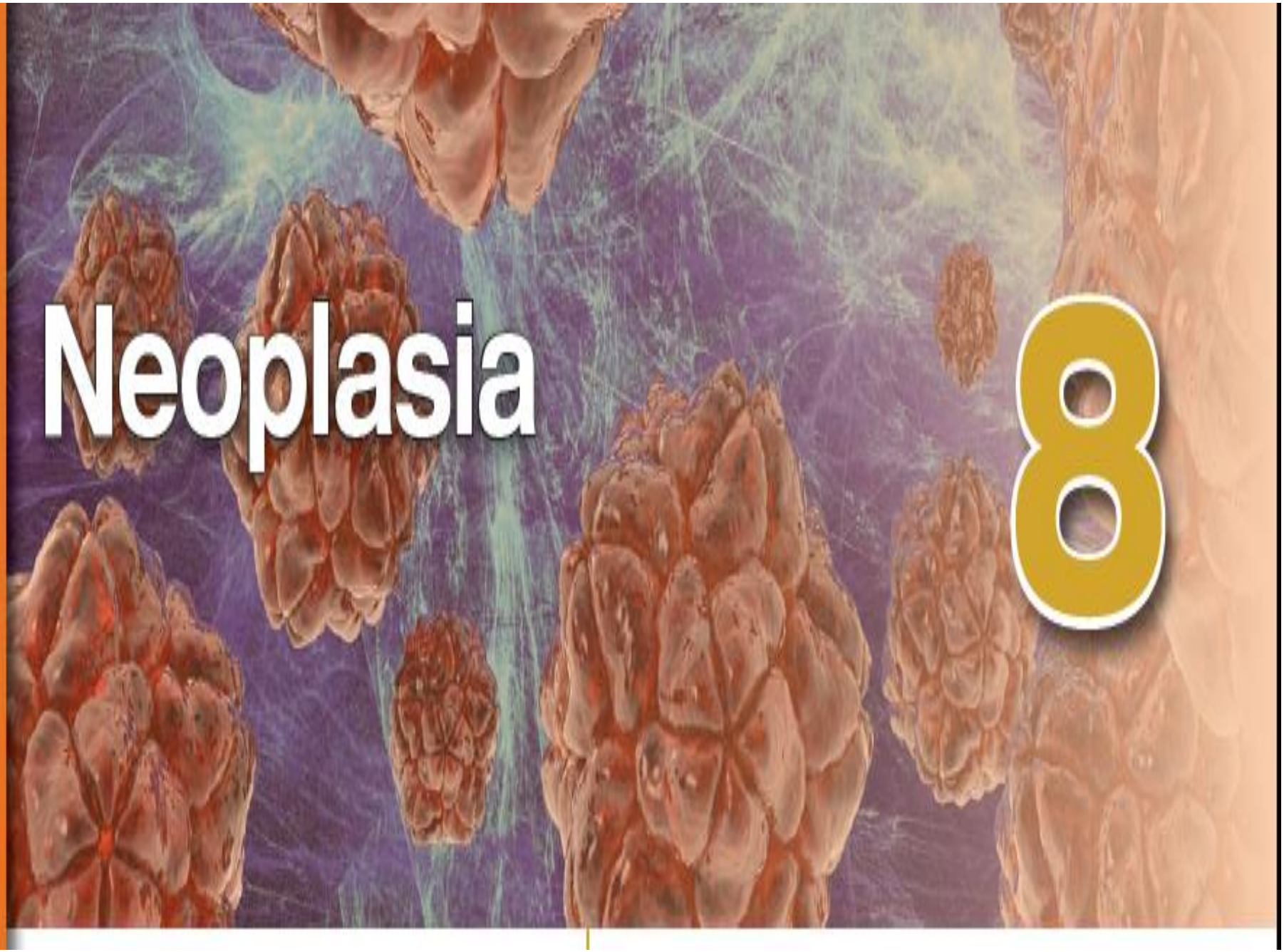

Neoplasia
8

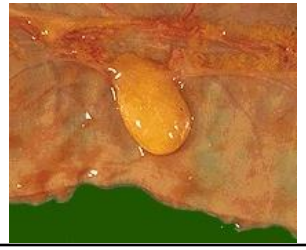
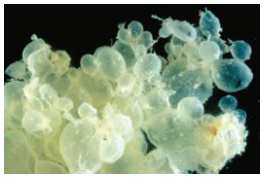
Definitions

- **Neoplasia** is the uncontrolled, disorderly proliferation of cells, resulting in the formation of tumour or neoplasm.
- **A tumor** : is a swelling that can be caused by a number of conditions, including inflammation and trauma. In addition, the term has been used to define an abnormal mass of cells that arises because of overgrowth.
- Unlike normal cellular adaptive processes such as hypertrophy and hyperplasia, neoplasms do not obey the laws of normal cell growth. They serve no useful purpose, they do not occur in response to an appropriate stimulus and they continue to grow at the expense of the host.
- **Neoplasms are classified as benign or malignant.**
- **Neoplasms that contain well-differentiated cells (Cell differentiation is the process whereby proliferating cells become progressively more specialized cell types) that are clustered together in a single mass are considered to be benign. These tumors usually do not cause death unless their location or size interferes with vital functions.**
- **In contrast, malignant neoplasms are less well differentiated and have the ability to break loose, enter the circulatory or lymphatic system, and form secondary malignant tumors at other sites.**

Continued…….

- Benign tumours of most tissues (including parenchymal (or called epithelial) and mesenchymal tissues, (comprising connective tissues, muscle and blood vessel)) are usually simply designated the suffix **-oma**. For example, a benign tumor of glandular epithelial tissue is called an **adenoma**, and a benign tumor of bone tissue is called an **osteoma**. **Papillomas** are benign epithelial, microscopic or macroscopic finger-like projections that grow on any surface.
- The term carcinoma is used to designate a malignant tumor of epithelial tissue origin. In the case of a malignant tumor of glandular epithelial tissue, the term adenocarcinoma is used. Malignant tumors of mesenchymal origin are called sarcomas (e.g., if it originated in bone (connective tissue) it is called osteosarcoma).
- Oncology is the study of tumors and their treatment.
- Anaplasia describes the loss of cell differentiation in cancer tissue

Nomenclature of Epithelial Neoplasms

Epithelial tissues	Benign neoplasms	Malignant neoplasms
Skin & Mucus	Papilloma 	Papillary carcinoma
Glandular Epithelium	Adenoma 	AdenoCarcinoma
Placental epithelium	Hydatidiform Mole 	Chorion Carcinoma

Nomenclature of Connective Tissue Neoplasms

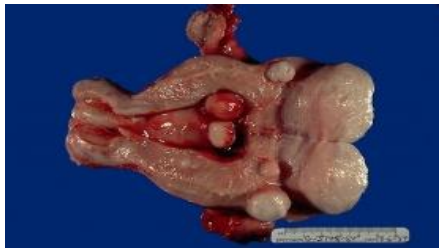
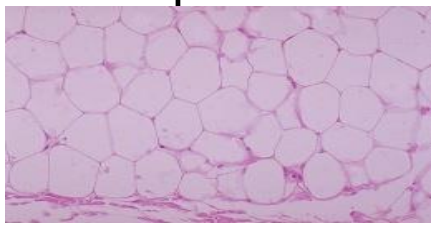
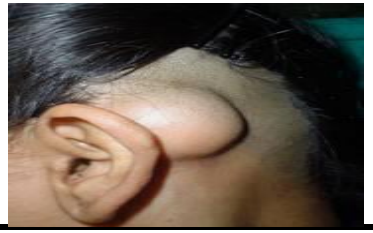
Connective tissues	Benign neoplasms	Malignant neoplasms
Fibrous tissue	Fibroma 	Fibrosarcoma
Fatty tissue	Lipoma 	Liposarcoma
Osteoid tissue	Osteoma 	Osteosarcoma 

TABLE 8.1 NAMES OF SELECTED BENIGN AND MALIGNANT TUMORS ACCORDING TO TISSUE TYPES

TISSUE TYPE	BENIGN TUMORS	MALIGNANT TUMORS
Epithelial		
Surface	Papilloma	Squamous cell carcinoma
Glandular	Adenoma	Adenocarcinoma
Connective		
Fibrous	Fibroma	Fibrosarcoma
Adipose	Lipoma	Liposarcoma
Cartilage	Chondroma	Chondrosarcoma
Bone	Osteoma	Osteosarcoma
Blood vessels	Hemangioma	Hemangiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
Lymph tissue		Lymphosarcoma
Muscle		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma
Neural Tissue		
Nerve cell	Neuroma	Neuroblastoma
Glial tissue	Glioma	Glioblastoma, astrocytoma, medulloblastoma, oligodendroglioma
Nerve sheaths	Neurilemmoma	Neurilemmal sarcoma
Meninges	Meningioma	Meningeal sarcoma
Hematologic		
Granulocytic		Myelocytic leukemia
Erythrocytic		Erythrocytic leukemia
Plasma cells		Multiple myeloma
Lymphocytic		Lymphocytic leukemia or lymphoma
Monocytic		Monocytic leukemia
Endothelial Tissue		
Blood vessels	Hemangioma	Hemangiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma

TABLE 8.3 COMPARISON OF NORMAL CELL CHARACTERISTICS WITH THOSE OF CANCER CELLS

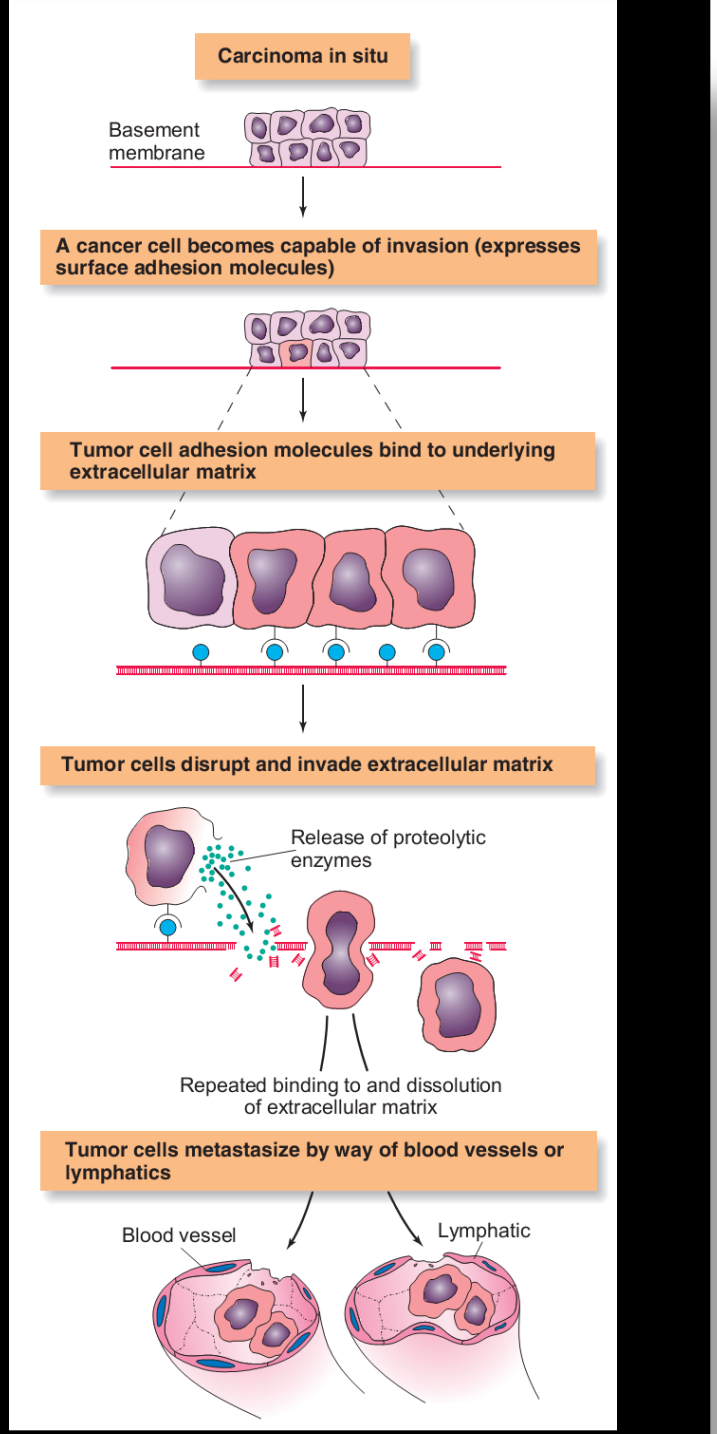
CHARACTERISTICS	NORMAL CELLS	CANCER CELLS
Growth	Regulated	Unregulated
Differentiation	High	Low
Genetic stability	Stable	Unstable
Growth factor dependence	Dependent	Independent
Density-dependent	High	Low inhibition
Cell-to-cell adhesion	High	Low
Anchorage dependence	High	Low
Cell-to-cell communication	High	Low
Cell life span	Limited	Unlimited
Antigen expression	Absent	May be present
Substance production (*e.g.*, proteases, hormones)	Normal	Abnormal
Cytoskeletal composition and arrangement	Normal	Abnormal

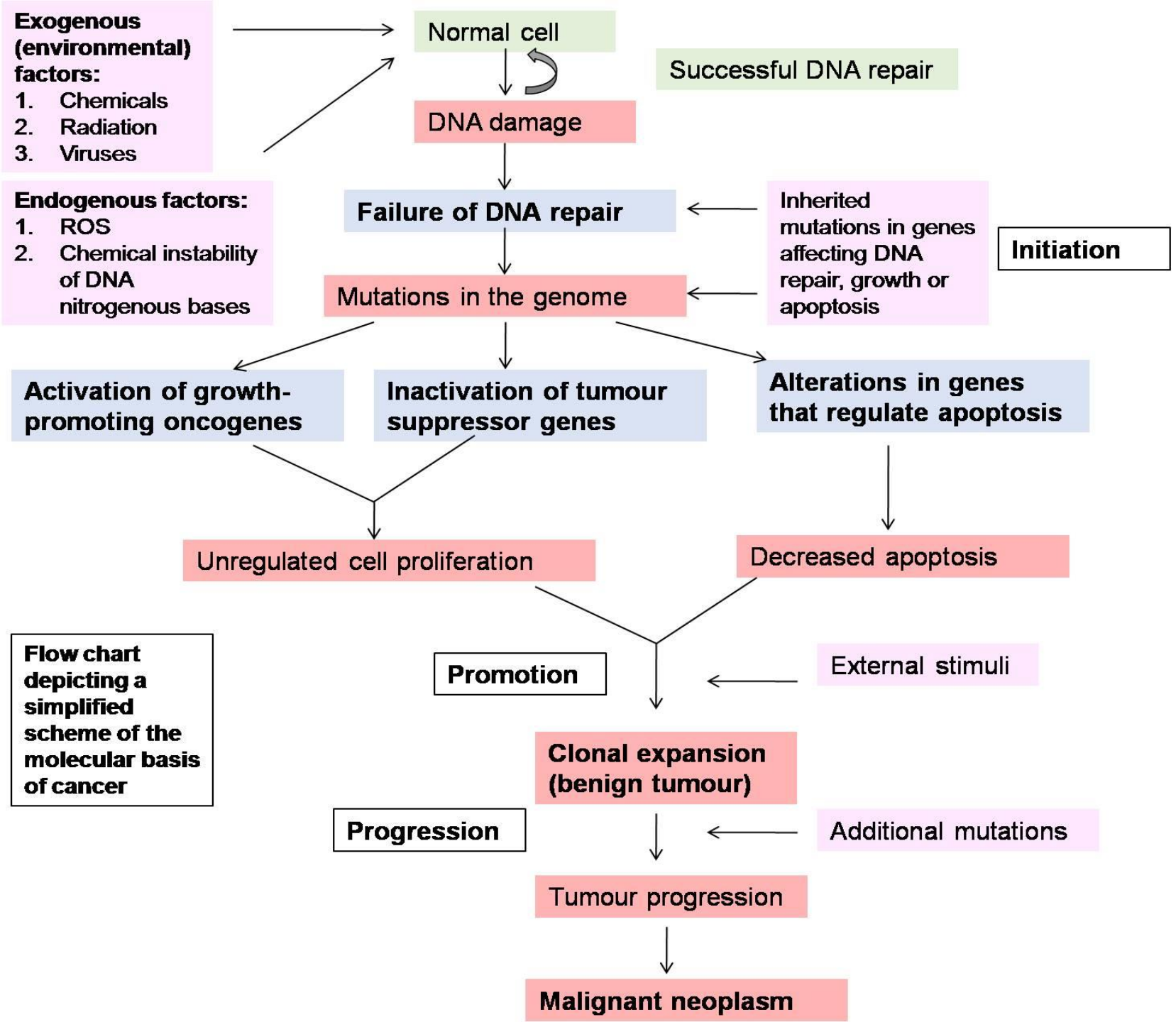
Characteristics	Benign neoplasms	Malignant neoplasms
Cell characteristics	Well-differentiated cells that resemble the cells of the tissues of origin.	Undifferentiated cells.
Rate of growth	Slow, progressive rate of growth that may come to regress.	Variable and depends on the level of differentiation, the more differentiated the cells, the more rapid the rate of growth.
Mode of growth & metastasis	Grow by expansion but remained localised to their site of origin, lacking the capacity to infiltrate, invade or metastasise to distant sites.	Grow by invasion and as the growth of primary solid tumour progress the cells detach from the original tumour mass and enter the blood and lymph systems to spread/metastasise to distant sites.
Encapsulation	Have ability to develop a fibrous capsule facilitating surgical removal.	Non-encapsulated with the lack of a sharp line of demarcation making the complete surgical removal more difficult.
Threat to health	Much less of a threat to health and do not cause death unless they interfere with vital functions because of their anatomic location. For instance, a benign tumours growing in the cranial cavity can eventually cause death by compressing brain structures. They also can cause disturbances in the function of adjacent or distant structures by producing pressure on tissue, blood vessels or nerves.	May compress blood vessels and outgrow their blood supply causing ischemia and tissue injury. Thus, they secrete vascular endothelial cell growth factor (VEGF) which increases the blood supply to the tumour and facilitates more rapid growth.
Categories	Solid tumour	Solid tumours and hematologic cancer

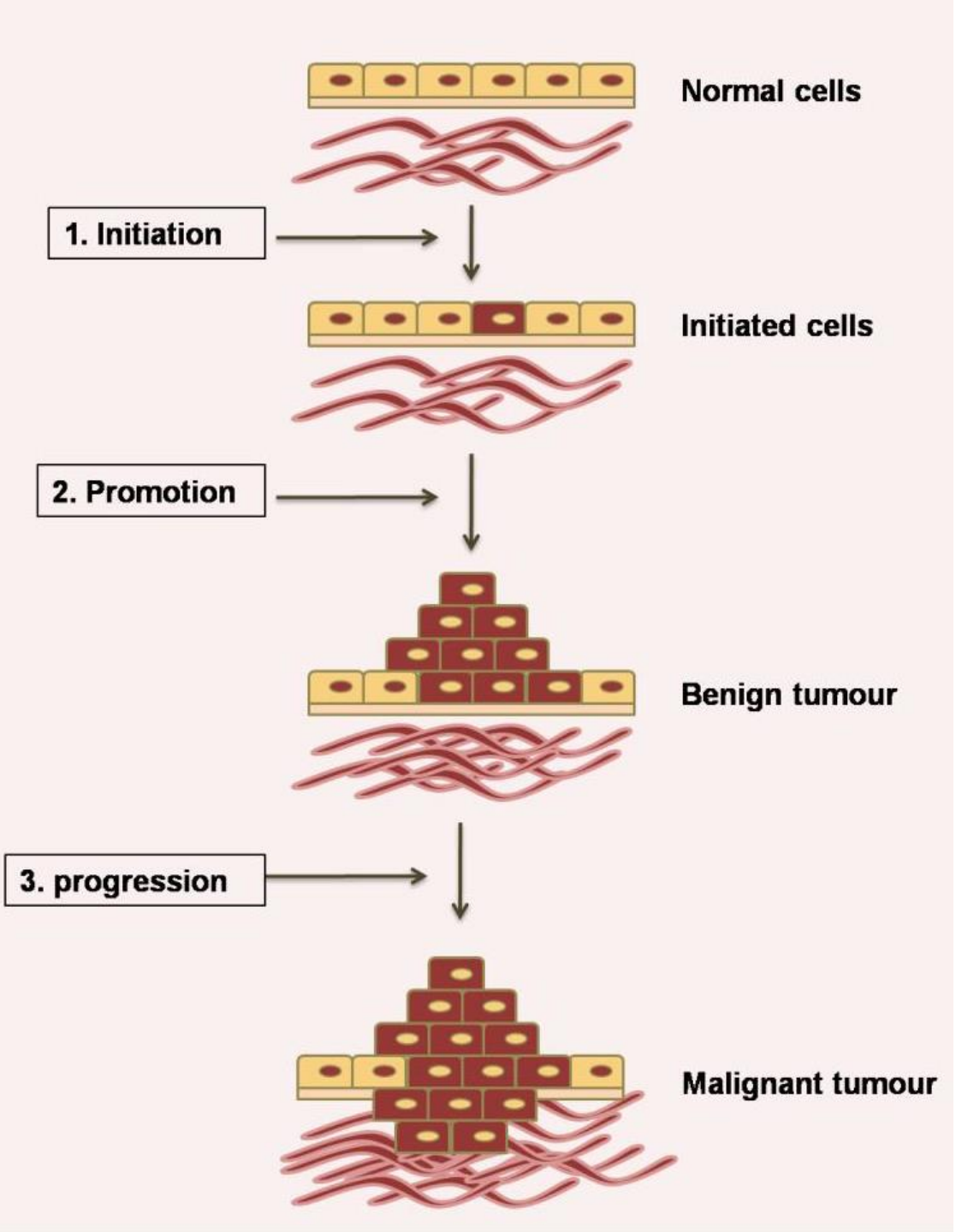
•***Carcinoma in situ*** is a localised preinvasive lesion or is an early stage cancer in which tumour is still confined to the site from which it started and has not spread to surrounding tissue or other organs in the body.

•The most common type of non-invasive breast cancer is breast ductal carcinoma in situ, in which the cells have not crossed the basement membrane.

•Depending on its location, in situ lesions usually can be removed surgically or treated so that the chance of recurrence are small. For example, carcinoma in situ of the cervix is essentially 100% curable.


Carcinoma in situ
Basement membrane
A cancer cell becomes capable of invasion (expresses surface adhesion molecules)
Tumor cell adhesion molecules bind to underlying extracellular matrix
Tumor cells disrupt and invade extracellular matrix
Release of proteolytic enzymes
Repeated binding to and dissolution of extracellular matrix
Tumor cells metastasize by way of blood vessels or lymphatics
Blood vessel
Lymphatic


Exogenous (environmental) factors:
1. Chemicals
2. Radiation
3. Viruses
Normal cell
Successful DNA repair
DNA damage
Endogenous factors:
1. ROS
2. Chemical instability of DNA nitrogenous bases
Failure of DNA repair
Inherited mutations in genes affecting DNA repair, growth or apoptosis
Initiation
Mutations in the genome
Activation of growth-promoting oncogenes
Inactivation of tumour suppressor genes
Alterations in genes that regulate apoptosis
Unregulated cell proliferation
Decreased apoptosis
Flow chart depicting a simplified scheme of the molecular basis of cancer
Promotion
External stimuli
Clonal expansion (benign tumour)
Progression
Additional mutations
Tumour progression
Malignant neoplasm


Normal cells
1. Initiation
Initiated cells
2. Promotion
Benign tumour
3. progression
Malignant tumour

Genetic theory of malignant transformation

- Stimulation of a gene causing hyperactivity (by mutation in a gene causing over expression of a growth gene). The gene is called **oncogene.e.g C-Myc is linked with oral squamous cell carcinoma.**
- Inhibition of a gene that causes inactivity. This is by inactivation of the differentiation gene frees the cell of controlled growth. This gene is called **tumor-suppressor gene. e.g. retinoblastoma (RB) gene, which normally prevent cell division and P53 gene which initiate apoptosis when the cell DNA is damaged.**

Causes of gene mutation

The mutant gene may be

(1) Inherited (some), makes the subject more susceptible to cancer (predisposing gene) e.g. retinoblastoma, Wilms tumor (nephroblastoma), neurofibromatosis

(2) Due to exposure to chemical carcinogens (agents capable of causing cancer) such as organic solvent, toothpaste, silicon, asbestos, or due to exposure of physical factors: radiation (ionized and non ionized), X-rays, nuclear radiaton and ultraviolet radiation(skin cancer).

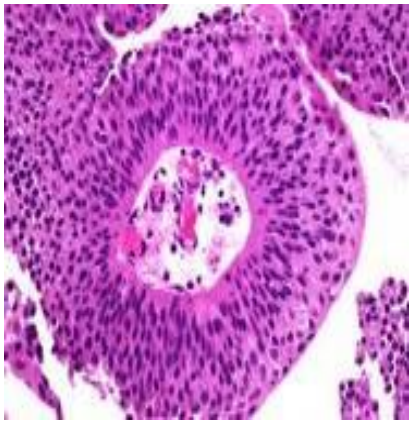
(3) Due to infection of the cell by viruses(some). DNA oncogenic viruses are papova viruses, adenoviruses and herpes viruses l; hepatitis B virus (hepatocellular cancer), Epstein-Barr virus (Burkitt lymphoma= is a cancer of the lymphatic system).

(4) RNA oncogenic viruses are retroviruses (reverse transcription) e.g. human T-cell leukemia-lymphoma virus.

❖HIV is not oncogenic virus but it leads to decrease the efficiency of the immune system. Decrease in immunity predispose more to cancer.

❖Some chemotherapeutic cytotoxic drugs are carcinogenic because it decreases the immunity and causes damage to DNA.

Pathohistological Characteristics of Tumors



1. Local increase in cell number .
2. Loss of normal arrangement of cells.
3. Variation of cell shape and size.
4. Increase in nuclear size and density of staining.
   Due to more DNA because more cells are in mitotic stage.
5. Increase of mitotic activity
6. Abnormal mitoses and chromosomes. aneuploidy

- Note !!!!! All of the above characteristics is more prominent in malignant than in benign tumor.

- The cytologic/histologic grading of tumors is based on the degree of differentiation and the number of proliferating cells. The closer the tumor cells resemble comparable normal tissue cells, both morphologically and functionally, the lower the grade. Accordingly, on a scale ranging from grades I to IV, grade I neoplasms are well differentiated and grade IV are poorly differentiated and display marked anaplasia

Characteristics of malignant tumors

- Invasion, infiltrating and destroying normal tissues surrounding them.
- Metastases. It is distant spread of the tumor

  (1)Spread into body cavities:(e.g. cancer in the stomach → peritoneal cavity, cancer in the lung → pleural cavity)

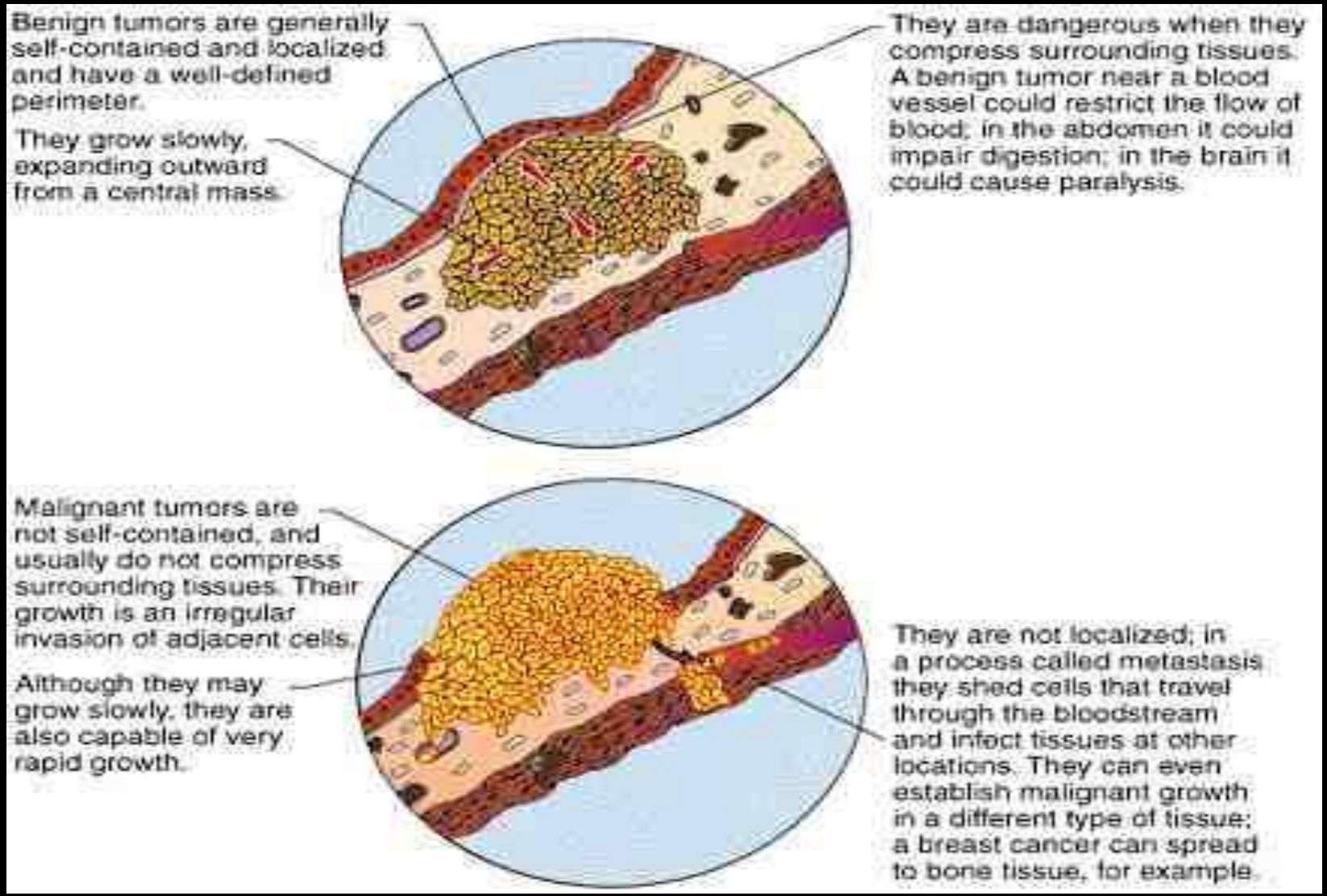
  (2)invasion of lymphatics: first to local lymph nodes then regional lymph nodes)(lymphadenopathy : enlarged hard lymph nodes)then(reticuloendothelial sytem:spleen, thymus, liver)

  (3)Hematogenous spread : into the blood stream,(depending in the direction of the blood flow and amount of blood) e.g colon cancer spread into liver. Lung,Brain, liver,-- has high blood supply so it is subjected more to metastasis.

❖Tumors may have Tumor cell Markers.(<u>are antigens expressed on the surface of tumor cells or substances released from normal cells in response to the presence of tumor.</u>)

These include

- Hormones e.g. ACTH (oat-cell carcinoma) **of** the lung : cancer cell of the lung produce hormones !!!! (so tumor cells may change their function).
- Alpha fetoprotein (AFP) tumor marker liver cancer
- Isoenzymes e.g. acid phosphatase (prostate carcinoma)
- Genes e.g. Philadelphia chromosome (chronic myelocytic leukemia (CML))
- Specific antigens or antibodies


Benign tumors are generally self-contained and localized and have a well-defined perimeter.
They grow slowly, expanding outward from a central mass.
They are dangerous when they compress surrounding tissues. A benign tumor near a blood vessel could restrict the flow of blood; in the abdomen it could impair digestion; in the brain it could cause paralysis.
Malignant tumors are not self-contained, and usually do not compress surrounding tissues. Their growth is an irregular invasion of adjacent cells.
Although they may grow slowly, they are also capable of very rapid growth.
They are not localized; in a process called metastasis they shed cells that travel through the bloodstream and infect tissues at other locations. They can even establish malignant growth in a different type of tissue; a breast cancer can spread to bone tissue, for example.