TUMOURS

3rd Stage of Vet. Medicine

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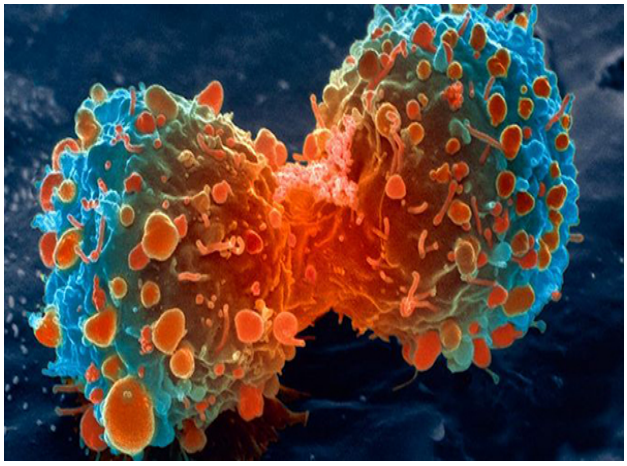
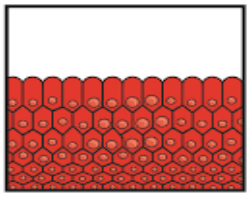
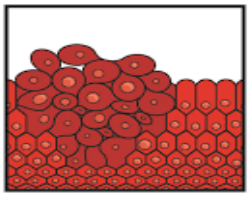


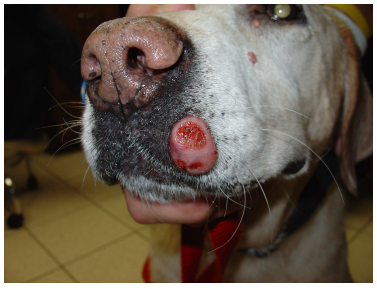
❑ General Definition of Tumours

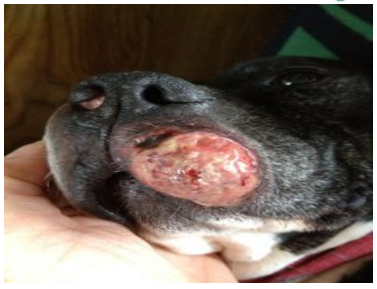
- Tumour is an abnormal mass of tissue resulting from abnormal growth of cells in the body, and the abnormal growth itself is called a neoplasm or tumour.

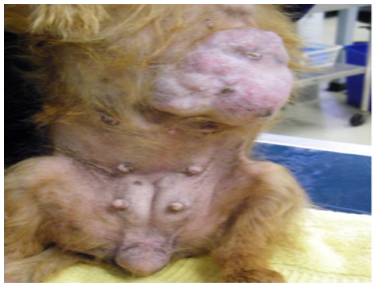




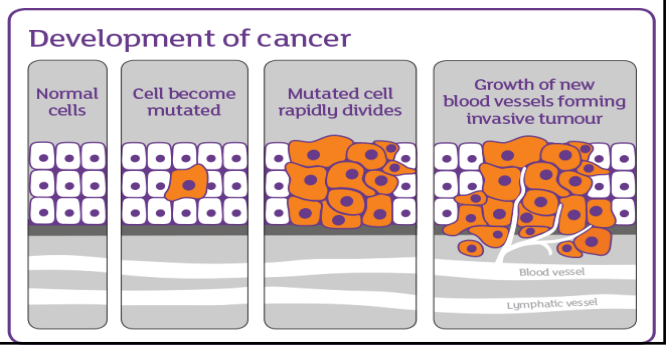
Normal cells Cells forming a tumour



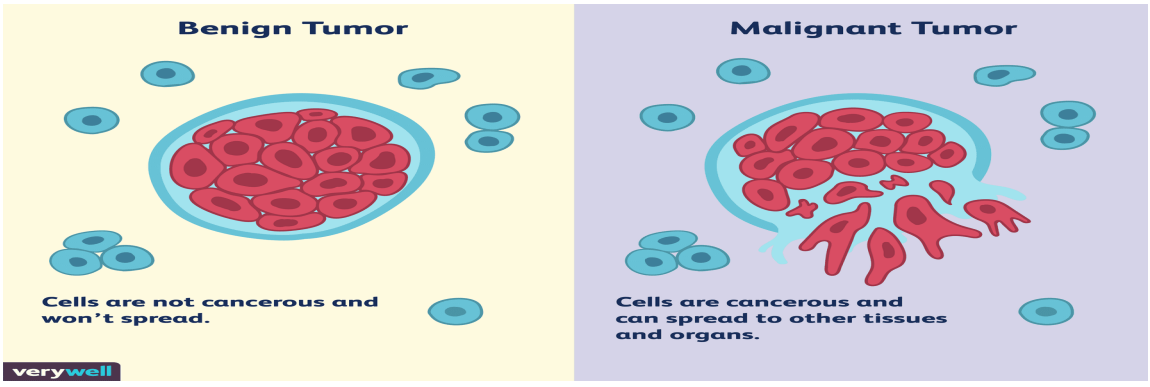




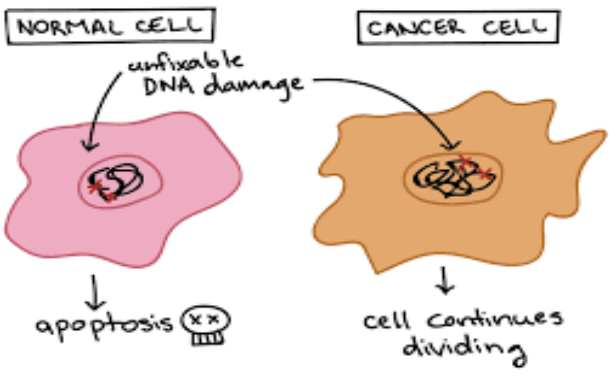
- It can be benign or malignant.
- The word tumour is often used to describe the actual swelling or other physical appearance of a neoplasm. The word cancer is often confused with neoplasia, but only malignant neoplasms are truly cancers.
- Tumours consist of cells are different from those of normal cells. Criteria for malignancy include increased cell proliferation, loss of differentiation, infiltrative growth and metastasis to other organs.

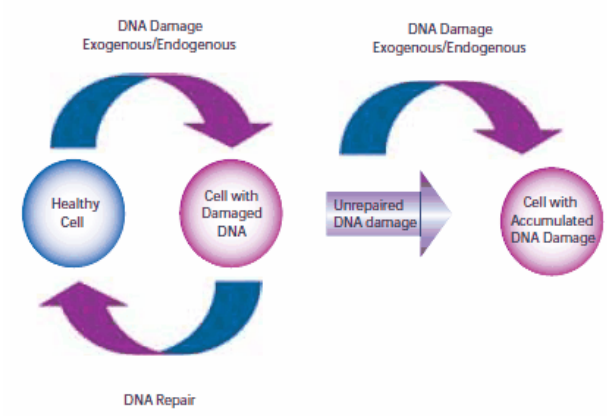


- Benign (harmless) tumours do not invade surrounding tissue or spread to new anatomic locations within the body; thus these tumours are rarely responsible for death of the animal.
- Malignant (harmful) tumours, if left untreated, invade locally, spread by metastasis (change of place), and ultimately kill the animal by interfering with critical body functions.



- The development of cancer may be initiated by environmental agents (chemical carcinogens, radiation, viruses) and inherited genetic factors (mutations).
- This evolution of malignant cells is caused by the sequential accumulation of alterations in genes responsible for the control of cellular proliferation, cell death and the maintenance of genetic integrity.



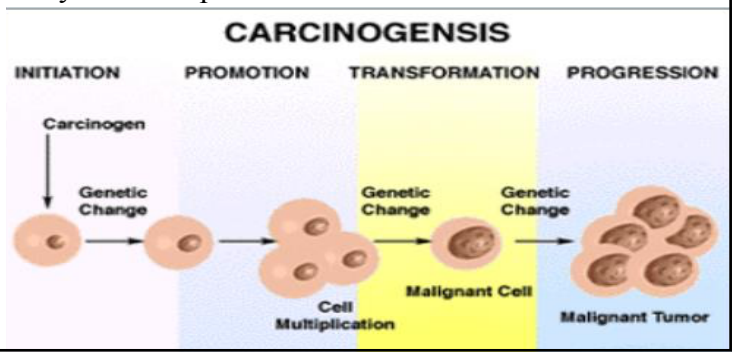


❑ Several terms are used in referring to malignant tumours:-

- ***Cancer*** is the common term for all malignant tumours.
- ***Carcinoma*** is the common term for malignant epithelial tumours.
- ***Sarcoma*** is the common term for malignant non-epithelial tumours.
- ***Solid tumours*** are circumscribed tumours such as carcinomas and sarcomas.
- ***Non-solid tumours*** are systemic autonomous proliferations of noncohesive individual cells, such as occur in leukemias.
- ***Neoplasm*** is a tumour that originates from a single cell and undergoes multiple duplications.
- ***Metastasis*** A metastasis occurs when a portion of a tumour which has left the original, or primary, tumour and traveled to another portion of the body.
- ***Primary tumour*** When metastasis has occurred, the term primary tumour is used to describe the original tumour which led to the metastasis.

❑ Carcinogenesis

- Carcinogenesis refers to the process by which a normal cell is transformed into a malignant cell and repeatedly divides to become a cancer.
- Carcinogenesis may take as long as 15-25 years in humans and in several animal models has been shown to involve two stages, initiation and promotion.
- Carcinogens are mutagens indicating that they have the potential to interact with DNA.



❑ Genetic mutations

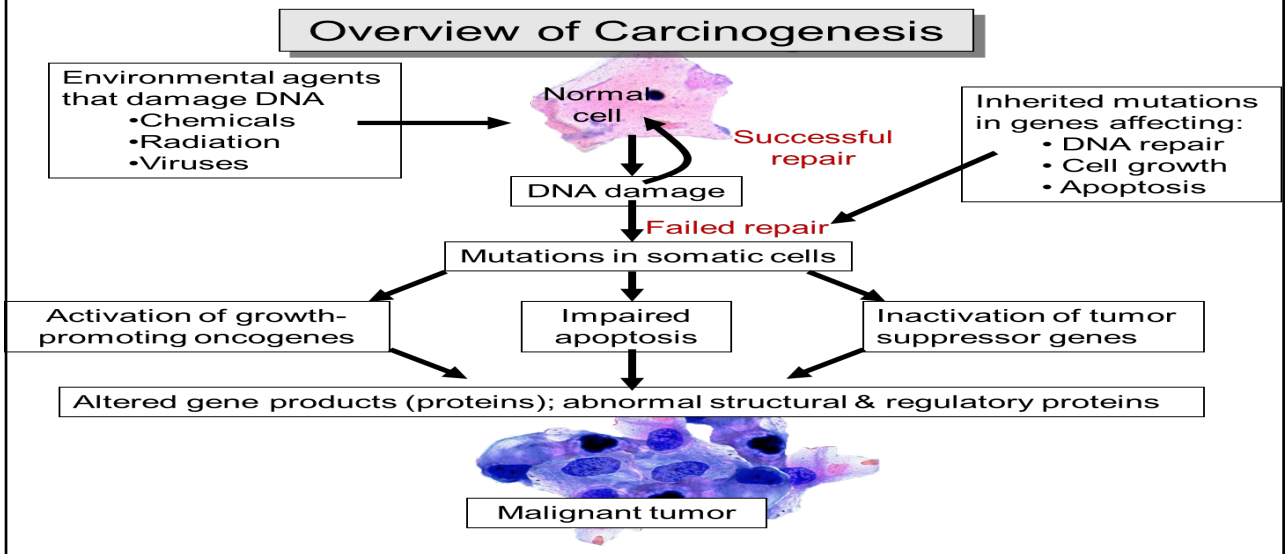
Genetic mutations are largely responsible for the generation of malignant cells.

Two major categories of mutated genes are:

- **Oncogenes** are abnormal forms of normal genes called proto-oncogenes that regulate cell growth. Mutation of these genes may result in direct and continuous stimulation of the molecular biologic pathways that control cellular growth and division.
- **Tumor suppressor genes, p53**, are inherent genes that play a role in cell division and DNA repair and are critical for detecting inappropriate growth signals in cells. If these genes, as a result of inherited or acquired mutations, become unable to function, genetic mutations in other genes can proceed unchecked, leading to neoplastic transformation.

❑ A General Theories of Carcinogenesis

The process by which normal, healthy cells transform into cancer cells is termed carcinogenesis.



❑ Classification of Cancers

The classification of cancers is based on: -

1- Classification by site of origin

By primary site of origin, cancers may be of specific types like lung cancer, prostate cancer, liver cancer and brain cancer etc.

2- Classification by tissue types

Based on tissue types cancers may be classified into six major categories:

1. Carcinoma

This type of cancer originates from the epithelial layer of cells that form the lining of external parts of the body or the internal linings of organs within the body. Carcinomas account for 80-90% of all cancer cases since epithelial tissues are most abundantly found in the body. Carcinomas usually affect organs or glands capable of secretion including lungs, bladder, colon and prostate.

Carcinomas are of two types – adenocarcinoma and squamous cell carcinoma. Adenocarcinoma develops in an organ or gland and squamous cell carcinoma originates in squamous epithelium.

Classification of Cancer by Histogenetic Site of Origin
Part 2: Epithelial Neoplasms

Tissue of Origin	Benign Neoplasm	Malignant Neoplasm
Epidermis	Epidermal papilloma	Epidermal carcinoma
Stomach	Gastric polyp	Gastric carcinoma
Adrenal cortex	Adrenocortical adenoma	Adrenocortical carcinoma
Surface Epithelium (Non-glandular)	Papilloma	Squamous carcinoma
Glandular Epithelium	Adenoma	Adenocarcinoma
Colon	Colon adenoma	Colon carcinoma
Breast	Mammary adenoma	Mammary carcinoma
Lung	Lung adenoma	Lung carcinoma

Carcinomas are malignant neoplasms of epithelial origin.

2. Sarcoma

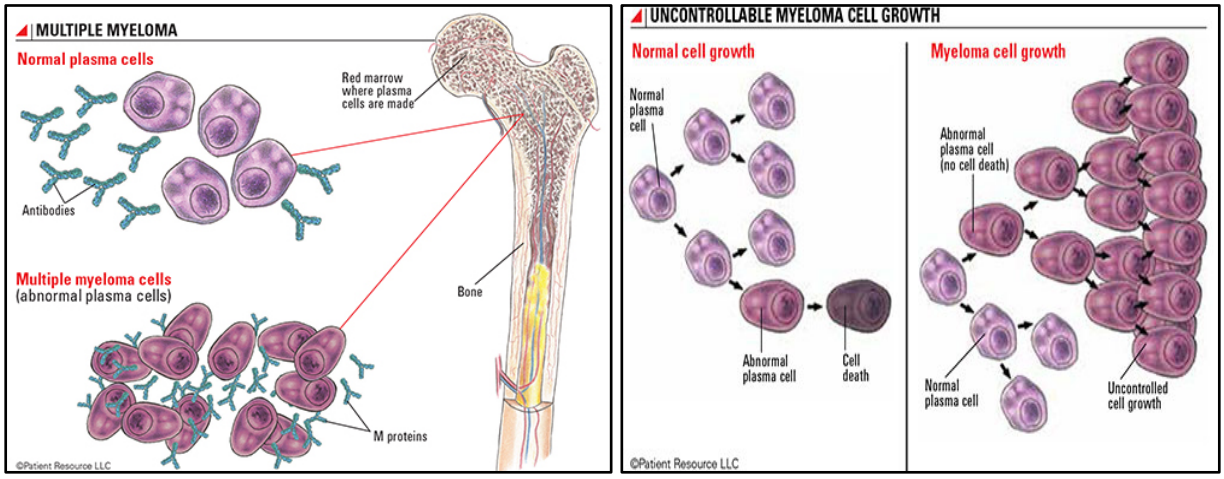
These cancers originate in connective and supportive tissues including muscles, bones, cartilage and fat. Bone cancer is one of the sarcomas termed osteosarcoma. Other examples include chondrosarcoma (of the cartilage), leiomyosarcoma (smooth muscles), rhabdomyosarcoma (skeletal muscles), Fibrosarcoma (fibrous tissue), Liposarcoma (adipose or fatty tissue), Glioma or astrocytoma (neurogenic connective tissue found in the brain).

- Sarcoma
  - Connective tissues (sarcoma)
    - Cartilage
    - Fat
    - Muscle
    - Bone

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

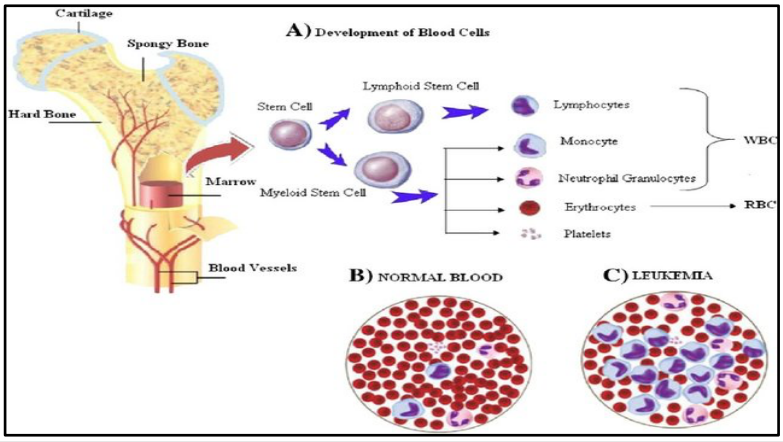
3. Myeloma

These originate in the plasma cells of bone marrow. Plasma cells are capable of producing various antibodies in response to infections. Myeloma is a type of blood cancer.



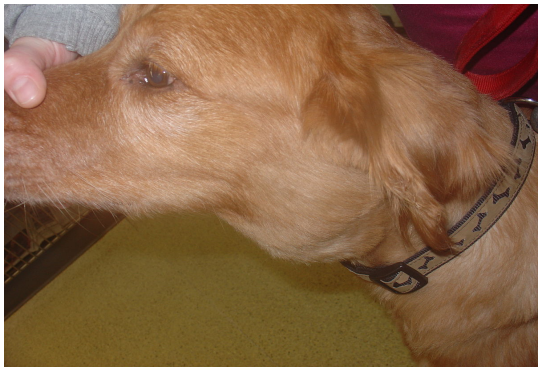
4. Leukemia

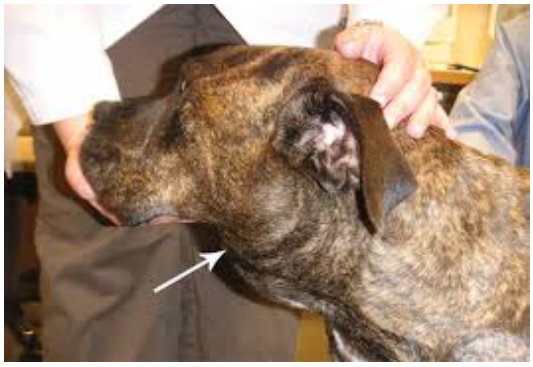
This a group of cancers that are grouped within blood cancers. These cancers affect the bone marrow which is the site for blood cell production. When cancerous, the bone marrow begins to produce excessive immature white blood cells that fail to perform their usual actions and the patient is often prone to infection.



5. Lymphoma

These are cancers of the lymphatic system. Unlike the leukemias, which affect the blood and are called "liquid cancers", lymphomas are "solid cancers". These may affect lymph nodes at specific sites like stomach, brain, intestines etc.





6. Mixed types

These have two or more components of the cancer. Some of the examples include mixed mesodermal tumour, carcinosarcoma, adenosquamous carcinoma.

3- Classification by stage

There are several types of staging methods. The most commonly used method uses classification in terms of tumour size (T), the degree of regional spread or node involvement (N), and distant metastasis (M). This is called the TNM staging.

For example, T0 signifies no evidence of tumour, T 1-4 signifies increasing tumour size and involvement. Similarly, N0 signifies no nodal involvement and N 1-4 signifies increasing degrees of lymph node involvement. Metastasis is further classified into two – M0 signifies no evidence of distant spread while M1 signifies evidence of distant spread.

Stages may be divided according to the TNM staging classification. Stage 0 indicates cancer being in situ or limited to surface cells while stage I indicates cancer being limited to the tissue of origin. Stage II indicates limited local spread, Stage III indicates extensive local and regional spread while stage IV is advanced cancer with distant spread and metastasis.

TNM classification (UICC)

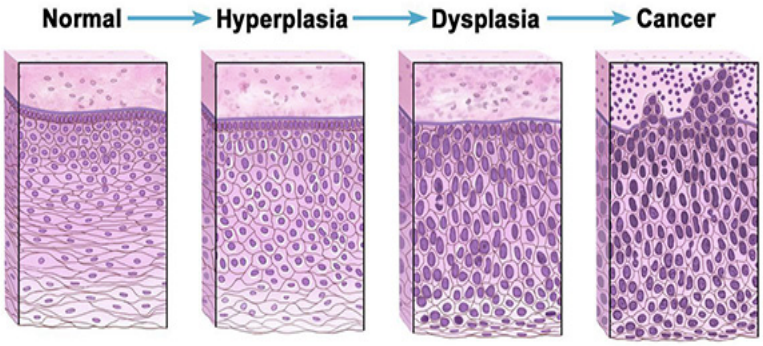
Stage	0	Tis	N0 M0
Stage	IA	T1	N0 M0
Stage	IB	T1	N1 M0
		T2	N0 M0
Stage	II	T1	N2 M0
		T2	N1 M0
		T3	N0 M0
Stage	IIIA	T2	N2 M0
		T3	N1 M0
		T4	N0 M0
Stage	IIIB	T3	N2 M0
Stage	IV	T4	N1-3 M0
		T1-3	N3 M0
		Any T	N M1

		M0			M1
	T \ N	N0	N1	N2	
M0	T1	Ia	Ib	II	
	T2	Ib	II	IIIa	
	T3	II	IIIa	IIIb	
	T4	IIIa	IIIb		IV
M1					

❑ Histological Characteristics of Cancer Cells

Cancer cells look different than normal cells and act differently because of their survival mechanisms.

Normal cells may become cancer cells. Before cancer cells form in tissues of the body, the cells go through abnormal changes called hyperplasia and dysplasia. In hyperplasia, there is an increase in the number of cells in an organ or tissue that appear normal under a microscope. In dysplasia, the cells look abnormal under a microscope but are not cancer. Hyperplasia and dysplasia may or may not become cancer.

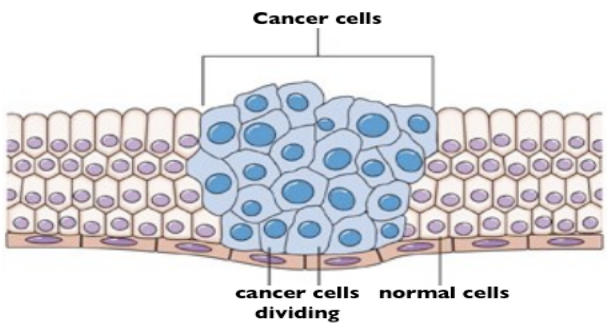


Cancer cells survival characters can generally be categorized by four unique features.

1. Cancer Cells Remain Undifferentiated (anaplasia).

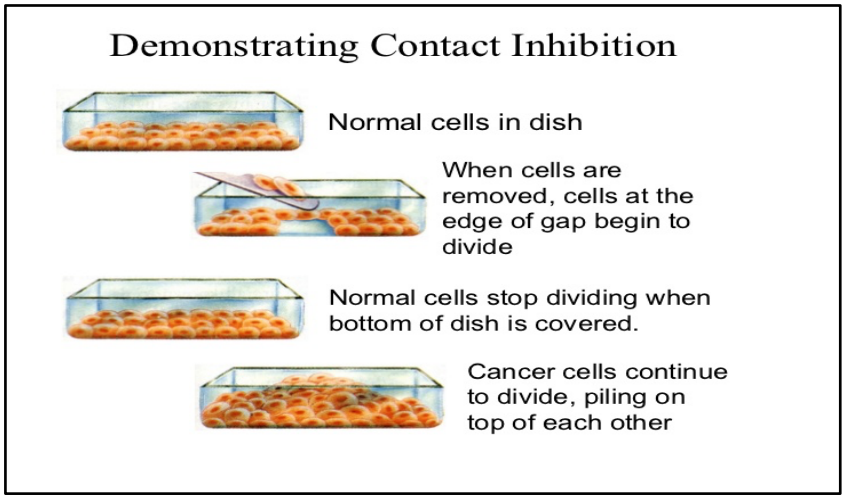
Normal cells are designed from their originating stem cell to fulfill a specific purpose in the human body. Although every cell has the same genetic code, cells with different purposes have different genes turned on so that they can perform a unique task in the body. Some cells may differentiate into cardiac muscle cells that make up heart tissue.

Cancer cells never differentiate. They continue to divide, cause more damage, and invade new tissue.



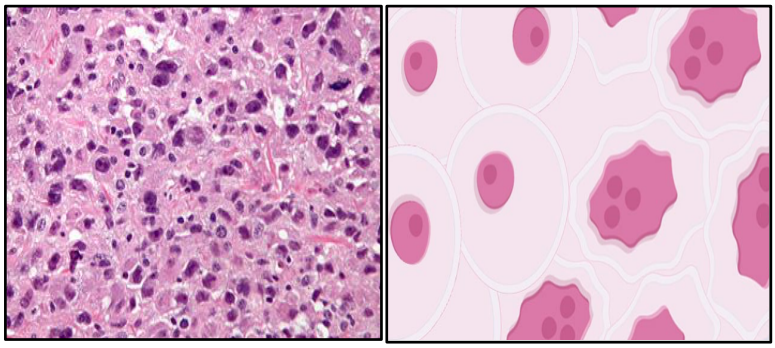
2. Cancer Cells Lack Normal Cell Signalling Responses

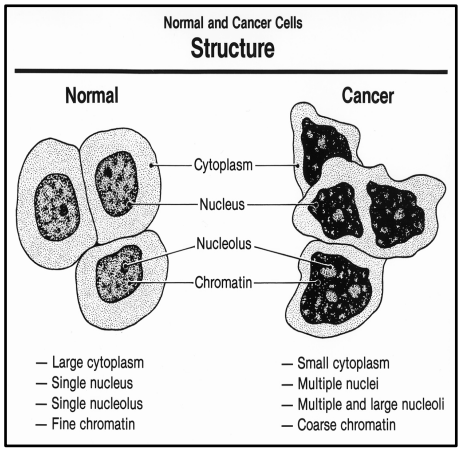
Cancer cells are able to proliferate, building layers on top of each other producing tumours. Healthy cells are programmed to stop proliferating upon reaching contact with a neighbouring cell. Key features of cancer cells and their inability to respond to internal and external communication signals include loss of contact inhibition and avoid apoptosis.



3. Cancer Cells Contain Abnormal Nuclei

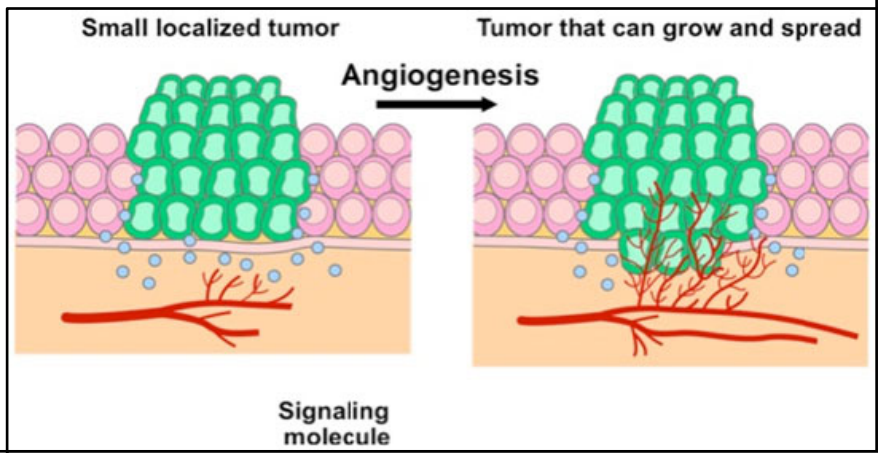
Under a microscope, Cancer cells have an asymmetrically-shaped nucleus that is larger than normal, resulting in the reduced presence of cytoplasm within the cell. Cancer cells nuclei have changes in chromatin and contain various genetic abnormalities such as mutations in gene sequencing (hyperchromatism).





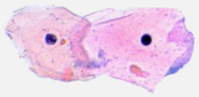
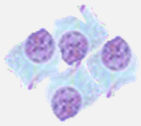
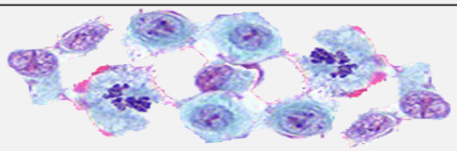
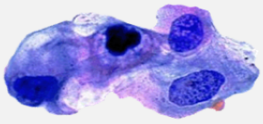
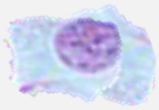
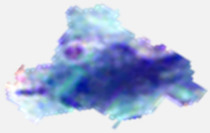
4. Cancer Cells Induce Vascularization

The four unique characteristic of cancer cells is their vascularizing properties, or ability to form new blood vessels. Specifically, cancer cells send out chemical signals that promote angiogenesis. New blood vessels provide the blood supply needed for growth by acting as a type of feeding tube for the delivery of oxygen and nutrients to the cancer cell. Angiogenesis is critical for allowing cancer cells to metastasize or invade neighboring tissue and distant regions of the body.



Thus, Cytological features of cancer cells include:

- Increased nuclear size (with increased nuclear/cytoplasmic ratio).
- Variation in nuclear or cell size (pleomorphism).
- Lack of differentiation (anaplasia).
- Increased nuclear DNA content with subsequent dark staining on H&E slides (hyperchromatism).
- Prominent nucleoli or irregular chromatin distribution within nuclei.

Normal	Cancer	
		Large, variably shaped nuclei
		Many dividing cells; Disorganized arrangement
		Variation in size and shape
		Loss of normal features

❑ Methods of Cancer Cells Transmission

The main reason cancer can be difficult to cure is that it can spread to a different part of the body from where it started. The cancer that grows where it first started in the body is called the primary cancer. The place a cancer spreads to and then starts growing is called the secondary cancer or metastasis.

In order cancer cells to spread:-

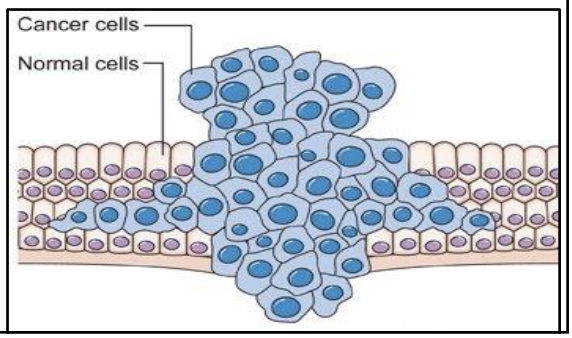
- Some cells from the primary cancer must break away, travel to another part of the body and start growing there.
- Cancer cells do not stick together as well as normal cells do.
- They also may produce substances that stimulate them to move.

There are four main ways a cancer cells spread:-

1- Local invasion

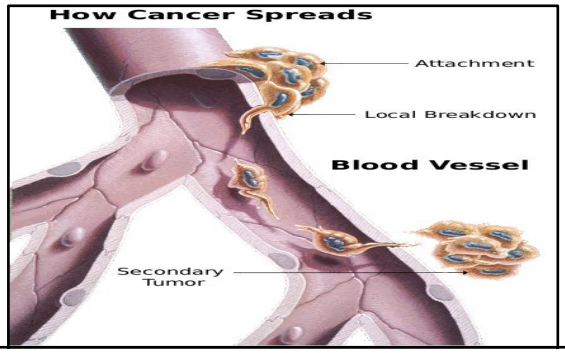
As a tumour gets bigger, it takes up more and more room in the body. Soon it begins to grow into the body structures nearby. This is called local invasion.

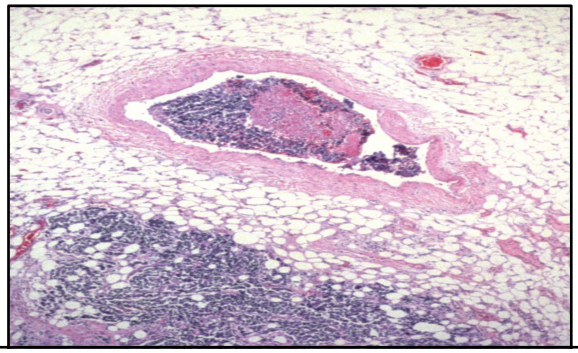
Research has pointed to 3 ways that the tumour is most likely to do this: pressure from the growing tumour, using enzymes and cancer cells moving through the tissue. A particular tumour will probably use all 3 of these ways of spreading.



2- Through the blood circulation (haematogenous spread)

In order to spread, the cancer cell must first become detached from the primary cancer. It must then move through the wall of a blood vessel to get into the blood stream. When it is in the bloodstream, it is swept along by the circulating blood until it gets stuck somewhere, usually in a very small blood vessel called a capillary. Then it must move back through the wall of the capillary and into the tissue of the organ close by. There it must start to multiply to grow a new tumour which is called secondary cancer or metastasis.





3- Lymphatic spread

The way a cancer spreads through the lymphatic system is very similar to the way it spreads through the bloodstream. The cancer cell must become detached from the primary tumour. Then it travels in the circulating lymph fluid until it gets stuck in the small channels inside a lymph node. There it begins to grow into a secondary cancer.

4- Transcoelomic spread

Transcoelomic (across the peritoneal cavity) metastasis refers to the dissemination of malignant tumours throughout the surfaces and organs of the abdominal and pelvic cavity covered by peritoneum. For example, ovarian tumours can spread transperitoneally to the surface of the liver. Mesothelioma and primary lung cancers can spread through the pleural cavity, often causing malignant pleural effusion.

❑ Benign and Malignant Tumours

The differentiation of a benign from a malignant tumour is very important so there are criteria by which benign and malignant tumours can be differentiated, and they behave accordingly. These differences can be discussed under the following headings:-

1. Differentiation

Tumours are often graded as to how closely they resemble the normal parent tissue that they are derived from, tumours can be

- Fully differentiated: exactly similar to normal-a feature of benign tumour.
- Well-differentiated" means the cells are very similar in appearance and architectural arrangement to normal tissue of that organ
- Poorly-differentiated" refers to tumours that show only minimal resemblance to the normal parent tissue they are derived from.
- Anaplastic" means the tumour shows no obvious similarity to it's parent tissue and almost always indicates malignancy.

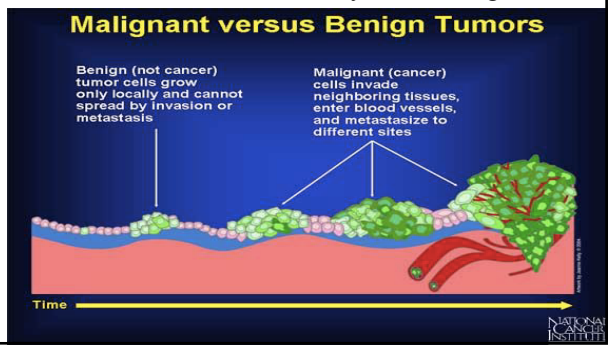
Benign tumours are always fully differentiated. Malignant tumours are well or moderately or poorly differentiated or undifferentiated (anaplastic).

2. Rate of growth

In general, the growth rate of tumours correlates with their level of differentiation, and thus most malignant tumours grow more rapidly than do benign lesions.

3. Local invasion and encapsulation

The local invasion is the most reliable feature that distinguishes malignant from benign tumours. Benign tumours are often encapsulated, and grow by expansion and they push other tissues away but they don't truly invade. Malignant tumours generally are not encapsulated. As they grow, they tend to infiltrate, invade, and destroy surrounding tissue.



4. Metastasis

Metastasis means that there is a secondary implant of a tumour in a distant tissue. Metastasis marks a tumour as malignant because benign neoplasms do not metastasize.

➢ **Comparisons between Benign and Malignant Tumours**

Characteristic	*Benign*	*Malignant*
Differentiation	• Fully-differentiated morphologic features and function. • Structure similar to tissue of origin. • Little or no anaplasia.	• Poorly differentiated morphologic features and function. • Tissue of origin sometimes unclear. • Variable degrees of anaplasia.
Growth rate	• Slow, progressive expansion. • Rare mitotic figures. • Normal mitotic figures. • Little necrosis.	• Rapid growth. • Frequent mitotic figures. • Abnormal mitotic figures. • Necrosis if poor blood supply.
Local invasion	• No invasion. • Capsule often present.	• Local invasion. • Capsule often absent or incomplete.
Metastasis	• No metastasis.	• Metastasis sometimes present