Neoplasia

Characteristics of benign and malignant tumours

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References:

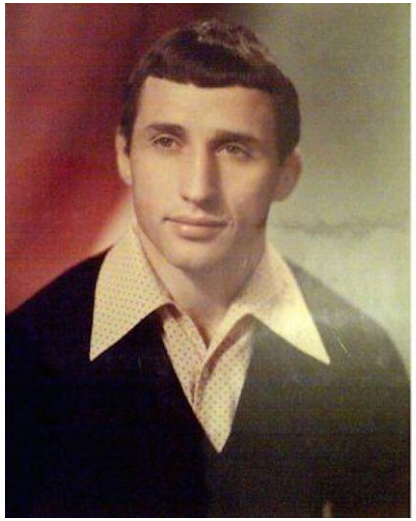
- **Robbins & Cotran Pathologic Basis of Disease- 9th edition**
- **IMAGES- Above mentioned book & internet**

Characteristics of benign and malignant tumours
KEYWORDS

- **Differentiation and Anaplasia**
- **Rate of growth**
- **Local Invasion**
- **Metastasis**

DIFFERENTIATION

DIFFERENTIATION



Father and son look similar in appearance
(resemble – morphologically similar)

DIFFERENTIATION

- Refers to the extent to which neoplastic parenchymal cells resemble the corresponding normal parenchymal cells both **morphologically** and **functionally**

DIFFERENTIATION

WELL DIFFERENTIATED → **Neoplastic cells resembling its normal counterpart**

POORLY DIFFERENTIATED → **Primitive appearing unspecialized cells**

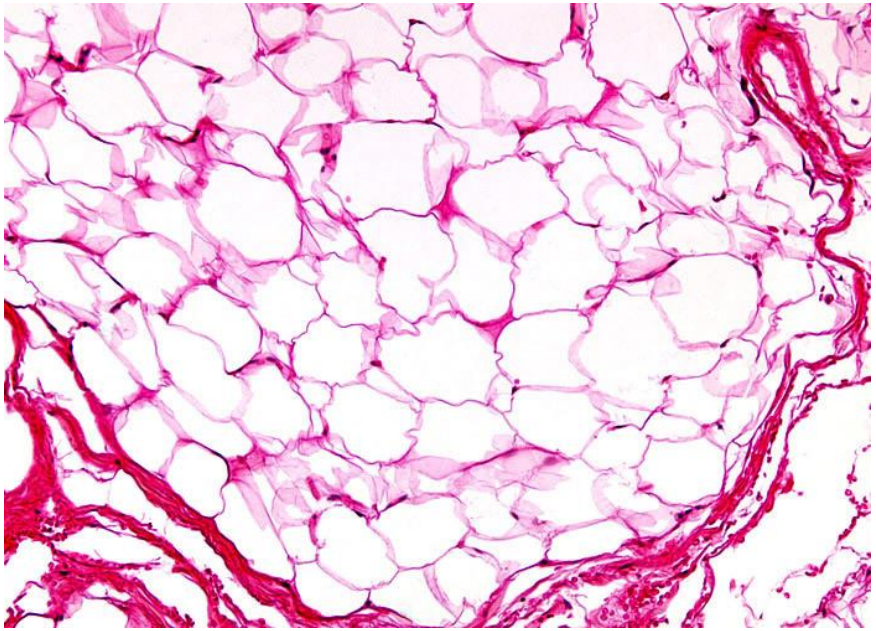
Benign Tumours

Benign tumours are well differentiated

DIFFERENTIATION

- The neoplastic cell in a lipoma closely resembles normal adipocytes
- Impossible to recognize the tumour by microscopic examination of an individual cell

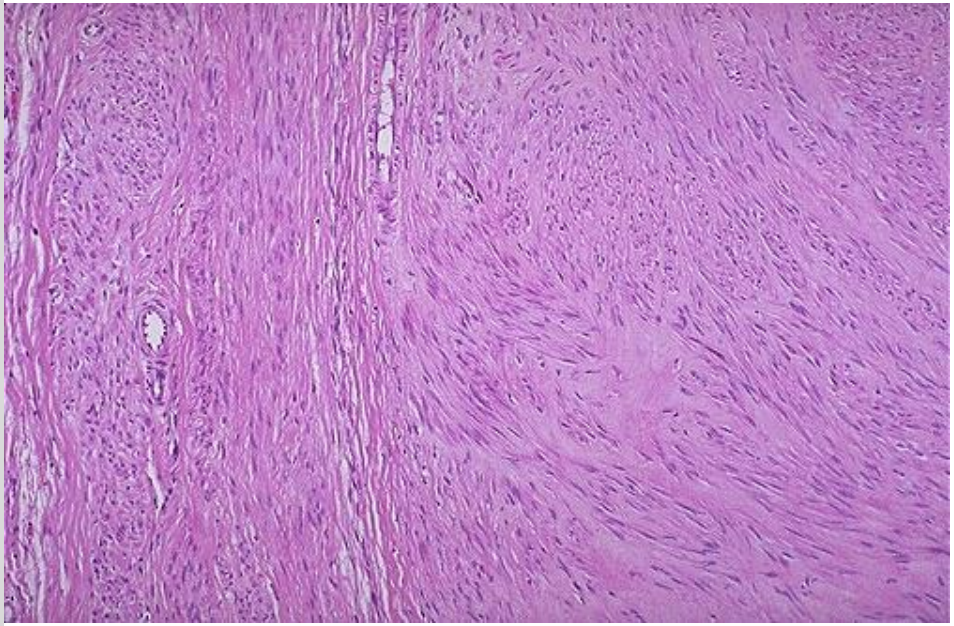
LIPOMA



DIFFERENTIATION

- Benign ,well differentiated tumour contains interlacing bundles of neoplastic smooth muscle cells
- That are virtually identical in appearance to ***normal smooth muscle cells of myometrium***

Leiomyoma



Malignant Tumours

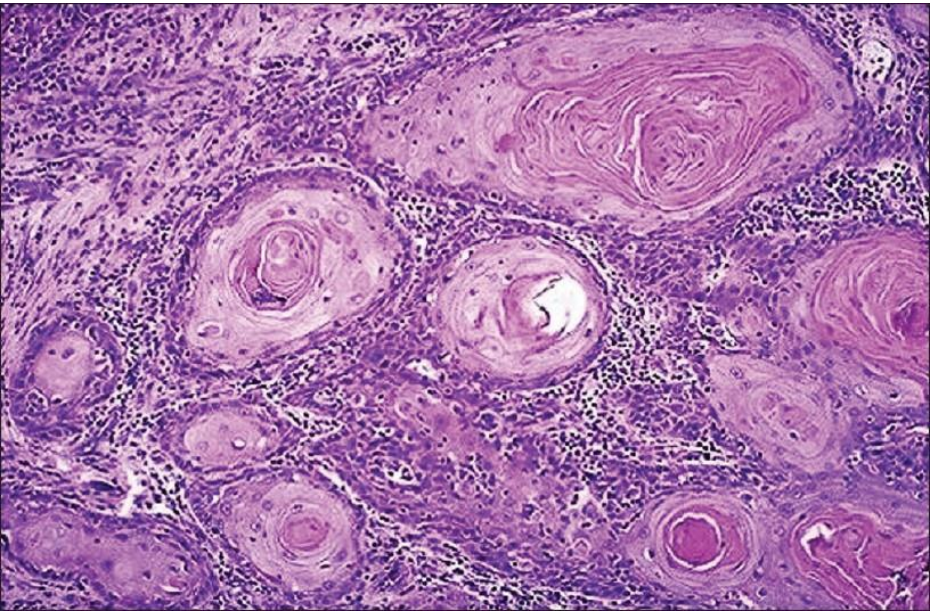
Malignant tumours shows a wide range of differentiation from **well** to **poorly** differentiated

In between lies **moderately** differentiated tumours

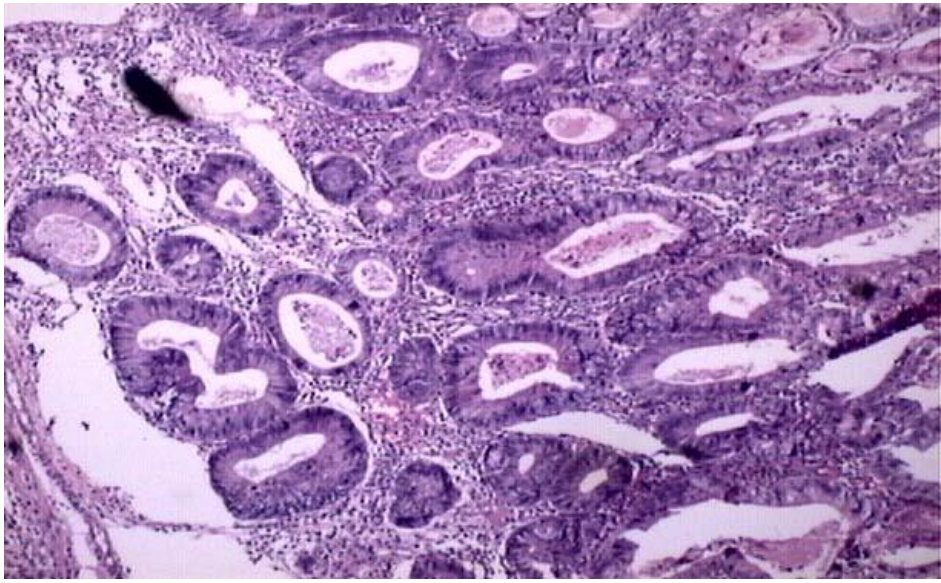
WELL DIFFERENTIATED

MORPHOLOGICAL DIFFERENTIATION

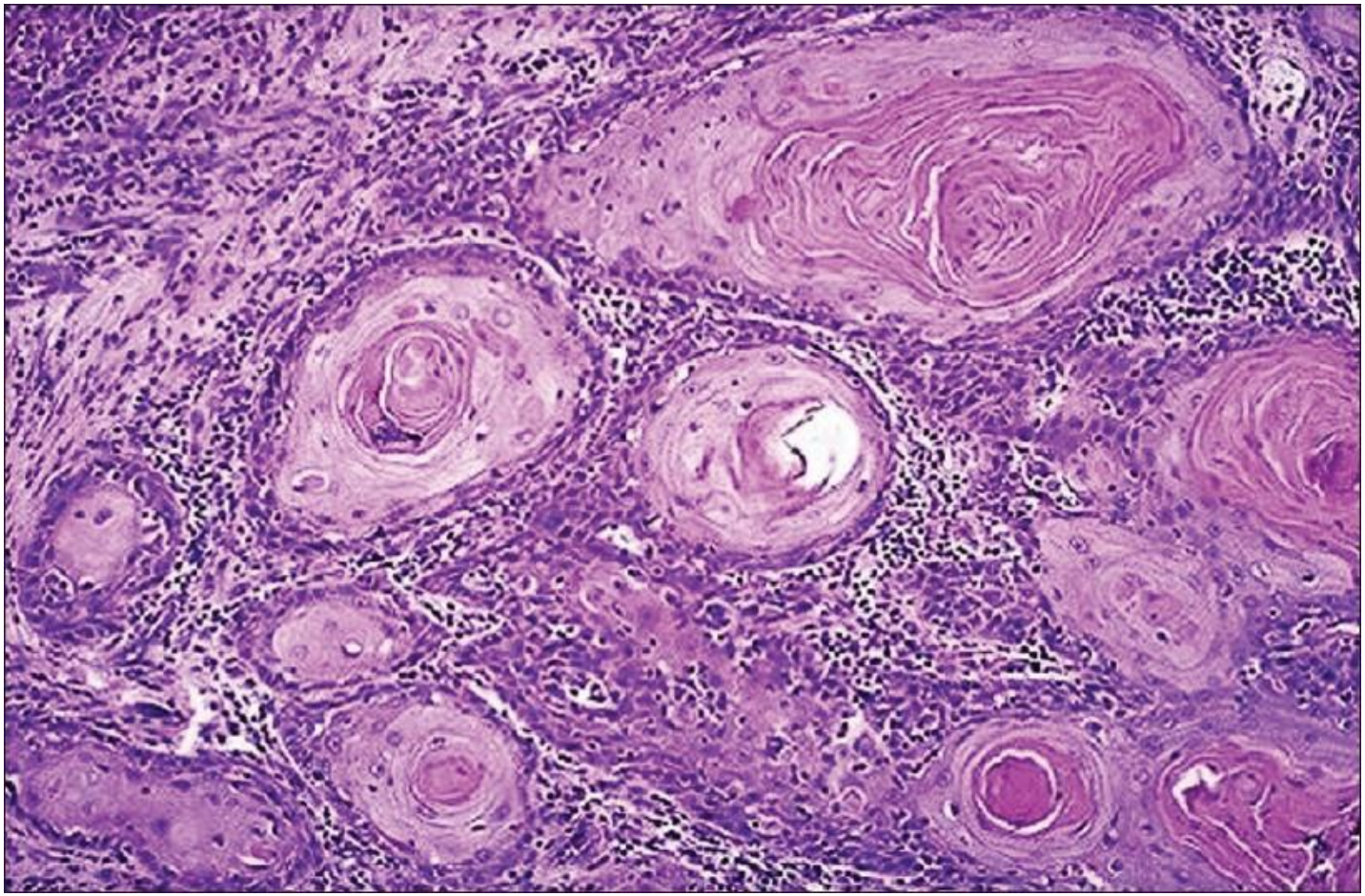
Well differentiated Squamous cell carcinoma
Identical to normal squamous epithelial cells



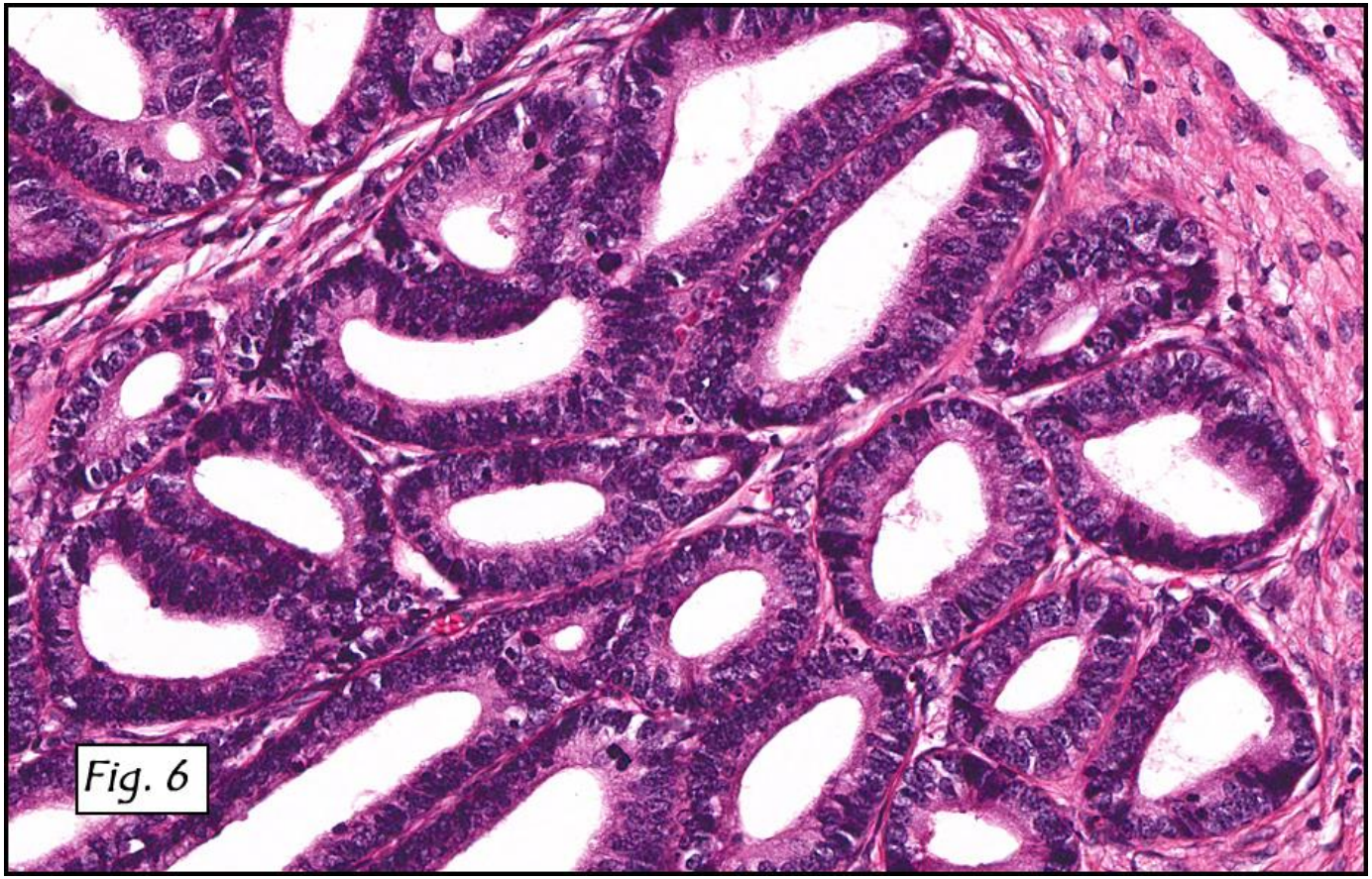
Well differentiated adenocarcinoma
Almost looks like normal glands



Well Differentiated Squamous cell carcinoma



Well differentiated adenocarcinoma

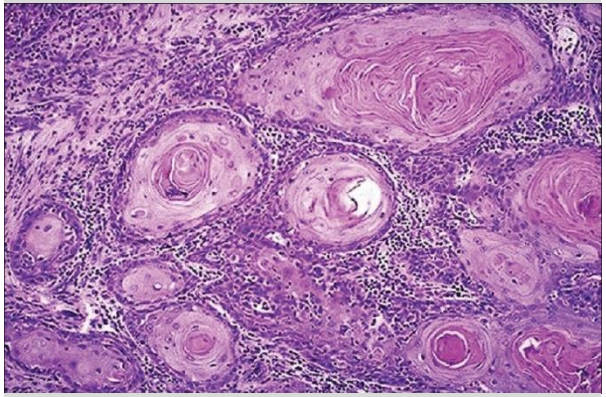


Well differentiated carcinoma

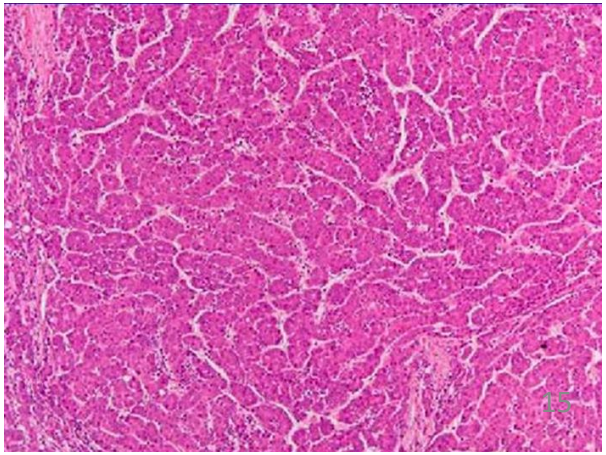
FUNCTIONAL DIFFERENTIATION

- Well differentiated Squamous cell carcinoma of epidermis synthesize keratin
- Well differentiated hepatocellular carcinoma elaborate bile

Well differentiated squamous cell carcinoma

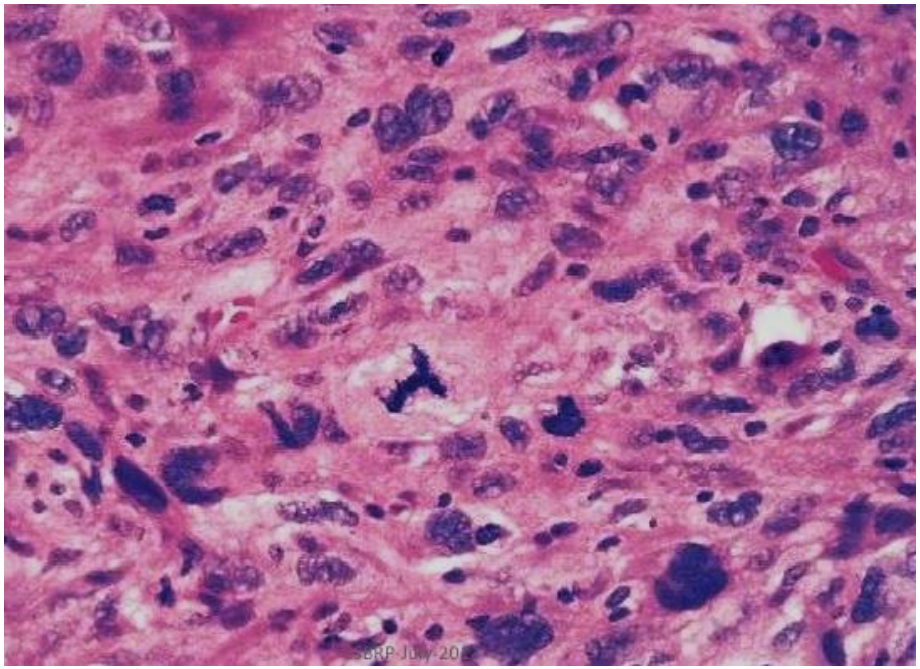


Well differentiated hepatocellular carcinoma



Poorly differentiated tumour

- **Little/no evidence of differentiation**



ANAPLASIA

Anaplasia

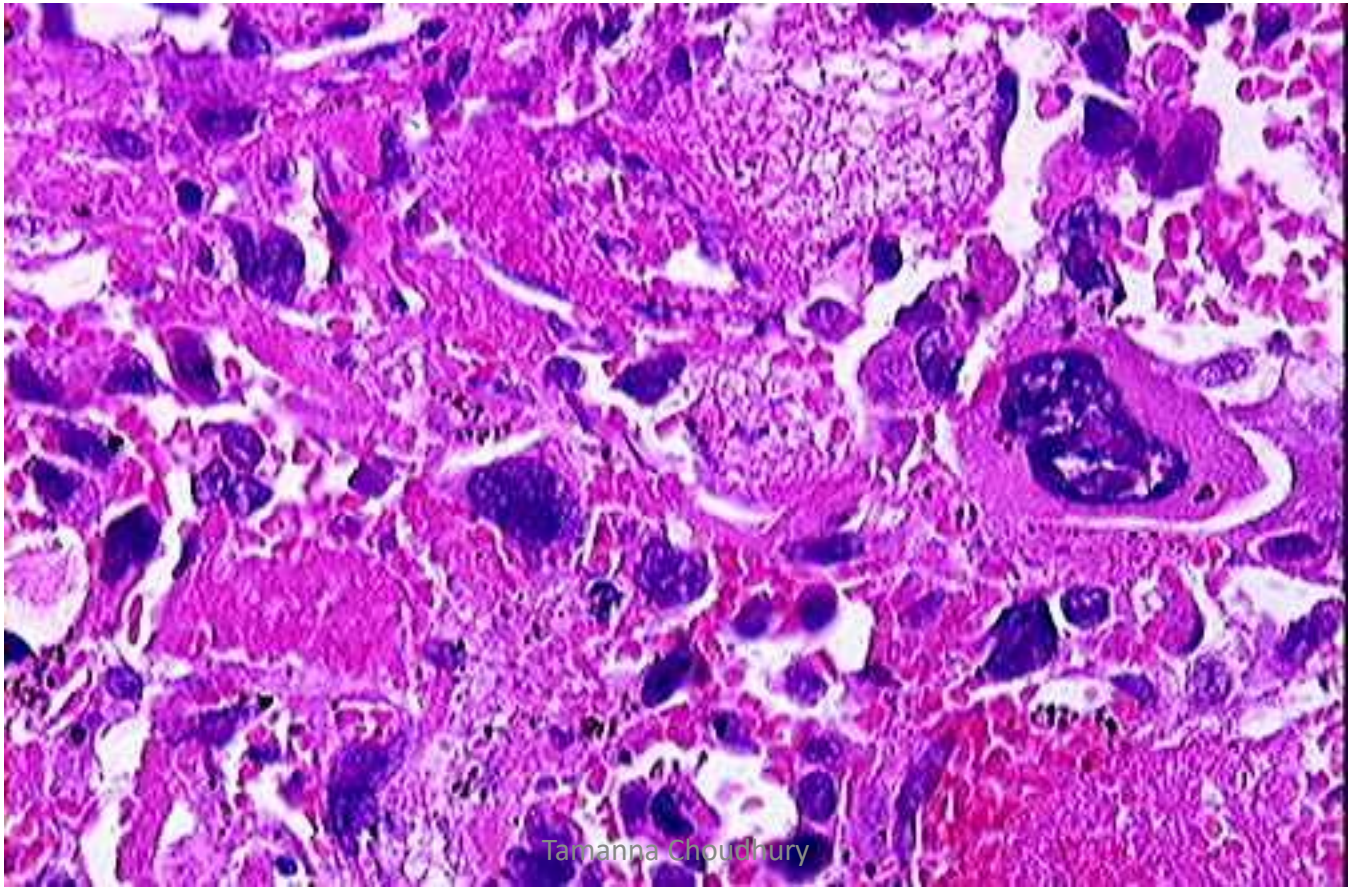
- Lack of differentiation
- It means “to form backward”
- Reversal differentiation to a more primitive level
- **ANAPLASIA is the HALLMARK of malignancy**

Anaplasia- morphologic changes

I. Pleomorphism
II. Abnormal nuclear morphology
III. Mitoses
IV. Loss of polarity/orientation
V. Other changes- ischemic necrosis

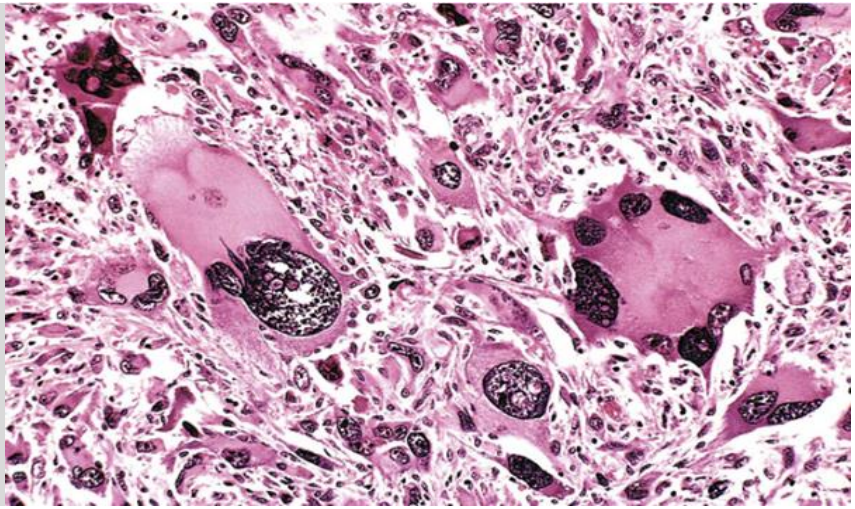
I. Pleomorphism

Variation in size and shape



Pleomorphism

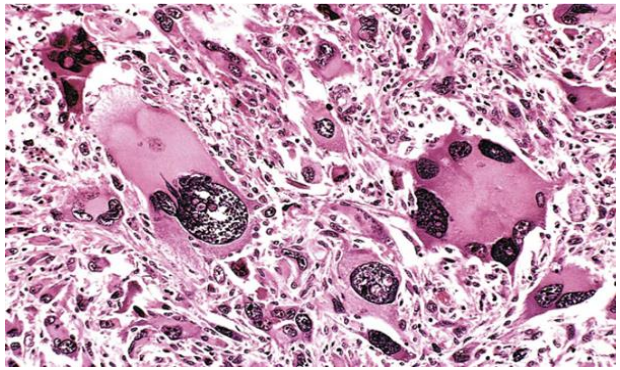
- **Cellular** as well as **nuclear** pleomorphism
- Tumour giant cells



Giant cell

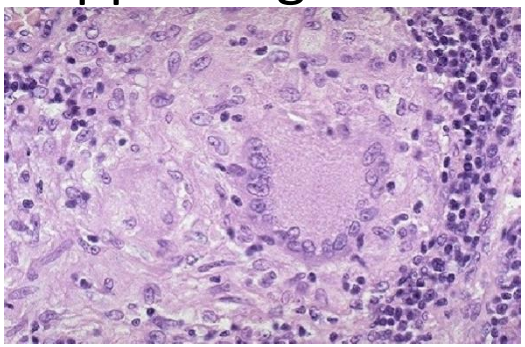
Tumour giant cell

- Single huge polymorphic nucleus
- Two or more hyperchromatic nuclei

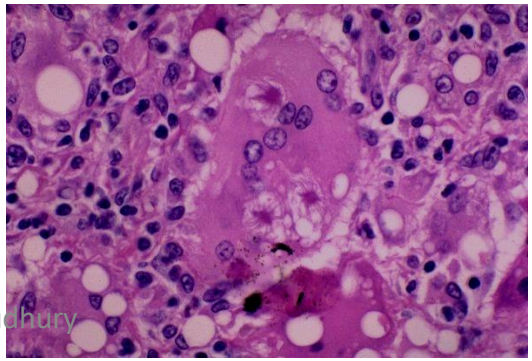


Inflammatory giant cell

- Derived from macrophages
- Contain many small, normal appearing nuclei



Langhan's type giant cell



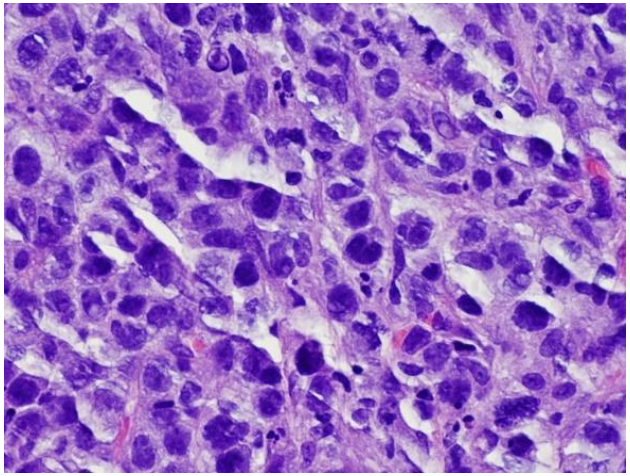
Foreign body type giant cell

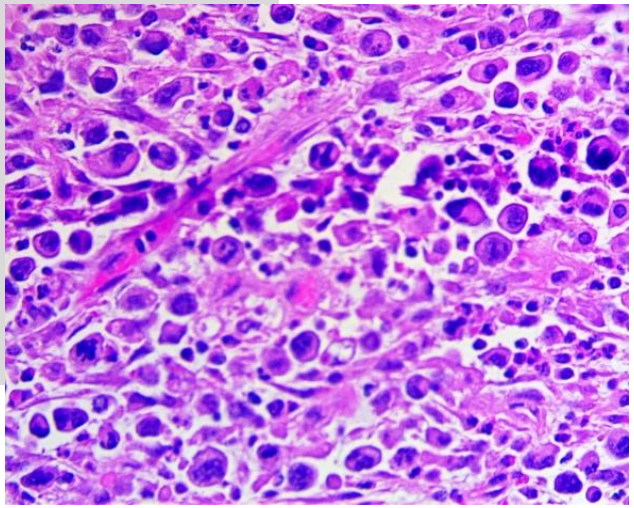
II. Abnormal Nuclear Morphology

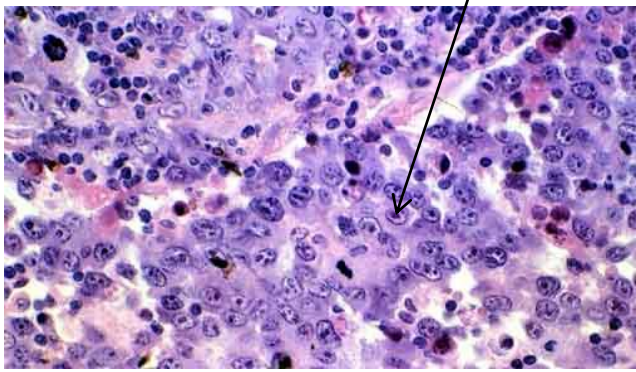
- **Hyperchromatic**
- **Disproportionately large**
- N:C ratio may reach 1:1

(normal ratio is 1:4 or 1:6)

- **Shape** is **variable** and often irregular
- **Coarse** clumped **chromatin**
- **Large nucleoli**

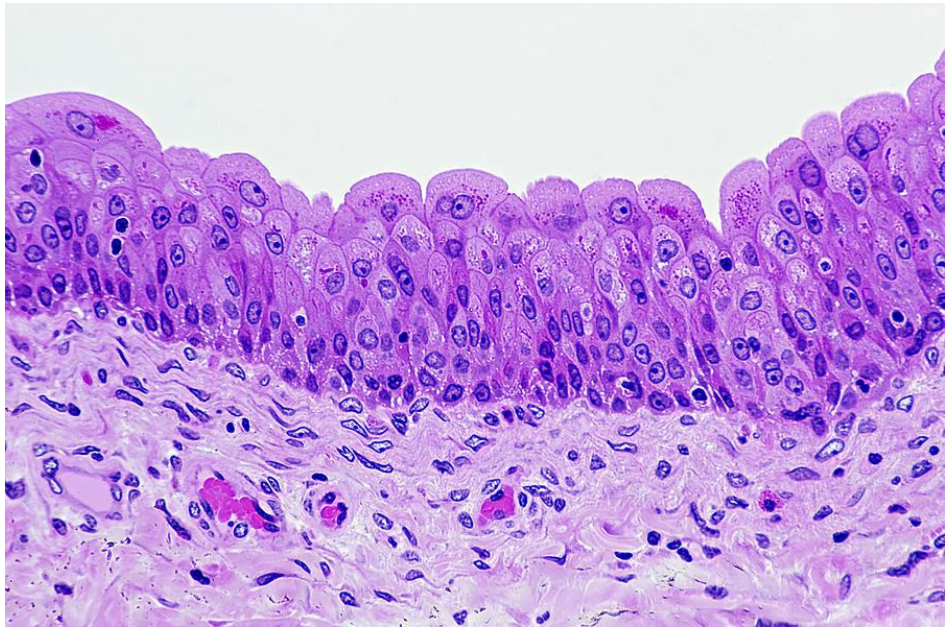




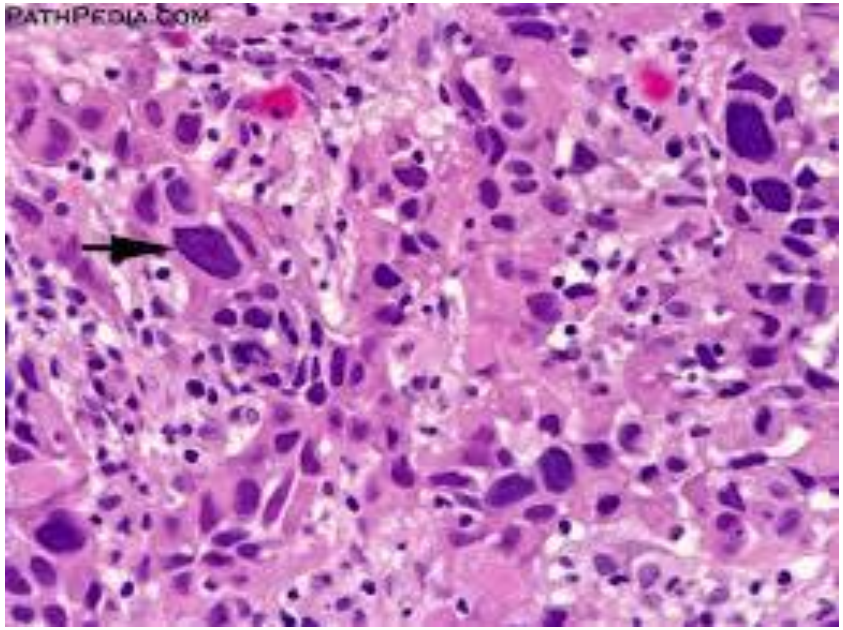


Abnormal Nuclear Morphology

Normal



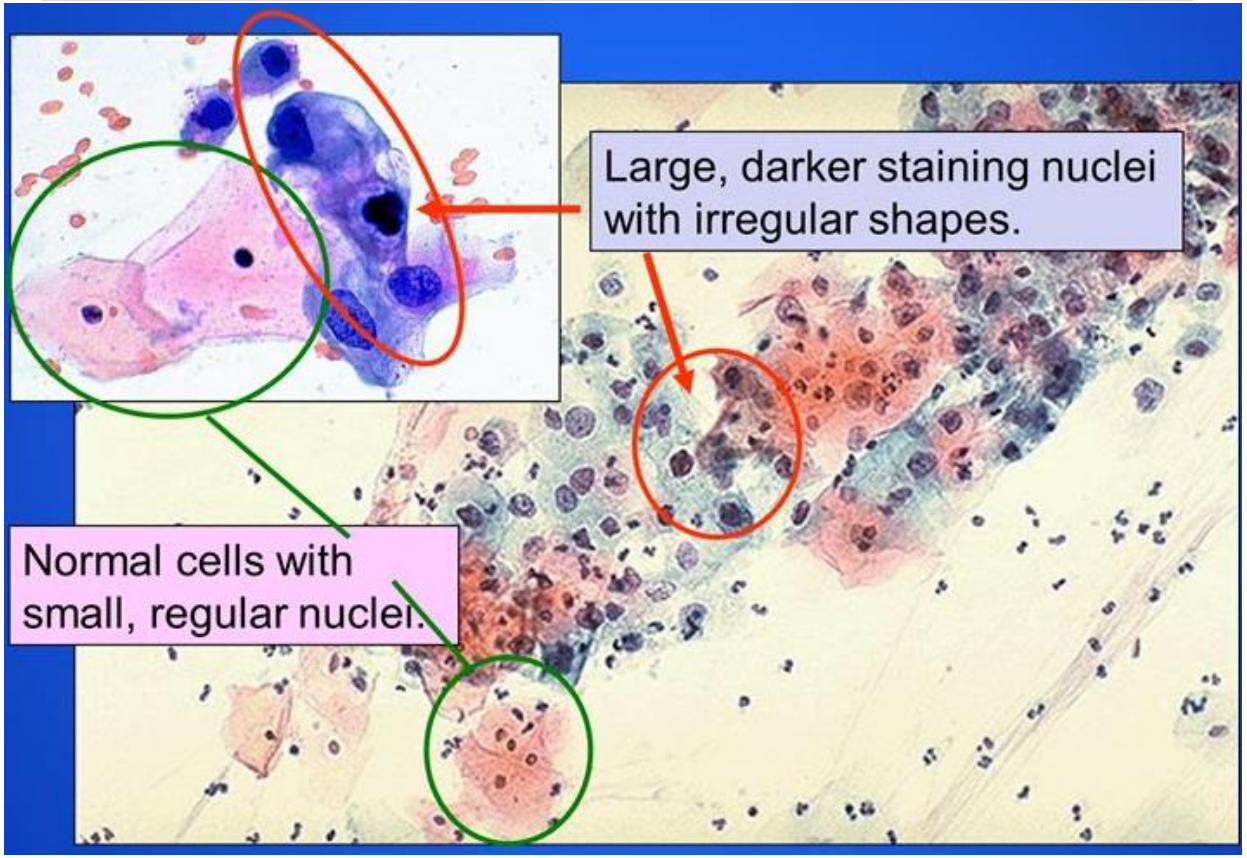
Anaplastic cells



- **Hyperchromatic**
- **N:C ratio increased**
- **Disproportionately large**
- **Variable shape**

Abnormal Nuclear Morphology

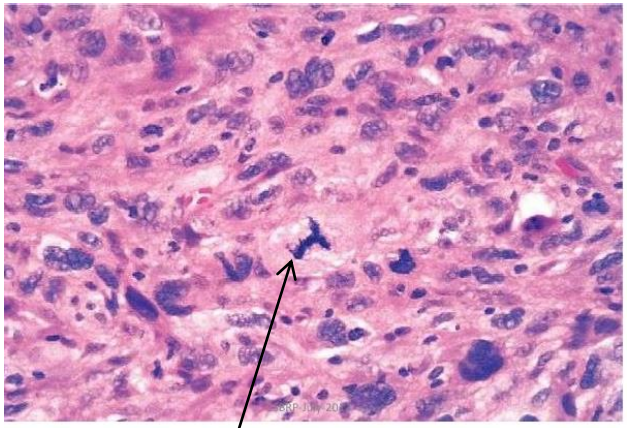
A cytology smear

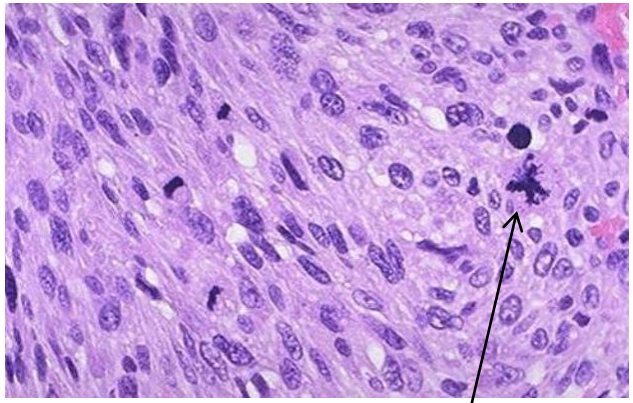


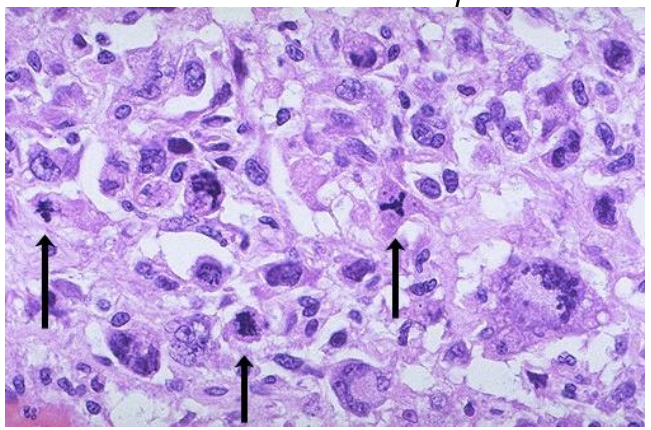
III. Mitoses

Atypical bizzare mitotic figures

(sometimes Tri, quadri or multipolar spindles)





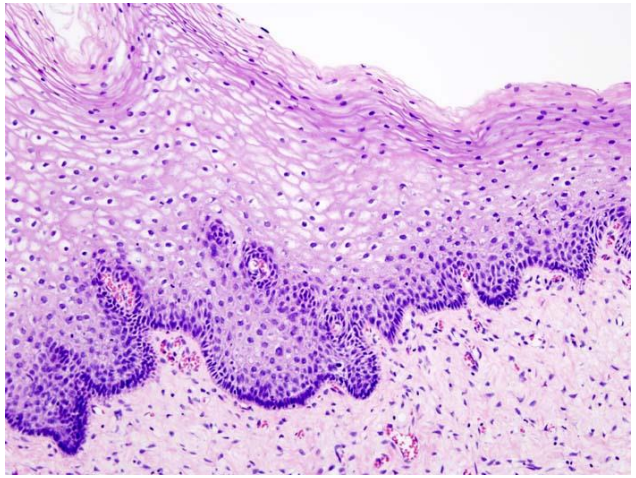


Abnormal mitoses are highly indicative of malignancy

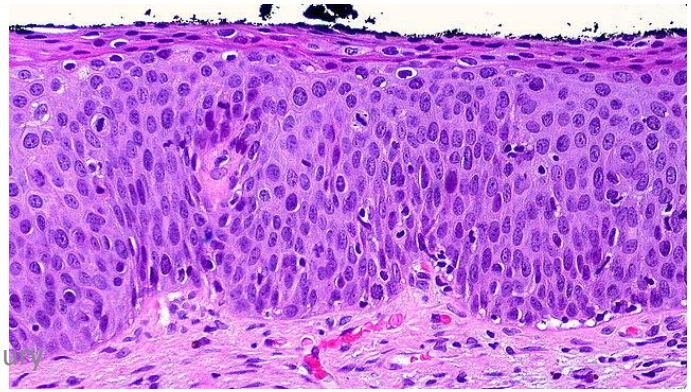
IV. Loss of polarity

- Orientation of anaplastic cells are markedly disturbed
- Anarchic , disorganized fashion

Normal ectocervical epithelium



Orientation is markedly disturbed



RATE OF GROWTH

RATE OF GROWTH

In general

- Benign tumours are **slow** growing
- Malignant tumours grow **faster**

LOCAL INVASION

Local invasion

Benign tumour	Malignant tumour
• Cohesive expansile mass • Usually have a **capsule** • Remain **localized** to their site of origin • **Lack the capacity to infiltrate, invade or metastasize to distant sites**	• **Poorly demarcated** from the surrounding normal tissue • Usually **unencapsulated** • No well defined cleavage plane • **Progressive infiltration , invasion and destruction of the surrounding tissue**

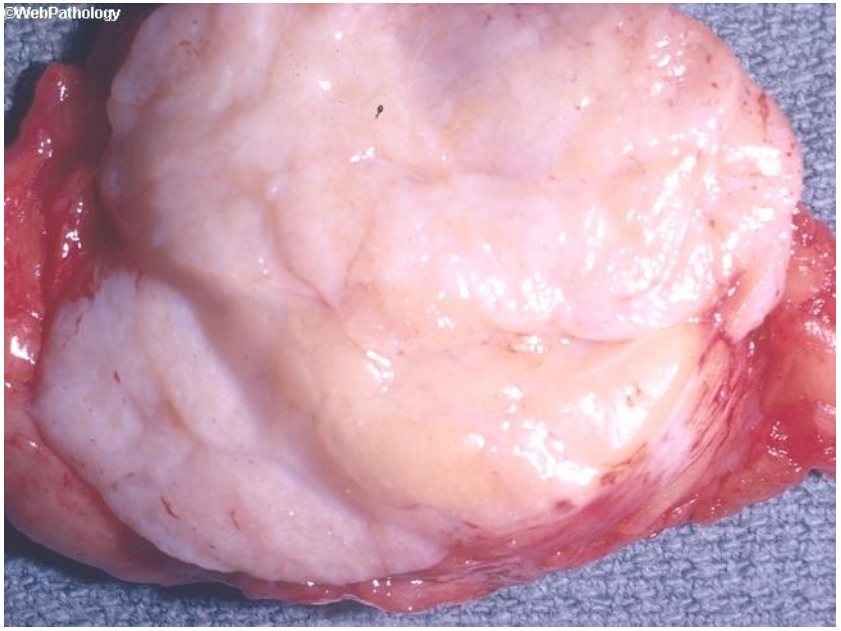
Local invasion

Contrasting Gross Features of Typical Infiltrating Carcinoma (left) & Fibroadenoma (right)

Diagnosis is strongly suspected based on the gross examination

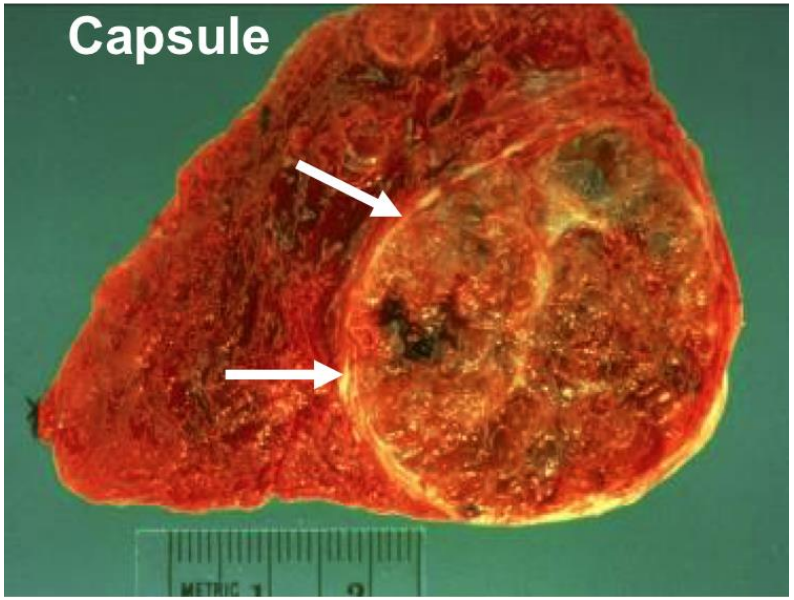
Cut section of carcinoma breast
Lesion is retracted & infiltrating into the surrounding tissue

Tan colored encapsulated small tumour sharply demarcated from the normal breast tissue



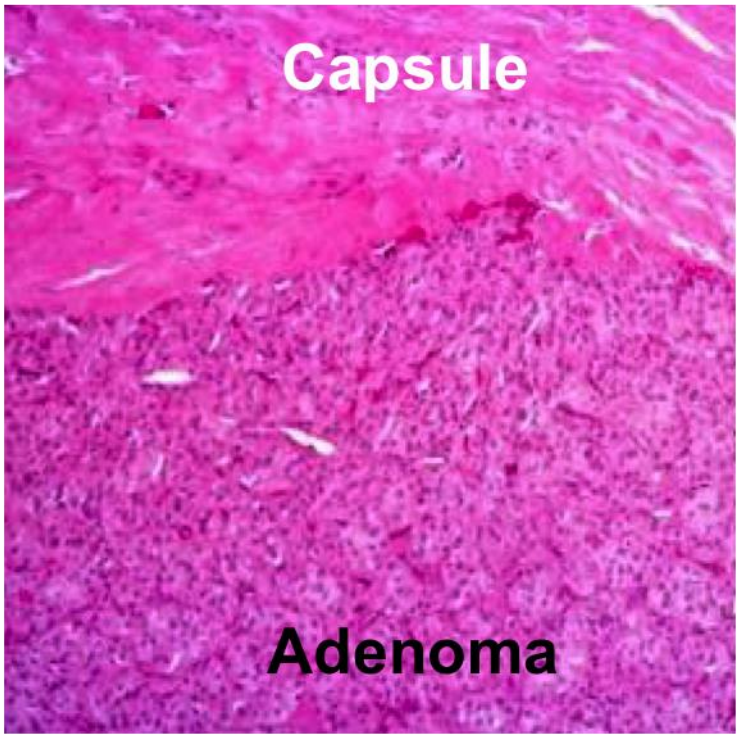
Capsule of a benign tumour

- Benign tumours grow slowly- develops a rim of compressed fibrous tissue- **capsule**
- Consists of extracellular matrix
- Deposited by stromal cells- fibroblasts
- Activated by hypoxic damage due to pressure from expanding tumour



Capsule of a benign tumour

- Does not prevent tumour growth
- Creates a tissue plane
- The benign tumours are
  - discrete
  - moveable
  - readily palpable
  - easily excisable



Capsule of a benign tumour

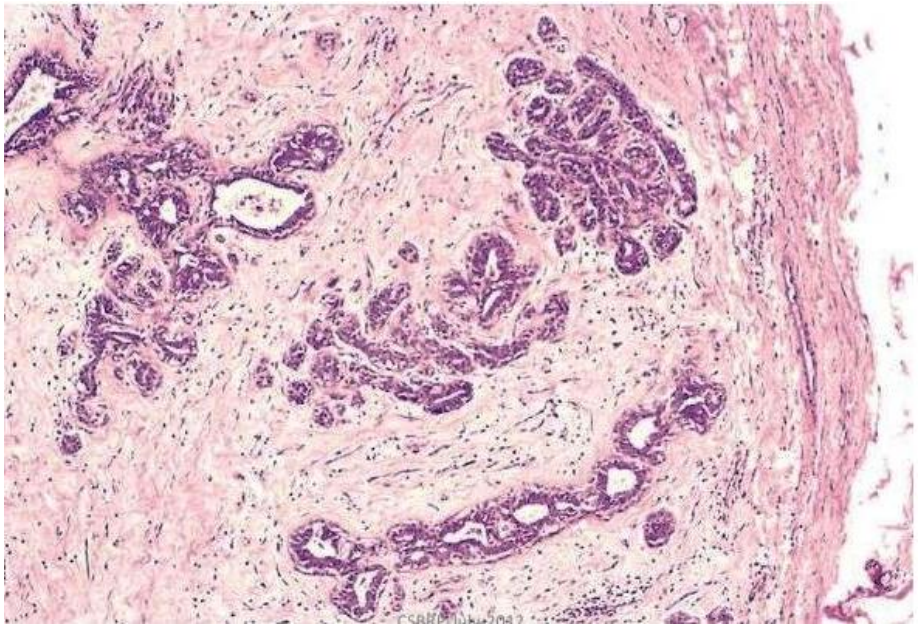
Exception

- **Haemangiomas often unencapsulated**

Local invasion

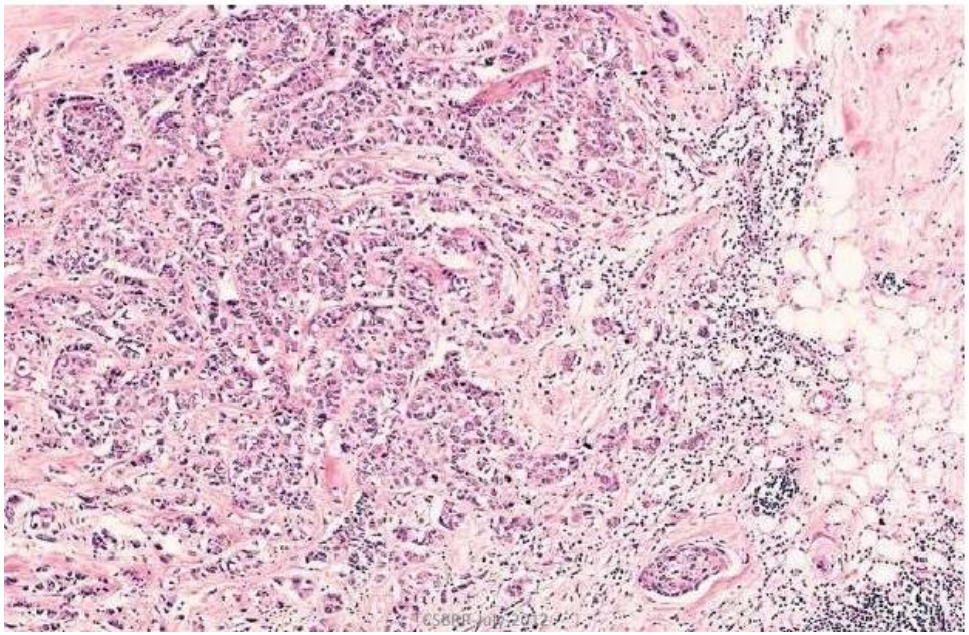
Fibroadenoma breast

Fibrous capsule delimits the tumour from the surrounding tissue



Breast carcinoma

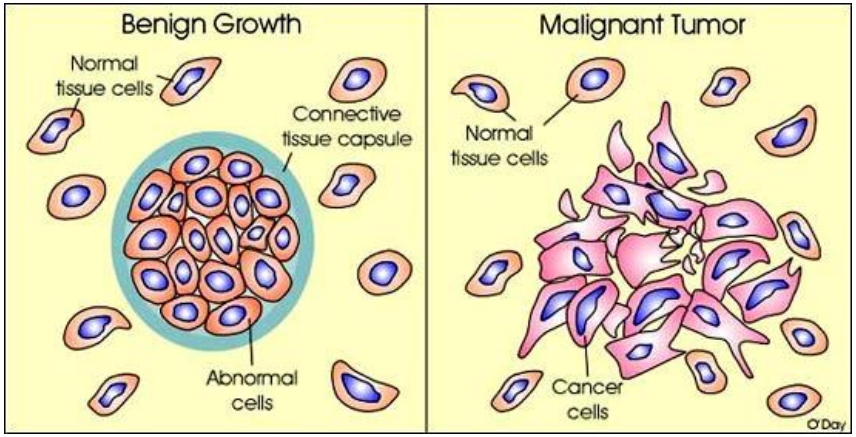
Invasion of breast stroma &fat by tumour cells

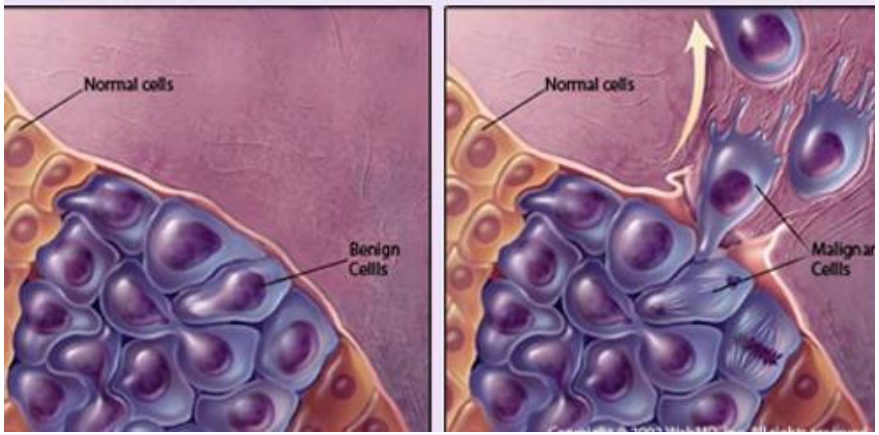


Poorly demarcated, well defined cleavage plane is lacking

Local invasion

Next to the development of **metastases**, ***invasiveness*** is the **most reliable feature** that differentiates cancer from benign tumours



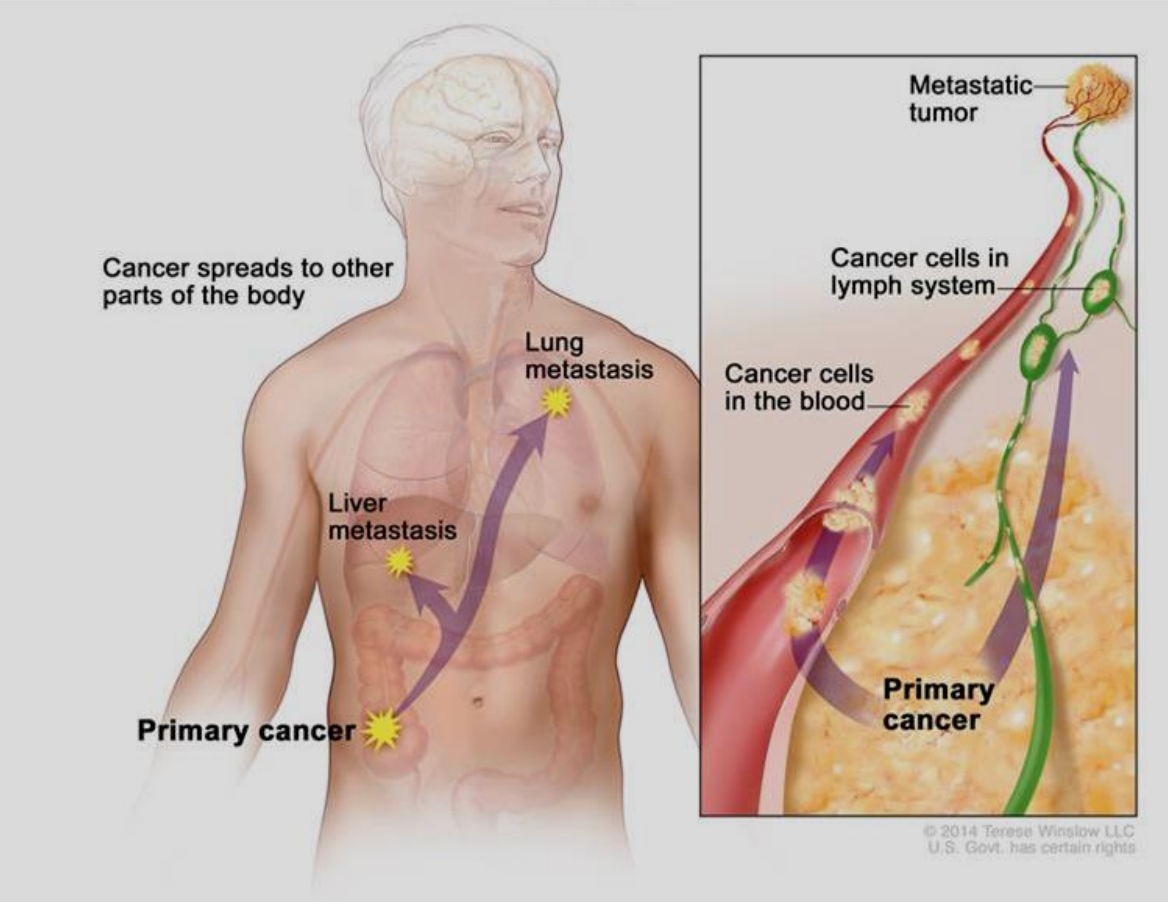


METASTASIS

METASTASIS

- **Defined** as spread of a tumour to sites that are physically **discontinuous** with the primary tumour and unequivocally marks a tumour as malignant

Metastases


Cancer spreads to other parts of the body
Lung metastasis
Liver metastasis
Primary cancer
Metastatic tumor
Cancer cells in lymph system
Cancer cells in the blood
Primary cancer
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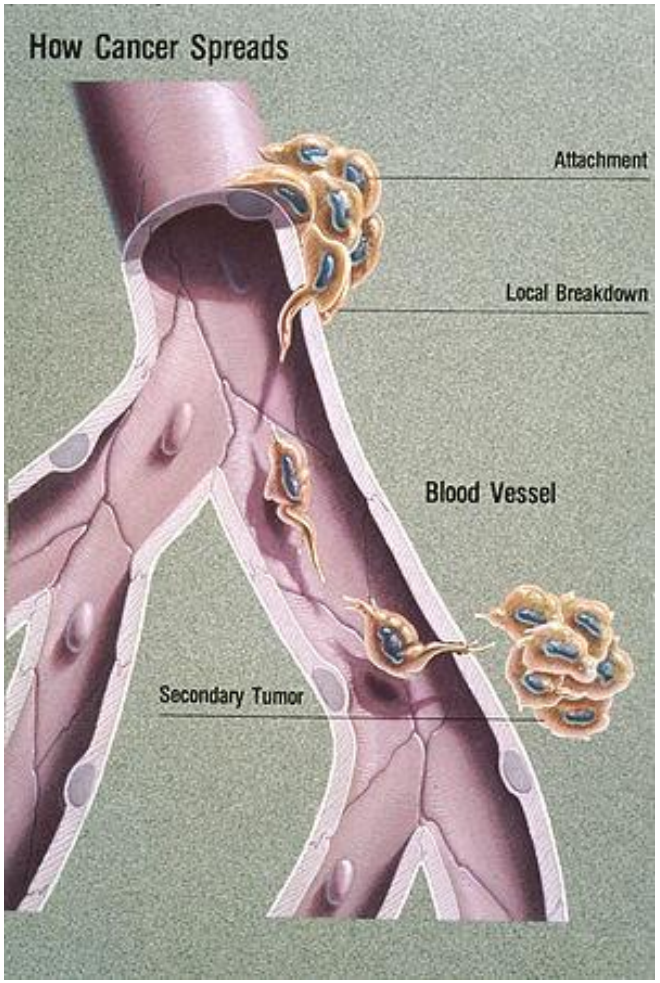
Metastasis

- Benign tumours- **do not** metastasize
- Malignant tumours- all **metastasize** with few exceptions



Metastasis

Some tumours metastasize very infrequently

- **Glioma**
- **Basal cell carcinoma of skin**

Pathways of spread

Three pathways

(1) **Direct seeding** of body cavities and surfaces

(2) **Lymphatic** spread

(3) **Haematogenous** spread

Iatrogenic spread- through surgical instruments

Pathways of spread

Direct seeding of body cavities or surfaces

When a malignant tumour penetrates into a natural **"open field"** lacking physical barriers

- Peritoneal cavity- most often
- Pleural
- Pericardial
- Subarachnoid
- Joint spaces

Pathways of spread

Direct seeding of body cavities or surfaces

- Particularly characteristic of **carcinoma of ovary**
- ***Psuedomyxoma peritonei*** - Mucus secreting carcinoma of **appendix or ovary** fill the abdominal cavity with a gelatinous neoplastic mass

Pathways of spread

Lymphatic spread

- **Most common** pathway for initial spread of ***carcinomas***
- ***S*arcomas** may use

Pathways of spread

Lymphatic spread

- The pattern of lymph node involvement follows natural routes of lymphatic drainage

Pathways of spread

Lymphatic spread

Breast carcinoma

- Upper outer quadrants- axillary LN
- Inner quadrants- infraclavicular & supraclavicular LN

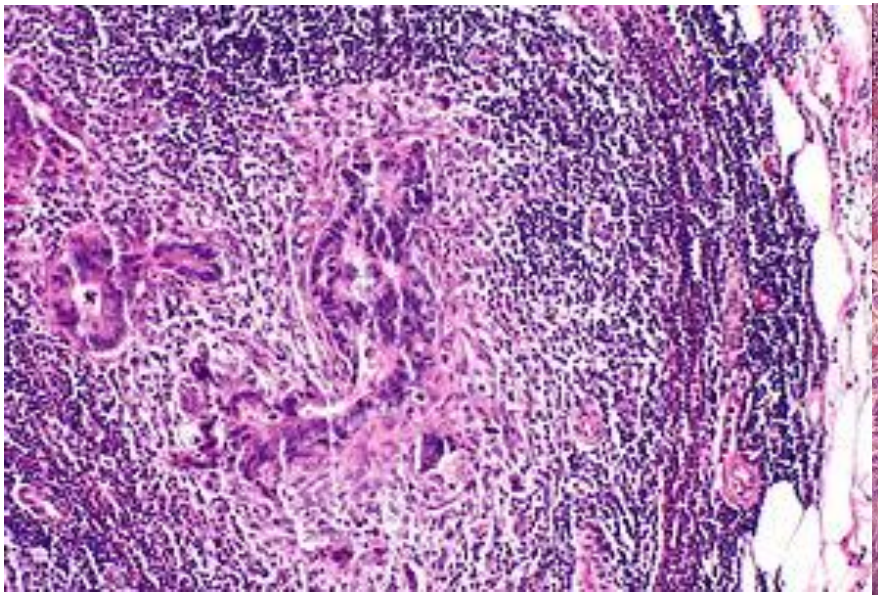
Carcinoma lung (major respiratory passages)

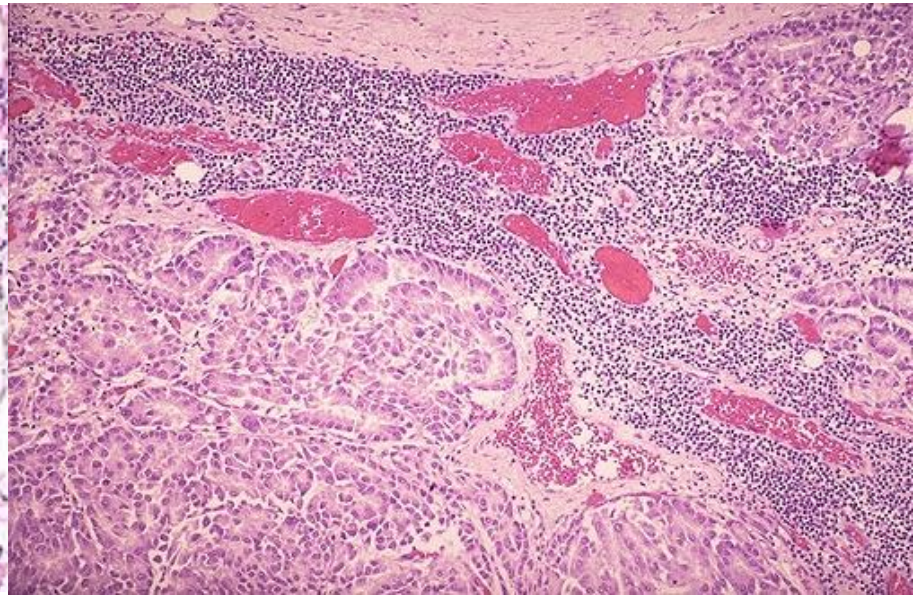
- Perihilar tracheobronchial LN &mediastinal LN

Pathways of spread

Lymphatic spread

Lymph nodes showing metastasis





Pathways of spread

Lymphatic spread

SKIP METASTASIS

- Local LN may be bypassed

1. Venous lymphatic anastomoes
2. Inflammation/radiation obliterating the lymphatic channels

Pathways of spread

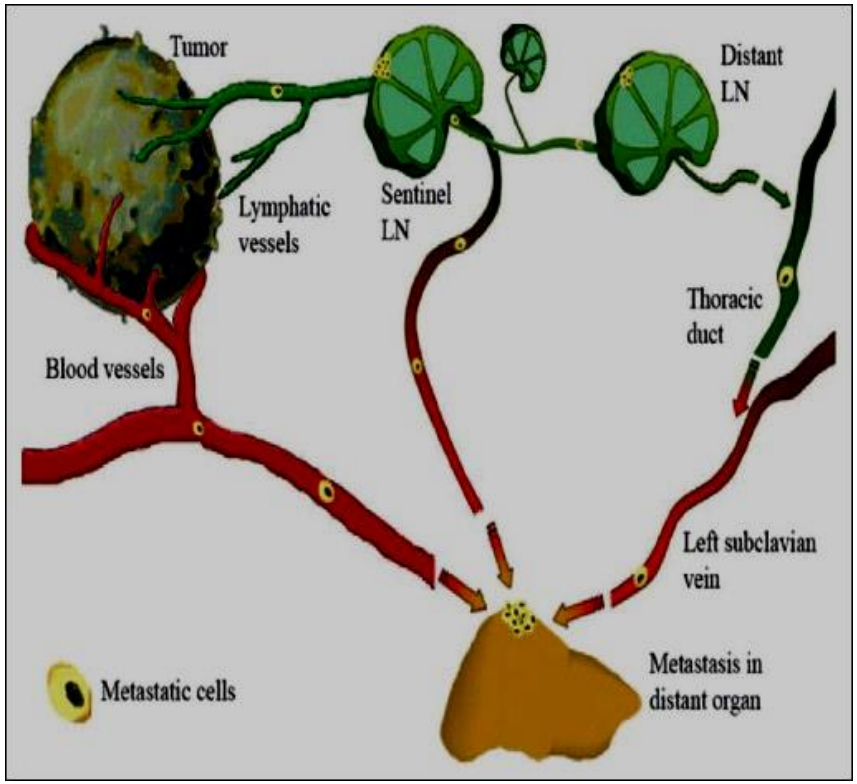
Lymphatic spread

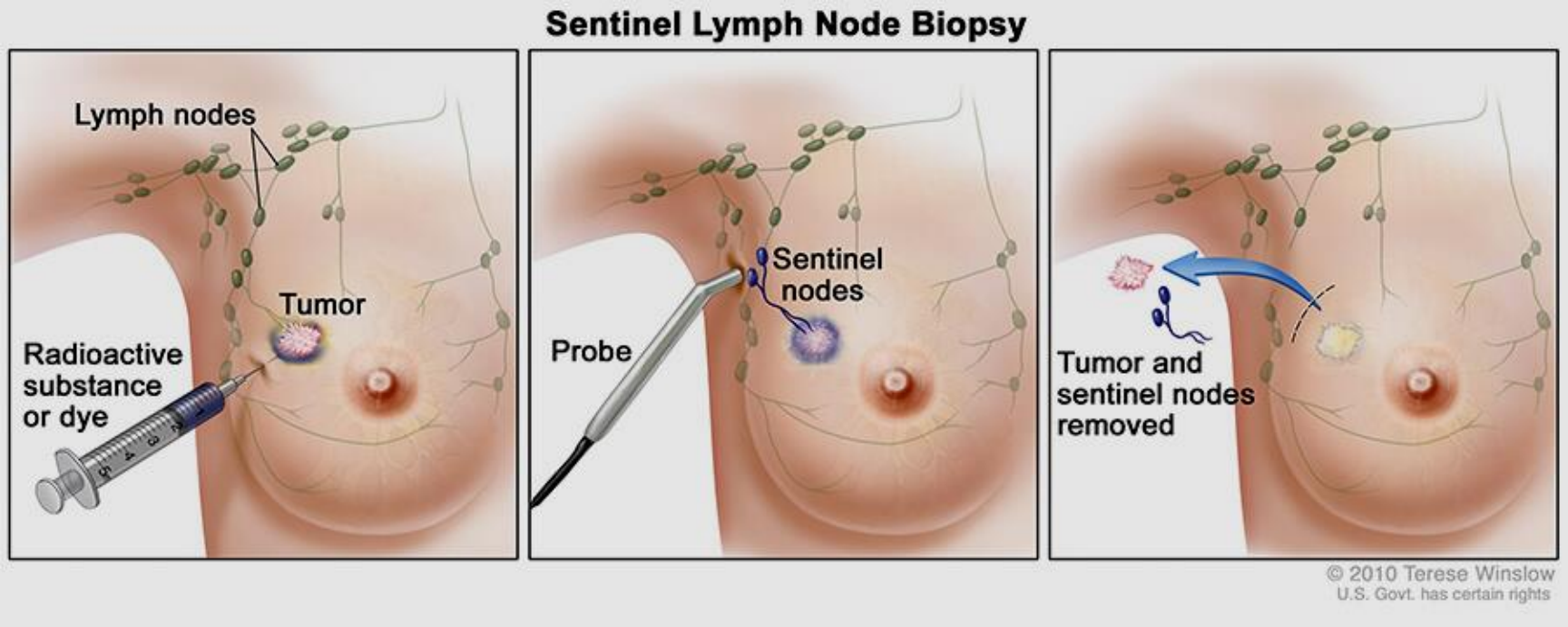
SENTINEL LYMPH NODES

- The **first** lymph node in a **regional lymphatic basin** that receives lymph flow from the primary tumour
- Sentinal LN **mapping** can be done by

a. Injection of radiolabeled tracer/coloured dyes

b. Frozen section examination




Sentinel Lymph Node Biopsy
Lymph nodes
Tumor
Radioactive substance or dye
Probe
Sentinel nodes
Tumor and sentinel nodes removed
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SENTINEL LYMPH NODE EXAMINATION

- **Breast**
- **Melanomas**
- **Colon cancers**

Pathways of spread

Haematogenous spread

- Typical of **sarcomas**
- Also seen in carcinomas

Pathways of spread

Haematogenous spread

- Arteries are less readily penetrated than veins
- Arterial spread may occur

a) When tumour cells pass through **pulmonary capillary** beds

b) Pulmonary **artreiovenous** shunts

c) Pulmonary **metastasis**

Pathways of spread

Haematogenous spread

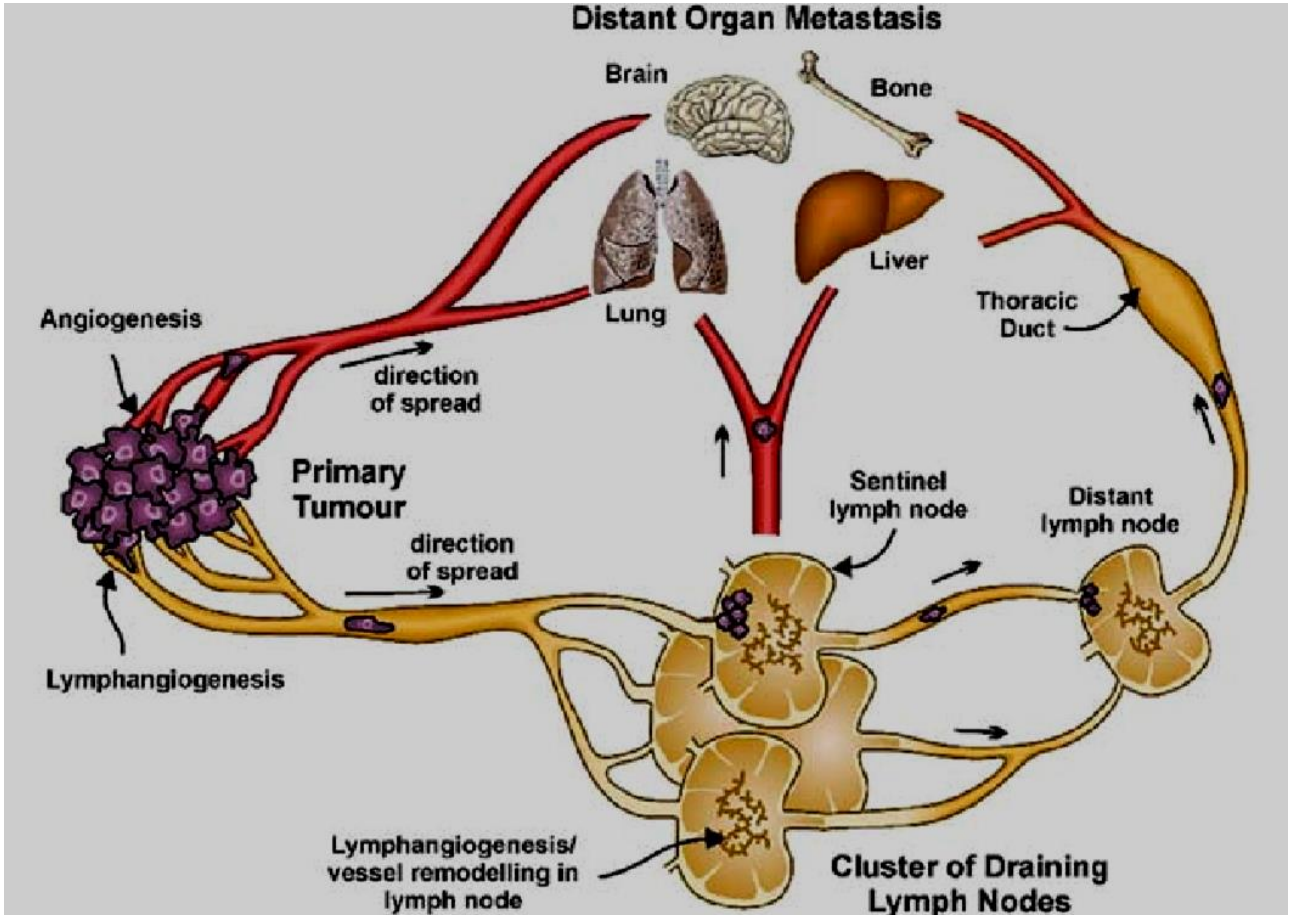
- With venous invasion

  The bloodborne cells follow the venous flow draining the site

i. The Liver

ii. The Lungs

} most frequently involved


Distant Organ Metastasis
Brain
Bone
Liver
Lung
Thoracic Duct
Angiogenesis
direction of spread
Primary Tumour
Sentinel lymph node
Distant lymph node
direction of spread
Lymphangiogenesis
Lymphangiogenesis/ vessel remodelling in lymph node
Cluster of Draining Lymph Nodes

Lung metastases

Pathways of spread

Haematogenous spread

A liver studded with metastatic cancer

Pathways of spread

Haematogenous spread

A liver studded with metastatic cancer

Pathways of spread

Haematogenous spread

Cancers arising in close proximity to the vertebral column

(carcinoma of thyroid & prostate)

Embolize through paravertebral plexus

Pathways of spread
Haematogenous spread

- Certain cancers have propensity to invade veins
- Such as **Renal cell carcinoma**

Invasion and Metastasis

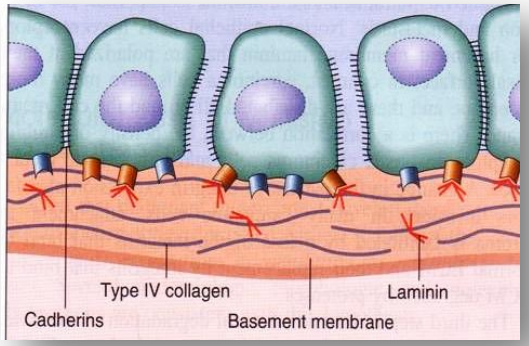
Invasion and Metastasis

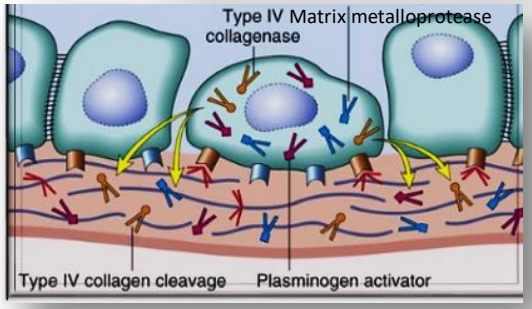
Ability to invade tissues

Hallmark of Malignancy

Sequence of events in the invasion of epithelial basement membranes by tumour cells

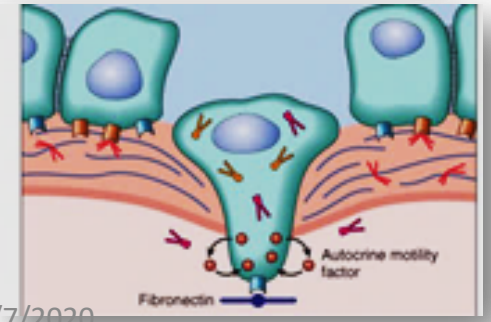
A





B

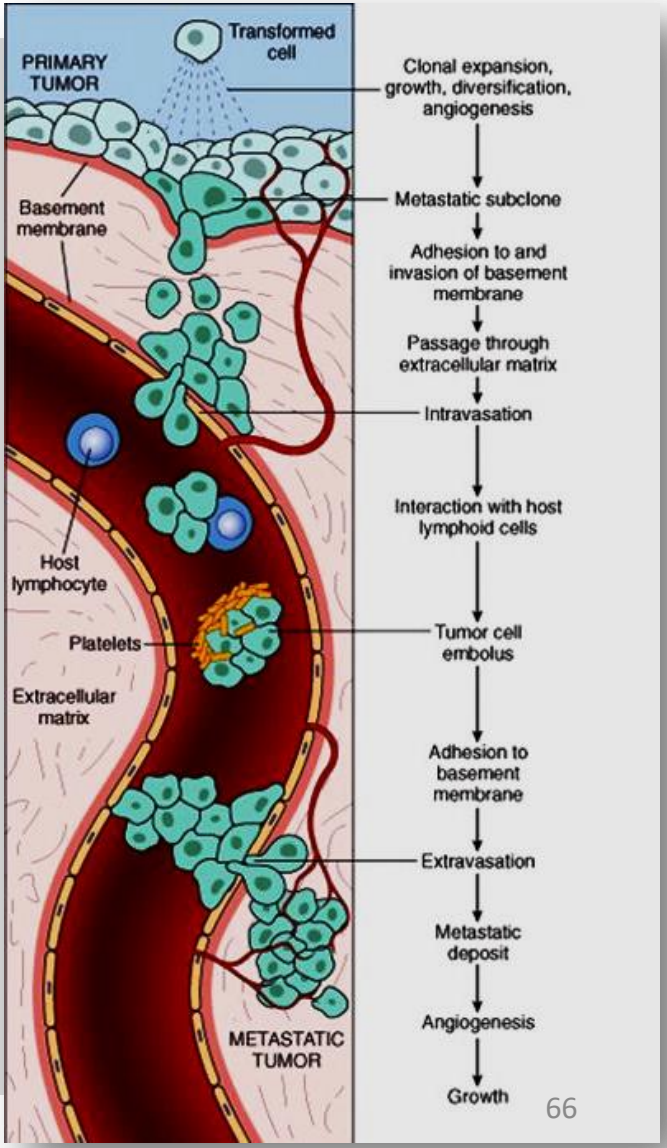
D



A. Loosening of Intercellular Junctions
B. Degradation of ECM
C. Attachment to ECM component
D. Migration and Invasion of tumour cells

Invasion and Metastasis

- **Loosening of intercellular junctions** E cadherin function lost
- **ECM degradation-** by proteolytic enzymes (elaborated by tumour cell/ stromal cell)
- **ECM attachment-** invading cells express adhesion molecules that allow interaction with ECM
- **Migration & invasion of tumour cells** diminished adhesivity, increased locomotion of tumour cells



Invasion and Metastasis

- Tumour cells **embolize** in the bloodstream as self aggregates and by adhering to the circulating leukocytes and platelets
- This may confer some protection from host antitumour effector mechanisms

DYSPLASIA

- Literally means "***disordered growth***"
- Encountered principally in epithelia
- Changes are

i. Loss of uniformity of individual cells

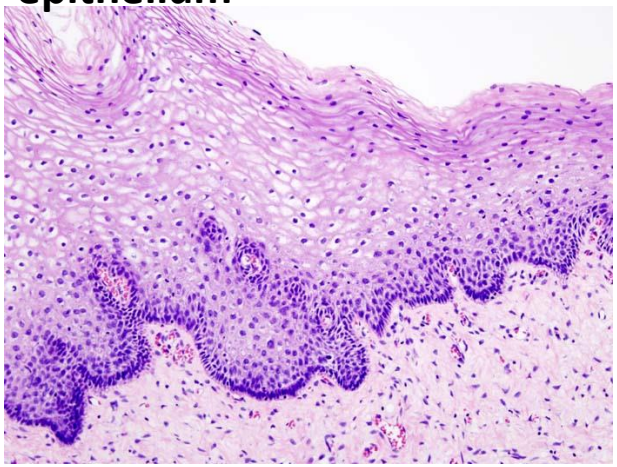
ii. Pleomorphism

iii. Large hyperchromatic nuclei

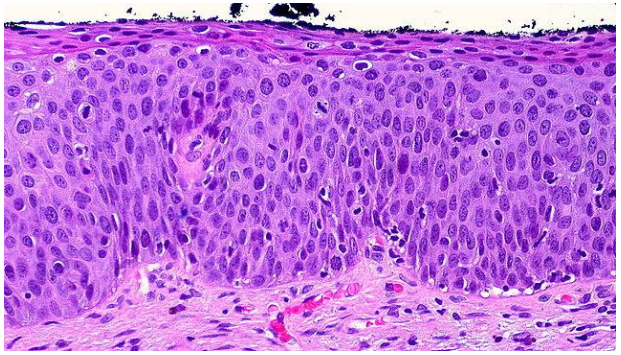
iv. High NC ratio

v. Architecture may be disorderly

Normal stratified squamous epithelium



Architecture is disorderly



DYSPLASIA

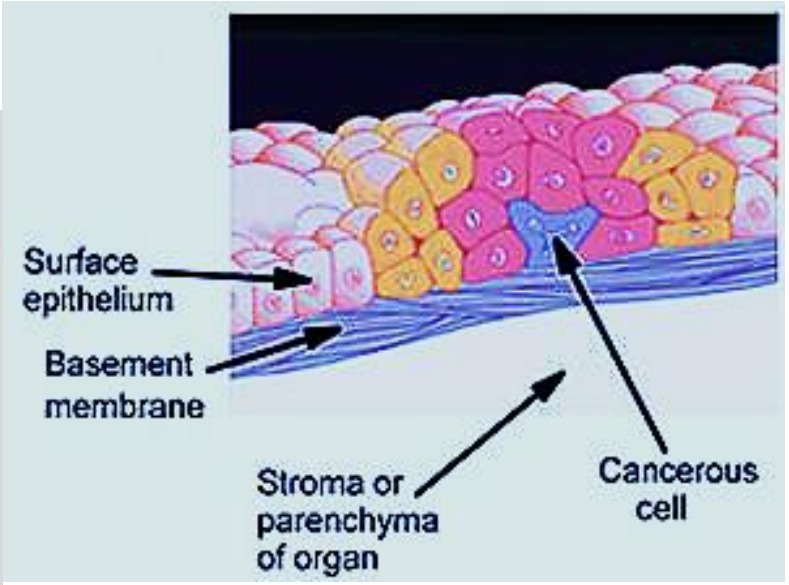
- Non neoplastic
- Dysplasia may be a **precursor** to malignant transformation
- Does not always progress to cancer
- Mild to moderate dysplasia may be completely **reversible** when the cause is removed

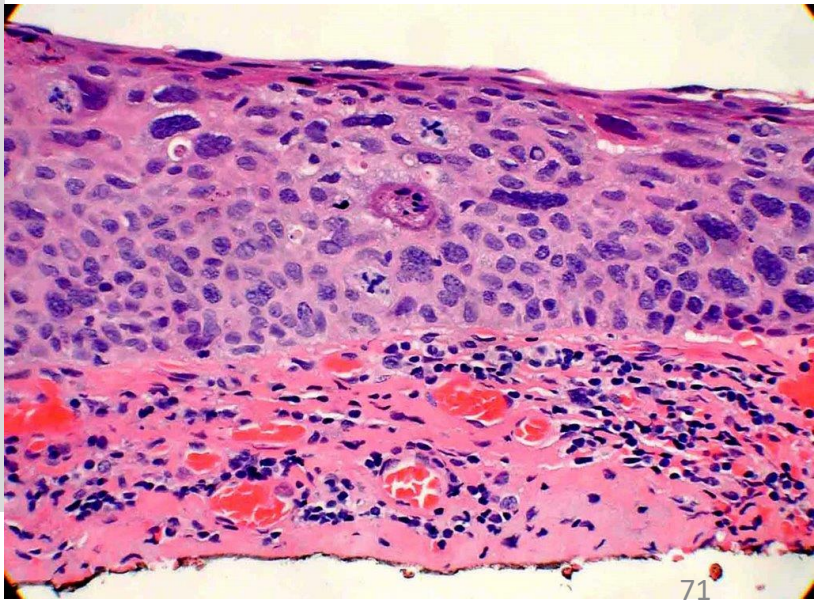
DYSPLASIA

DYSPLASIA	CANCER
Non invasive	Invasive
Reversible (mild to moderate)	Irreversible

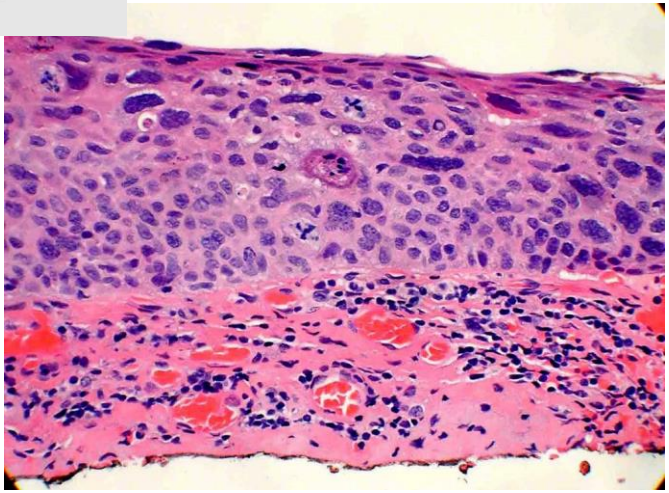
Carcinoma in situ

- **Applicable** to only **epithelial** neoplasms
- When dysplastic changes are marked/severe
- Involve the **full thickness** of the epithelium
- **Lesion does not penetrate the basement membrane**
- No tumour in the subepithelial stroma



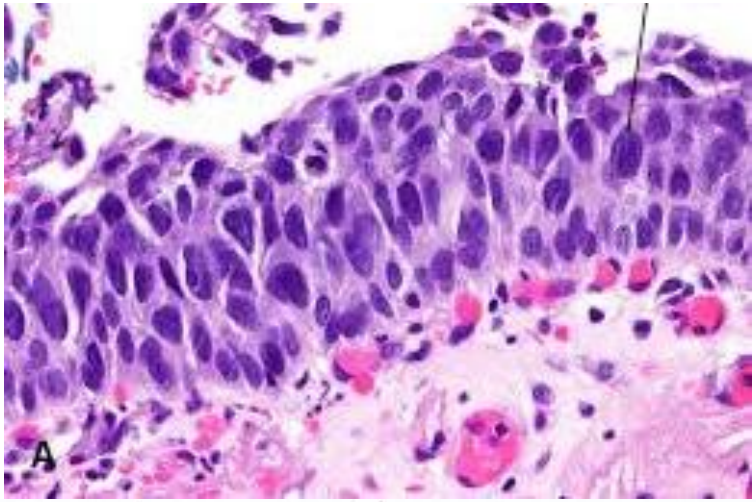


Carcinoma in situ

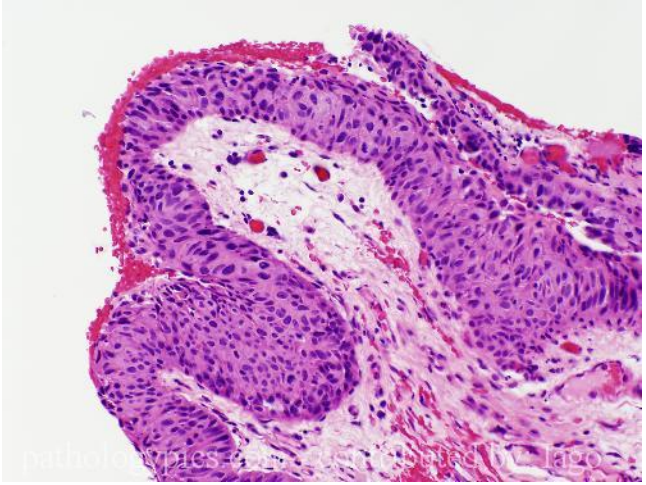


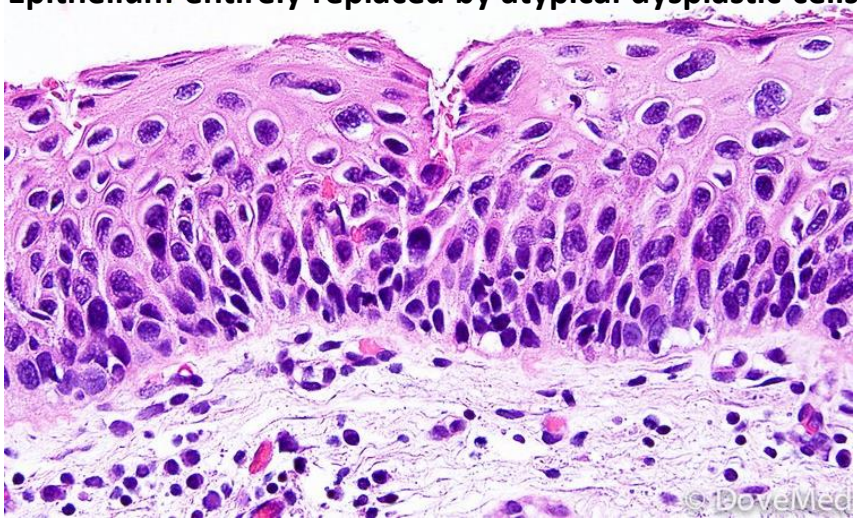
Numerous mitotic figures extending toward the surface

Large dark nucleus



Epithelium entirely replaced by atypical dysplastic cells





Carcinoma in situ

Some examples

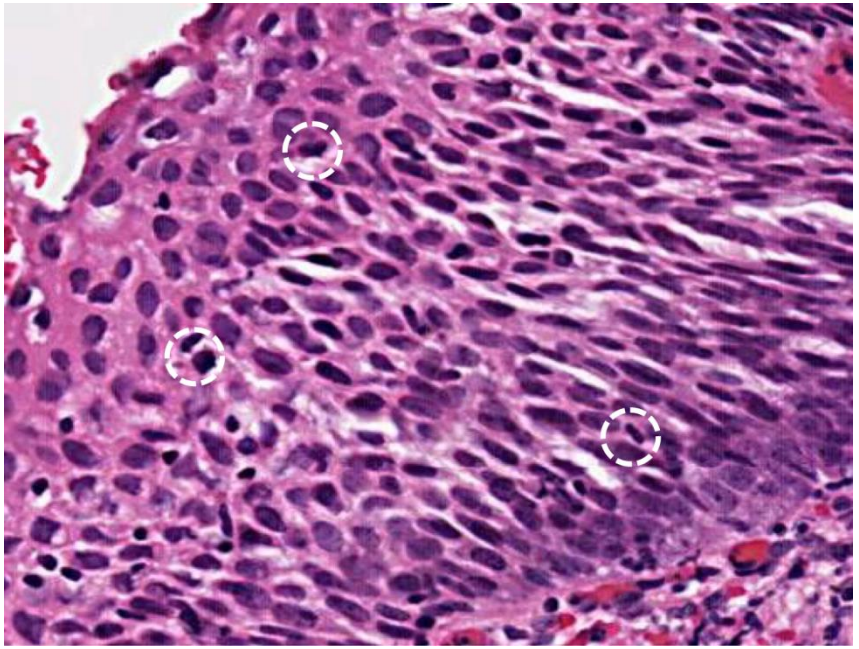
- **Uterine cervix**
- **Skin (Bowens disease)**
- **Bronchial epithelium**

Carcinoma in situ

- It is a **preinvasive** neoplasm
- No chance of metastasis
- Prognosis is excellent
- May **persist for years** before it becomes invasive

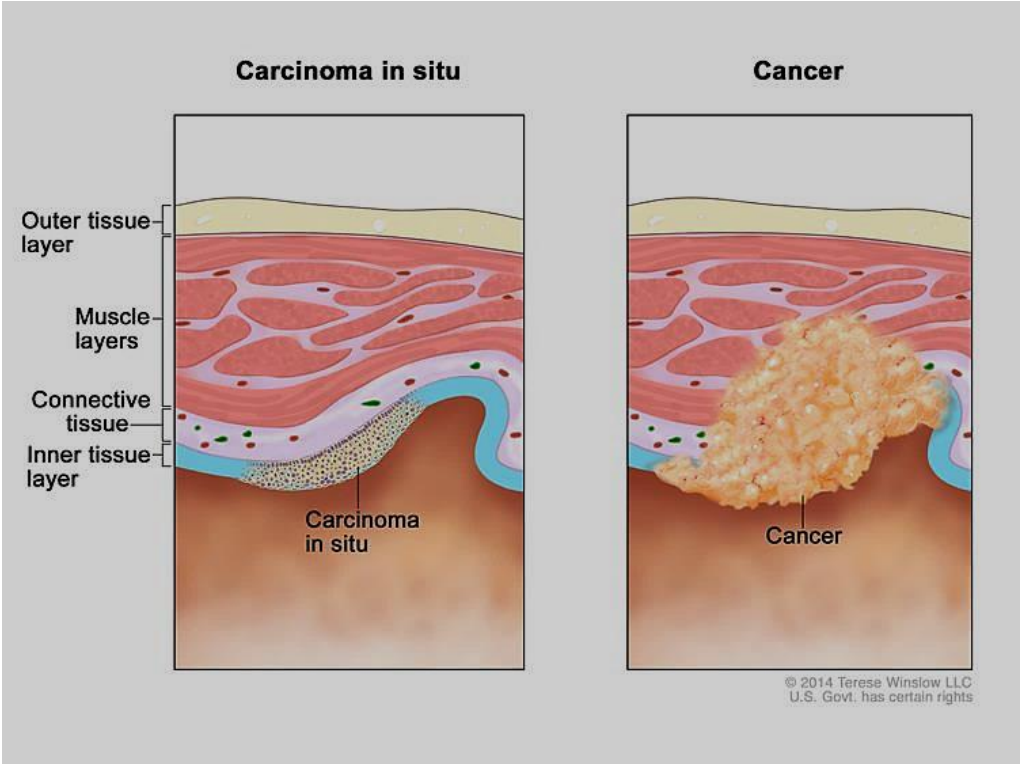
Normal stratified squamous epithelium

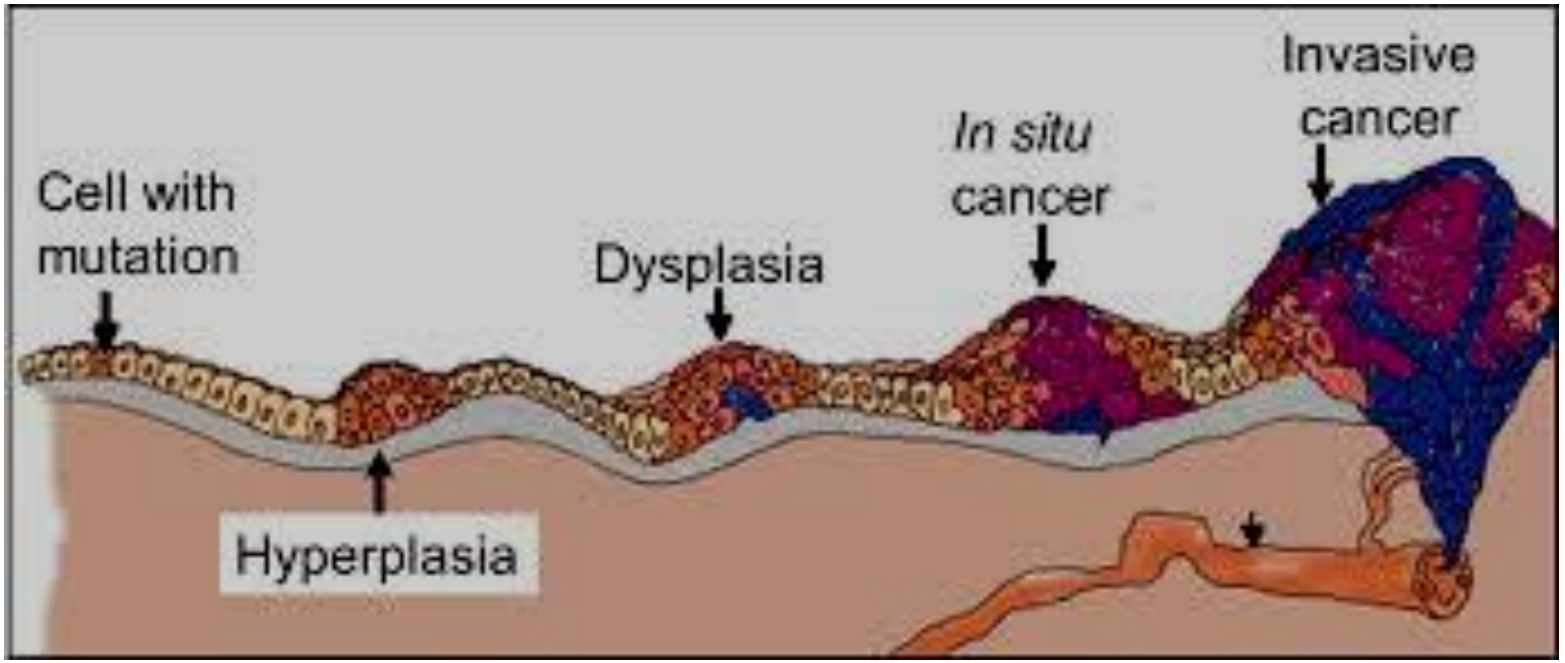
Carcinoma in situ



INVASIVE

- Once the tumour cells breach the basement membrane the tumour is said to be **INVASIVE**




Invasive
cancer
In situ
cancer
Cell with
mutation
Dysplasia
Hyperplasia

LOCALLY MALIGNANT TUMOUR

Groups of tumours that spread only locally with no distant spread

Examples:

- **Basal cell carcinoma of skin**
- **Glioma**
- **Adamantinoma/ ameloblastoma**

LATENT CANCER

- A cancer that grows slowly
- Has no important health effect on a patient
- Also called occult cancer
- Example- **Prostate cancer**

DORMANT CANCER

- **Dormancy** is a stage in **cancer** progression where the cells cease dividing
- but survive in a quiescent state while
- waiting for appropriate environmental conditions to begin proliferation again.
- Quiescence is the state where cells are not dividing but at arrest in the cell cycle in G0-G1.

Today's Lecture topics

Characteristics of benign and malignant tumours

1. Differentiation and Anaplasia-
   - Pleomorphism
   - Abnormal nuclear morphology
   - Mitoses
   - Loss of polarity/orientation
2. Rate of growth
3. Local Invasion
4. Metastasis

Today's Lecture topics

- Local Invasion
- Metastasis

Three pathways

(1) direct seeding of body cavities or surfaces

(2) lymphatic spread

(3) haematogenous spread

Iatrogenic spread

Today's Lecture topics

- Dysplasia
- Carcinoma in situ
- Locally malignant tumour
- Latent tumour
- Dormant tumour


THANK YOU