LABORATORY DIAGNOSIS OF CANCER

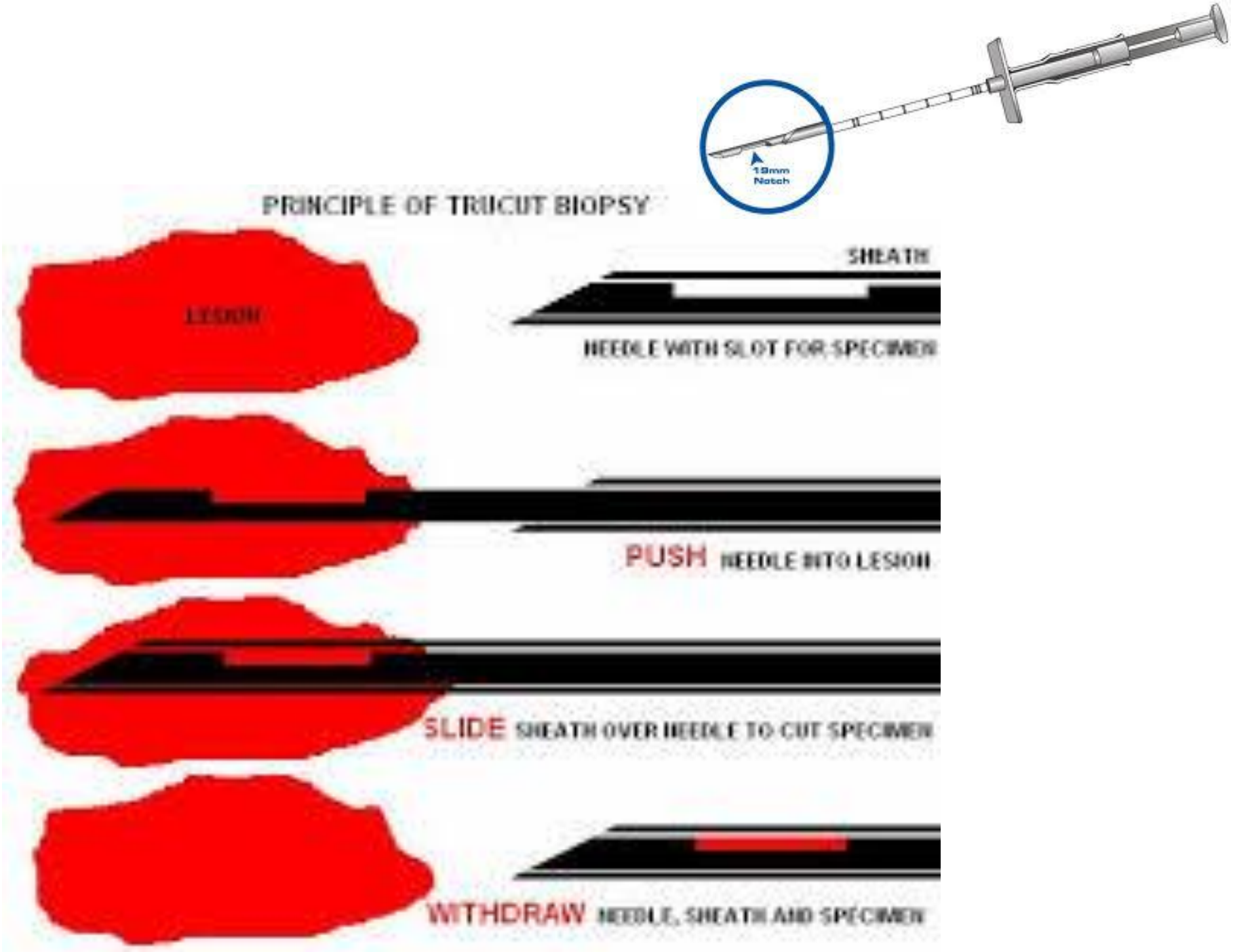
Histologic and Cytologic Methods

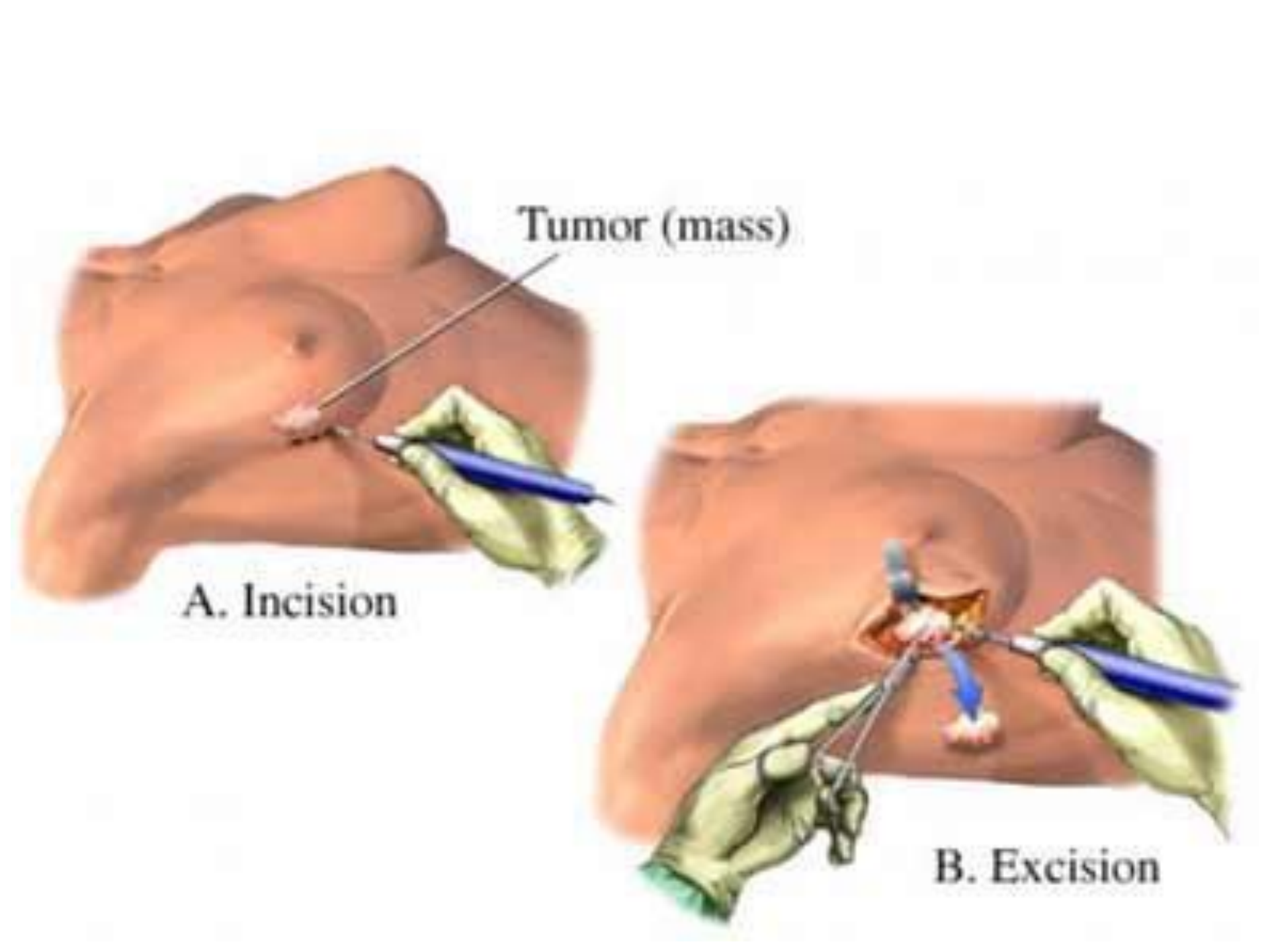
Clinical data

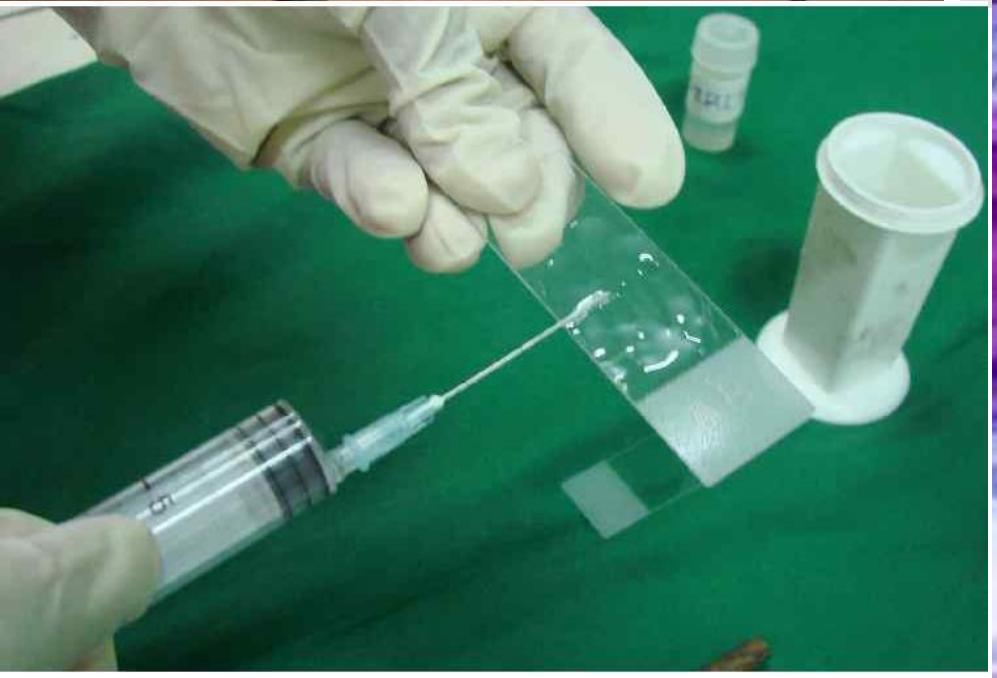
- Radiation changes in the skin or mucosa
- Sections taken from a healing fracture
- Specimen must be adequate, representative, and properly preserved.

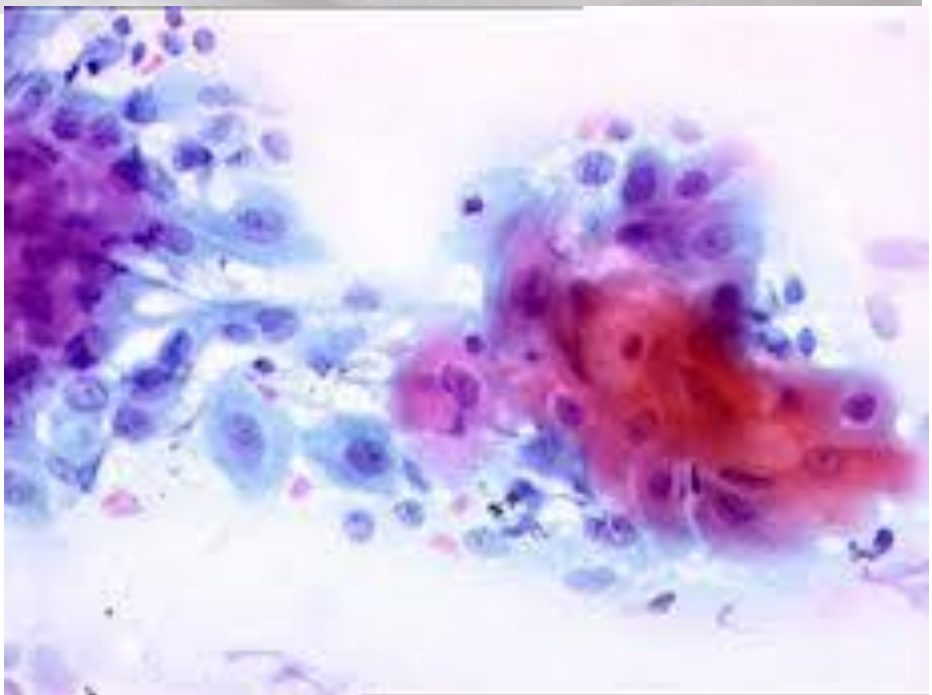
Sampling Approaches

- (1) Excision or biopsy,
- (2) Needle aspiration, and
- (3) Cytologic smears


19mm
Notch
PRINCIPLE OF TRUCUT BIOPSY
LESION
SHEATH
NEEDLE WITH SLOT FOR SPECIMEN
PUSH NEEDLE INTO LESION
SLIDE SHEATH OVER NEEDLE TO CUT SPECIMEN
WITHDRAW NEEDLE, SHEATH AND SPECIMEN

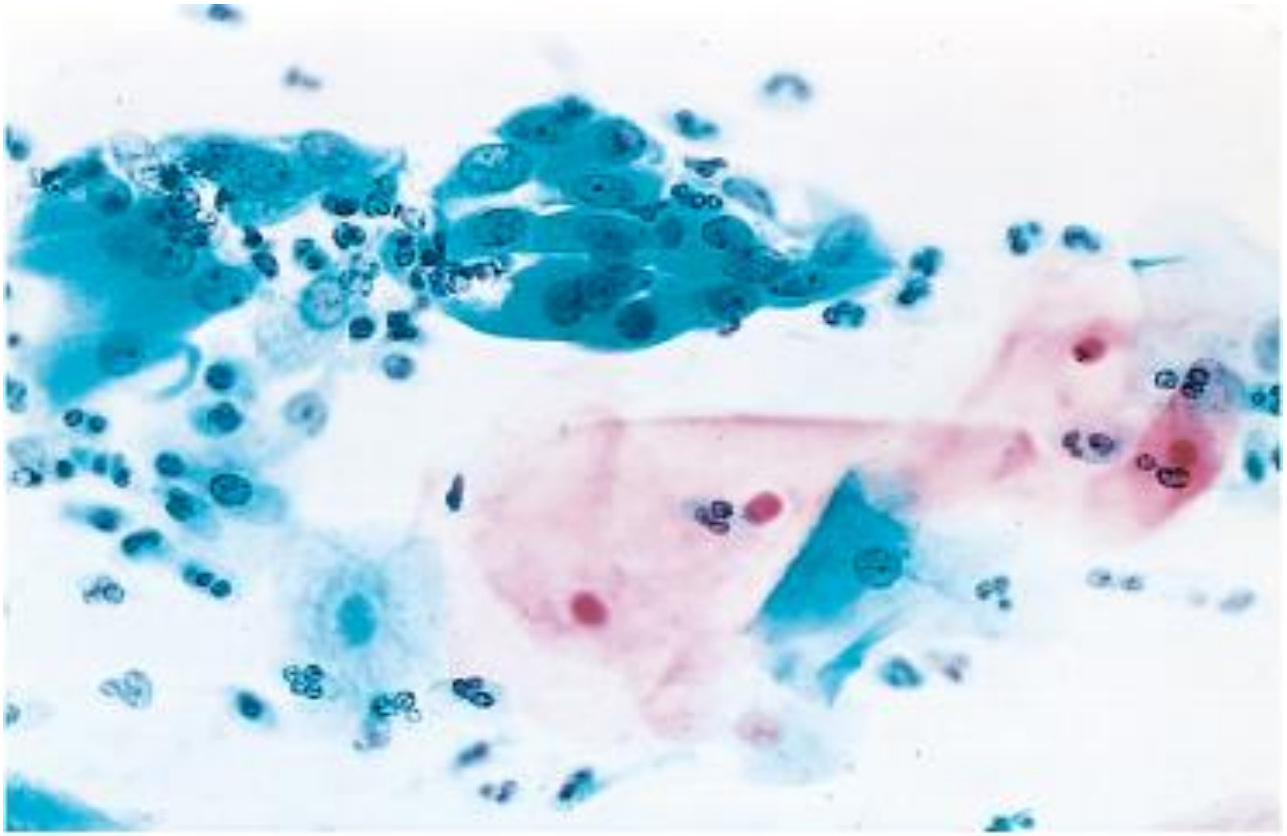

Tumor (mass)
A. Incision
B. Excision



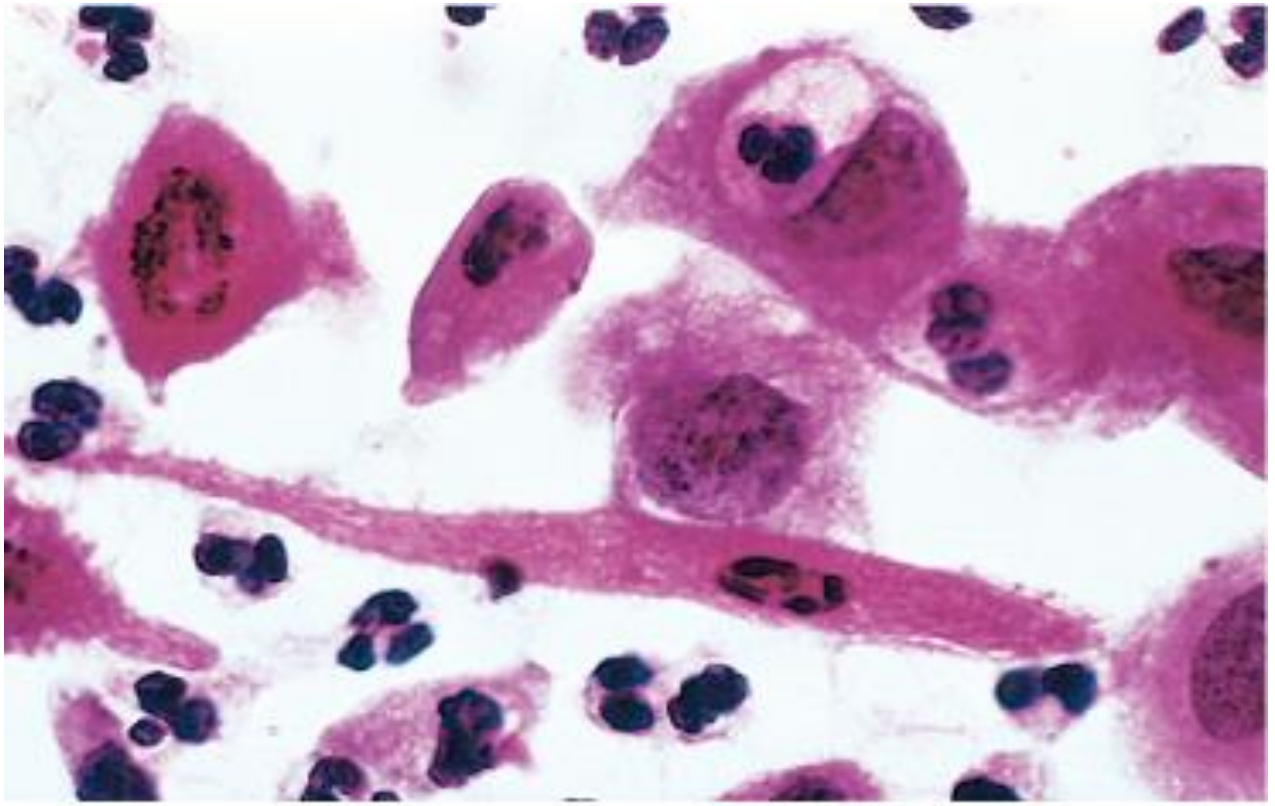


Appropriate preservation of the specimen

- Commonly formalin solution
- Special fixative (Glutaraldehyde) for EM
- Prompt refrigeration to permit optimal hormone, receptor, or other types of molecular analysis
- Quick-frozen section



A normal cervicovaginal smear shows large, flattened squamous cells and groups of metaplastic cells; interspersed are some neutrophils. There are no malignant cells



An abnormal cervicovaginal smear shows numerous malignant cells that have pleomorphic, hyperchromatic nuclei; interspersed are some normal polymorphonuclear leukocyte

Fine-needle aspiration

- Aspirating cells and attendant fluid with a small-bore needle
- Readily palpable lesions in sites
- Modern imaging techniques

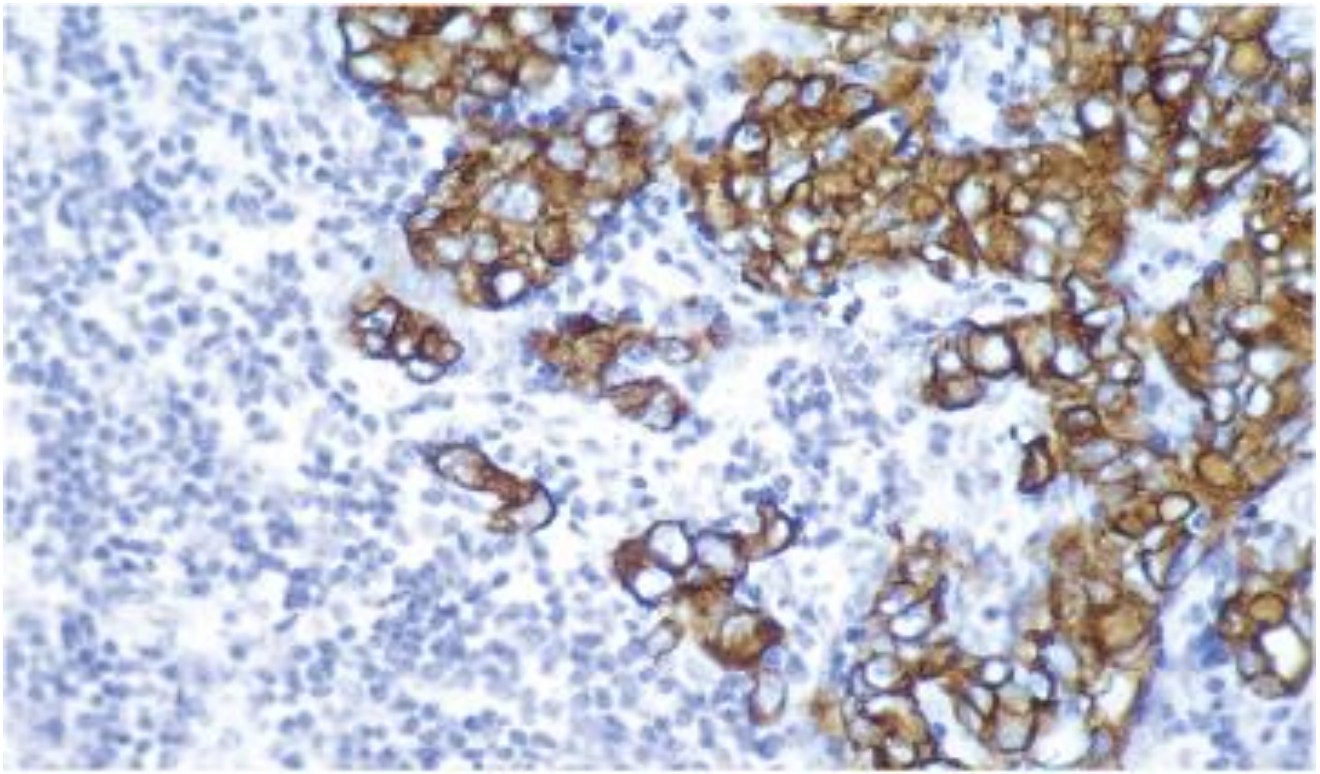
- Exfoliative cytology
- *Cytologic (pap) smears*

Immunohistochemistry

Specific Monoclonal Antibodies : The Identification Of Cell Products Or Surface Markers

- *Categorization of undifferentiated malignant tumors*
- *Categorization of leukemias and lymphomas:*
- *Determination of site of origin of metastatic tumors*
- *Detection of molecules that have prognostic or therapeutic significance*

Anticytokeratin immunoperoxidase stain
of a tumor of epithelial origin (carcinoma)



Flow Cytometry

- Rapidly and quantitatively measure several individual cell characteristics,

- Membrane antigens
- DNA content of tumor cells

- Classification of leukemias and lymphomas
- Flow cytometric detection of PLOIDY

- Aneuploidy seems to be associated with poorer prognosis in early-stage breast cancer, carcinoma of the urinary bladder, lung cancer, colorectal cancer, and prostate cancer.

Molecular diagnosis

- PCR

- FISH

Several molecular techniques—some established, others emerging

- For diagnosis, in some cases,
- for predicting behavior of tumors

Diagnosis of malignant neoplasms:

- Not the primary modality of cancer diagnosis,
- Considerable value in selected cases.

- Molecular techniques are useful in differentiating benign (polyclonal) proliferations of T OR B cells from malignant (monoclonal) proliferations

- Many hematopoietic neoplasms (leukemias and lymphomas) are associated with specific translocations that activate oncogenes.

- Detection of such translocations, usually by routine cytogenetic analysis or by FISH technique is often extremely helpful in diagnosis

PCR,

- Can detect residual disease in cases that appear negative by conventional analysis.

- Diagnosis of sarcomas with characteristic translocations is also aided by molecular techniques, because chromosome preparations are often difficult to obtain from solid tumors.

- Many sarcomas of childhood, **ROUND BLUE CELL TUMORS** can be difficult to distinguish from each other on the basis of morphology.

- The characteristic [t(11;22)(q24;q12)] translocation, established by PCR, in one of these tumors confirms the diagnosis of EWING SARCOMA.

Prognosis of malignant neoplasms:

- Certain genetic alterations are associated with poor prognosis,
- Stratification of patients for therapy
- Amplification of *HER-2/NEU* in breast cancer is an indication that therapy with antibodies against the ERBB2 receptor may be effective.
- These can be detected by routine cytogenetics and also by FISH or PCR assays

Detection of minimal residual disease:

- After treatment of leukemia or lymphoma, the presence of minimal disease or the onset of relapse can be monitored by PCR-based amplification of nucleic acid sequences unique to the malignant clone

- For example, detection of *BCR-ABL* transcripts by PCR gives a measure of the residual leukemia cells in treated patients with CML.

- Specific *KRAS* mutations in stool samples of persons previously treated for colon cancer

Diagnosis of hereditary predisposition to cancer:

- Germ-line mutations in several tumor suppressor genes, including *BRCA1*, *BRCA2*, and the *RET* proto-oncogene, are associated with a high risk of developing specific cancers.

Tumor Markers

Biochemical indicators of the presence of a tumor.

Include

- Cell-surface antigens,
- Cytoplasmic proteins,
- Enzymes, and
- Hormones.
- In clinical practice, refers to a molecule that can be detected in plasma or other body fluids

CEA

- Normally produced in embryonic tissue of the gut, pancreas, and liver
- Complex glycoprotein elaborated by many different neoplasms

positive in

- 60% to 90% of colorectal,
- 50% to 80% of pancreatic, and
- 25% to 50% of gastric and breast carcinomas

CEA assays lack both specificity & sensitivity required for the detection of early cancers

- Preoperative CEA levels have some bearing on prognosis
- In patients with CEA-positive colon cancers, the presence of elevated CEA levels 6 weeks after therapy indicates residual disease.
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- A rising CEA level indicates recurrence,
- With an increase in tumor marker level often preceding clinically detectable disease.
- Serum CEA is also useful in monitoring the treatment of metastatic breast cancer.

AFP

- Glycoprotein
- Early in fetal life by the yolk sac, fetal liver, and fetal GIT
- Abnormal plasma elevations are encountered in adults with cancer arising principally in the liver and germ cells of the testis.
- Less regularly in carcinomas of the colon, lung, and pancreas.

Markers	Associated Cancers
Hormones	
Human chorionic gonadotropin	Trophoblastic tumors, nonseminomatous testicular tumors
Calcitonin	Medullary carcinoma of thyroid
Catecholamine and metabolites	Pheochromocytoma and related tumors
Ectopic hormones	Paraneoplastic Syndromes

Oncofetal Antigens	
α-Fetoprotein	Liver cell cancer, nonseminomatous germ cell tumors of testis
Carcinoembryonic antigen	Carcinomas of the colon, pancreas, lung, stomach, and heart

Isoenzymes	
Prostatic acid phosphatase	Prostate cancer
Neuron-specific enolase	Small cell cancer of lung, neuroblastoma

Specific Proteins	
Immunoglobulins	Multiple myeloma and other gammopathies
Prostate-specific antigen and prostate-specific membrane antigen	Prostate cancer

Mucins and Other Glycoproteins	
CA-125	Ovarian cancer
CA-19-9	Colon cancer, pancreatic cancer
CA-15-3	Breast cancer

New Molecular Markers

***p53, APC, RAS* mutations in stool and serum**	**Colon cancer**
p53 and *RAS* mutations in stool and serum	Pancreatic cancer
p53 and *RAS* mutations in sputum and serum	Lung cancer
p53 mutations in urine	Bladder cancer