Pathology

Subject :

Lec no : lec-27-

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وَقُل رَّبِّ زِدْنِي عِلْمًا

NEOPLASIA

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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:

* السرطان بكل انواعه حميد/خبيث يؤثر على المصاب ب & تعتمد شدته على عدة عوامل

(1) **Location and impingement on adjacent structures**:

مناطق حساسة جداً & خطيرة حتى لو كان ال (tumor) benign

- 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.

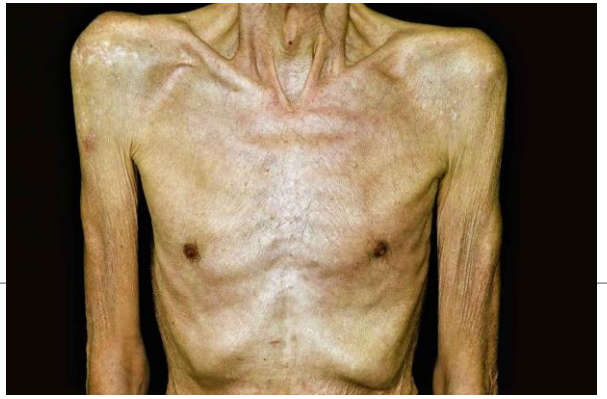
(2) Functional activity such as hormone synthesis or the development of paraneoplastic syndromes.

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

(4) Symptoms from rupture or infarction

(5) Cachexia or wasting

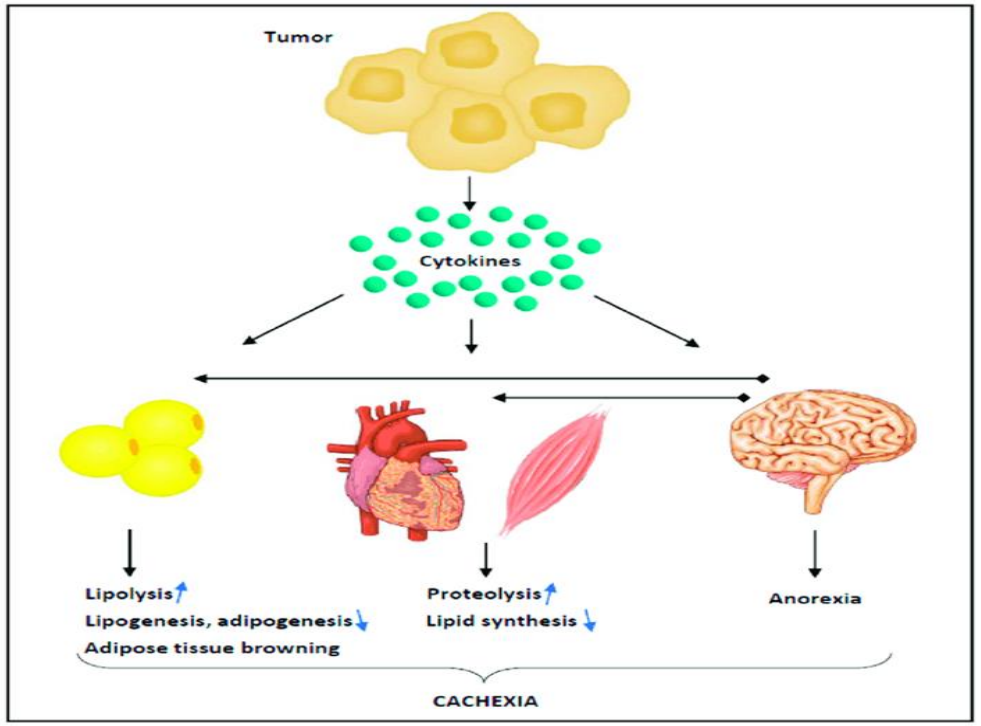
Cancer Cachexia:



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

فقدان الشهية

- 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.**

* يحدث هذا الشيء بسبب ان (cancer cells) تزيد (metabolic rate) اكثر من الطبيعي

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 (بحدث بسبب زيادة مستوى الكورتيزول)
2. Thrombotic endocarditis (thrombosis + inflamation → in the heart) (caused by زيادة عوامل التخلط) hypercoagulability of blood.
3. Hypercalcemia.

Examples of paraneoplastic syndromes:

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)**

Finger Clubbing

Examples (continued)

- Squamous Cell CA lung
- Breast CA
- Renal Carcinoma

الذي يحدث بسبب (PTHrP) يكون paraneoplastic syndrome

Hypercalcemia (PTHrP)

parathyroid hormon

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

- **Hepatic & Renal CA →** Polycythemia (↑RBC) (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 (شراسة السرطان) of a neoplasm and its extent and spread to arrive at an accurate prognosis and treatment protocols.

Based on microscope

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.

* كل (tumor) الـ (grading system) مختلف عن الـ حر

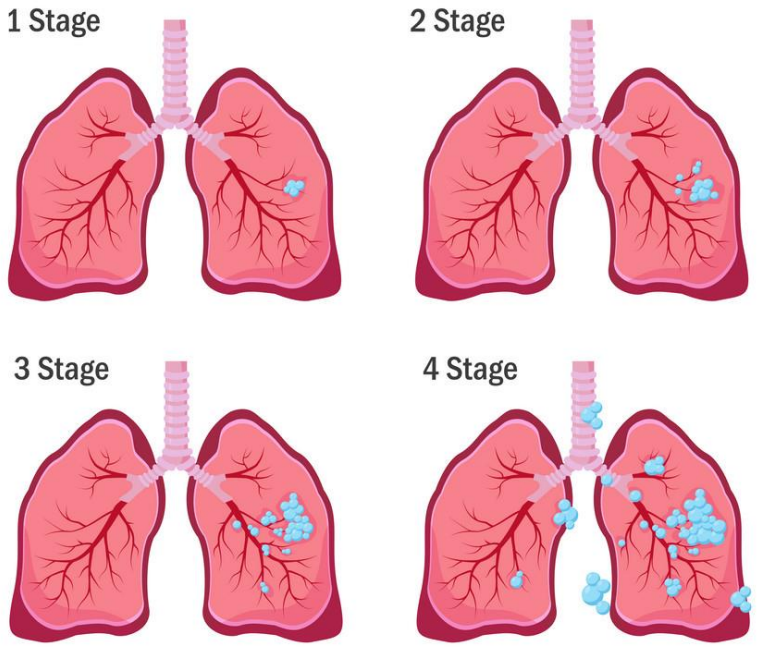
1. Grade I: Well-differentiated tumor
2. Grade II: Moderately differentiated tumor
3. Grade III: Poorly differentiated tumor
4. Grade IV: Anaplastic tumor

Complete lose of differentiated

معدل انتشار السرطان Cancer

STAGE of Tumor:

- This indicates the extent of the spread of tumor.
- It depends on:
  1. * Size of tumor
  2. * Regional lymph node involvement
  3. * 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.

advanced stage المرحلة اكبر كانت الرقم كل ما كان

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

No metastasis

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:

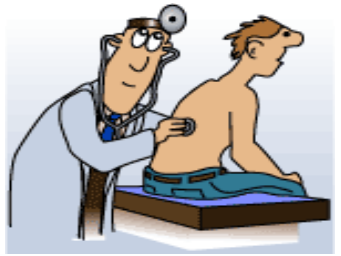
1. **Tumor Type**
2. **Tumor Grade & Stage**
3. **Host reactions**

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 → sub type ادوات تحديه { benign / malignant } ← ادوات تحديه لكن وجود mass هنا يظهر

- 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 <u>histopathological examination</u>.

A- Cytological Methods:

Study of cells: تدرس الخلايا تحت الميكروسكوب

- Brush, Fluid tapping…etc

- FNA: This method is most commonly used with

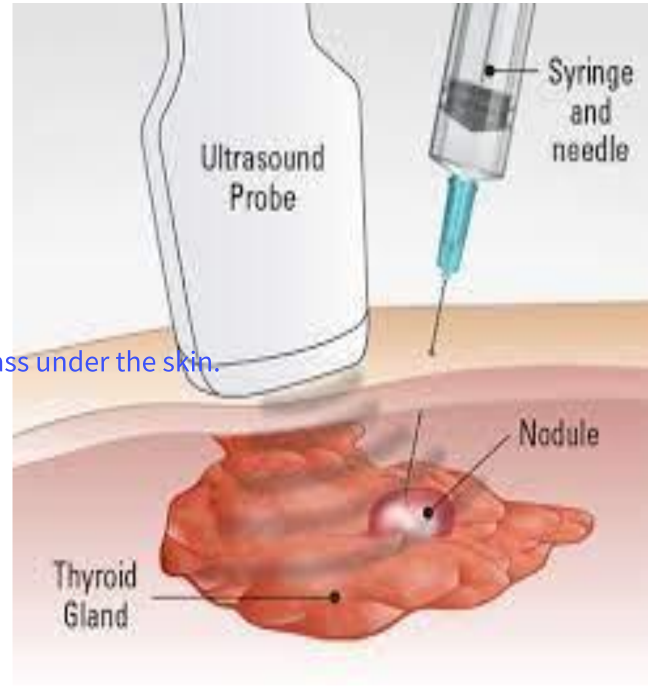
Fine needle aspiration a procedure in which a thin needle is used to draw cells or fluid from a lump or mass under the skin.

palpable masses in the breast, thyroid, LN

- Smear.

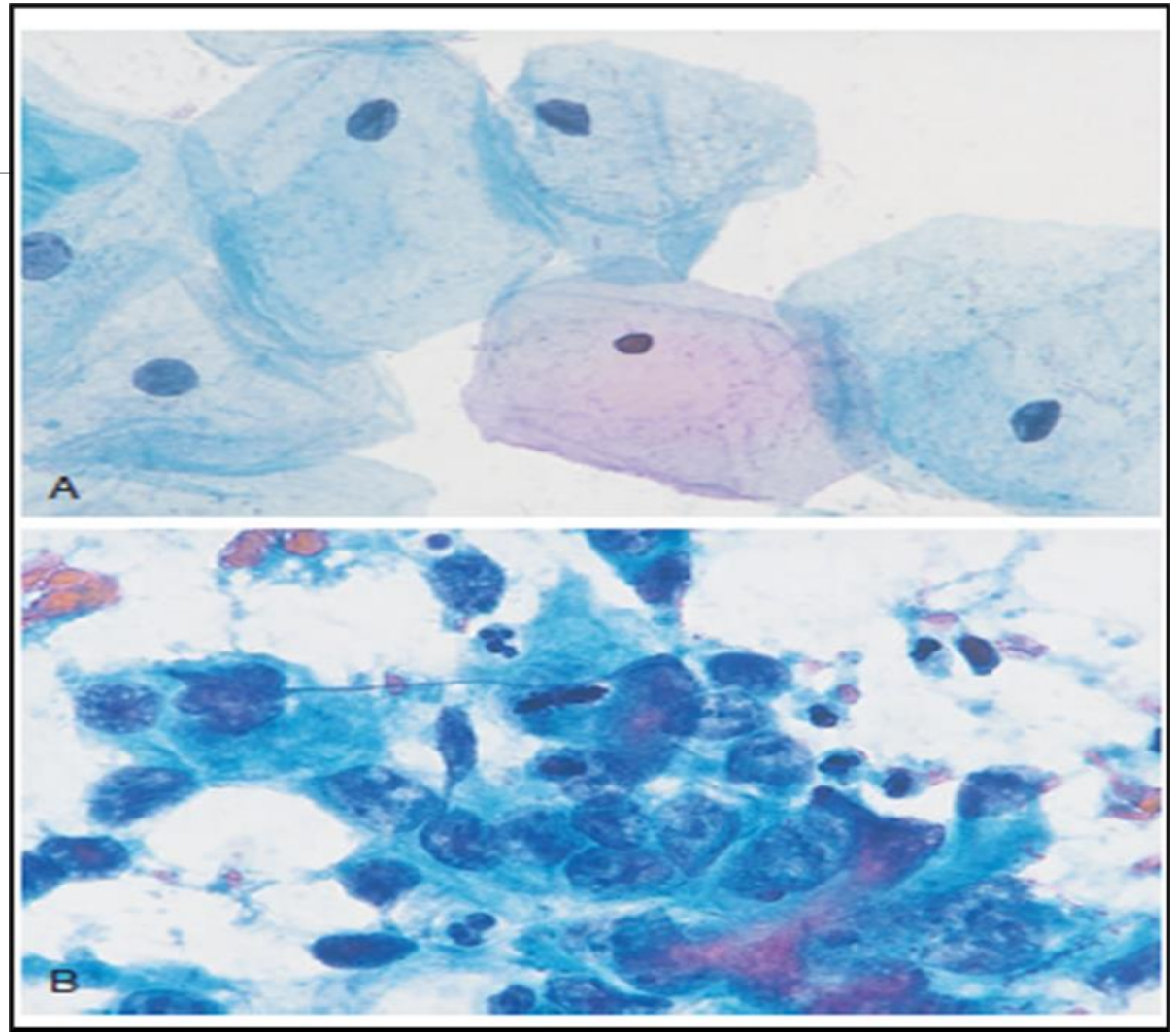
- Papanicolaou stain (Pap) used.

يتم صبغ الخلايا البطانية بصبغة تسمى (pap)



(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.

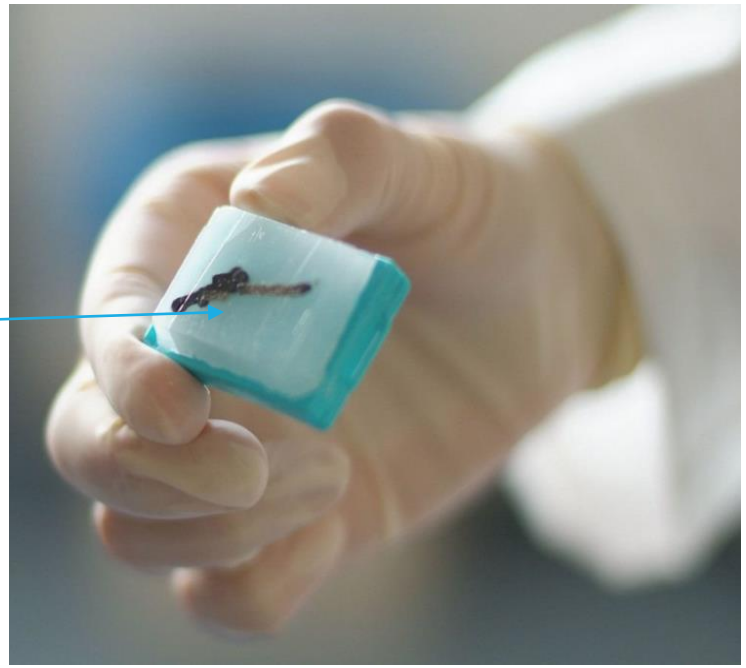


B- Histological methods:

- 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 Stain

- Special stains, e.g. (PAS, CONGO RED, PEARL's iron stains)

- Immunohistochemical methods (IHC)

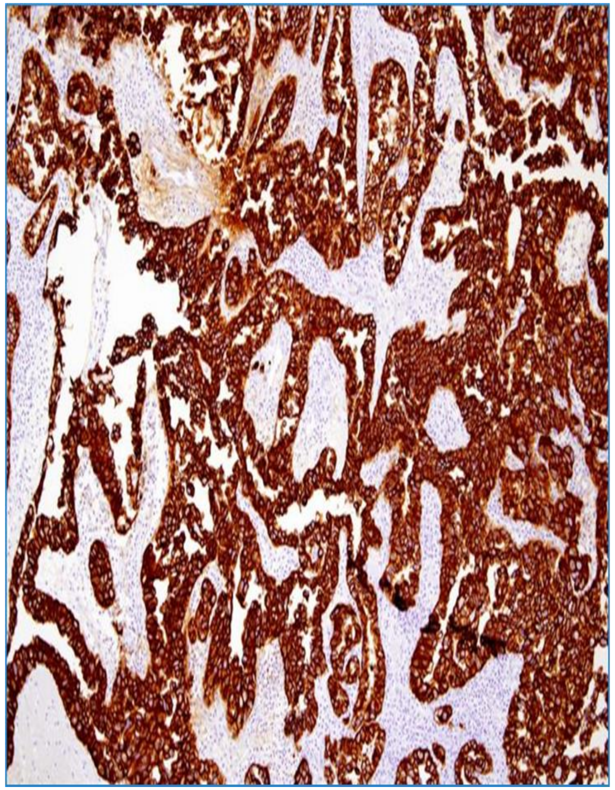
C- Immunohistochemistry:

- 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.

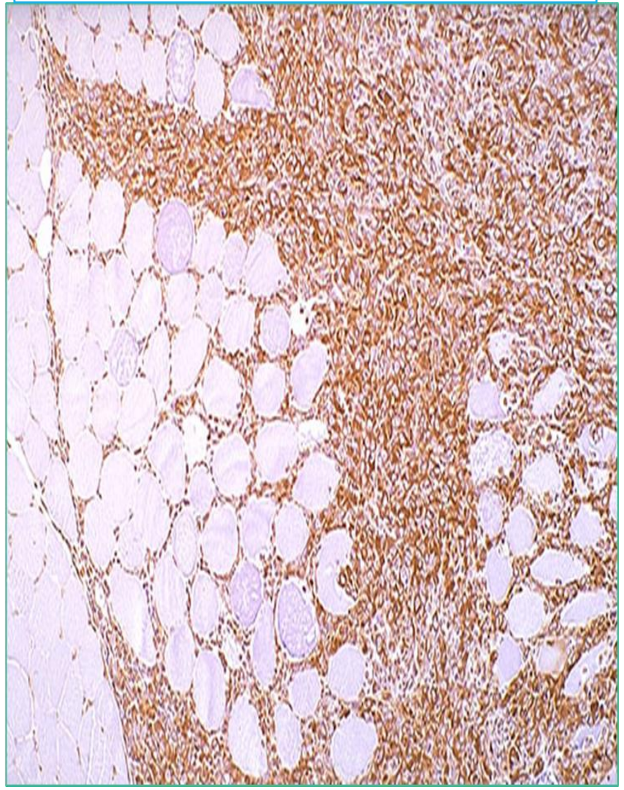
- **Cytokeratin→ Carcinoma** for keratin in epithelial tissue
- Leukocyte Common Antigen → Lymphoma
- S 100→ Neural tissue, melanocytic lesions
- **Vimentin, Desmin → Sarcoma** connective tissue
  - Desmin → muscle
  - Vimentin → CT But not specific

Brown → positive

Cytokeratin for epithelial cells indicating Carcinoma



Vimentin Positive for connective tissue indicating Sarcoma

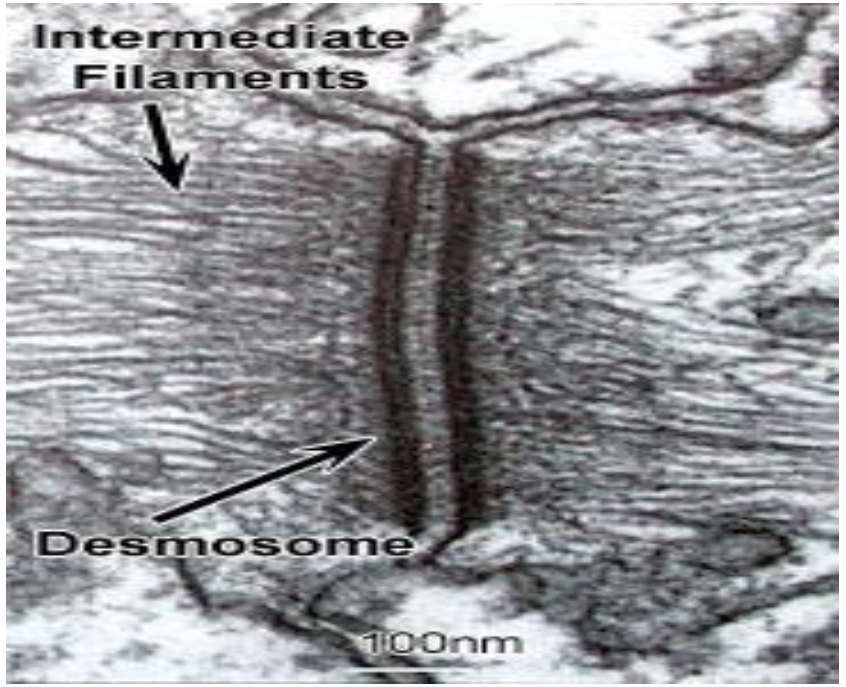


D- Electron microscopy:

- For recognition of intracellular structures e.g. desmosomes, or neurosecretory granules….etc.

- Not considered a practical tool for diagnosis.

→ we use it in special situation



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

استجابة الـ tumor إلى علاج معين نتيجة ذلك يجب ان يقل مستوى الهرمون الذي يفرزه الـ tumor في الدم

III- Detect early relapse. → عودة الـ cancer بعد علاجه

-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:

presents only in the development of the fetus

- **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

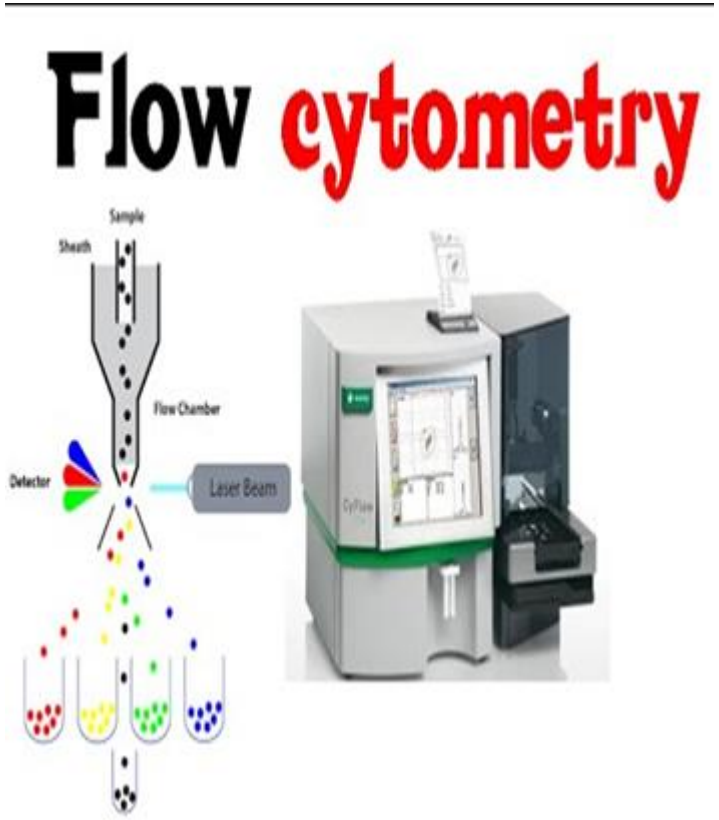
- **MUC-1** in breast CA
- **CA-125** in ovarian CA
- **CA-19.9** in colon ca

3- Flow Cytometry:

مش كتير مهم

- 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:

we use it to check genetic changes mutations DNA abnormalities

- 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.