

NEOPLASIA

Neoplasia is the second leading cause of death after cardiovascular diseases .

Even more agonizing than the associated mortality is the emotional and physical suffering caused by neoplasms , the only hope for controlling cancer lies in learning more about its pathogenesis, and understanding the molecular basis of cancer .

Fundamental and shared characteristics of cancers:

- Cancer is a genetic disorder caused by DNA mutations . Most pathogenic mutations are either induced by exposure to **mutagens** or occur spontaneously as **part of aging** .
- Genetic alterations in cancer cells are heritable, being passed to daughter cells during cell division.
- Mutations and epigenetic alterations impart to cancer cells a set of properties that are referred to collectively as **cancer hallmarks** . These properties produce the cellular phenotypes that dictate the natural history of cancers as well as their response to various therapies .

Basic research has illustrated many of the cellular and molecular abnormalities that give rise to cancer and govern its malignant behavior . These in turn leading to diagnosis and treatment of cancer .

Neoplasia literally means " **Neo** -new **plasia** -growth or proliferation .

Neoplasm is defined as "an abnormal growth of tissue which exceeds and is uncoordinated with that of the adjacent normal tissues and persists in the same excessive manner even after removing of the causative agent ." this term is interchangeably with a **tumor** (swelling) because the most tumors present as mass .

Oncology (from oncos , "tumor," and logos, "study of") .

In oncology , **neoplasms** based on **clinical behavior** is divided in to **benign** and **malignant** tumors .

A tumor is said to be **benign** when its microscopic and gross characteristics are innocent , remain localized and cannot spread to other sites , and is amenable to surgical removal; the affected patient is survives . It should be noted, that benign tumors can produce more than localized lumps, and sometimes they produce morbidity or are even lethal .

Malignant tumors are also called **cancers** , derived from the Latin word for **crab**- that is similar to a crab's behavior, adhere to any part that they seize in an obstinate manner, its means the lesion can invade and destroy adjacent tissues and spread to distant sites (metastasize) to cause death .

Basic components of tumors

(1) **The parenchyma**, made up of **transformed or neoplastic cells** ,The parenchyma of the neoplasm largely determines its biologic behavior, and it is the component from which the tumor derives its name .

(2) **Stroma** (the supporting, host-derived , non-neoplastic) made up of **connective tissue, blood vessels and host-derived inflammatory cells** .

Stroma is crucial to the growth of the neoplasm , because it carries the blood supply and provides support for the growth of parenchymal cells .

Stromal cells and neoplastic cells influences the growth of the tumor by two ways :- **neoplastic cell** release substances that stimulate the endothelial cell to form a new blood vessels with in the tumor and **stromal cell** release growth factors that encourage tumor cell growth .

Nomenclature of neoplasm

A- Benign Tumors

In general, benign tumors are designated by attaching the suffix - **oma** to the cell type from which the tumor arises .

- **Benign mesenchymal tumors are named after their tissue of origin + “oma”**

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- A benign tumor arising in fibrous tissue is called **fibroma**

- A benign cartilaginous tumor is called **chondroma** .

- A benign tumor of fat tissue (lipocytes) called **Lipoma** .

- A benign tumor of smooth muscle is **leomyoma** .

- A benign tumor of schwann cells is **schwannoma** . etc

- **Benign epithelial tumors** is more complex and are named after their tissue of origin, sometimes combined with architecture + “oma”.

- **Adenoma** is benign epithelial neoplasms that produce glandlike structures or neoplasms derived from glands but lack a glandular growth pattern .

- **Papillomas** are benign epithelial neoplasms, growing on any surface, that produce microscopic or macroscopic finger-like fronds e.g papilloma in skin .

- **Polyp** is a mass that projects above a mucosal surface, as in the gut. Although this term is commonly used for benign tumors, some malignant tumors also may grow as polyps . Nasal polyps are **not neoplastic** but inflammatory in origin .

- **Cystadenomas** are hollow cystic masses ; typically they are seen in the ovary.

B- Malignant Tumors

The nomenclature of malignant tumors essentially follows that of benign tumors, with certain additions and exceptions .

- **Sarcomas** are malignant neoplasms arising from “solid” **mesenchymal tissue or its derivatives**.

leukemias or lymphomas are malignant neoplasms arising from the mesenchymal cells of the blood .

Sarcomas are designated by cell of origin + sarcoma .

Examples include :-

-**Fibrosarcoma** is a cancer of fibrous tissue origin .

-**Chondrosarcoma** is a malignant neoplasm of chondrocytes.

-**Liposarcoma** malignant tumor of lipocytes

-**Leiomyosarcoma** malignant tumor of smooth muscle cells .

-**Rhabdomyosarcoma** malignant tumor of striated muscle cells .

- **Carcinomas** are malignant neoplasms of epithelial cell . the epithelia of the body are derived from all three germ-cell layers. thus a malignant neoplasm arising in the renal tubular epithelium (**mesoderm**), in the skin (**ectoderm**) and lining epithelium of the gut and respiratory tract (**endoderm**) are all considered **carcinomas** .

Carcinomas are subdivided further.

Adenocarcinomas are Carcinomas that grow in a glandular pattern .

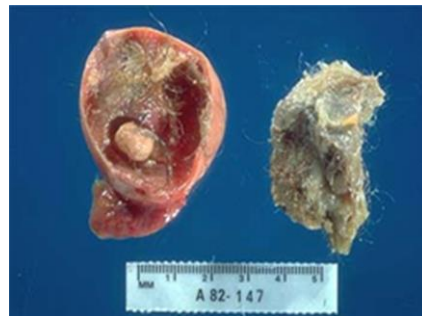
Squamous cell carcinomas are malignant neoplasms of squamous cell in any epithelium of the body (e.g. skin , esophagus ,and uterine cervix).

Some tumors have more than one parenchymal cell type , these include :-

1- Teratomas, which are tumors of germ cell origin , derived from more than one germ cell layer, and sometimes all three . (**Ectoderm**: like skin and hair follicles and sebaceous glands, **Endoderm**: like gut epithelia and **Mesoderm**: like bone, cartilage, muscle, etc), **thus a variety of parenchymal cell types may be seen in any one of these neoplasms .**

Examples include

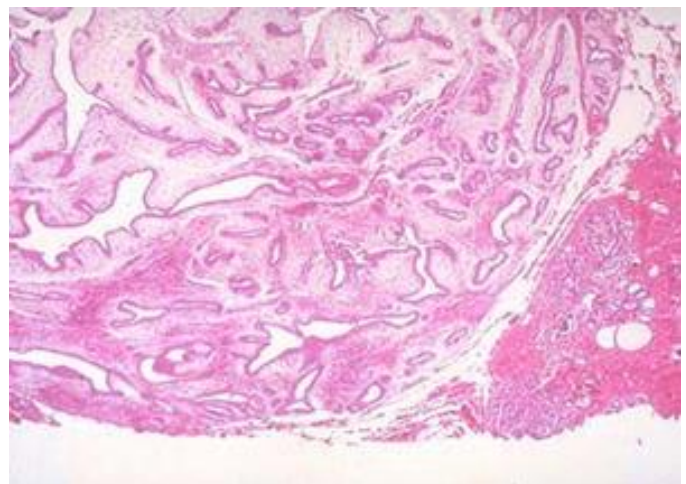
- Teratoma of the ovary
- Teratoma of the testis



2- Mixed tumors; these differ from teratomas in that they are derived from one germ cell layer , that differentiates into more than one parenchymal cell type .

Examples include

- Pleomorphic adenoma of salivary glands
- Fibroadenoma of breast



Some names that do not follow the principles of nomenclature that are always malignant :-

- **Melanoma** carcinoma of melanocytes.
- **lymphomas or leukemias** cancer arising from the mesenchymal cells of the blood .
- **Seminoma** is testicular germ cell carcinoma .
- **Hamartoma** is a malformation that presents as a mass of disorganized tissue indigenous to the particular site such as a mass of mature but disorganized hepatic cells, blood vessels, and possibly bile ducts within the liver, or nodule in the lung containing islands of cartilage, bronchi, and blood vessels .
- **Choristoma** is congenital anomaly consist of heterotopic nest of cells . For example, a small nodule of pancreatic tissue may be found in the submucosa of the stomach, or small intestine.

Characteristics of benign and malignant neoplasms

there are three fundamental features by which benign and malignant tumors can be distinguished.

A- Differentiation and Anaplasia

B- Local invasion

C- Metastasis

A- Differentiation and anaplasia

The differentiation means extent to which neoplastic cell resemble their normal parenchymal cells of origin morphologically and functionally.

Lack of differentiation called **anaplasia** .

Benign neoplasms are composed of well-differentiated cells that closely resemble their normal counterparts . Ex. A lipoma is made up of mature fat cells laden with cytoplasmic lipid vacuoles , and a chondroma is made up of mature cartilage cells that synthesize their usual cartilaginous tissue is evidence of morphologic and functional differentiation .

In well-differentiated benign tumors , mitoses are usually rare and are of normal configuration .

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

1-well differentiated neoplasms : - For example, well-differentiated adenocarcinomas of the thyroid may contain normal follicles difficult to distinguish from benign neoplasm .

2-moderately well differentiated neoplasm :- lies between well differentiated and undifferentiated neoplasms .

3- undifferentiated neoplasms:-are composed of undifferentiated cells are said to be anaplastic. a feature that is indicator of malignancy. The term **anaplasia** literally means “**backward formation**” Its dedifferentiation, or loss of the structural and functional differentiation of normal cells .

Morphologic feature of undifferentiated neoplastic cells (anaplastic cells) include :-

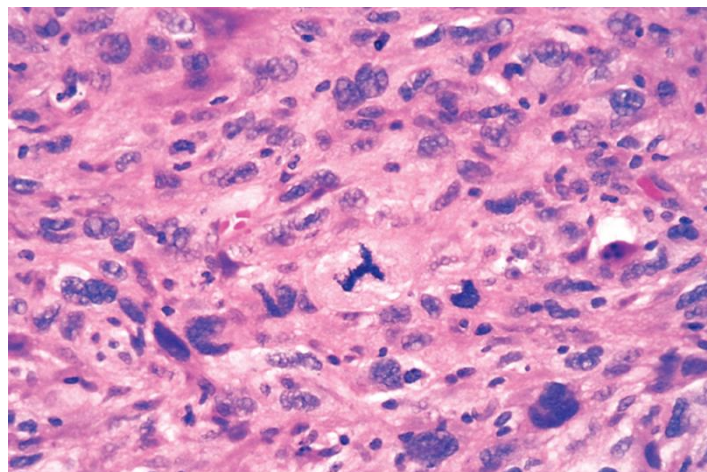
1-Pleomorphism i.e., variation in size and shape of neoplastic cells .

2- Abnormal nuclear morphology

- **hyperchromatism** :- the nuclei are extremely hyperchromatic (darkly stained) ,

- **variation in nuclear size and shape** .

- **Enlargement of nuclei** may result in increased nuclear-to-cytoplasmic ratio may approach 1 : 1 instead of the normal 1 : 4 or 1 : 6 .

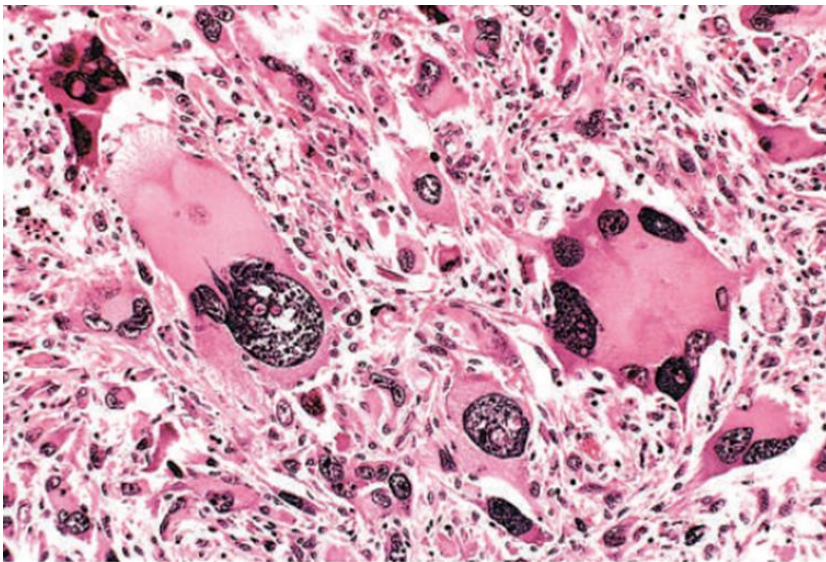


tumor cells shows cellular and nuclear variation in size and shape

3-Tumor giant cells may be formed. These are considerably larger than neighboring cells and may possess either one enormous nucleus or several nuclei.

4- Abnormal mitosis:- malignant cells possess large number of mitosis , reflecting to high proliferative activity . The more important morphologic feature of malignancy is the presence of mitotic figures which may be tripolar or quadripolar .

5- Loss of normal polarity :- means disturbed in arrangement of cells. In malignancy , the tumor cells grow in disorganized fashion . As in normal epidermis shows normally stratified cells , oriented from below to up, there are basal cells followed by spinous cells and then granular cells and finally upper layer of flattened , keratinized cells. While squamous cell carcinoma there is disorder of this arrangement and there is loss of stratification that seen in normal skin .



B-Local Invasion

benign tumors grow as cohesive expansile masses that remain localized to their sites of origin. Because benign tumors grow and expand slowly, they usually develop a rim of compressed fibrous tissue or “capsule” at the periphery . They don’t penetrate the capsule or the surrounding normal tissues. The line of cleavage between the capsule and the surrounding normal tissues facilitates surgical enucleation .

Not all benign neoplasms are encapsulated. For example, **the leiomyoma** of the uterus is demarcated from the surrounding smooth muscle by a zone of compressed and attenuated normal myometrium, but lacks a capsule .

Malignant tumors is accompanied by progressive infiltration, invasion, and destruction of surrounding tissues . They usually lack of capsule or line of cleavage, thus, their enucleation is impossible , and their surgical removal requires removal of a considerable margin of healthy tissues .

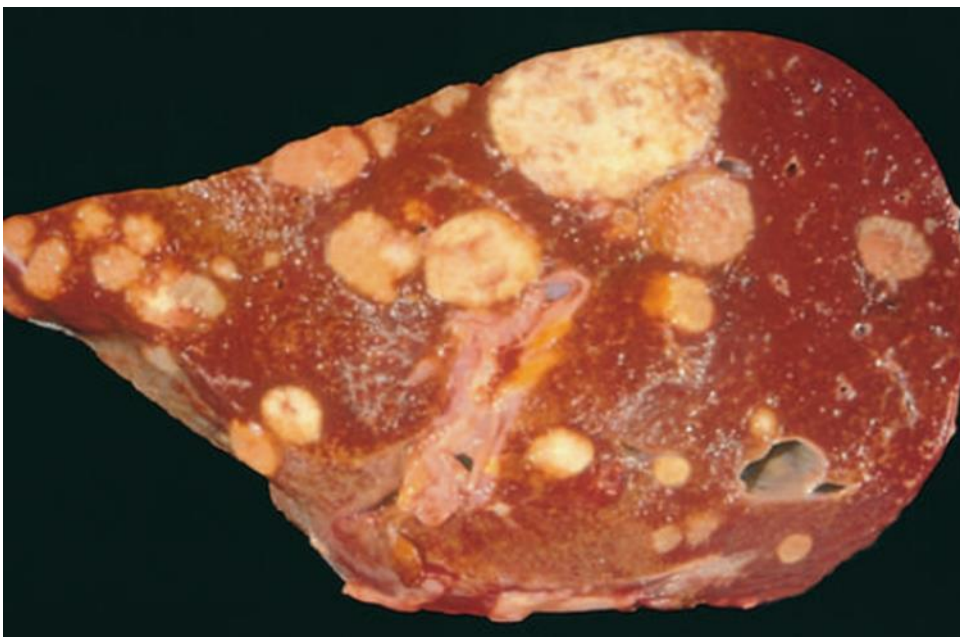
C- Metastasis

The term metastasis is defined by the spread of a tumor to sites that are discontinuous or distant with the primary tumor and it marks a tumor as malignant. Benign neoplasms do not metastasize.

Almost all cancer can metastasized except :-

1- Basal cell carcinomas of the skin .

2- Most tumors of the central nervous system that are highly invasive in their primary sites of origin but rarely metastasize.



Malignant neoplasms disseminate by one of three pathways:

(1) Seeding within body cavities, (2) Lymphatic spread, or (3) Hematogenous spread.

(1) Seeding within body cavities :- occurs when neoplasms invade a natural body cavity as peritoneal, pleural, pericardial and subarachnoid spaces. Cancer of ovary spreads transperitoneally to the liver or other abdominal viscera

(2) Lymphatic spread

Is the most common pathway for dissemination of carcinomas . This pattern depends on the site of the primary neoplasm and the natural pathways of lymphatic drainage . Lung carcinomas arising in the respiratory passages metastasize first to the regional bronchial lymph nodes, then to the tracheobronchial and hilar nodes. Carcinoma of the

breast usually arises in the upper outer quadrant and first spreads to the axillary nodes then drain to the nodes along the mammary artery.

Sentinel lymph node'' is the first regional lymph node that receives lymph flow from a primary tumor.

(3) hematogenous spread

It is the favored pathway for sarcomas, but carcinomas use it . Veins are more readily penetrated than arteries because of their thinner wall. With venous invasion, the blood-borne tumor cells follow the venous flow draining from the site of the neoplasm, the tumor cells stopping in the first capillary bed they encounter . the liver and lung are most frequently secondary sites of metastases because the portal drainage flows to the liver , and vena cava flows to the lung. Cancers arising near the vertebral column often embolize through the paravertebral plexus; this pathway involved in the vertebral metastases of carcinomas of the thyroid and prostate .

Differences between benign and malignant tumors

Feature	Benign tumor	Malignant tumor
Degree of differentiation	Well differentiated	Poorly or completely undifferentiated
Rate of growth	Slow in growing	Grow faster
Local invasion	Well circumscribed and have capsule	Poorly circumscribed and invade surrounding normal tissues
metastasis	Localized to the site of origin	Locally invasive and metastasize to distant site.