Diagnosis of Malignancy

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Objectives

- How to approach a case of cancer?

- Describe modalities available in diagnosing cancer.

- Before any form of evaluation clinical history and examination is a must

Inspection

Palpation

Aims of investigations

- Confirm diagnosis
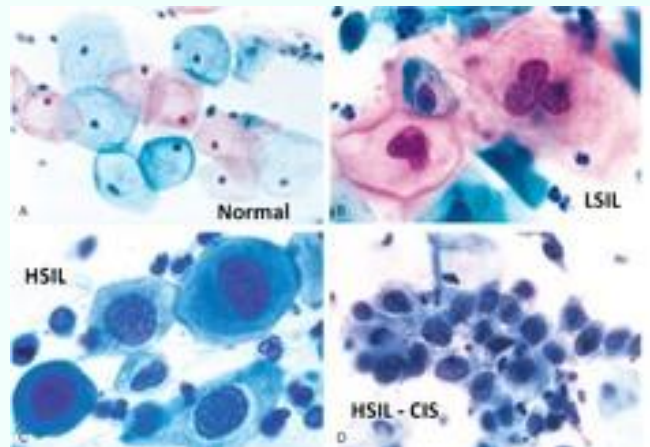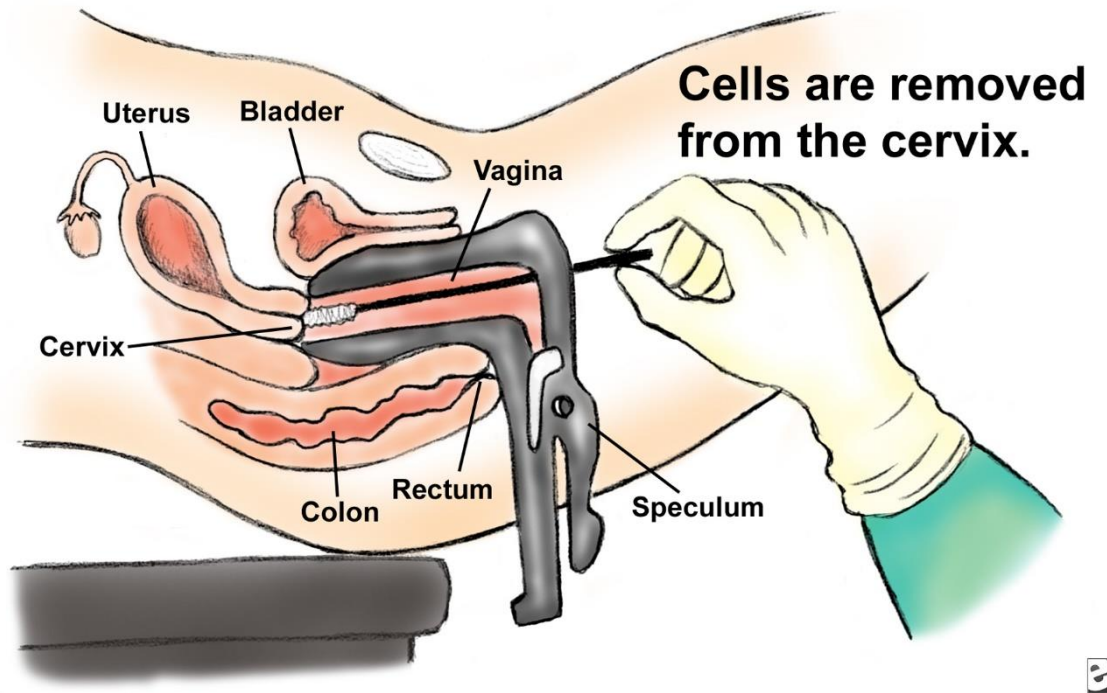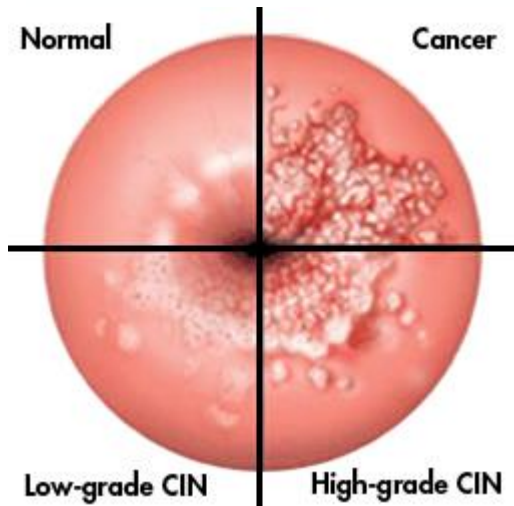- Grading
- Staging
- Prognosis

METHODS OF EVALUATION

1.Cytologic methods

2.Histologic methods

3.Special tests

i. Tumour markers

ii. Immunohistochemistry

iii. Molecular diagnosis

iv. Flow cytometry

CYTOLOGIC METHODS

- EXFOLIATIVE CYTOLOGY

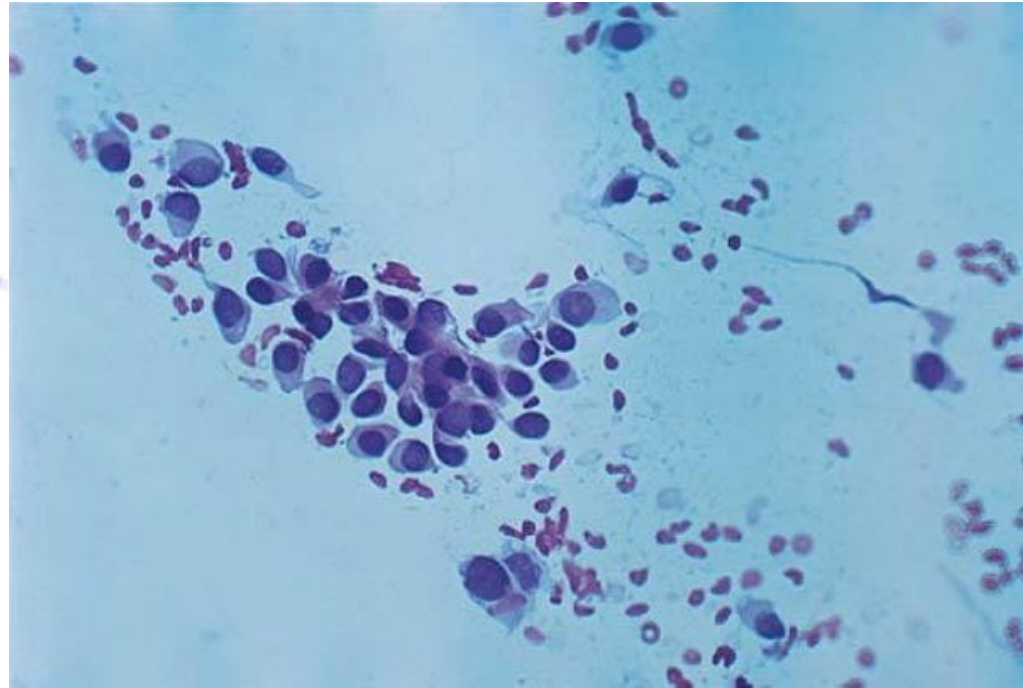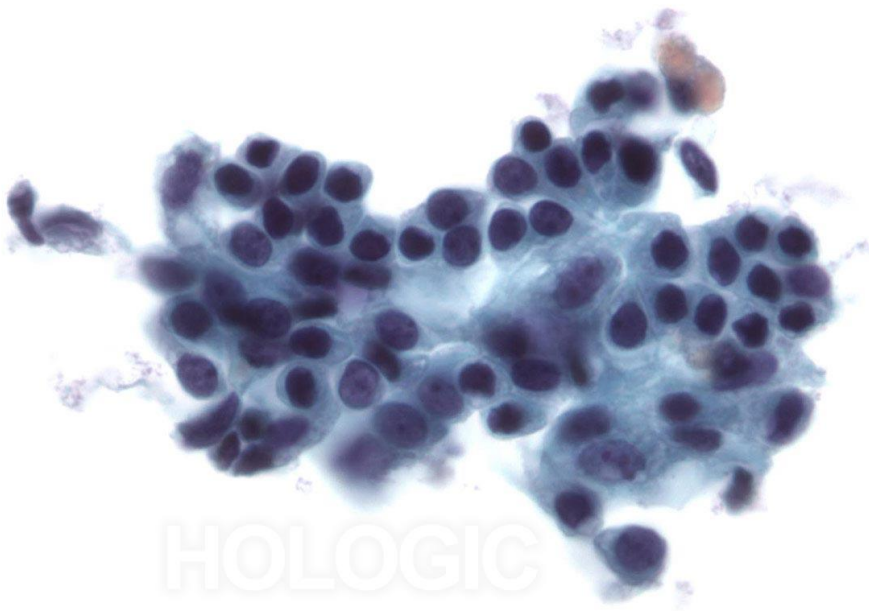- ASPIRATION CYTOLOGY

Exfoliative cytology

Normal | Cancer

Low-grade CIN | High-grade CIN

Uterus | Bladder

Vagina

Cells are removed from the cervix.

Cervix

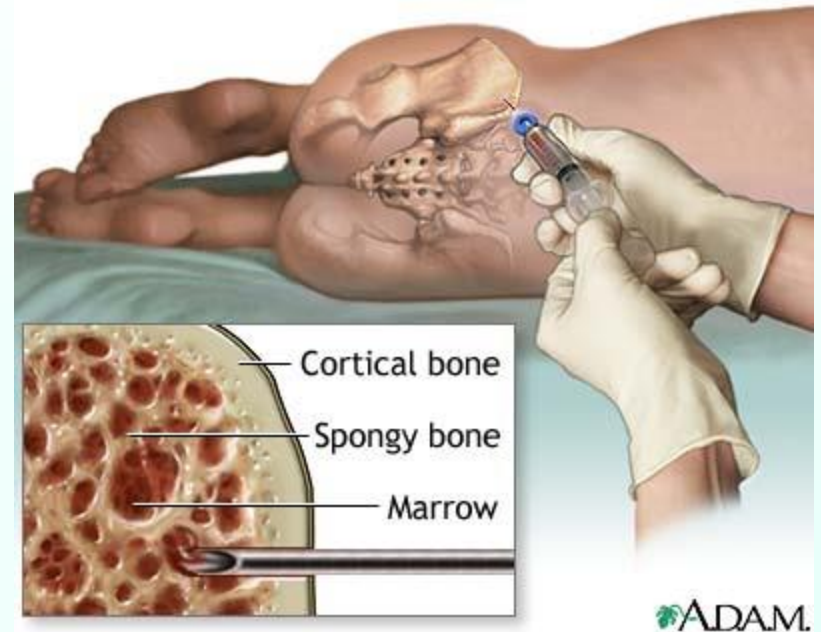Rectum

Colon | Speculum

Normal | LSIL

HSIL | HSIL - CIS

F
N
A
C

Fine needle aspiration

HISTOLOGY

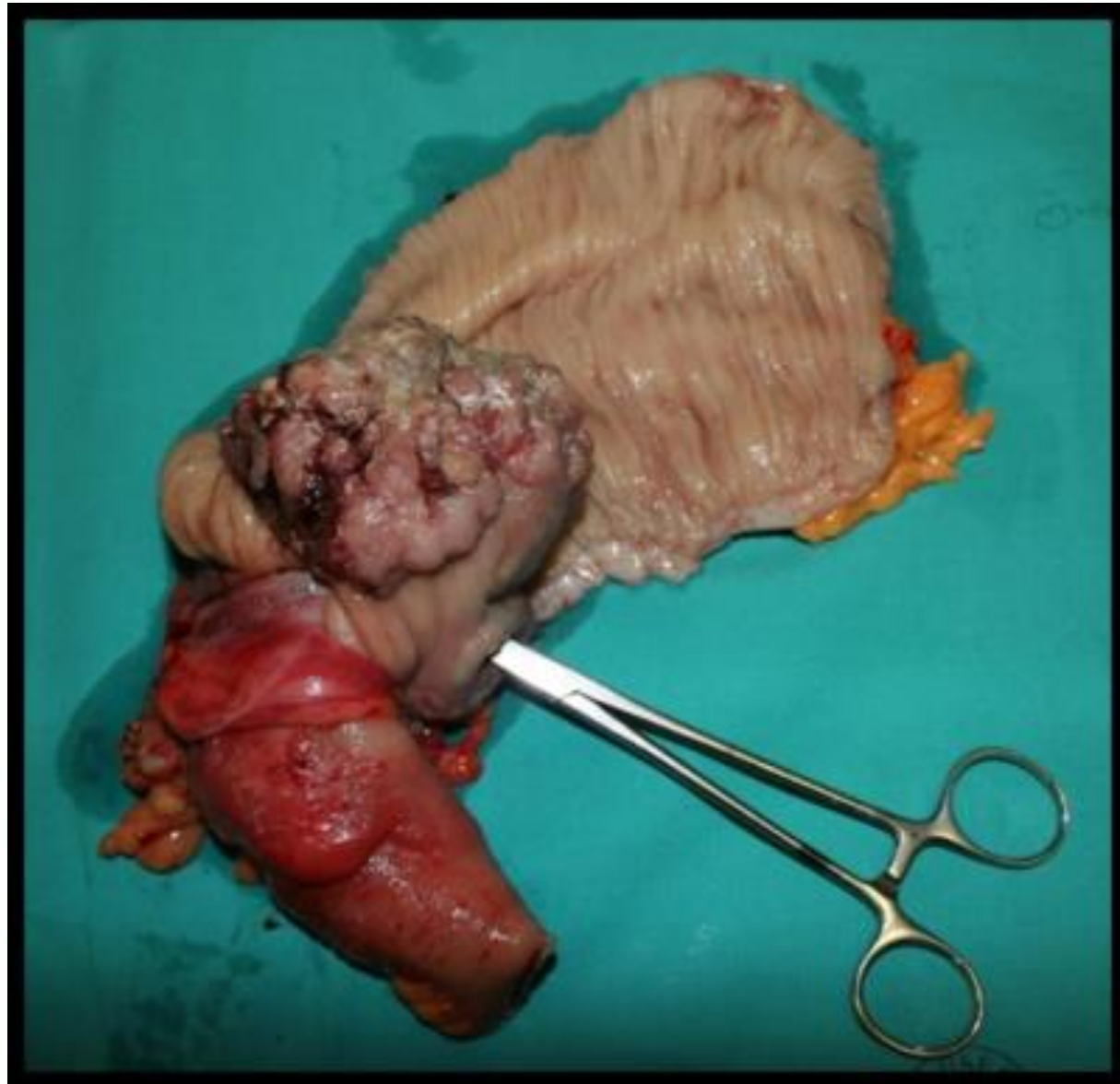- Tissue Diagnosis
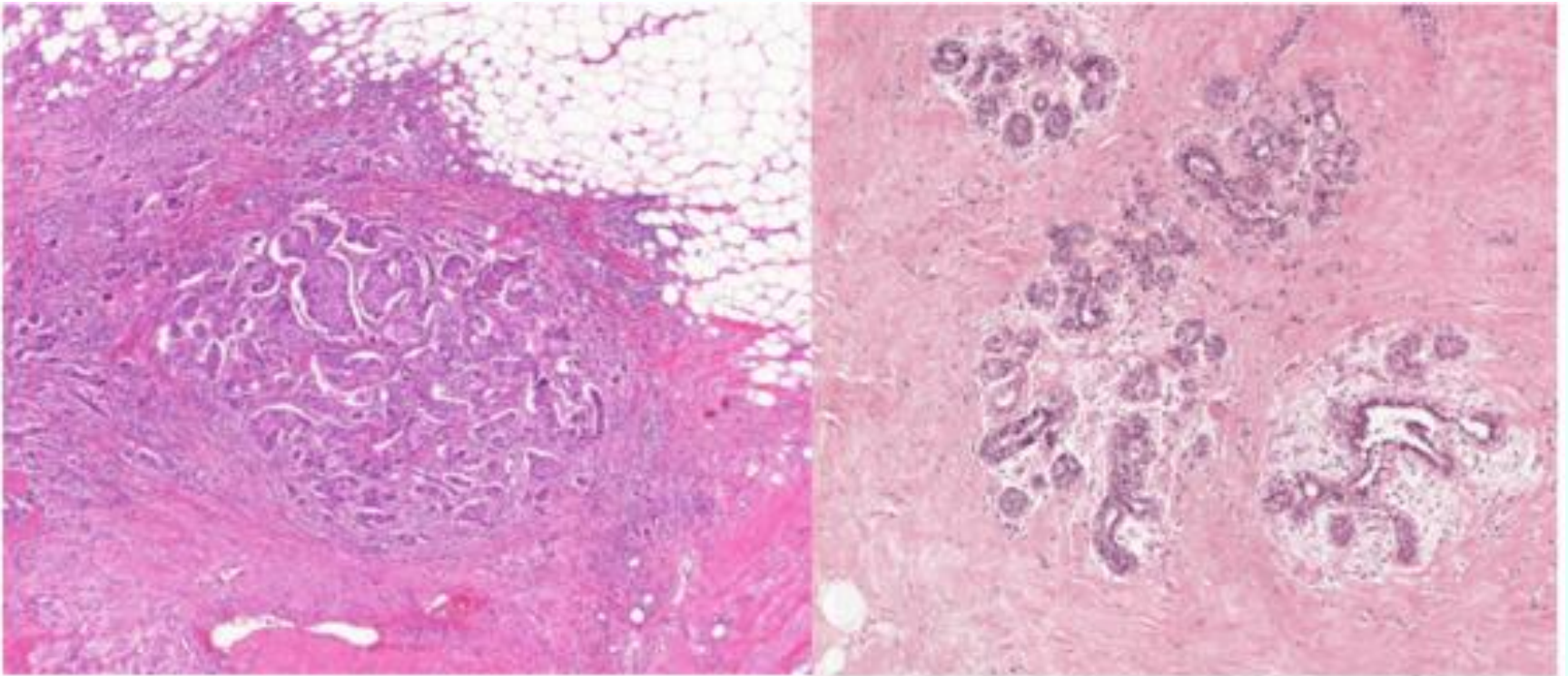

Cortical bone
Spongy bone
Marrow

A.D.A.M.
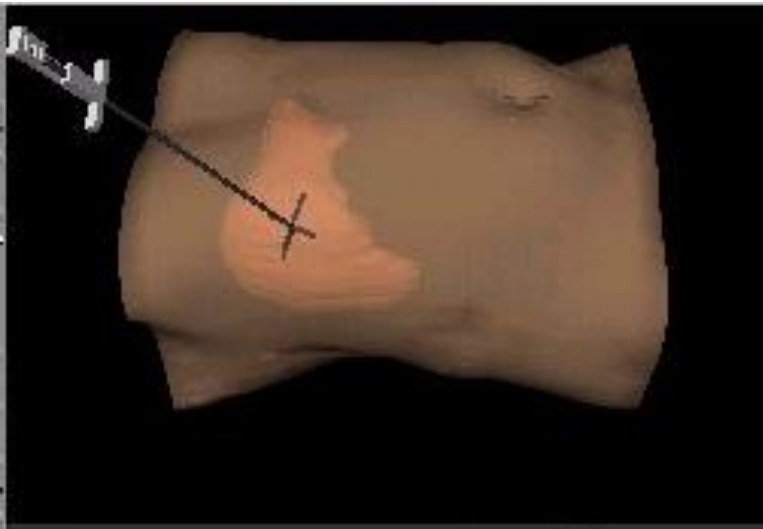
Excision/incision biopsy

Surgical specimens

Histology- H&E stain

Home work – specimen transport

TUMOUR MARKERS

- They are biochemical indicators for the presence of a tumour
- They only support a diagnosis of cancer
- Screening
- Response of a cancer to therapy
- Detecting relapse during follow up period

CLASSES OF TUMOUR MARKERS

1. HORMONES
2. ONCOFETAL ANTIGENS
3. ISO ENZYMES
4. SPECIFIC PROTEINS
5. MUCINS AND GLYCOPROTEINS
6. NEW MOLECULAR MARKERS

Hormone	Cancer
HCG	Trophoblastic tumours, non seminomatous germ cell tumours
Calcitonin	Medullary carcinoma of thyroid
Catecholamine and metabolites	Pheochromocytoma and related tumours
Ectopic hormones Ex:ACTH	Paraneoplastic syndromes of many cancers

ONCO FETAL ANTIGENS

- These are the antigens which are normally expressed during embryonic life
- These get re expressed in many diseased states including malignancy
- They are not specific for any cancer
- The two main onco fetal antigens are

1. α feto protein
2. Carcino embryonic antigen(CEA)

Elevated α feto protein

Non neoplastic conditions

1.Cirrhosis

2.Toxic liver injury

3.Hepatitis

4.Pregnancy especially with fetal distress or death

Neoplastic conditions

1.Hepato cellular carcinoma

2.Germ cell tumour of testis

Less commonly elevated in

3.Carcinoma colon

4.Carcinoma lung

5.Carcinoma pancreas

CARCINO EMBRYONIC ANTIGEN(CEA)

- It is a complex glycoprotein
- Normally synthesised in the embryonic tissue of - gut- pancreas- liver

Elevated CEA

Non neoplastic

1. Alcoholic cirrhosis
2. Hepatitis
3. Ulcerative colitis
4. Crohn disease
5. Smokers

Neoplastic

1. **Colorectal carcinoma –60-90%**
2. Pancreatic carcinoma – 50-80%
3. Gastric carcinoma – 25-50%
4. Breast carcinoma – 25-50%

- SPECIFIC PROTEINS

- Immunoglobulins-Multiple myeloma
- Prostate specific antigen (PSA)-Carcinoma prostate

- ISO ENZYMES

- Prostatic acidphosphatase-Prostate cancer
- Neuron specific enolase-Small cell cancer lung, neuroblastoma

MUCINS AND OTHER GLYCOPROTEINS

- CA-125   Ovarian cancer
- CA 19-9   Colon cancer, pancreatic cancer
- CA 15-3   Breast cancer

IMMUNOHISTOCHEMISTRY

- This is the special branch of pathology where antibodies against cellular antigens are used in identification of cellular products or surface markers

- The components are visualized using chromogens which stain up when the antigen antibody reaction is completed.

IHC
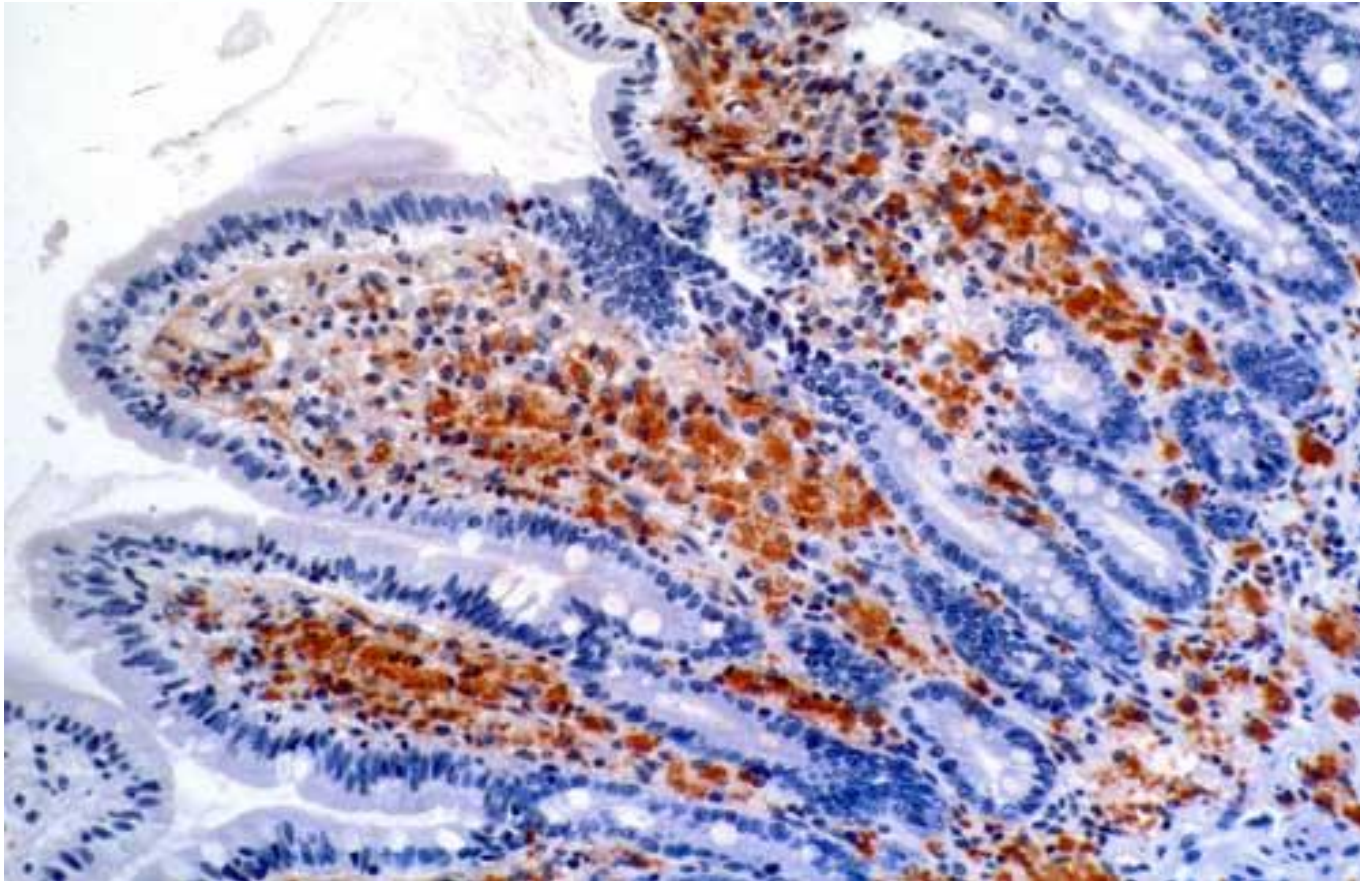
UTILITY OF IHC IN NEOPLASMS

1. Categorisation of undifferentiated malignant tumours

2. Categorisation of leukemias and lymphomas

3. Determination of site of origin of metastatic tumours

4. Detection of molecules that have prognostic or therapeutic significance
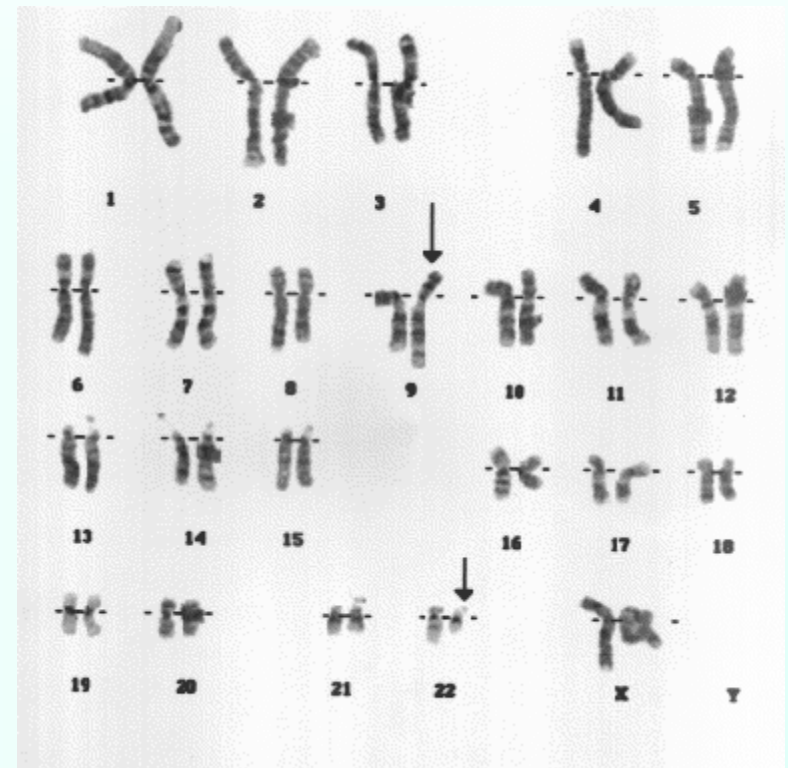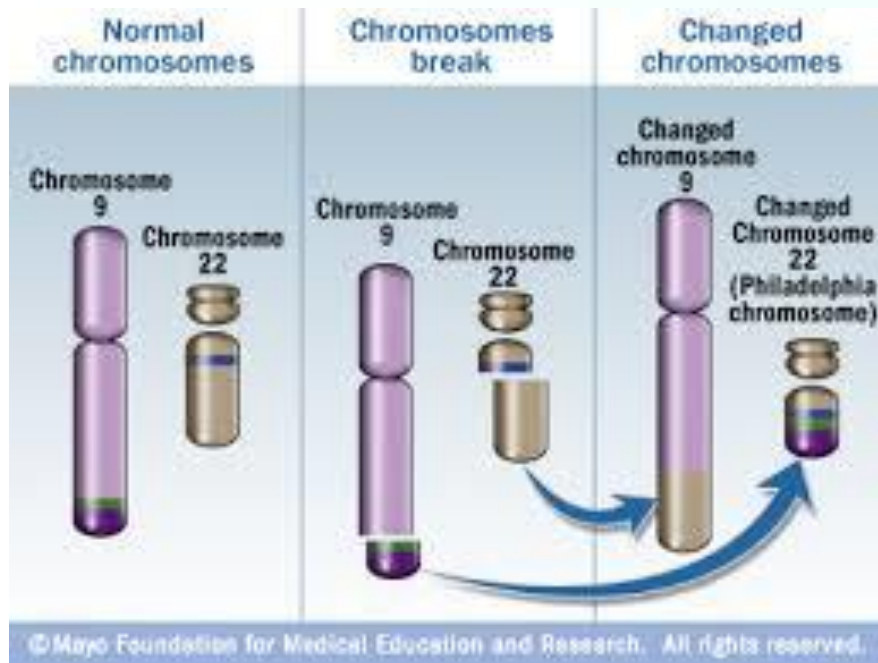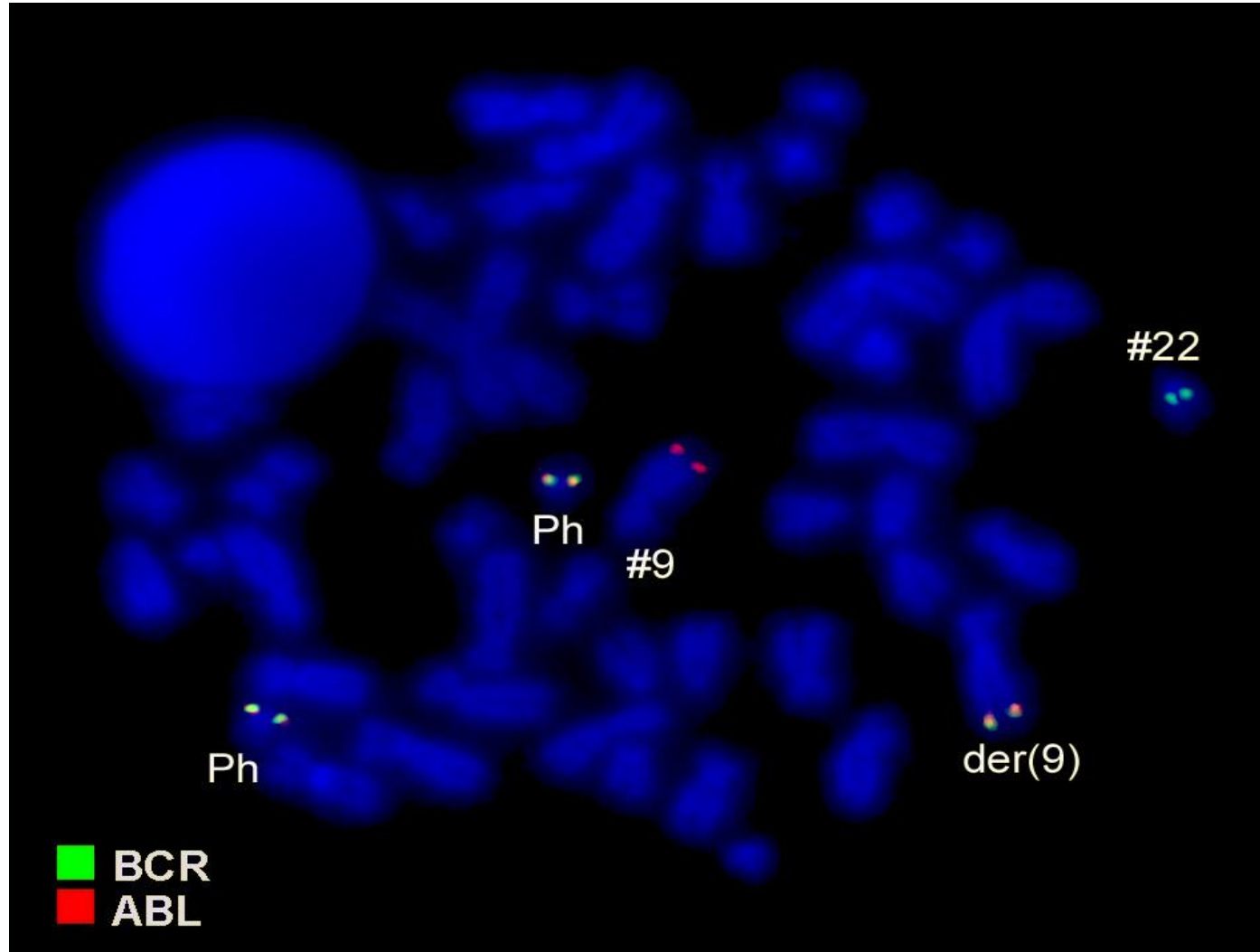
Genetic markers

- Philadelphia chromosome – in CML
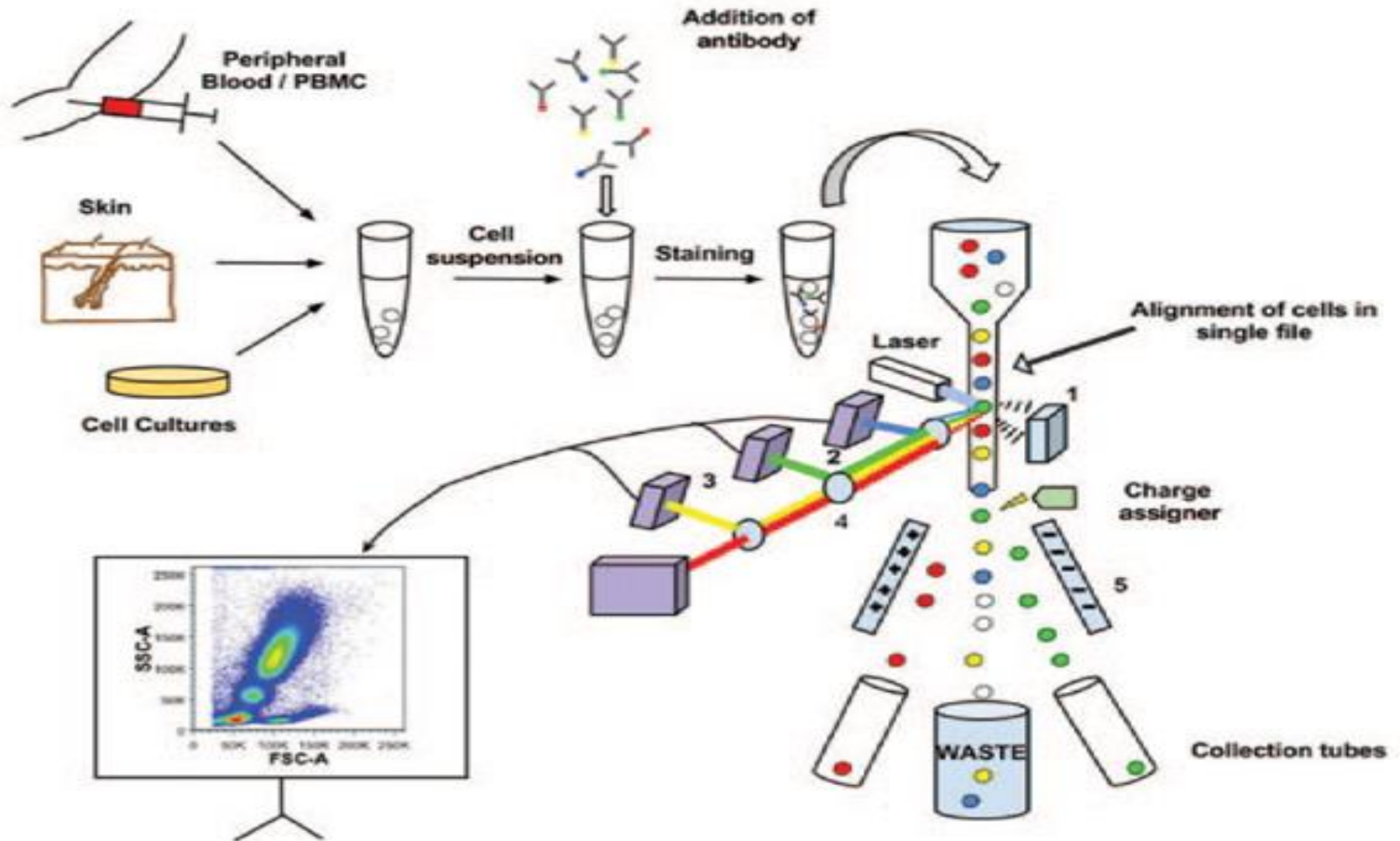
Karyotype

FISH

PCR

FISH
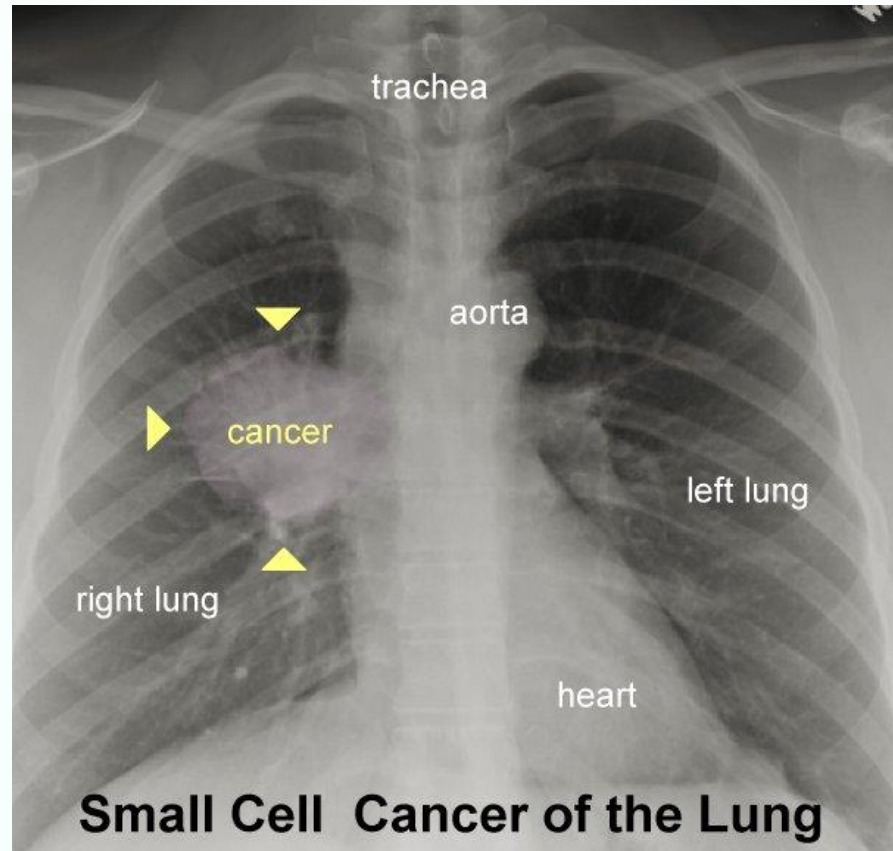
MOLECULAR DIAGNOSIS

- Diagnosis of malignant neoplasms

- Prognosis of malignant neoplasms

- Detection of minimal residual disease

- Diagnosis of hereditary predisposition to cancer
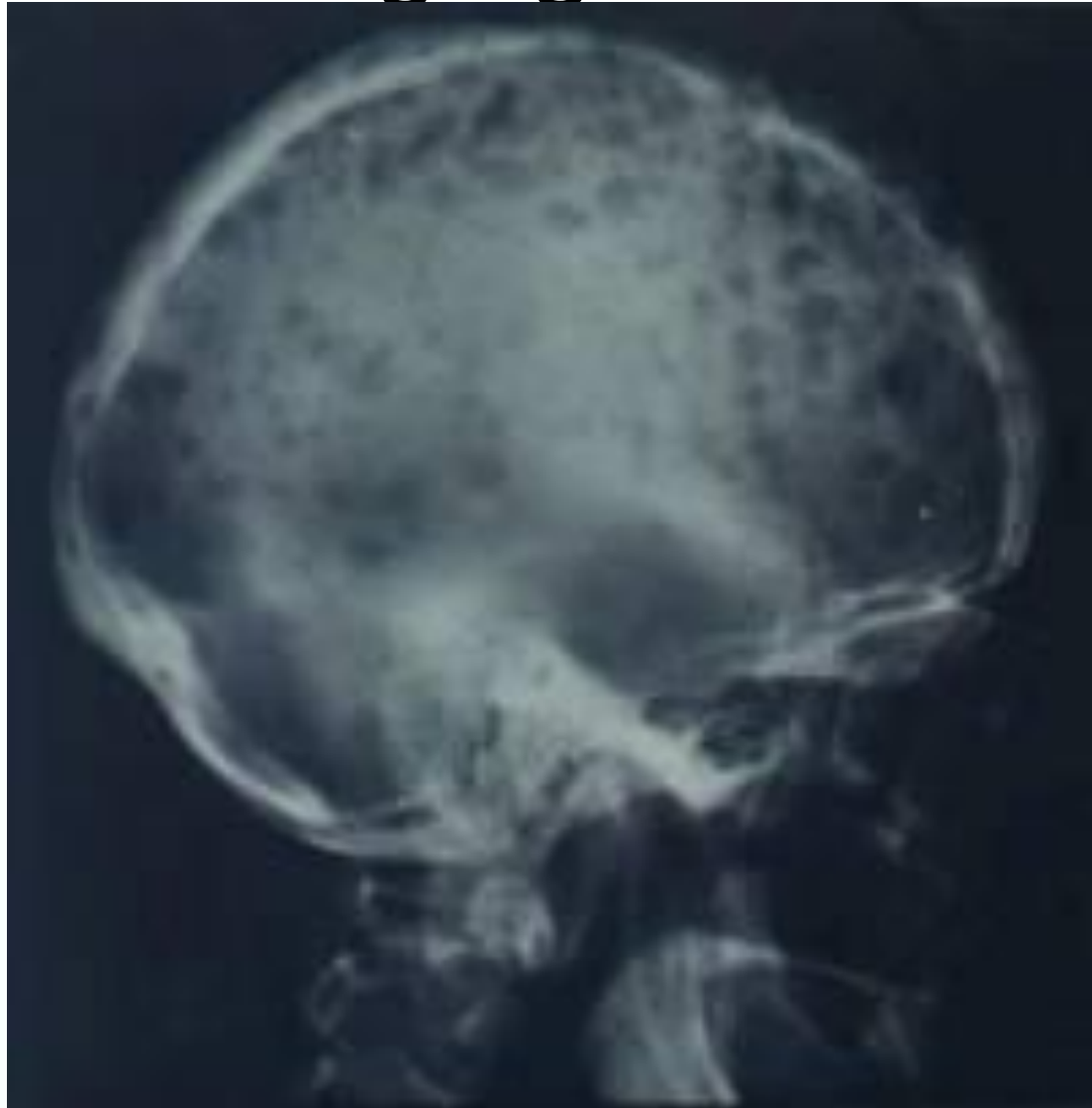
Flowcytometry
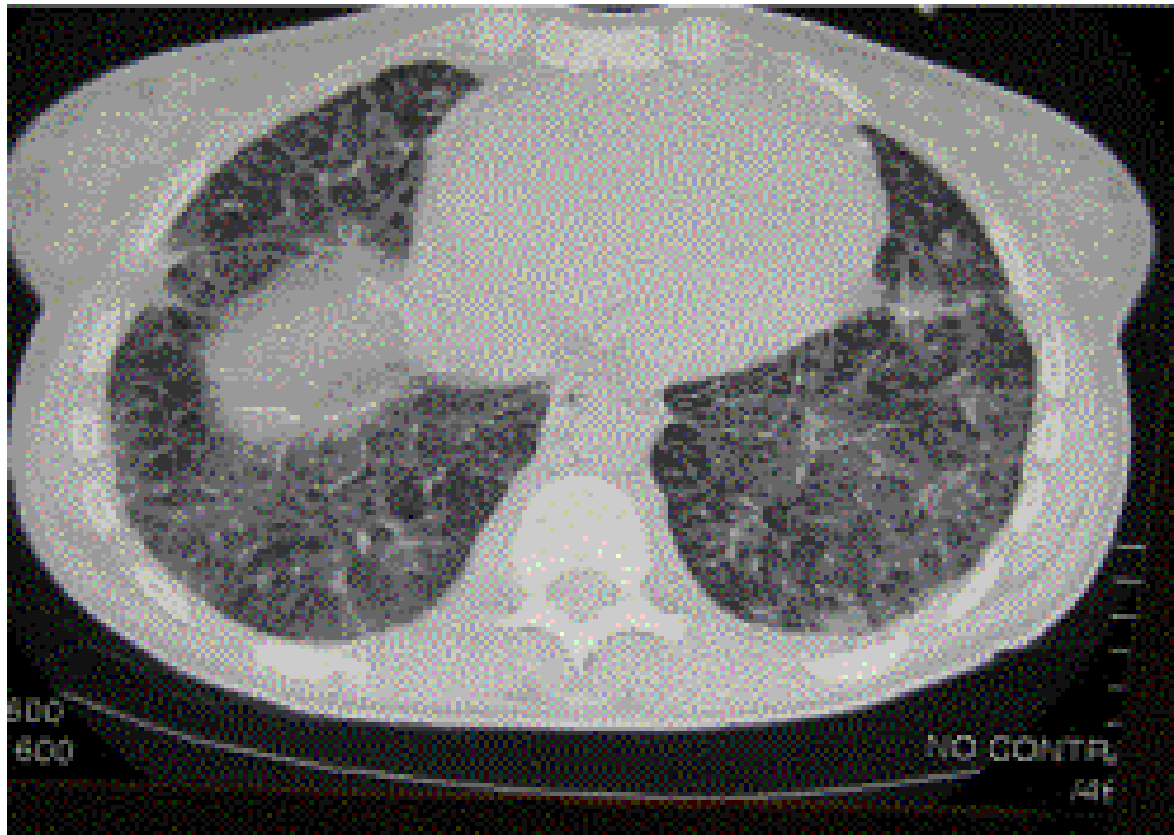
Imaging

- X-rays

Imaging

- X-rays
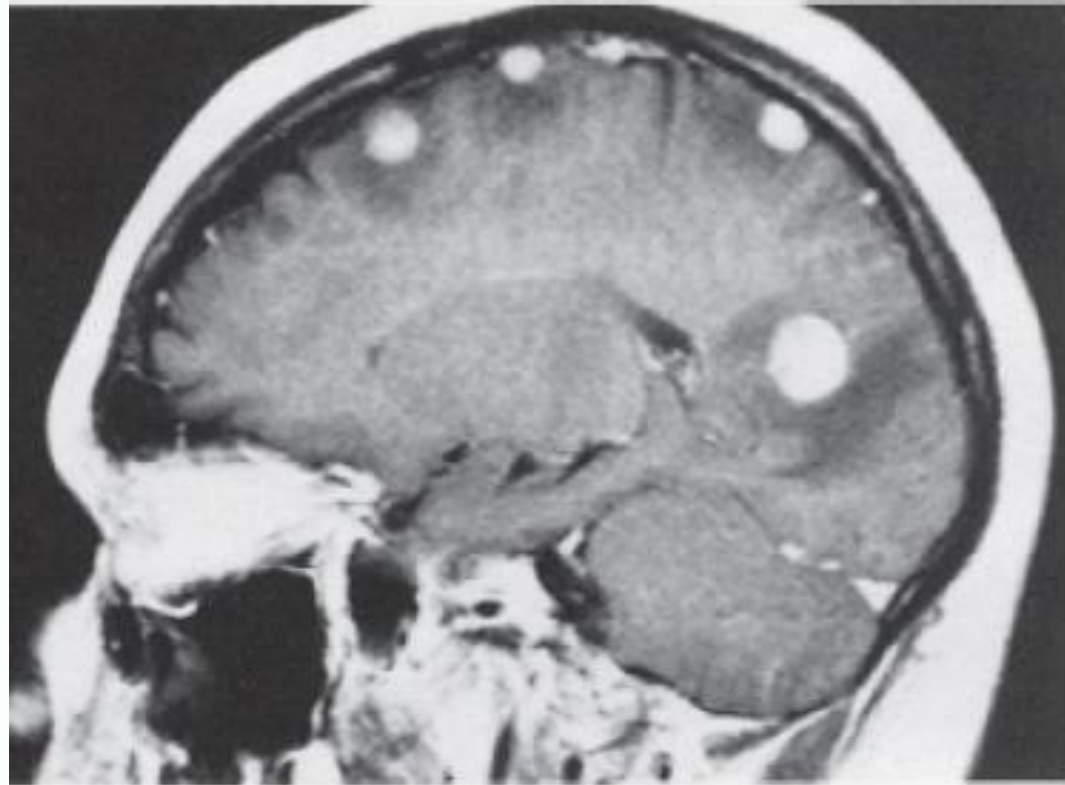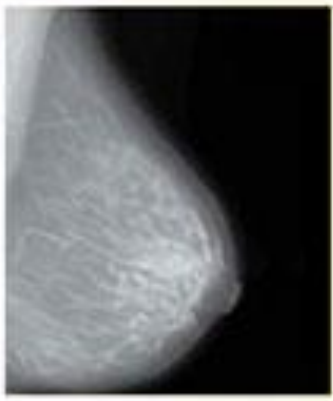
Imaging

- USS

Imaging

- CT scans

Imaging

- MRI scans

Mammogram

Normal mammogram

Benign cyst (not cancer)

Cancer

Calcium in your diet does not cause calcium deposits (calcifications) in the breast.

Grading-Breast CA

Tubule Formation

Tubule Formation is the percentage of the tumour that is made up of tubular structures.

1 – The tumour is made up of more than 75% tubules.

2 – The tumour is made up of 10%–75% tubules.

3 – The tumour is made up of less than 10% tubules.
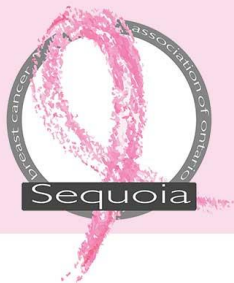
Nuclear Pleomorphism

Nuclear Pleomorphism is the degree of change in the size and shape of the tumour cells' nuclei (the part of the cell that holds the chromosomes, which contain genetic information)

1 – The nuclei are small and uniform in size and shape.

2 – The nuclei are medium to large in size, but are mostly the same size and shape.

3 – The nuclei are large and vary in size and shape.

Mitotic Count

Mitiotic Count is the number of cells that are actively dividing

1 – The tumour cells are dividing at a slow rate.

2 – The tumour cells are dividing at a moderate rate.

3 – The tumour cells are dividing at a fast rate.

The individual scores from these 3 features are added together to give a total score between 3 and 9. A tumour grade is then assigned based on the total score.

Staging

- Macroscopy and microscopy

ex:Tumour size,LN involvement

- Imaging-Distant organ involvement

ex: CT scans

- Bone marrow biopsy

ex:Lymphoma

Staging breast CA

Tumor size T	Tumor size < 2 cm	Tumor size 2-5 cm	Tumor size > 5 cm	Tumor extends to skin or chest wall
	T1	T2	T3	T4
Lymph Nodes N	**N0** No lymph node metastasis	**N1** Metastasis to ipsilateral, movable, axillary LNs	**N2** Metastasis to ipsilateral fixed axillary, or IM LNs	**N3** Metastasis to infraclavicular/ supraclavicular LN, or to axillary and IM LNs
Metastasis M	**M0** No distant metastasis	**M1** Distant metastasis		

أحسن اونكولوجيست

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LNs= Lymph Nodes; IM= Internal Mammary

Prognostic markers

- Beta 2 microglobulin
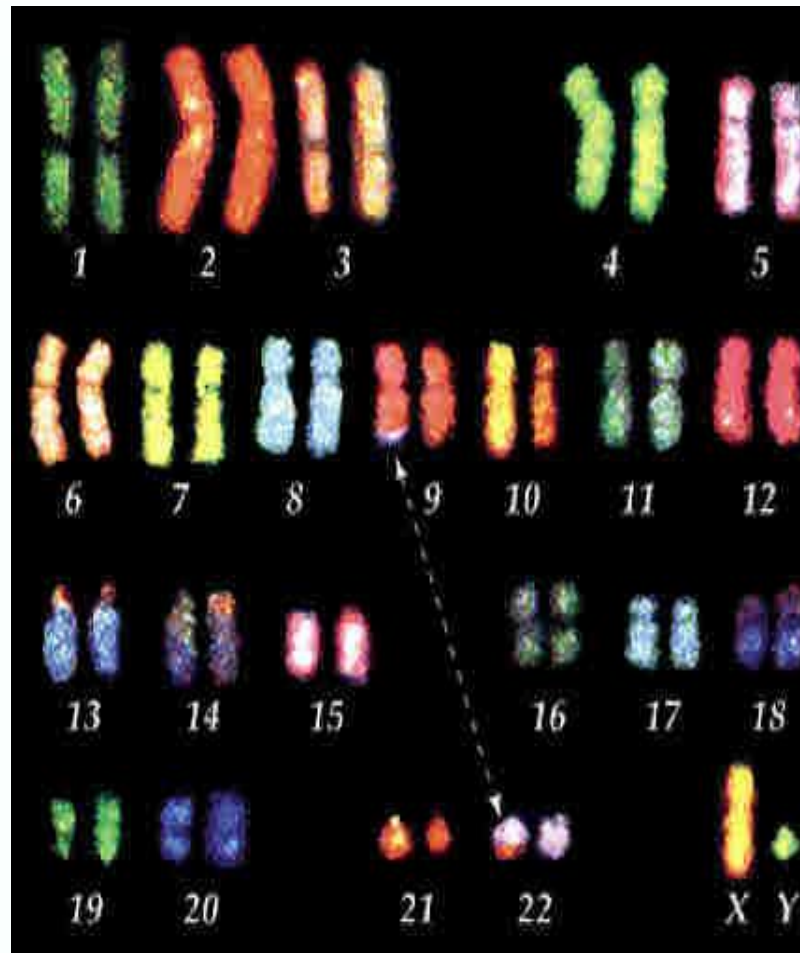
Ancillary markers

- ESR
- Serum LDH
- Serum protein electrophoresis – monoclonal gamma band
- Serum Ca
- Ectopic ACTH - lung
- Ectopic ADH – lung
- Serum uric acid

NEWER TECHNIQUES

1. Spectral karyotyping
2. Comparative genomic hybridisation
3. DNA micro array analysis
4. Proteomics
5. Tissue arrays
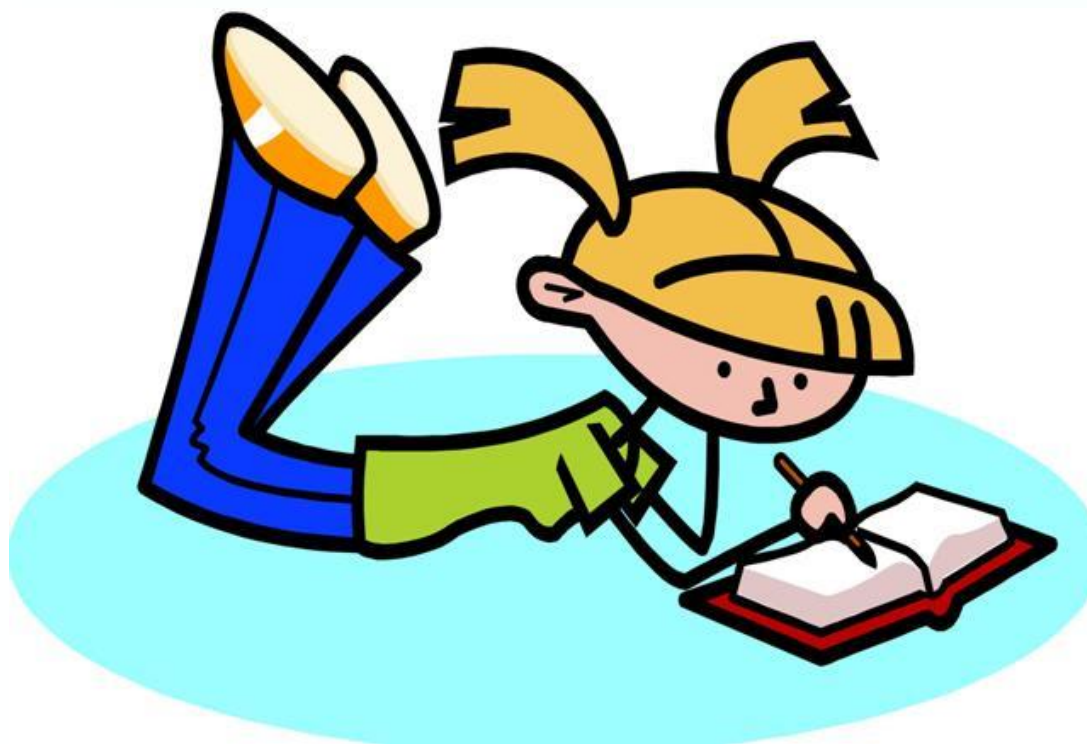6. Electron microscopy

Whole genome sequencing

Spectral karyotyping

Summary

- Clinical history and examination is a must in evaluation of a tumour

- Hematoxylin and eosin stained tissue sections first line of investigation in solid cancers

- Additional newer techniques should be used judiciously

Thank you