MIPER Kurnool

NEOPLASTIC DISEASES

BY

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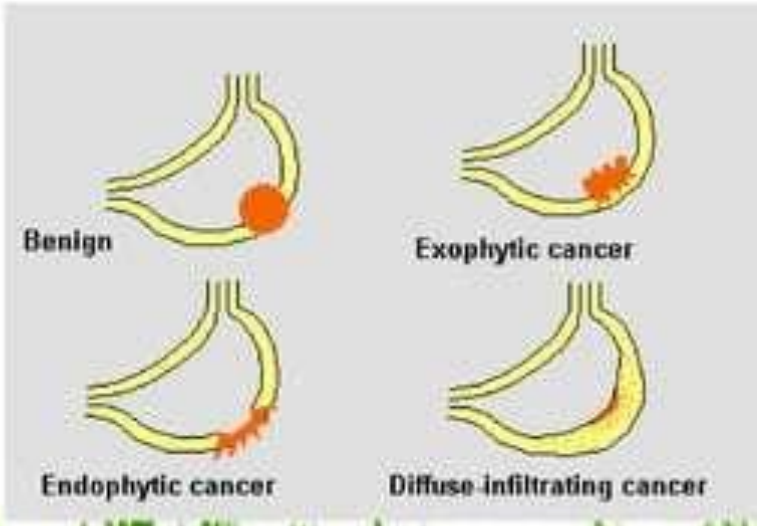
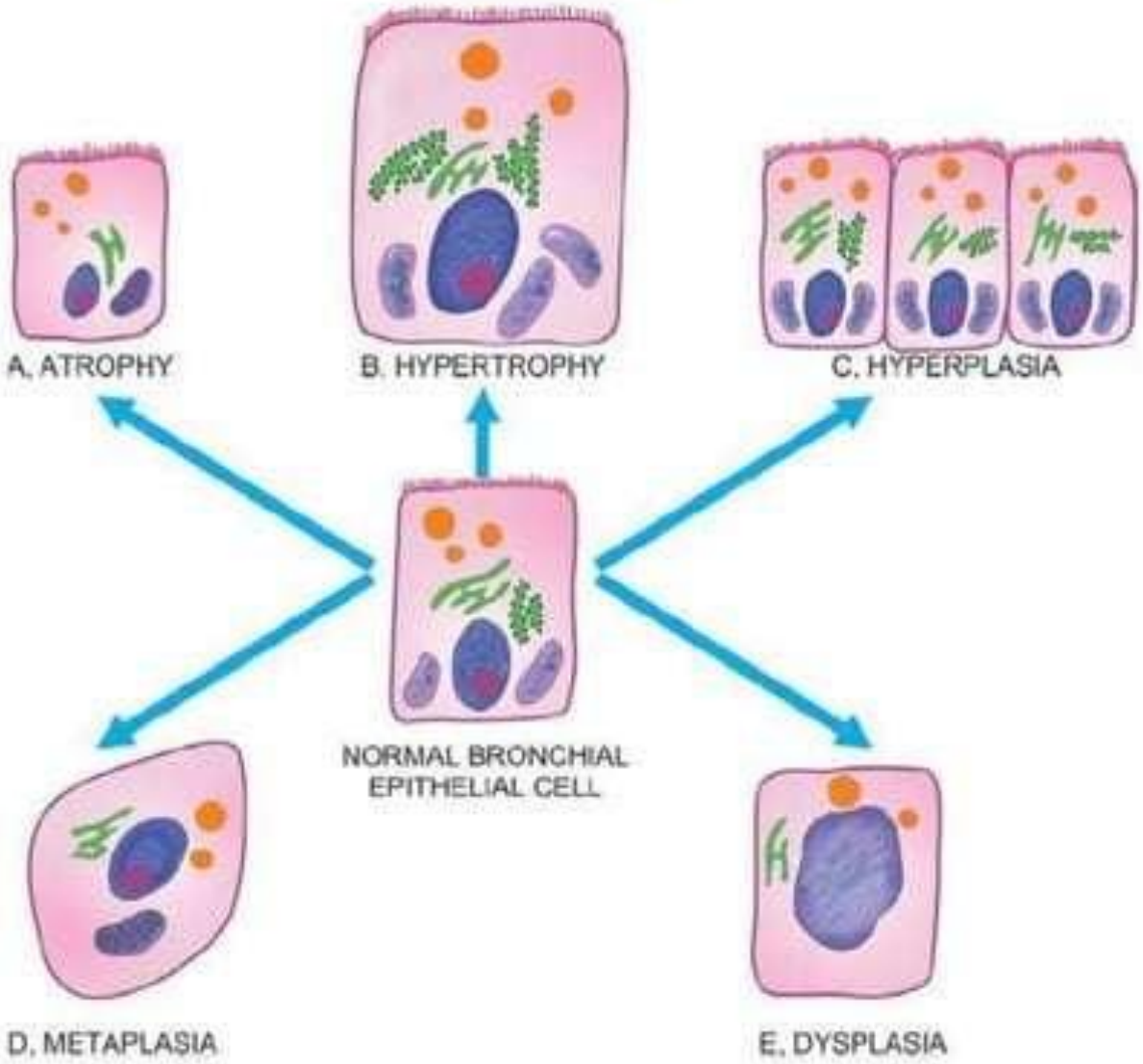
Definition

- Neoplasia means 'new growth'
- Neoplasm means 'tumour/ cancer'
- Cancer is an uncontrolled proliferation of cells that express varying degree of fidelity to their precursors.
- It can be benign or malignant.

- Benign: Cells grow as a compact mass and remain at their site of origin
- Malignant:
  Growth of cells is uncontrolled
  Cells can spread into surrounding tissue and spread to distant sites.



Cellular adaptations



Cellular adaptations

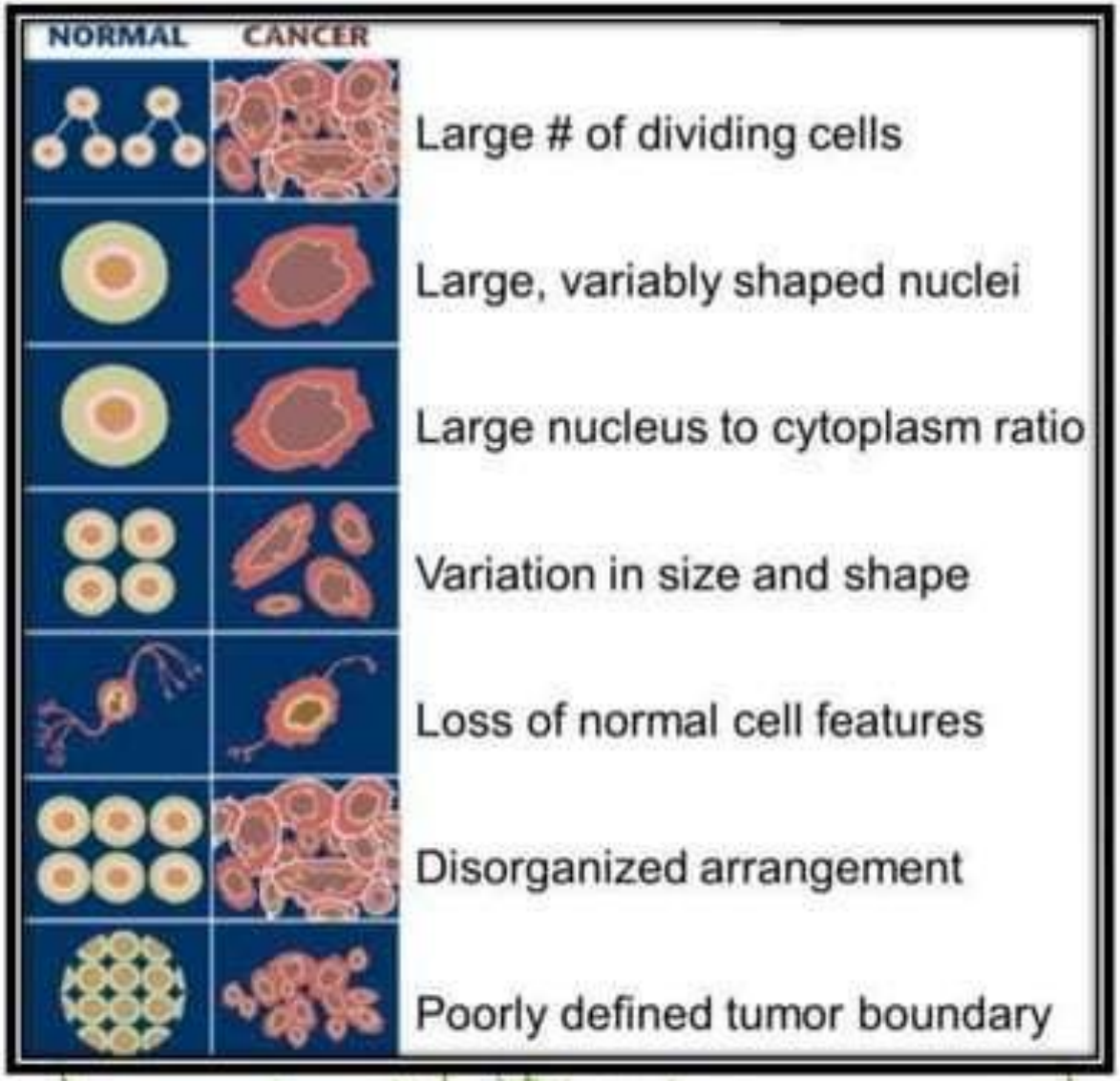
- Atrophy: Reduction of number and size of parenchymal cells of an organ or its parts which was once normal is called atrophy. E.g.: ischemic atrophy, neuropathic atrophy.

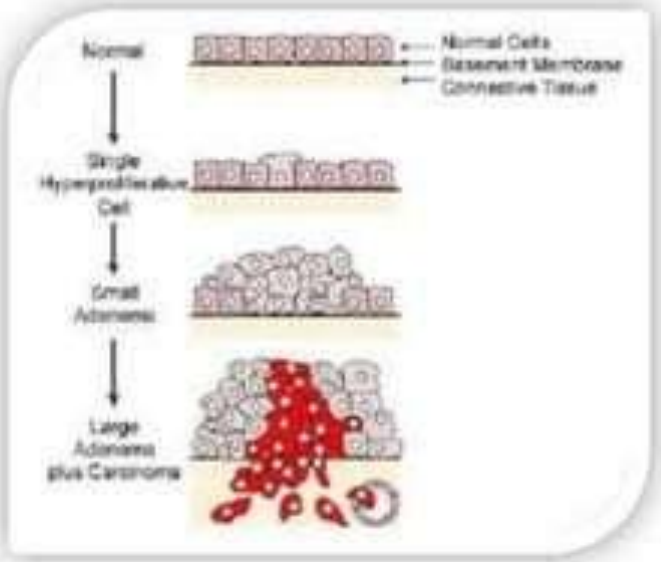
- Hypertrophy: Increase is an size of parenchymal cells resulting in enlargement of the organ. E.g.: enlarged size of uterus in pregnancy (physiological), hypertrophy of cardiac muscle (pathological).

Cellular adaptations

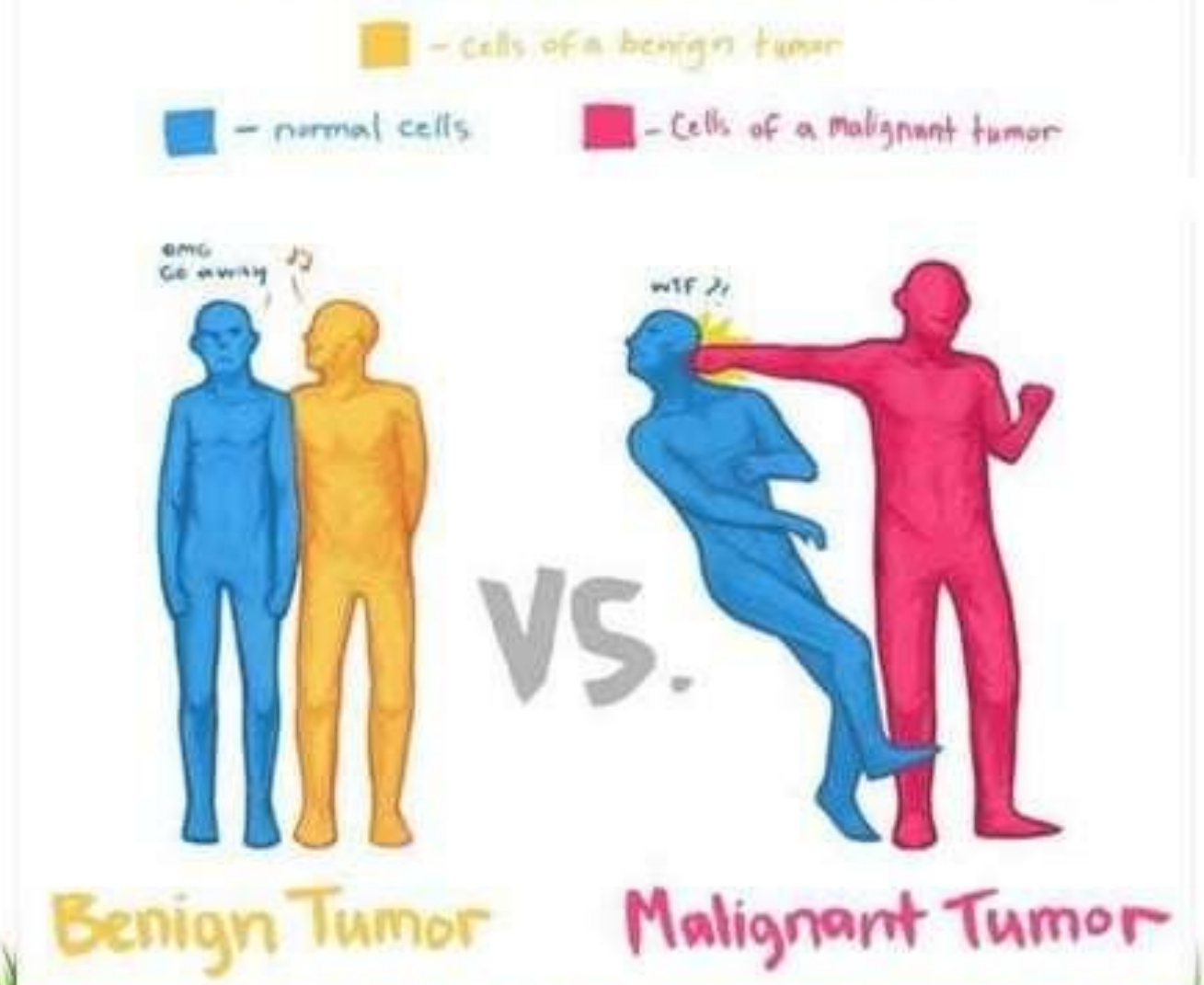
- Hyperplasia: Increased number of parenchymal cells resulting in enlargement of the organ. E.g.: Hyperplasia of female breast at puberty, during pregnancy and lactation (physiological), wound healing (pathological; formation of granulation tissue due to proliferation of fibroblasts and endothelial cells)
- Dysplasia: Disordered cellular development (pleomorphism, nuclear hyperchromasia, mitosis, loss of polarity) accompanied with metaplasia and hyperplasia.
- Metaplasia: Reversible changes in one type of epithelial or mesenchymal adult cell to another type of epithelial or mesenchymal adult cell .
  - Epithelial → Squamous and Columnar metaplasia
  - Mesenchymal → Osseous and Cartilaginous metaplasia

Differences between normal and cancer cell



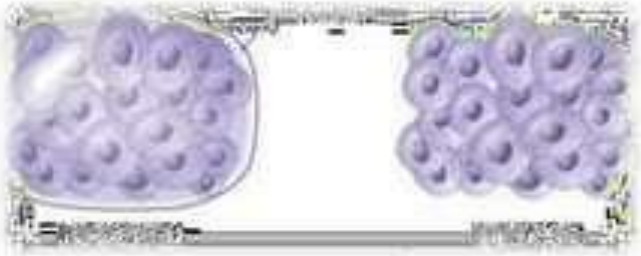


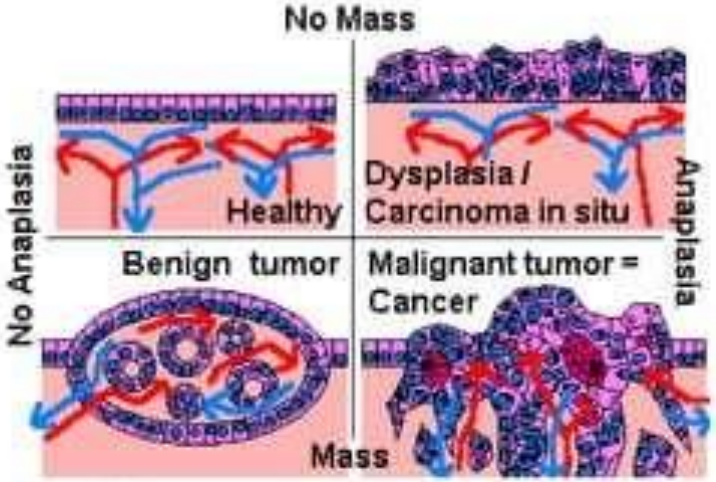
Differences between benign and malignant neoplasms

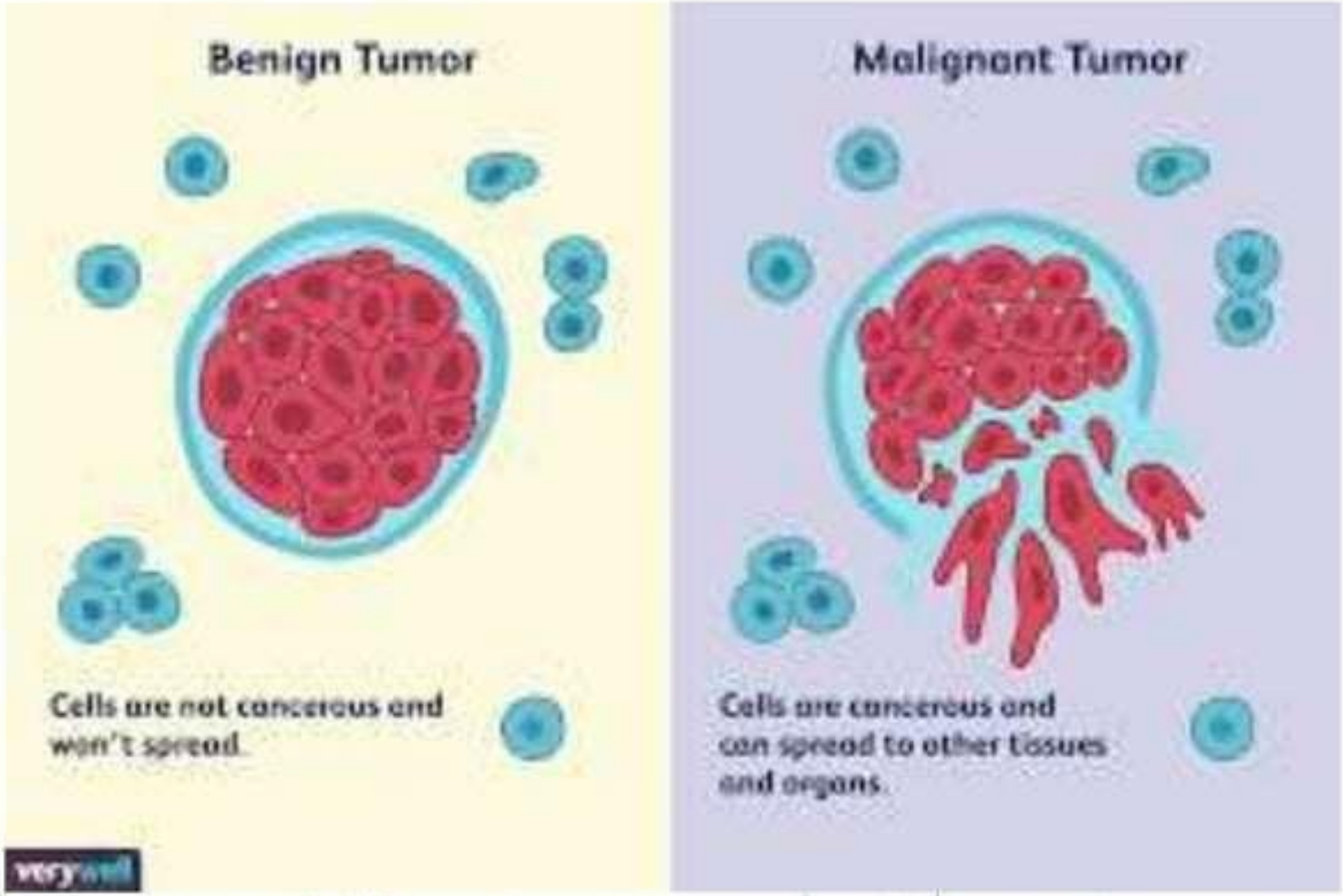


Differences between benign and *malignant neoplasms*

BENIGN	MALIGNANT
Nuclear variation in size and shape minimal	Nuclear variation in size and shape minimal to marked, often variable
Diploid	Range of ploidy
Low mitotic count, normal mitosis	Low to high mitotic count, abnormal mitosis
Retention of specialisation	Loss of specialisation
Structural differentiation retained	Structural differentiation shows wide range of changes
Organised	Not organised
Functional differentiation usually	Functional differentiation often lost



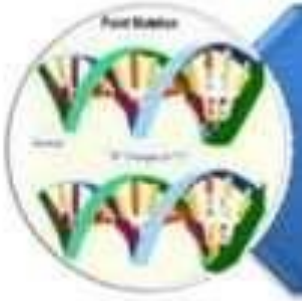



Benign Tumor
Cells are not cancerous and won't spread.
Malignant Tumor
Cells are cancerous and can spread to other tissues and organs.

Benign tumors	Malignant tumor
Slowly growing mass	Rapidly growing mass
Regular surface, capsulated, not attached to deep structures	Irregular surfaces, Non-capsulated attached to deep structures
Noninvasive to another organ or tissues	Invasive to other organs
No spread or metastasis	Spread and metastasis
Well differentiated all the them	Poorly differentiated, moderately or well differentiated
No recurrence after surgery	Recurrence after surgery
No bleeding in cut surfaces	Bleeding from cut surfaces is common
Named by adding suffix –oma	Named by adding suffix sarcoma or carcinoma
Slight pressure effect on the neighboring organ	Remarkable pressure effect on neighboring tissue

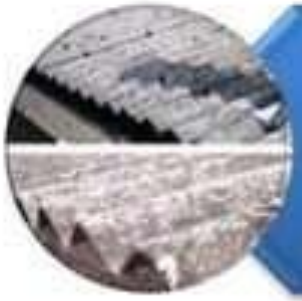
Causes of cancer

Three major type of carcinogens



Chemical carcinogenesis

- Mutagens
- Chemical carcinogenesis and their metabolism



Physical carcinogenesis (radiation)

- Ultraviolet radiation, Asbestos

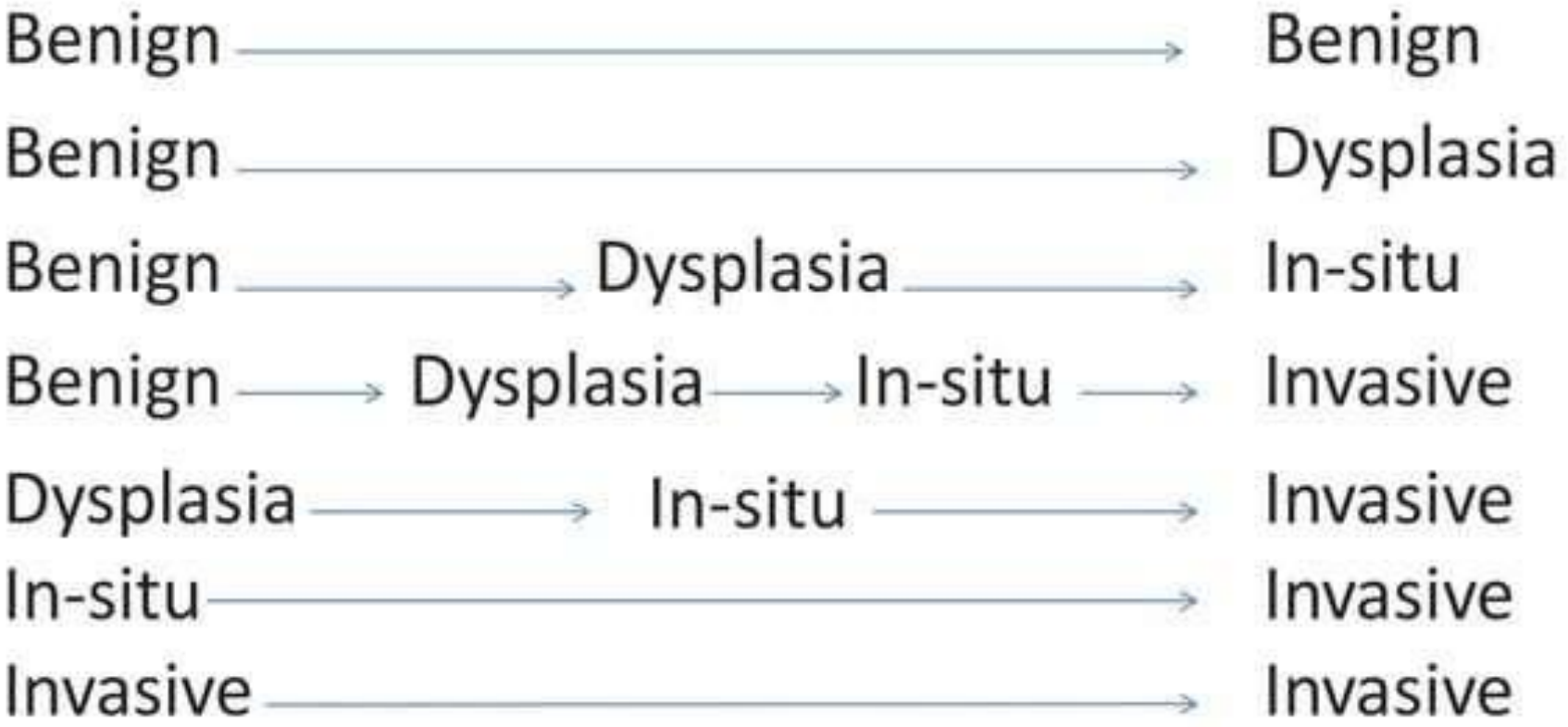
Infectious Pathogens (Viral)

- Human T-cell leukemia viruses, DNA viruses, Human papillomaviruses
- Epstein-Barr virus, Hepatitis B virus

Development of cancer

- Changes in DNA (mutation)
- The change must cause an alteration in cell growth and behaviour
- The change must be non-lethal and be passed onto daughter cells
- Alterations in more than one gene
- Genes concerned are oncogenes/tumour suppressor genes
- Sequence of gene alterations from normal to benign to malignant
- Intrinsic and extrinsic / inheritance and environment key factors

Possible events

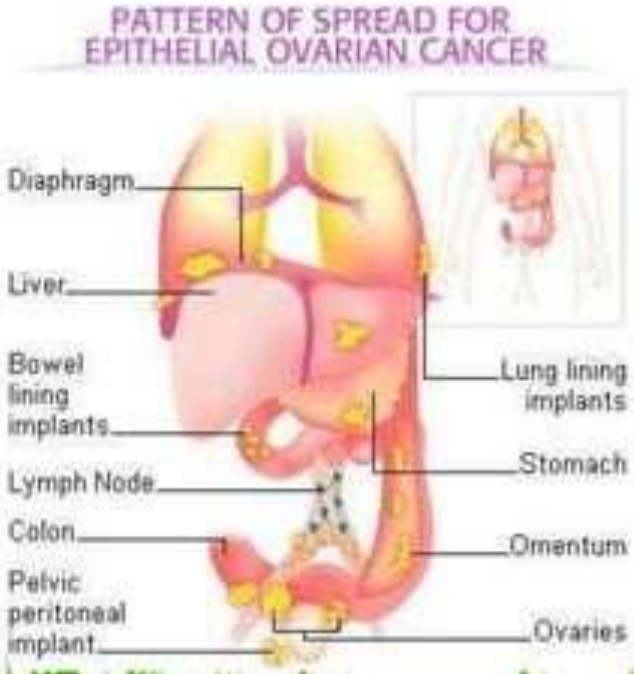


Properties of cancer cells

- Two unique properties of cancer cells are
  - **ability to invade locally**
  - **capacity to metastasize to distant sites to distant sites – cancer spreading (patterns of spread)**

Patterns of spread:

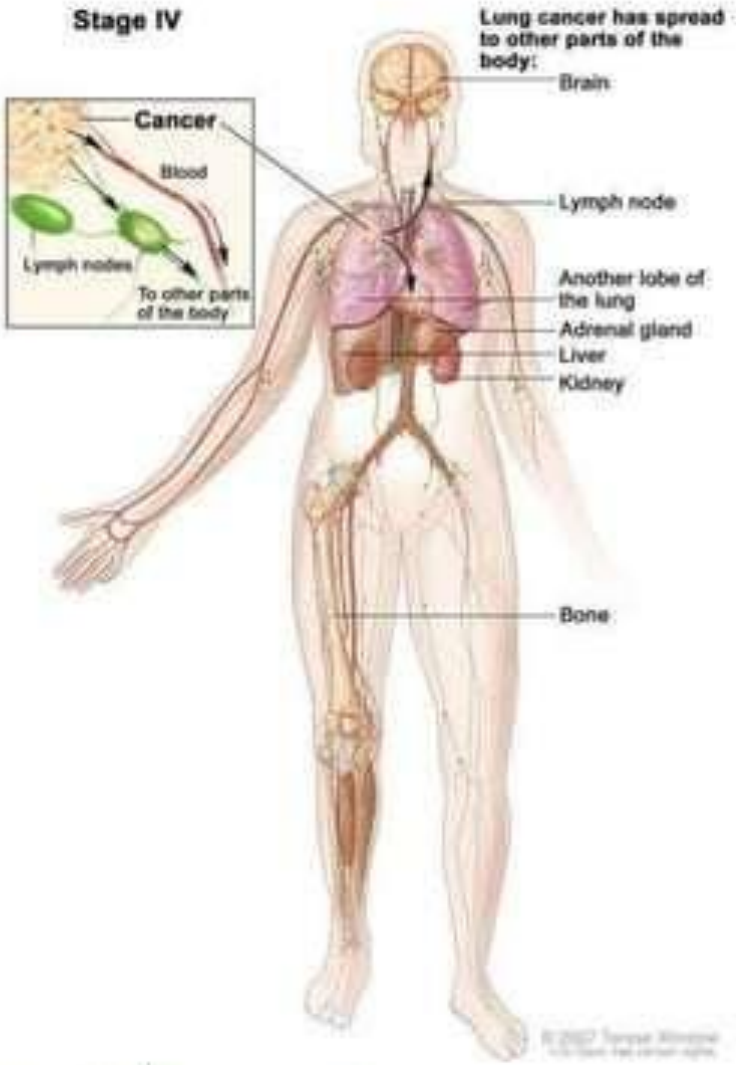
Direct extension: Carcinomas begin as localized growths (direct seeding of body cavities or surface), when they arise. In early cancers do not penetrate the basement membrane (carcinoma in situ). When the in situ tumor acquires invasive potential extends directly to compromise neighboring cells and to metastasize. E.g. Peritoneal carcinomatosis (metastatic ovarian carcinoma)



Properties of cancer cells

Patterns of spread:

- ❑Direct extension
- ❑Metastatic spread: Transfer of malignant cells from one site to another (not directly connected with it). Invasive properties of malignant tumors bring them into contact with blood and lymphatic vessels.
  - Hematogenous metastases
  - Lymphatic metastases



Nomenclature

- Benign tumors:
  - Suffix- *oma* to cell of origin
  - Name of origin cell + morphologic character + oma (skin pailoma, ovarian cyst adenoma)

E.g.:

- tumors of squamous epithelium- epitheli*oma*
- tumors arising from the glandular gland (colon/ endocrine glands)- aden*oma*

– lipoma ,fiboma, chondroma, osteoma papilloma

Nomenclature

- Malignant tumors:
  - mesenchymal tissue are usually called **sarcoma**
  - Epithelial cell origin are usually called **carcinoma**
  - Name of origin cell + morphologic character + carcinoma/ sarcoma
  - E.g.:
    - Malignant tumor of the stomach is a gastric adenocarcinoma or adenocarcinoma of the stomach.

Special nomenclature

- Blastoma: tumors rigging in immature tissue or nervous tissue, most of them are malignant
  - E.g.: medulloblastoma, retinoblastoma, nephroblastoma
- Some tumors atacching the suffix- oma, but they are malignant

Malignant tumor of the liver: Hepatoma

Melanoma of the skin: Seminoma

Lymphoproferative tumor: Lymphoma (Hodgkin's and non Hodgkin's)

Malignant proliferation of leukocytes: Leukemia

Special nomenclature

- Mixed tumors: Derived from one from one germ layer may undergo divergent defferentiation creating
  - E.g.: Mixed tumor of salivary gland
- Teratomas: Tumors containing mature or immature cells
- Hamartoma: tumor-like malformation composed of a haphazard arrangement of tissues indigenous to the particular site, which is totally benign.

Classification of tumours

Tissue or origin	Benign	Malignant
Epithelial tumours		
1. Squamous epithelium	Squamous cell papilloma	Squamous cell carcinoma
2. Transitional epithelium	Transitional cell papilloma	Transitional cell carcinoma
3. Glandular epithelium	Adenoma	Adenocarcinoma
4. Basal cell layer skin	--	Basal cell carcinoma
5. Neuroectoderm	Naevus	Melanoma (melanocarcinoma)
6. Hepatocytes	Liver cell adenoma	Hepatoma (Hepatocellular carcinoma)
7. Placenta (chorionic epithelium)	Hydatidiform mole	Choriocarcinoma

Classification of tumours

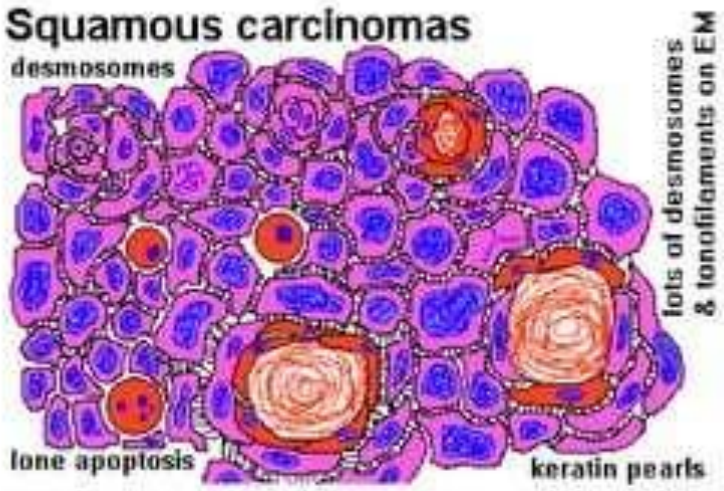
Tissue or origin	Benign	Malignant
Non-epithelial (mesenchymal) tumours		
1. Adipose tissue	Lipoma	Liposarcoma
2. Adult fibrous tissue	Fibroma	Fibrosarcoma
3. Embryonic fibrous tissue	Myxoma	Myxosarcoma
4. Cartilage	Chondroma	Chondrosarcoma
5. bone	Osteoma	Osteosarcoma
6. Synovium	Benign synovioma	Synovial sarcoma
7. Smooth muscle	Leiomyoma	Leiomyosarcoma
8. Embryonic fibrous tissue	Rhabdomyoma	Rhabdomysarcoma

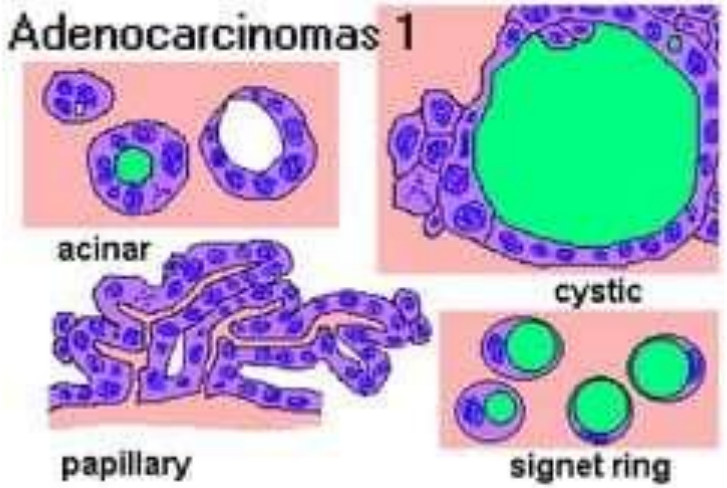
Classification of tumours

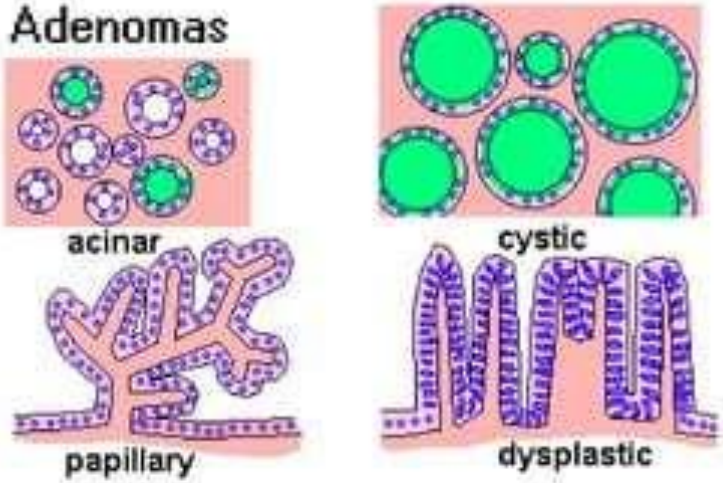
Tissue or origin	Benign	Malignant
Non-epithelial (mesenchymal) tumours		
9. Mesothelium	--	Mesothelioma
10. Blood vessels	Haemangioma	Angiosarcoma
11. Lymph vessels	Lymphangioma	Lymphangiosarcoma
12. Glomus	Glomus tumour	--
13. Meninges	Meningioma	Invasive meningioma
14. Haematopoietic cells	--	Leukaemias
15. Lymphoid tissue	Pseudolymphoma	Malignant lymphomas
16. Nerve sheath	Neurilemmoma, Neurofibroma	Neurogenic sarcoma
17. Nerve cells	Ganglioneuroma	Neuroblastoma

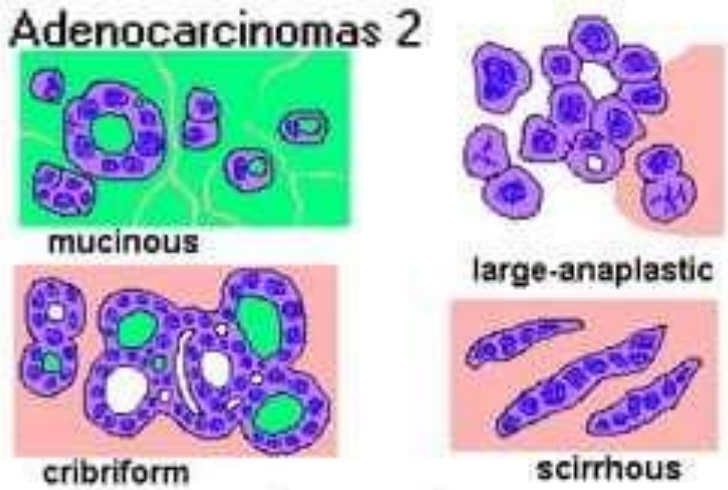
Classification of tumours

Tissue or origin	Benign	Malignant
Mixed Tumours		
Salivary glands	Pleomorphic adenoma	Malignant mixed salivary tumour
Tumours of more than one germ cell layer		
Totipotent cells in gonads or in embryonal rests	Mature teratoma	Immature teratoma


Squamous carcinomas
desmosomes
lots of desmosomes & tonofilaments on EM
lone apoptosis
keratin pearls


Adenocarcinomas 1
acinar
cystic
papillary
signet ring


Adenomas
acinar
cystic
papillary
dysplastic


Adenocarcinomas 2
mucinous
large-anaplastic
cribriform
scirrhous

Characteristics of tumours

- Majority of neoplasms can be categorized clinically and morphological into **benign and malignant** on the basis of certain characteristics listed bellow
  - Rate of growth
  - Cancer phenotype and stem cells
  - Clinical and gross features
  - Microscopic features
  - Local invasion (direct spread)
  - Metastasis (distant spread)

Characteristics of tumours

- ***Rate of growth***
  - The tumour cell proliferate more rapidly than the normal cells.
  - The tumour enlarge rate is depends upon
    1. **Rate of cell production, growth fraction and rate of cell loss**
    2. **Degree of differentiation of the tumour**

1. Rate of growth of a tumour depends upon

- Doubling time (mitotic rate) of tumour cells
- Number of cells remaining in preoperative pool (growth fraction)
- Rate of loss of tumour cells by cell shedding

Cancer cell do not follow the normal cell controls in cells, and are immortal. The cell division rate is high and center of tumor do not receive adequate nourishment and undergo ischemic necrosis, loss shedding.

Death tumour cells appear as apoptotic figures and dividing tumours are seen as normal/ abnormal mitotic figure→ ultimately tumour grow in size.

Characteristics of tumours

- ***Rate of growth***

  2. Degree of differentiation

  - Rate of growth of malignant tumour is directly proportionate to the degree of differentiation.
  - Poorly differentiated tumours show aggressive growth pattern compare to better differentiated tumours.
  - Rarely, a malignant tumour may disappear spontaneously from the primary site, due to good host immune attack.

Characteristics of tumours

- ***Cancer phenotype and stem cells***

Cancer cells

1. disobey the growth control – ***proliferate rapidly***
2. escape from death signals – ***immortality***
3. imbalance between cell proliferation and cell death – ***excessive growth***
4. lose differentiation properties – ***no function***
5. are unstable – ***newer mutations***
6. overrun their neighboring tissue – ***invade locally***
7. have the ability to travel from the site of origin to other part of body – ***distant metastasis***

Cancer stem cells/ tumour-initiating cells have the properties of self-renewal, asymmetric replication and transdifferentiation (i.e. plasticity).

Characteristics of tumours

- ***Clinical and gross features***
  - Benign tumour are generally slow growing and depending upon location remains asymptomatic (subcutaneous lipoma) or may cause serous symptoms (meningioma in the nervous system). Benign tumours are generally spherical or ovoid shape.
  - Malignant tumor grow rapidly, invade locally into deeper tissue and spread to distant sites (metastasis). Malignant tumours are usually irregular in shape, poor-circumscribed and extend into adjacent tissues.

Characteristics of tumours

- ***Microscopic features***
  - Microscopic pattern
  - Cytomorphology of neoplastic cells
  - Tumor angiogenesis and stroma
  - Inflammatory reaction

Characteristics of tumours

- ***Local invasion (direct spread)***
  - Benign: expand and push aside without invading, infiltrating or metastasising.
  - Malignant: expand, invasion, infiltration and destruction of the surrounding tissue.
- ***Metastasis (distant spread)***
  - Metastasis (meta= transformation, stasis= residence): spread of tumour by invasion.
  - Routes of metastasis
    - Lymphatic spread
    - Haematogenous spread
    - Spread along body cavities and natural passages

Tumours grading

Grading is based on (1) the degree of anaplasia

(2) the rate of growth

- Grade-I : Well-differentiated (less than 25% anaplastic cells)
- Grade-II : Moderately-differentiated (25-50% anaplastic cells)
- Grade-III : Moderately-differentiated (50-75% anaplastic cells)
- Grade-IV : Poorly-differentiated or anaplastic (more than 75% anaplastic cells)

Tumours staging

- International TNM system is commonly used for solid tumours (less applicable to lymphomas and leukaemias).
  - T: Tumour (size of primary tumour), N: Nodes (local/ regional node involvement), M: Metastases (distant metastases)

T0	No evidence of tumour	N0	Regional lymph nodes not involved
Tis	Carcinoma in situ	NX	Regional lymph nodes can't be assessed
TX	Tumour can't be assessed	N1-4	Progressive increase in number of local/ regional lymph nodes involved
T1-4	Progressive increase in tumour size	M0	No evidence of distant metastases
		MX	distant metastases can't be assessed
		M1-3	Increasing involvement of distant metastases

THANK YOU