

## *Terms*

**Histotechnique**- The technique for processing the tissue ,whether biopsies ,large specimen removed at surgery or tissues autopsy to produce microscopic slides that are viewed under microscope by pathologist .

**Pathologist** :- are physicians who diagnose disease in living patients by examining biopsies. The vast majority of cancer diagnosis are made or confirmed by a pathologist. Pathologist may also conduct autopsies to investigate causes of death.

**Forensic pathology** -Is a branch of pathology concerning with determining the cause of death by examination of tissue .

**Lesion** - Macroscopic and Microscopic changes which occur on the tissues after injury .

**Disease** - Any anatomica or chemical or physiologica deviation from normal.

**Etiology** -Is the study of disease , and the etiological agents mean disease factors which can divided in to four groups,chemical,physica,biological and genetic.

**Clinical symptoms** – These are the symptoms that feel by patient and can not seen grossly.

**Clinical signs** – The signs which are seen by physician on the patient such as swelling ,congestion and fever.

**Prognosis** – The termination of the disease which is suspected by physician which end either with recovery or invalidism or death of patient.

**Termination of disease**- Is the result of disease which either recovery or invalidism or death.

## Inflammation

Inflammation is part of the body's immune response. Caused by:

- Microbial mediators: bacteria, virus, fungi, parasites etc...
- Physical mediators: Burns, stress, ionizing radiation etc...
- Chemical mediators: Alcohol, toxins etc...
- Mechanical mediators: Trauma, injuries etc...

Cardinal signs of inflammation:

- Pain:
- Redness:
- Immobility:
- Swelling:
- Heat:

Types of inflammation:

- 1- Normal (Tears, sneezing, vomiting, ear wax etc...)
- 2- Acute inflammation.
- 3- Chronic inflammation.

The following table shows the key differences between acute and chronic inflammation:

	<b>Acute</b>	<b>Chronic</b>
<b>Caused by</b>	Harmful bacteria or tissue injury	Pathogens that the body cannot break down, including some types of virus, foreign bodies that remain in the system, or overactive immune responses
<b>Onset</b>	Rapid	Slow
<b>Duration</b>	A few days	From months to years
<b>Outcomes</b>	Inflammation improves, turns into an abscess, or becomes chronic	Tissue death and the thickening and scarring of connective tissue

## **Tissue changes post infection**

Vascular changes  $\implies$  Vasodilation  $\implies$  permeability increase

Cellular events  $\implies$  recognition  $\implies$  removal

Mediators  $\implies$  Cell derived  $\implies$  plasma-derived

## **Cells involved:**

**Neutrophil granulocyte:** major cell of acute inflammation phagocytes, produce cytokines, antimicrobial agents.

**Eosinophil granulocyte:** IgE-mediated reaction - allergic reaction, parasite antimicrobial agents has a part in chronic inflammation as well.

**Basophil granulocyte:** IgE-mediated reaction antimicrobial agents has a part in chronic inflammation as well IgE receptors produce histamine, chemotactic factors, leukotriene relatives of mast cells.

**Monocyte/macrophage:** Kupfer-cell, microglia, alveolar macrophage phagocytes, produce cytokines major cells of reparation/chronic inflammation.

**Lymphocyte:** major cell of adaptive immunity chronic inflammation.

Other important cells:

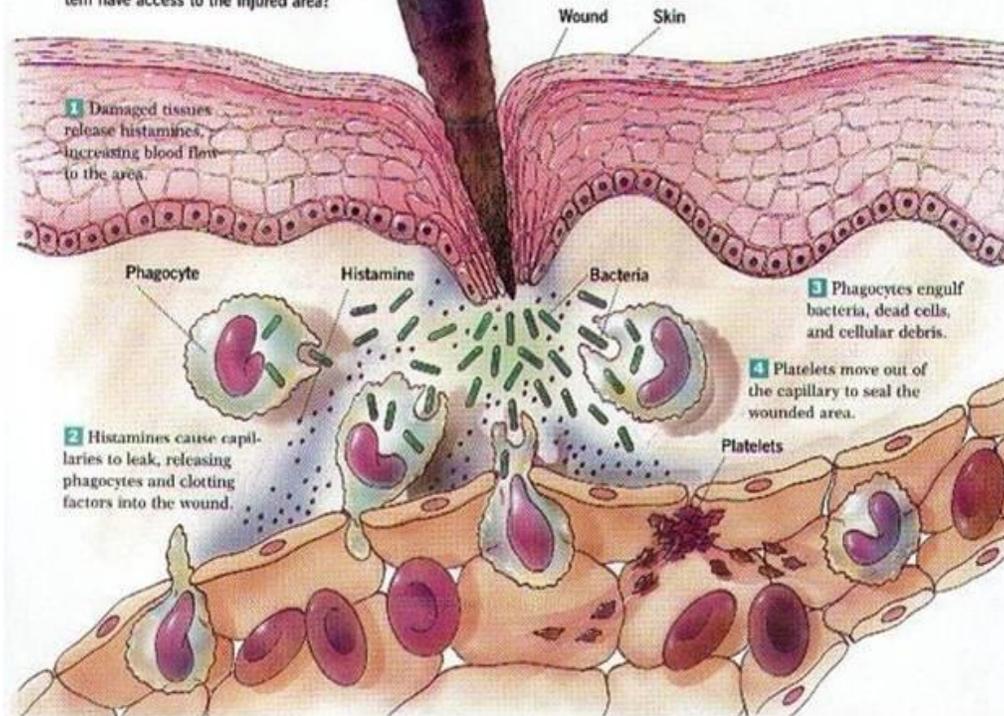
- Platelet

-Endothelial cell

-Fibroblast

### Steps of the Inflammatory Response

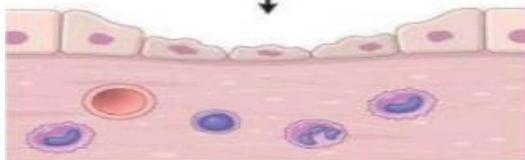
The inflammatory response is a body's second line of defense against invasion by pathogens. Why is it important that clotting factors from the circulatory system have access to the injured area?



### NORMAL



### Mild, superficial injury



### REGENERATION



### Severe injury



### SCAR FORMATION



# Gangrene

**Gangrene:** is a condition that occurs when body tissue dies. It is caused by a loss of blood supply due to an underlying illness, injury, and/or infection. Fingers, toes, and limbs are most often affected, but gangrene can also occur inside the body, damaging organs and muscles. There are different types of gangrene and all require immediate medical attention.

## Gangrene Causes

- Diabetes
- Atherosclerosis
- Peripheral arterial disease
- Smoking
- Trauma or serious injury
- Obesity
- Weakened immune system

## Gangrene Symptoms

You may notice the following symptoms at the site of the dry gangrene:

- Dry skin that changes color from blue to black and eventually sloughs off
- Cold and numb skin
- Pain may or may not be present

Symptoms of wet gangrene may include:

- Swelling and pain at the site of infection
- Change in skin color from red to brown to black
- Blisters or sores that produce a bad-smelling discharge (pus)
- Fever and feeling unwell
- A crackling noise that comes from the affected area.

## **Gangrene Types**

There are two main types of gangrene:

**Dry gangrene:** More common in people with blood vessel disease, diabetes, and autoimmune diseases, dry gangrene usually affects the hands and feet. It develops when blood flow to the affected area is impaired, usually as a result of poor circulation. In this type, the tissue dries up and may be brown to purplish-blue to black in color and often falls off. Unlike other types of gangrene, infection is typically not present in dry gangrene. However, dry gangrene can lead to wet gangrene if it becomes infected.

**Wet gangrene:** Injury from burns or trauma where a body part is crushed or squeezed can rapidly cut off blood supply to the affected area, causing tissue death and increased risk of infection. The tissue swells and blisters and is called "wet" because of pus.

**Types of wet gangrene include:**

**Internal gangrene:** If gangrene occurs inside the body due to blocked blood flow to an internal organ, then it is referred to as internal gangrene. This is usually related to an infected organ such as colon.

**Gas gangrene:** Gas gangrene is rare but dangerous. It occurs when infection develops deep inside the body, such as inside muscles or organs, usually as a result of trauma. The bacteria that causes gas gangrene, called *clostridia*, release dangerous toxins or poisons that wreak havoc throughout the body, along with gas which can be trapped within body tissue. As the condition progresses, the skin may become pale and gray, and make a crackling sound when pressed, due to the gas within the tissue.

**Fournier's gangrene:** Also a rare condition, Fournier's gangrene is caused by an infection in the genital area. Men are affected more often than women.

## **Gangrene Treatments:**

**1-Surgery.**

**2-Maggot therapy.**

**3-Antibiotics.**

**4-Oxygen therapy.**



**Wet  
gangrene**

**Intestine**

## **Cell damage**

variety or changes of stress that a cell suffers due to external as well internal environmental changes. Among other causes, this can be due to physical, chemical, infectious, biological, nutritional or immunological factors. Cell damage can be reversible or irreversible.

### **Causes**

Physical agents such as heat or radiation can damage a cell by literally cooking or coagulating their contents.

Impaired nutrient supply, such as lack of oxygen or glucose, or impaired production of adenosine triphosphate (ATP) may deprive the cell of essential materials needed to survive.

### **Targets**

The most notable components of the cell that are targets of cell damage are the DNA and the cell membrane.

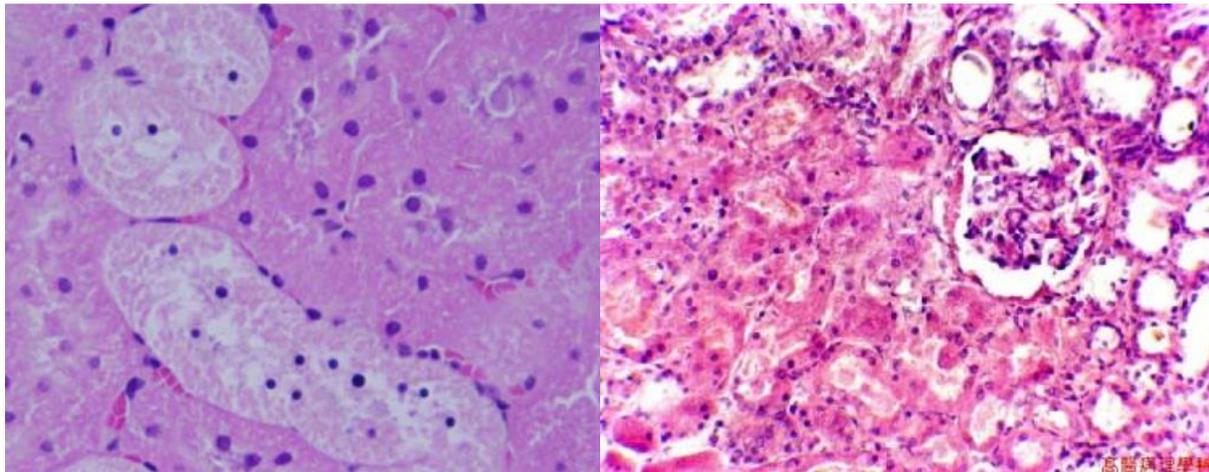
### **Types of damage**

#### **Sub-lethal (reversible)**

##### **Cellular swelling**

Cellular swelling (or cloudy swelling) may occur due to cellular hypoxia, which damages the sodium-potassium membrane pump; it is reversible when the cause is eliminated. On microscopic examination, small clear vacuoles may be seen

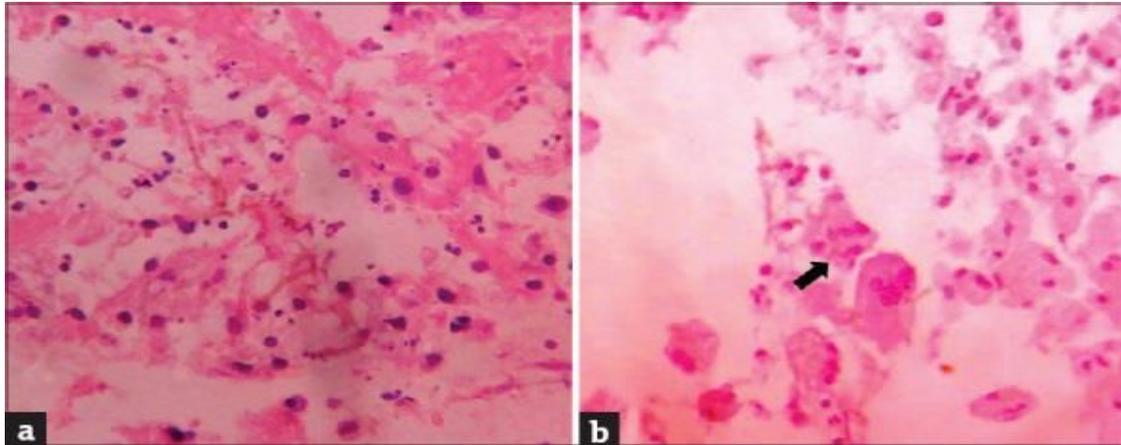
within the cytoplasm; these represent distended and pinched-off segments of the endoplasmic reticulum. This pattern of non-lethal injury is sometimes called Hydropic change or vacuolar degeneration. Hydropic degeneration is a severe form of cloudy swelling. It occurs with hypokalemia due to vomiting or diarrhea.



## **Lethal**

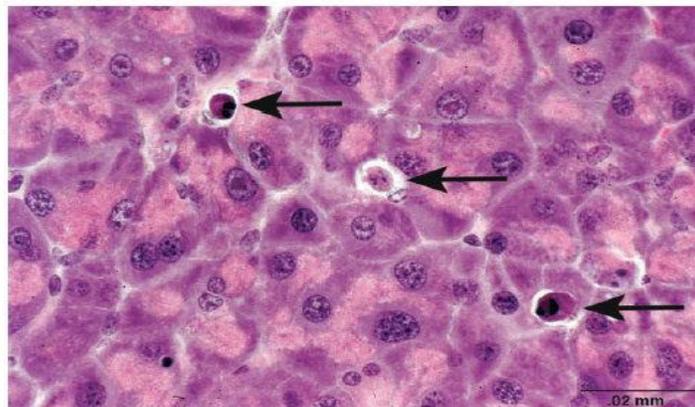
### **Necrosis:**

Necrosis is characterized by cytoplasmic swelling, irreversible damage to the plasma membrane, and organelle breakdown leading to cell death. The stages of cellular necrosis include psychosis; clumping of chromosomes and shrinking of the nucleus of the cell, karyorrhexis; fragmentation of the nucleus and breakup of the chromatin into unstructured granules, and karyolytic; dissolution of the cell nucleus.



## Apoptosis:

Apoptosis is the programmed cell death of potentially harmful cells in the body. It is an energy dependent process mediated by proteolytic enzymes called caspases, which trigger cell death through the cleaving of specific proteins in the cytoplasm and nucleus. The dying cells shrink and condense into apoptotic bodies. The cell surface is altered so as to display properties which lead to rapid phagocytosis by macrophages or neighboring cells.



**Figure 2.** Apoptosis of exocrine pancreatic cells with cytoplasmic and nuclear condensation and nuclear fragmentation (arrows). Image courtesy of National Toxicology Program (NTP) archives.

# Tumors

Is an abnormal mass of tissue that may be solid or fluid-filled.

## Tumor types:

- **Benign:** These are not cancerous and cannot spread. A benign tumor will remain in its current form. They do not generally return after being removed.
- **Premalignant:** A premalignant tumor is not yet cancerous but appears to be developing the properties of cancer.
- **Malignant:** Malignant tumors are cancerous. They can grow, spread, and get worse.

## BENIGN

A tumor is an abnormal growth of cells that serves no purpose. A benign tumor is not a malignant tumor, which is cancer.

## Causes of Benign Tumors

Often the cause is unknown. But the growth of a benign tumor might be linked to:

- Environmental toxins, such as exposure to radiation
- Genetics
- Diet
- Stress
- Local trauma or injury
- Inflammation or infection.

## **Examples of benign tumors include:**

### **Adenomas**

Adenomas are tumors that arise from glandular epithelial tissue, the thin membrane that covers glands, organs, and other structures in the body.



### **Hemangiomas**

Hemangiomas are benign tumors that consist of excessive blood cells.

They can sometimes be seen on the surface of the skin and are known as strawberry marks. The majority of Hemangiomas appears at birth and gradually goes away after some months or years.

Hemangiomas do not usually require any treatment. If they affect the ability of an individual to eat, hear, or see, the doctor may recommend treatment with corticosteroids.

If the patient is over 10 years of age, they are more commonly removed using laser surgery.



## Lipoma

Lipoma is the most common form of soft-tissue tumor. They consist of fat cells. Most of them are very small, painless, soft to the touch, and generally movable. They are more common among people aged over 40 years. Experts disagree on whether Lipoma can change and become cancerous.



## MALIGNANT TUMORS

A term for diseases in which abnormal cells divide without control and can invade nearby tissues. Malignant cells can also spread to other parts of the body through the blood and lymph systems. There are several main types of malignancy. **Carcinoma** is a malignancy that begins in the skin or in tissues that line or cover internal organs. **Sarcoma** is a malignancy that begins in bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue. **Leukemia** is a malignancy that starts in blood-forming tissue, such as the bone marrow, and causes large numbers of abnormal blood cells to be produced and enter the blood. **Lymphoma** and multiple myeloma are malignancies that begin in the cells of the immune system. **Central nervous system cancers** are malignancies that begin in the tissues of the brain and spinal cord. Also called cancer

Cancer, also called malignancy, is an abnormal growth of cells. There are more than 100 types of cancer, including breast cancer, skin cancer, lung cancer, colon cancer, prostate cancer, and lymphoma. Symptoms vary depending on the type. Cancer treatment may include chemotherapy, radiation, and/or surgery.

### **Cancer epidemiology:**

- Over years the incidence of cancers increased in males more than in females (the screening techniques of breast and cervix play a role).
- In males the most common cancer is of the lung, in females the breast cancer.
- Most cancers occur in older age group (> 55 yrs.) While those < 15 yrs. More susceptible for blood tumors leukemia, neuroblastoma, wilms tumor etc....

- Geographic factors: there are differences in incidence rates of cancers are seen worldwide. Stomach carcinoma common in Japan, lung cancer in USA, skin cancer in Newzeland.
- Environmental factors: occupational like asbestos that related to mesothelioma, benzene to leukemia.

## **Clinical features of tumors**

(effects of tumor on the host), can occur in both benign and malignant tumors:

- Pressure on adjacent tissue.
- Functional activities (hormones).
- Bleeding and secondary infection when ulcerate through adjacent natural surface.
- Acute symptoms like infarction rupture.
- Cancer cachexia (progressive loss of body fat and mass).
- Para neoplastic syndromes: complex of symptoms that cannot be explained, by local or distant spread of the tumor.

## **Tumor diagnosis:**

- History and clinical examination.
- Imaging – X-ray, US, CT, MRI
- Tumor markers.
- Biopsy – histopathology.
- Molecular techniques- gene detection.
- Flow cytometry.

## **Histologic and cytological methods:**

- Excisional or incisional biopsy.
- Cytological smears:
  - . Fine needle aspiration (guided or without)

- . Pap smear (cervical smear)
- . Fluid cytology (exfoliative)

## **Treatment**

### **1-Surgery**

In many cases, surgery offers the best chance of getting rid of the disease, especially if it hasn't spread to other parts of the body.

Along with a traditional operation, doctors can also fight some types of cancer with:

- Laser surgery (beams of light)
- Electro surgery (electric currents)
- Cryosurgery (very cold temperatures to freeze cancer cells)

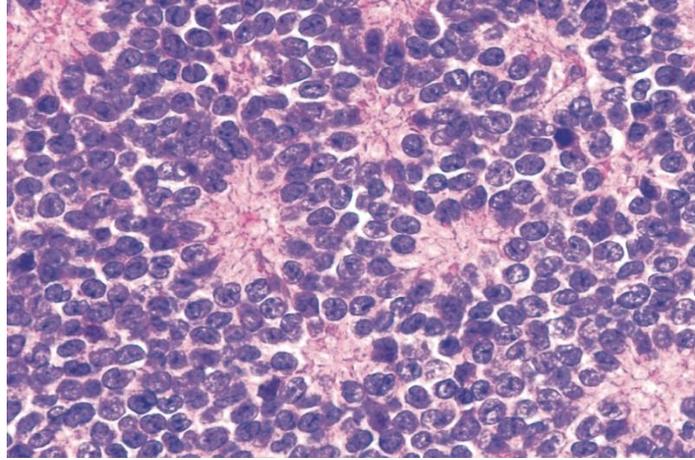
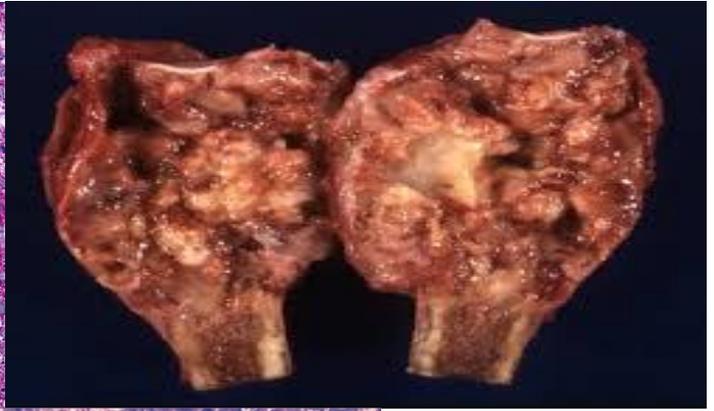
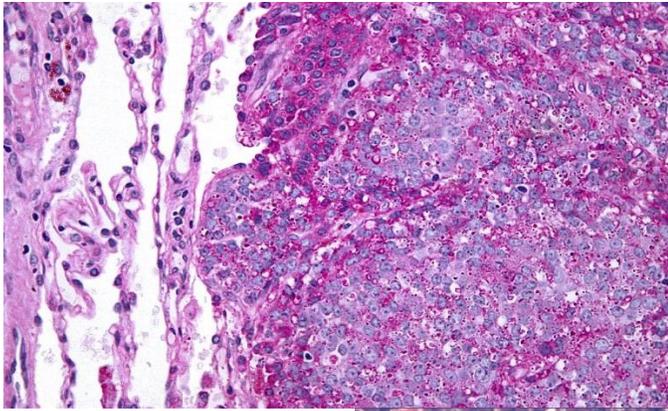
### **2-Chemotherapy**

Chemotherapy uses drugs to kill cancer cells. There are two ways to get it:

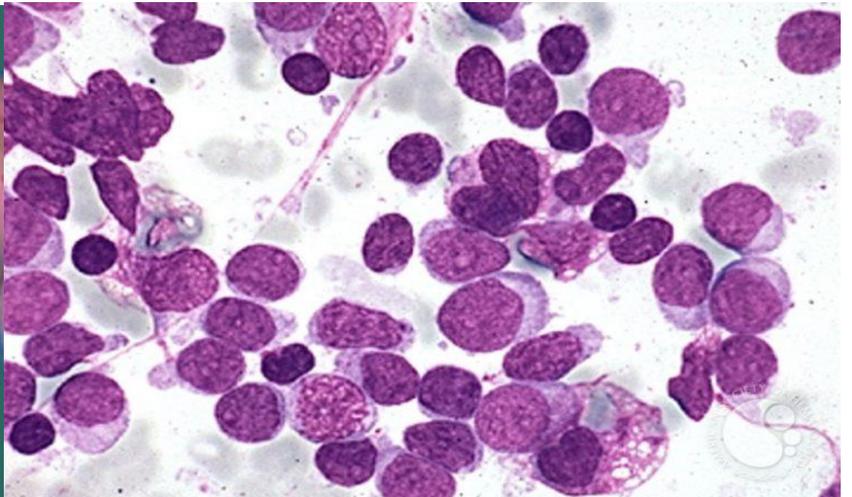
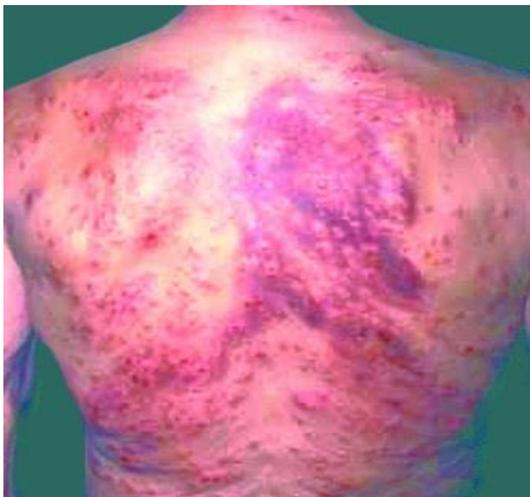
- Traditional Chemotherapy
- Oral Chemotherapy
- Radiation

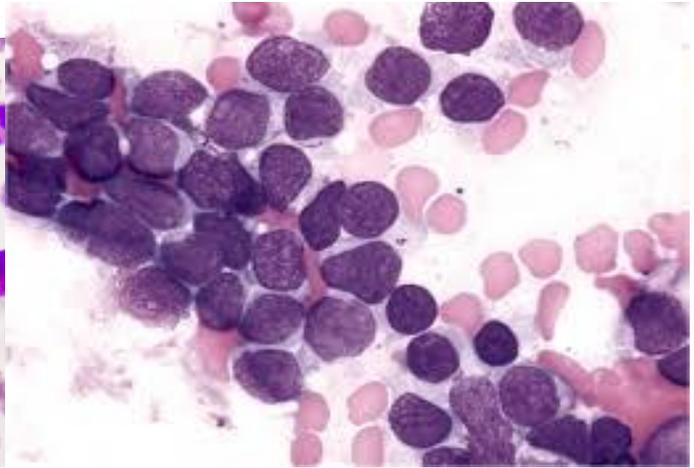
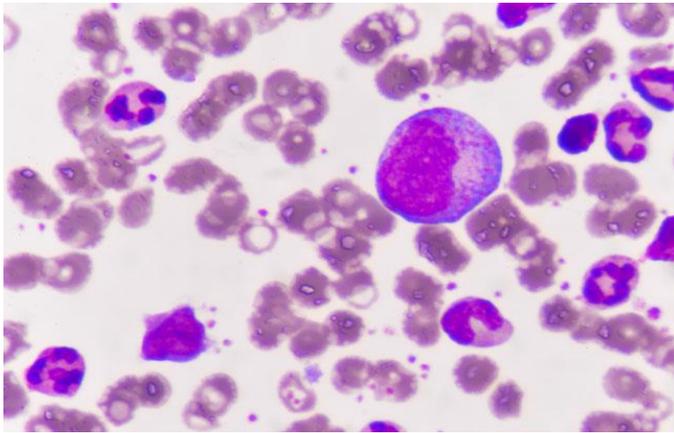


**Carcinoma (skin cancer)**

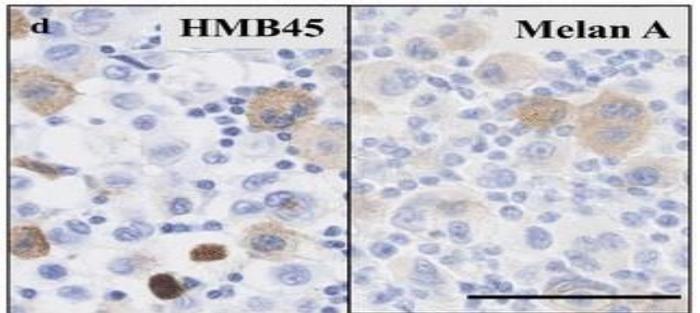
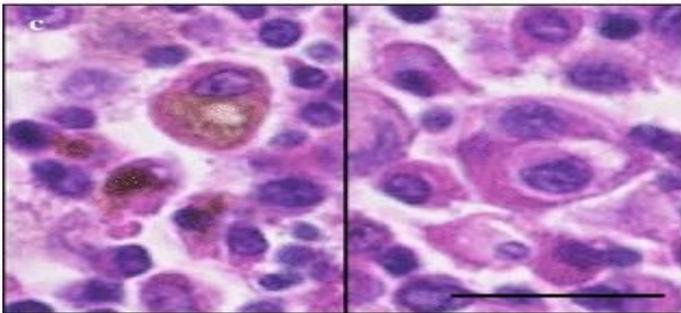
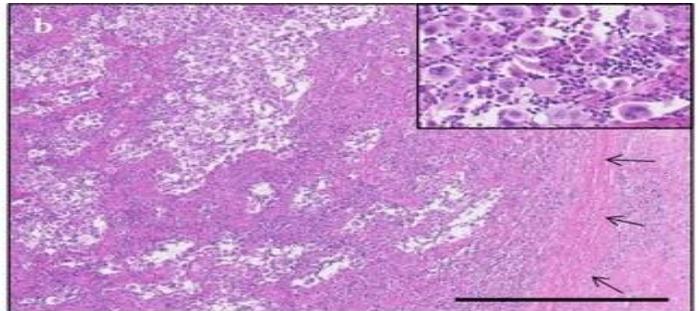


**Sarcoma (bone cancer)**

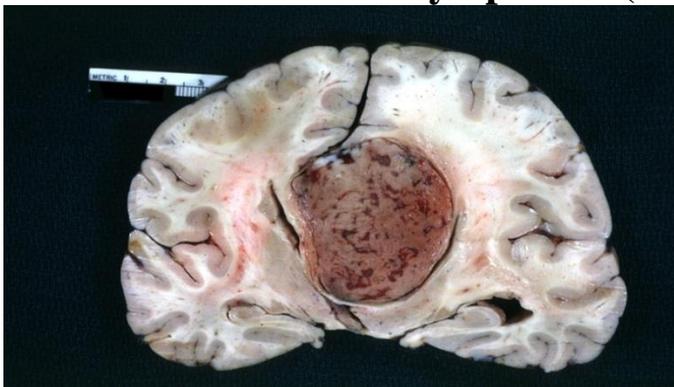




**Leukemia**



**Lymphoma (colon tonsils cancer)**



**Brain cancer**