

NEOPLASIA



Dr. Ola Abu Al Karsaneh

Clinical Aspects of Neoplasia

The importance of neoplasms ultimately lies in their effects on patients.

- 1. Effects of Tumor on Host**
- 2. Grading and Staging of Cancer**
- 3. Cancer diagnosis**

1. Effects of tumor on the host

Both malignant and benign tumors may cause problems:

(1) Location and impingement on adjacent structures:

- A 1 cm pituitary adenoma can destroy the surrounding normal gland & give rise to hypopituitarism.
- A 0.5 cm tumor within the: ureter, common bile duct, may induce unilateral hydronephrosis or fatal biliary tract obstruction, respectively.

(2) Functional activity such as hormone synthesis or the development of paraneoplastic syndromes.

(3) Bleeding and infections when the tumor ulcerates through adjacent surfaces

(4) Symptoms from rupture or infarction

(5) Cachexia or wasting

Cancer Cachexia:

-Wasting syndrome characterized by progressive loss of body fat, weight & lean body mass, with MUSCLE LOSS marked by weakness, anorexia, anemia & fever.

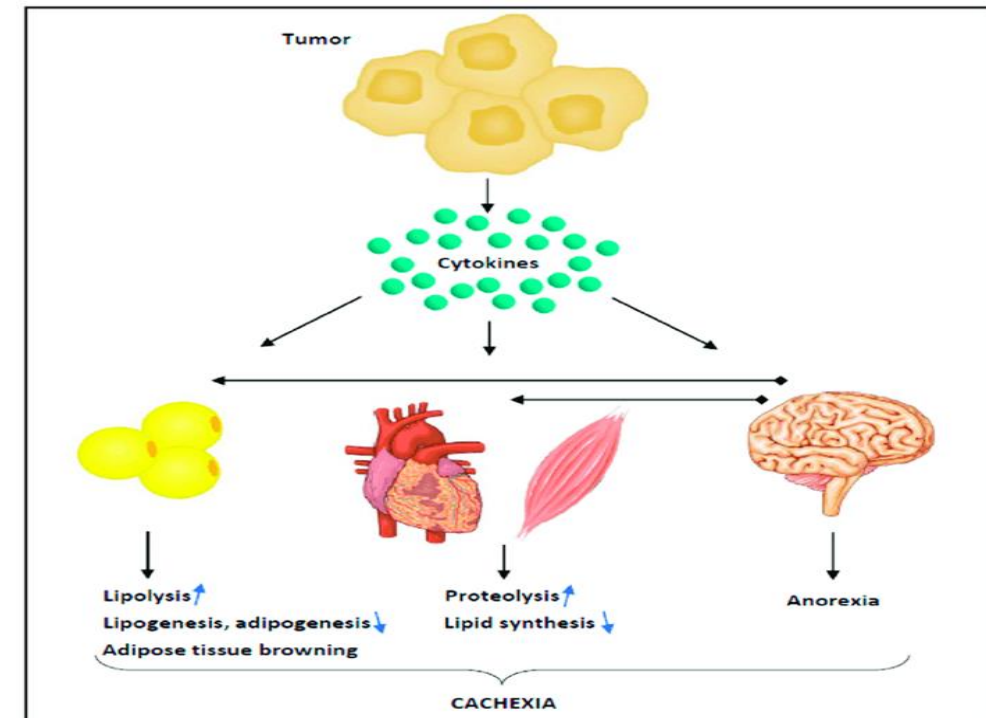
- Cachexia is usually seen in advanced cancer.



► The causes of cachexia are multiple:

(1) Anorexia is a loss of appetite.

(2) The BMR {basal metabolic rate} is **↑** in patients with cancer, despite reduced food intake, in contrast to the lower BMR that occurs as an adaptational response in starvation.



Paraneoplastic Syndromes:

- Symptom complexes that occur in patients with cancer and cannot be explained by the local or distant spread of the tumor or by the elaboration of hormones indigenous to the tissue of origin of the tumor.
- Due to ectopic production of hormones or other factors.
- May precede the tumor (occult cancer) or mimic metastases.
- Occur in 10%-15% of cancers.

Types of paraneoplastic syndromes:

- Endocrinopathies.
 - Nerve and Muscle Syndrome
 - Osseous, Articular and Soft-Tissue Changes
 - Dermatologic Disorders
 - Vascular & hematological changes
- MANY OTHERS !**

Commonest 3 syndromes reported:

- 1.Cushing syndrome
- 2.Thrombotic endocarditis (caused by hypercoagulability of blood.
- 3.Hypercalcemia.

Examples of paraneoplastic syndromes:

Finger Clubbing

❑ Carcinoma of Lung

- Cushing Syndrome(ectopic ACTH or ACTH- like polypeptides.
- ADH secretion
- Hypertrophic osteoarthropathy & finger clubbing
- Venous thrombosis (Trousseau phenomenon) (**Also in Pancreatic CA**)



Examples (continued)

Squamous Cell CA lung

Breast CA

Renal Carcinoma

Hypercalcemia (PTHrP)

- Note: Hypercalcemia due to skeletal metastasis is not a paraneoplastic syndrome!

Hepatic & Renal CA → Polycythemia (Erythropoietin)

Advanced Cancers → Nonbacterial thrombotic endocarditis.

Fibrosarcoma → Hypoglycemia (Insulin-like substance)

2-Grading & Staging of Tumors (for cancers)

- Methods to quantify the probable clinical aggressiveness of a neoplasm and its extent and spread to arrive at an accurate prognosis and treatment protocols.

**CANCER
STAGES**



**TUMOR
GRADES**

GRADE of tumor:

- Based on level of **differentiation and** the number of **mitoses** and is based on **microscopic** criteria.
- Grading schemes have evolved for each type of malignancy and generally range from two categories (low grade and high grade) to four categories.

Grade I: Well-differentiated tumor

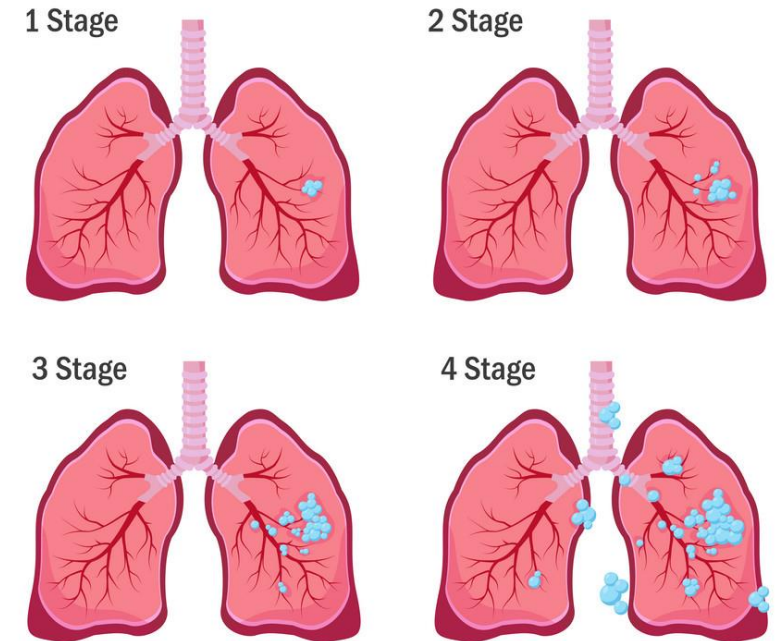
Grade II: Moderately differentiated tumor

Grade III: Poorly differentiated tumor

Grade IV: Anaplastic tumor

STAGE of Tumor:

- This indicates the extent of the spread of tumor.
- It depends on:
 - * Size of tumor
 - * Regional lymph node involvement
 - * Metastases to distant organs



The major staging system in use is the **American Joint Committee on Cancer Staging**. This system uses a classification called the **TNM** system.

TNM Staging System

- **T** : Size and extent of primary tumor.
- **N** : Presence and extent of lymph node involvement.
- **M** : Presence or absence of distant Metastasis.

e.g. **T1,N1, M0**



Staging is more important than grading because it affects treatment

Prognosis:

- This indicates the final outcome of the disease in terms of **5-year or 10-year survival**.
- This is influenced by:

Tumor Type

Tumor Grade & Stage

Host reactions

3. Laboratory Cancer diagnosis

General outline:

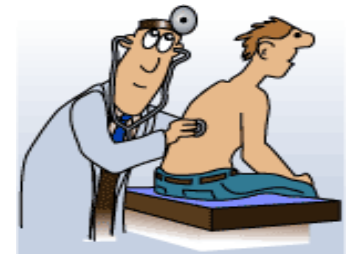
- History & clinical examination

- Symptoms: What the health care worker learns from the patient.
- Signs: Physical examination of the patient



- Radiographic techniques

- X-ray
- CT scan
- MRI
- Ultrasound



- Laboratory tests:

- General such as blood picture, stool for occult blood, blood sugar, **biopsy**.....etc



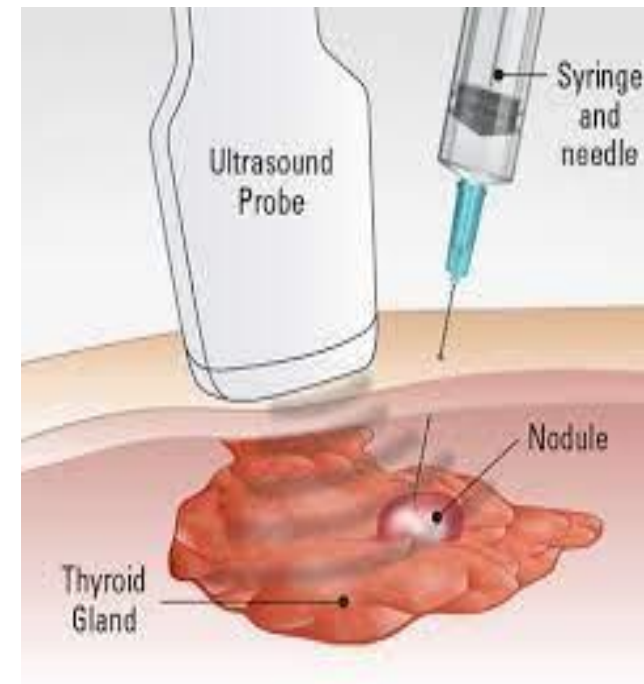
1- Morphological Methods:

Sufficient clinical data should accompany requests for the histopathological examination.

A- Cytological Methods:

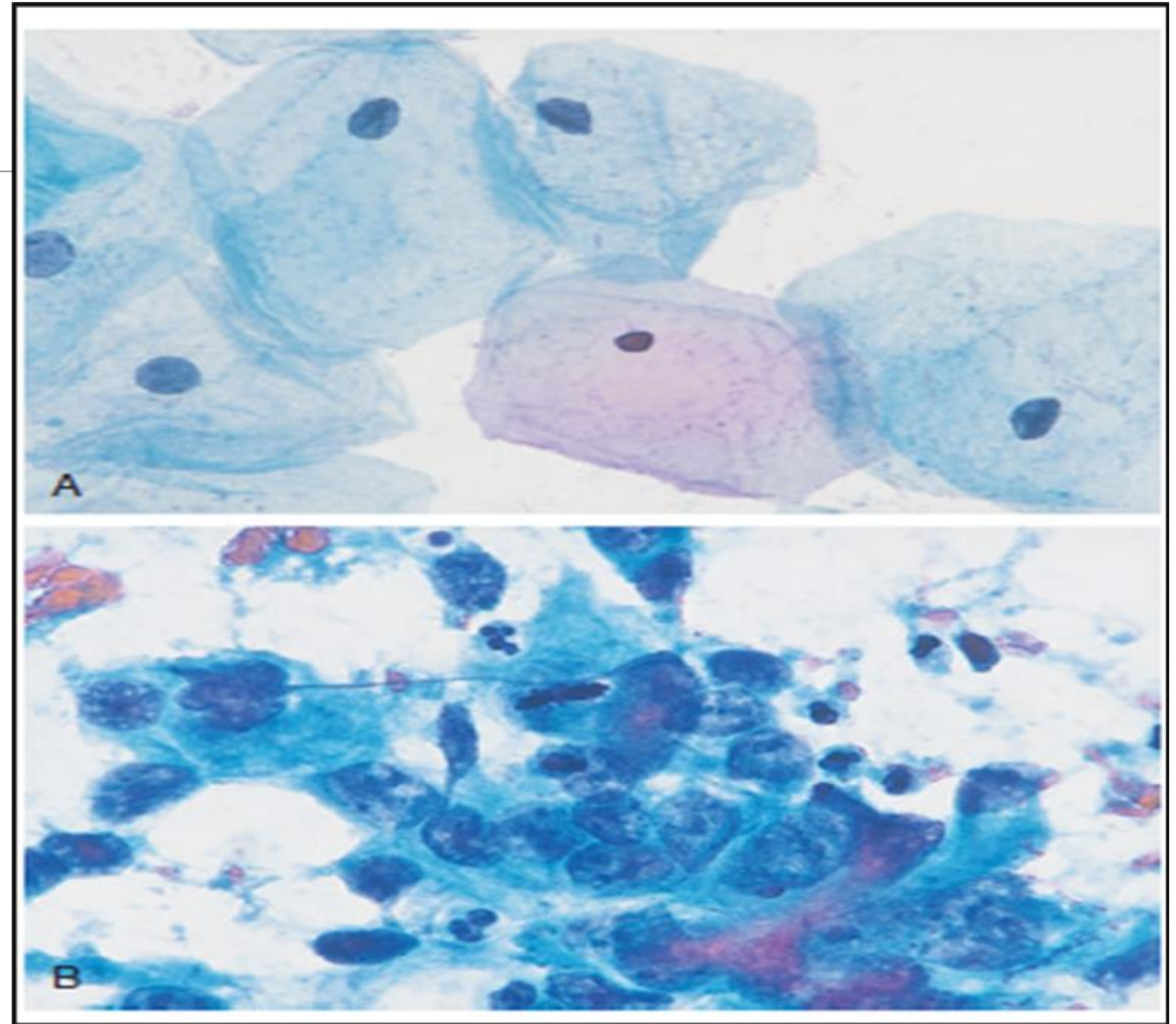
Study of cells:

- Brush, Fluid tapping...etc
- FNA: This method is most commonly used with **palpable masses** in the breast, thyroid, LN
 - Smear.
 - Papanicolaou stain (Pap) used.



(A) Normal Papanicolaou smear from the uterine cervix. Large, flat cells with small nuclei are typical.

(B) Abnormal smear containing a sheet of malignant cells with large hyperchromatic nuclei. Nuclear pleomorphism is evident, and one cell is in mitosis.



B- Histological methods:

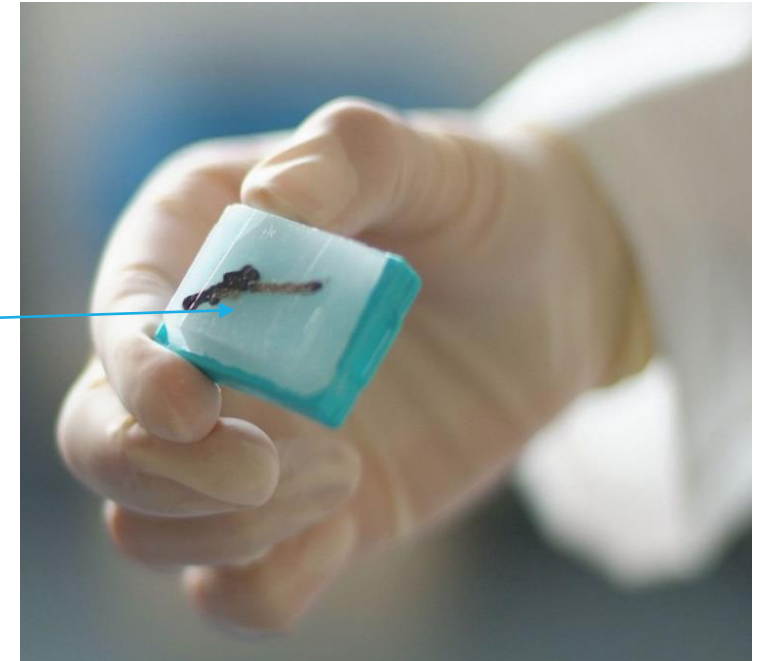
- Biopsy of tissue:

Needle core biopsy, Endoscopic Biopsy, or open surgical biopsy

- **Frozen Section (Rapid technique)**, done while the patient is already anesthetized in the surgical theater, in which the sample is quick-frozen (e.g., by CO₂ gas), allowing histopathological evaluation within 20 minutes)

- Paraffin Section.

- H&E
- Special stains, e.g. (PAS, CONGO RED, PEARL's iron stains)
- Immunohistochemical methods (IHC)



C- Immunohistochemistry:

- Staining by use of monoclonal AB directed against various components in cells: May help in the diagnosis of undifferentiated cancers or help in identifying the source of a metastatic tumor.

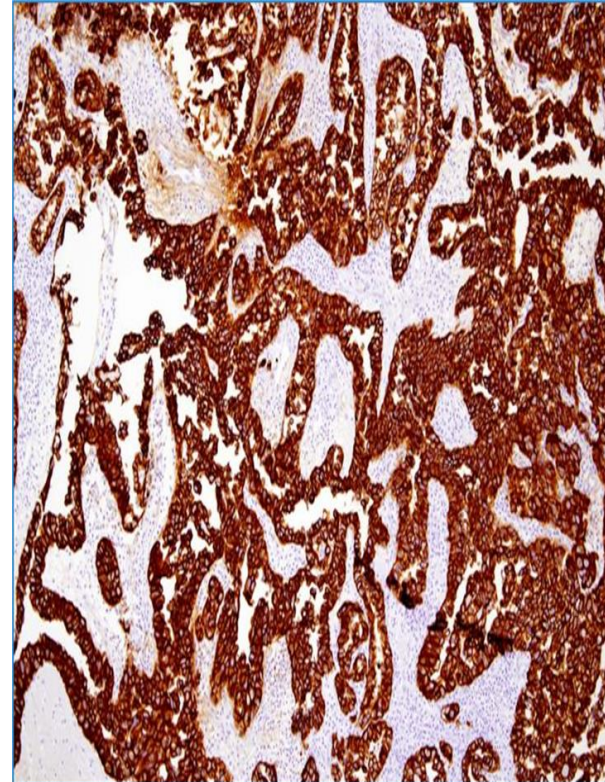
- **Cytokeratin** → **Carcinoma**

- Leukocyte Common Antigen → Lymphoma

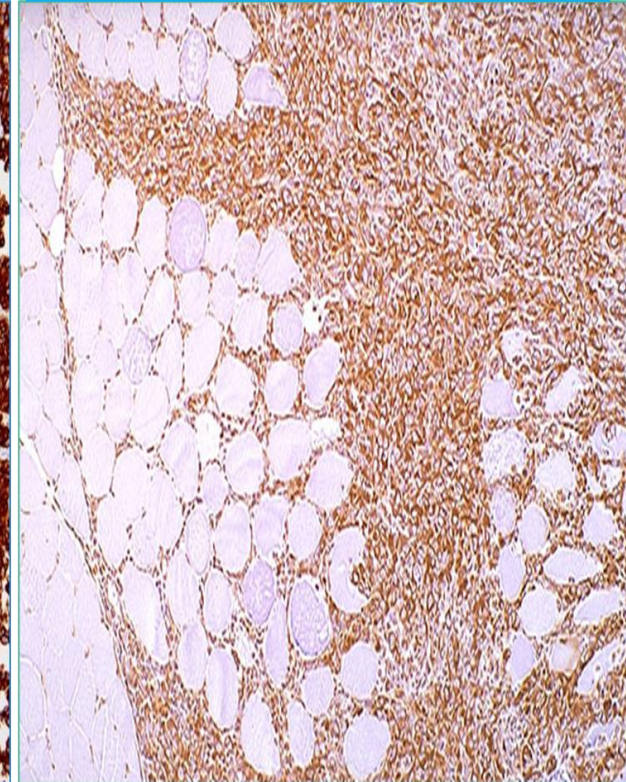
- S 100 → Neural tissue, melanocytic lesions

- **Vimentin, Desmin** → **Sarcoma**

Cytokeratin for epithelial cells indicating
Carcinoma

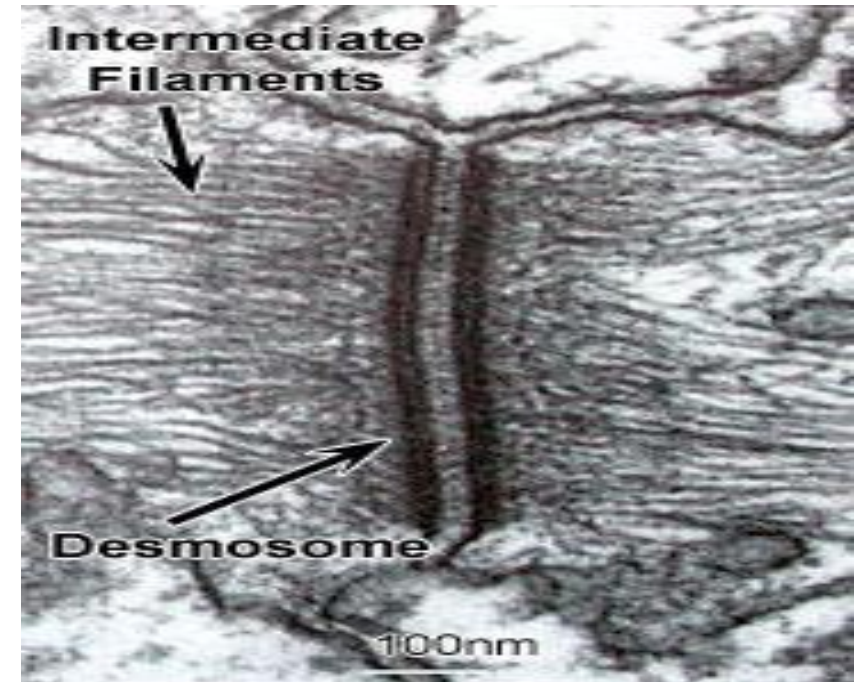


Vimentin Positive for
connective tissue indicating
Sarcoma



D- Electron microscopy:

- For recognition of intracellular structures e.g. desmosomes, or neurosecretory granules....etc.
- Not considered a practical tool for diagnosis.



2- Tumor Markers:

-Used to identify tumor associated enzymes, hormones, antigens ... etc

-Their uses are to:

I - Confirm diagnosis.

II -Determine the response to treatment

III- Detect early relapse.

-Present in serum or urine.

-Many are present in normal & tumor tissue, so not specific, but level is important.

Types of tumor markers

1- Hormones:

- Human Chorionic Gonadotrophic Hormone (β -HCG)

- Elevated levels are seen in Pregnancy & Gestational Trophoblastic Disease (Choriocarcinoma)
- Also high in some testicular tumors

2- Oncofetal Antigens:

- Carcinoembryonic Antigen (CEA):

- In fetal tissue & some malignancies – Colorectal CA

- Alpha-Fetoprotein (AFP):

- Cirrhosis: Elevated
- Hepatocellular carcinoma: Extremely high

3- Isoenzymes:

- Prostatic Acid Phosphatase (PAP)

↑ levels are seen in prostatic CA

4- Specific Proteins:

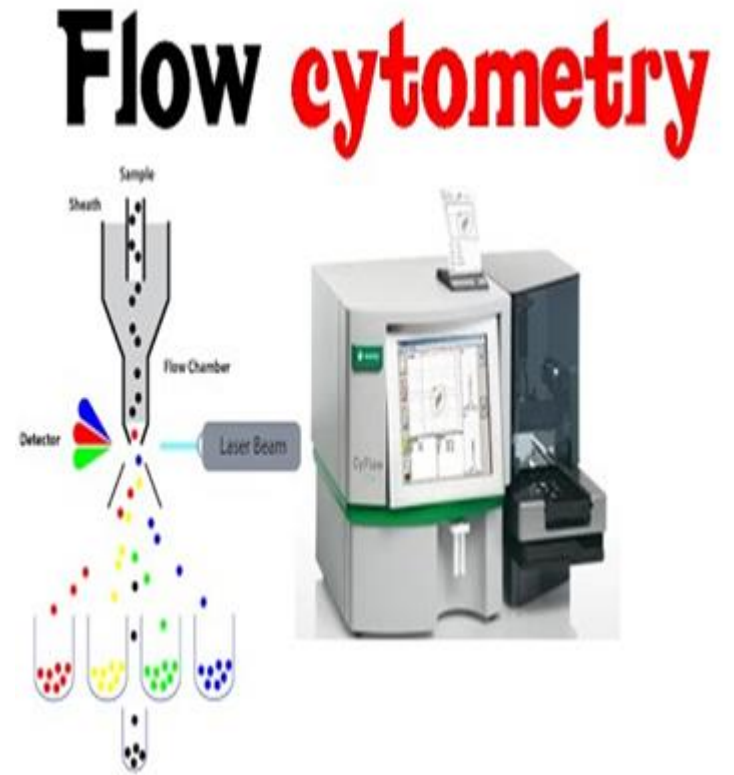
- **Immunoglobulins** secreted in Multiple Myeloma
- **Prostate-specific antigen (PSA)**: Present in epithelium of prostatic ducts.
 - * ↑ Prostatic hyperplasia
 - * ↑↑↑ in Prostatic CA

5- Several mucins

- **MUC-1** in breast CA
- **CA-125** in ovarian CA
- **CA-19.9** in colon ca

3- Flow Cytometry:

- In this method, fluorescently labeled antibodies against cell surface molecules and differentiation antigens are used to obtain the phenotype of malignant cells.
- Useful in the diagnosis & classification of Lymphoma & Leukemia



4- Molecular diagnosis:

- Methods used include:

- PCR (Polymerase Chain Reaction)
- FISH (Fluorescent In Situ Hybridization)

Used for:

1) Diagnosis of malignancy to detect gene rearrangement, translocations, amplifications...etc

- BCR-ABL in Chronic Myeloid Leukemia

2) For prognosis: gene amplification

- HER-2 NEU in breast carcinoma
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3) Detection of residual disease:

- In chronic myeloid leukemia(detection of *BCR-ABL* transcripts by PCR)

4) Detection of hereditary predisposition to cancer:

e.g. BRCA-1 in breast cancer

5) Useful in therapeutic decision-making (Targeted Therapy):

- V600E BRAF mutation in Melanomas.

