International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

Diagnostic Techniques of Cancer

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Date of Submission: 15-10-2020 Date of Acceptance: 05-11-2020

INTRODUCTION:

Cancer is a leading cause of death group worldwide and accounted for 7.4 million deaths (around 13% of all deaths) in 2004.Cancer is a 2nd most death causing disease in the world wide after the heart disease. Cancer is also known as malignancy, malignant neoplasm. Cancer might regarded as

- Abnormal and uncontrolled cell growth.
- Has ability to invade the other lymph nodes and into the distant organs.
- Progression of the tumours leads to the mortality of the patients.

Major categories of the cancer are:

1. Carcinoma: Common type of cancer .It originates from the epithelial cells which lines he inner and outer surfaces of the body.
2. Sarcoma: It begins in the connective tissues like muscles, bone.
3. Lymphoma, myeloma and leukaemia: Arising from the immune system and bone marrow.

Some types of cancer cause rapid cell growth, while the others cause cells to grow and divide at slower rate. Certain forms of cancer results in visible growths called tumours, while others, such as leukemia, do not.

Most of the body`s cells have respective specific functions and fixed lifespan. It seems bad thing .But the cell death is a part of the natural process and the phenomenon is known as apoptosis. Cells receive the instructions to die so that the body can replaces it with the newer cell that function better. Cancerous cells lack the components that instruct them to stop dividing and then to stop dividing and to die as a result the cancerous cells can form tumours, impair the immune system and cause other changes that prevent the body from functioning normally. Usually cancerous cells firstly appear one localized area of the body and it eventually spread to the other parts of the parts of the body and become malignant.

Two main classifications of the tumours are:

1. Benign - the tumour is extent to only certain localized area
2. Malignant -the tumour that may invade its surrounding cells, tissues or spread to the nodes around the body.

Benign tumours grow very slowly, while the malignant tumours grow very quickly in size that is just in a few weeks. But not all the tumours are malignant or cancerous and not all are more aggressive. Sometimes the benign tumours are painful and dangerous and but not much as aggressive as malignant.

BENIGN TUMOURS DO NOT GENERALLY INVADE .BUT THEY ACTUALLY PUSH THE NORMAL TISSUE TO THE SIDE.

Tumours grow due to malfunctioning in the cells of the DNA, mainly in the genes like p53 gene which control the growth of the cells .If the apoptosis is altered the cells gets confused when it's time to die and persists. Because of it develops the ability to proliferate, abnormal continuous cells growth happens and tumours are formed which grow rapidly. Some of the mutations lead to rapid growth of the tumours.

The prevention and controlling of malignant tumours required early detection, mainly depending on the histological examination as a first step in the diagnosis.

GRADING AND STAGING:

Grading and staging of cancer are the two historically used ways in the diagnosis of cancer and which helps in the detection of the tumour behaviour and malignant tumour.

GRADING:

Grading is done based on the features like degree of anaplasia (loss of mature and characteristics features of the cell, tissue)and rate of the growth and it was characterized as

- GRADE -1 : Well differentiated (about less than 25% anaplasia cells)

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

- GRADE-2 : Moderately differentiated (about 25 -50% anaplasia cells)
- GRADE-3: Moderately differentiated (about 50 –75% anaplasia cells)
- GARDE-4:Poorly differentiated (about more than 75% anaplasia cells)

Many pathologists giving the grading in the terms like differentiated, well differentiated, undifferentiated, keratinising and non-keratinising.

STAGING:

TNM Staging is the most widely used method in the cancer reporting.

- T – Extent of primary tumour
- N – Invasive of primary tumour into the lymph nodes .Counting of the number near the lymph nodes that have the tumour cells which are invaded.
- M – Refers to whether the cancer has metastasized (from primary tumour to the other parts of the body).

PRIMARY TUMOUR (T) :

1. TX- Main tumour cannot be measured
2. T0 –Main tumour cannot be found
3. T1, T2, T3, T4 - Refers to the size and extent of the main tumour and location.

As the higher the number after the T1 the larger the tumour or the more it is extent to the nearby tissues or deeper into the organ.

REGINAL LYMPH NODES (N):

NX – Cannot be measured in the nodal region.

1. NO – No tumour extension to the lymph nodes.
2. N1, N2, N3: Refers to the number and location of lymph nodes that contain cancer.
3. N3 – means spread to the lymph nodes.

Higher the number, more lymph nodes contains tumour cells.

DISTANT METASTASIS (M):

1. MX –Metastasis cannot be measured.
2. M0 –No extension of tumour cell to the other parts of the body.
3. M1 – metastasis is spread to the other parts of the body.

Main factors in TNM Staging are:

- Size of the tumour cells.

Type of the tissue involved, whether tumour is a localized spread or generalized spread.

Grading and staging of the cancer helps the doctors and patients to understand how serious the condition was and form a treatment plan. The grading describes the appearance of the cancerous cells. Once the staging was assigned, it never changes, even after the treatment. For instance stage-1 cervical cancer is treated, it will remain a stage -1 cervical cancer even if it recurrent after few years or later and has metastasized to the lung however,it is possible for some type of cancers to restaged. Staging helps in the treatment plan for the care takers to determine the appropriate treatment and provide the prognosis.

Cancer that is diagnosed at an early stage (stage 1 or 2) ,before it has spread that had the chance to get too big or has spread to the other areas of the body is more likely to thebe treated successfully ,if the cancer is late stage (stage3 or 4) and has spread into the surrounding tissue or to the other organs than its more difficult to treat and the chances of survival are much lower. Any cancer is diagnosed late due to:

- When the patient fails to recognise the symptoms of cancer
- Poor public awareness on early symptoms of the cancer is considered to be the predominant reason in the late detection of the cancer.
- If the Screening tests are suggested but sometimes they show false positive test results are possible.

False positive tests results may leads to the progression of the benign tumour to a malignant tumour.

So early detection and standard diagnosis of the cancer plays a key role in the controlling the tumour progression and form a treatment plan.

Over the past few decades the most and standard technique is histological examination of the tissue biopsy is used for the confirmation of the cancer.

Currently available and widely used techniques all over the world wide are:

1. Histological methods
2. Cytological methods
3. Histochemistry and Cytochemistry
4. Immunohistochemistry
5. Electron microscopy
6. Tumour markers: level of the tumour marker can contributes to the prognostic factor.

DIAGNOSIS TECHNIQUES OF THE CANCER

Establishing a diagnosis of cancer begins with a thorough history and physical examination of the patient. Few times where the diagnosis of malignancy is made in the absence of pathological confirmation, particularly as diagnostic procedure

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

have become less invasive over the past few decades .

The most standard and reliable methods in diagnosis of cancer and confirmation stood from the past decades to now is histological examination of tissue biopsy.

Grading and staging are the two widely used applications to determine the prognosis and choice of treatment after the malignant tumour is detected.

SCREENING TETS:

A screening test that works the way it should and it helps in:

- Early detection of cancer
- Easier to treat early

Screening test usually do not diagnose and confirm the cancer , because screening tests has results in the false positive and false negative possibilities.

False positive results :

Screening tests results may appear to be normal even though there is no cancer, it mean a positive test result.

False negative tests results:

Screening tests results may appear to be normal even though there is a cancer, it means a false positive test results.

The cause for these possibilities might be the machines give false reading.

Screening tests should be suggested for people who have cancer risk factors and it doesn't means that not having the high risk factors that you may not get the cancer.

People known to have high risk of cancer than others include:

- Personal history of malignancy
- Family history
- Reliable gene mutations which lead to the development of malignancy
- Exposure to the carcinogenic agents such as tobacco, smoke, or occupational chemicals.
- Exposure the high radiations mainly the gamma radiations.
- Repeated exposures to the x-rays may sometimes leads to the cancer.

Different methods of screening tests:

1. PHYSICAL EXAMINATION:

A procedure of body examination of checking the general signs of the heath issues, including lumps and any unusual findings.

2. LABORATORY TETS :

Laboratory tests are the tests that collect the samples of tissues, blood, urine, serum or other substances in the body to check out the abnormality levels of the body.

3. IMAGING PROCEDURES :

- Before performing the histological and cytological procedures the imaging procedures play a role in spotting the abnormal area in the body.
- Imaging procedures are non-invasive procedures include the X-rays, CT scan (computerized tomography), MRI –magnetic resonance imaging ,spinal x-rays ,chest x-rays.

4. GENETIC TESTS :

- Provide information on the analysis of changes in the genes and chromosomes.
- Genetic tests performed on samples on the blood, hair, saliva amniotic fluid.

➢ Screening tests are not meant for cancer confirmation. If a screening test results are abnormal, other diagnostic techniques are suggested to find the specific reason for the abnormality. Ex: A screening test mammography find lump in the breast , but more other tests are suggested by the physicians to check out whether it is lump or tumour , other diagnostic tests include tissue biopsy in which the removal of the cells or tissue for the examination by the pathologists.

➢ Two procedures of the biopsy:

1. Biopsy :

Incisional biopsy: sample of tissue is removed.

Excisional biopsy: an entire lump and suspicious area is removed.

2. Fine needle biopsy:

Sample of the tissue smear or fluid is removed from the needle followed by the sectioning, observing and evaluation of optical images.

✓ Needle used is wide one during the biopsy – core biopsy.

✓ Needle used is thin during the biopsy – fine needle aspiration biopsy.

The prevention and controlling of malignancy tumour required early detection, mainly depending on the histological examination as a primary step in the diagnosis.

1. HISTOLOGICAL METHODS:

There are many methods in diagnosis of cancer with more benefits in technologies in order to understand type of the cancer much better.

Several number of diagnosis tools which helps in the cancer detection .The histological

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

methods mainly performed under the experienced pathologists and oncopathologists.
Most of the cancers needs a confirmation of type or staging and form a certain treatment plan.

Histology studies related to the microscopically study of the anatomy of cells and tissues of the organs. It is performed by examination of a slice of a tissue under a fluorescent light and images are analysed.Histopathologies examine the regularities of cell shape and tissue progression to known the tissue is in the benign or malignant exclusively in the histological diagnosis is mainly effective in the cancer category of carcinoma.

As we know that carcinoma rises from the epithelial cells. Carcinoma cancer such as prostate cancer, breast cancer, cervix cancer, lung cancer and other cancers related to the epithelial cells.
Histological diagnosis involves in the removal of the tissue is called biopsy and the biopsy can be performed by the three methods:

Endoscopy

- Needle biopsy
- Surgical biopsy

Biopsy often needed to confirm a cancer diagnosis. Biopsies also be needed to find out a lump felt on the exam of something seen on an imaging test in another part of the body is really from the spread of cancer. During the biopsy, the doctor removes the tumour or pieces of the tumour to be investigated in the laboratory.
Some of the biopsies are done during the surgery .But biopsies can also be done using a thin, hollow needle or through an endoscope.

ENDOSCOPY:

Endoscopy can also helps in indentifying the inflammation, ulcers and tumours. Endoscopy is more accurate than the X-rays for detecting the abnormal growths such as cancers and for examining the inside of the gastro-intestine system. In addition, abnormalities can be treated through the endoscopy.

This test examines the oesophagus and stomach using a thin, lighted tube called an endoscope, which is passed through the mouth to the stomach. Through the endoscope, the doctor can look directly inside the gastro- intestine tract. If an abnormal area is found, the doctor will remove some tissue to be examined under a microscope (called as biopsy).A biopsy is the only one the reliable way to detect the cancer.

Biopsy and the endoscopy are the best ways to found out the stomach cancer.

NEEDLE BIOPSY:

During the needle biopsy, doctors use the special needle called Fine gauge needle, to extract the cells from a suspicious area. A needle biopsy is performed to detect the non-cancerous and malignant tumours, infections, lumps of breasts.
The needle biopsy can determines the
A mass or lump – A needle biopsy may reveal
NEEDLE BIOPSY PROCEDURES INCLUDE:

- The whether a mass or lump is a cyst, an infection a benign tumour or cancer.
- An infection
- Inflammation

Before the examination with the needle biopsy if the imaging tests are done it is useful for the detection of the suspicious area for the needle biopsy where should be spot the area.
Needle biopsy includes:

1. FINE NEEDLE ASPIRATION: During the fine needle aspiration, a long needle gauge is inserted into the suspicious area .A syringe used to draw out the fluid and cells for analysis.
2. CORE NEEDLE BIOPSY: A fine larger needle is inserted into the suspicious area and the syringe draws out the columns of tissues.
3. IMAGING GUIDED BIOPSY: It combines with the imaging procedures like X-rays, Computerized tomography (CT), magnetic resonance imaging (MRI) with a needle biopsy.

SURGICAL BIOPSY:

If the cells can't be assessed with biopsy the doctor suggests the surgical biopsy.

During the surgical biopsy, a surgeon makes an incision in your skin to access the suspicious area of cells. For instance, the surgical procedures are used to remove the breast lumps for a possible breasts cancer diagnosis and surgery to remove a lymph node for a possible lymphoma diagnosis.

Histology analysis:

Tissue processing:

1. After collecting the tissues through the needle biopsy procedure the tissues are fixed by the fixatives by precipitate fixative like ethanol, acetone, and chloroform.
2. Fixed tissue samples are dehydrated by the removing the lipids and reducing the solubility of the proteins.

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

3. The fixed sample tissues are frozen or embedded in a solid mould.
4. Those frozen samples are sectioned into thin slices for the microscopical examination.
5. The fixed tissues and embed with a stable medium such as paraffin wax, plastic resin.
6. After the sectioning into thin slices of tissues, it is placed on a slide.
7. The transparent sections are floated in warm water or smooth out any wrinkles
8. Then they are ready for the staining ,they are placed on a glass slide variety of dyes such as haematoxylin stains the cells dark blue and eosin stains the cells in varying shades of the pink.

Histology imaging technologies:

After the completion of the tissue processing the, light and electron microscopes, equipped with a variety of imaging technologies are used to take the digital histology images on the stained tissue techniques.

- Light microscopy: It is most commonly used technology helps to identify the tissue structures by using the visible light.
- Fluorescence microscopy: In the fluorescence microscopy, acridine orange stain is used which is very sensitive stain .The stain intercalate with nucleic acids, and changing the optical characteristics of the stain which is bright orange colour when viewed under the electron microscopy if the malignant cells are stained.
- Electron microscopy: This technique involves in obtaining the high –resolution images of the biological and non-biological specimens .In the electron microscopy the electrons are used for radiation through the cells and results in the complete information on the structural basis of the cell function.

There are the two main electron microscopy:

1. Transmission electron microscopy (TEM)
2. Scanning electron microscopy (SEM)

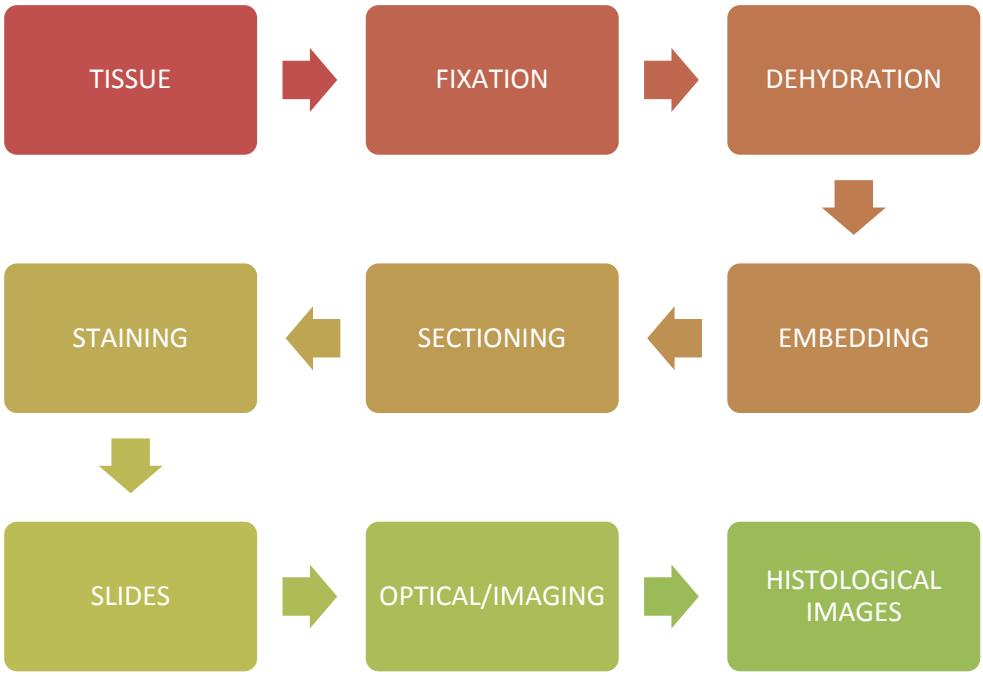

Fig 1.1 histological procedure – tissue processing and histological images.

2.CYTOLOGICAL METHODS :

Cytological technique is the analysis of the cell from the body a microscope .This test usually to find out the cancers and pre-cancerous changes, and it also used to look for the viral infections in the cells.

Cytopathology is cost effective, quick and sample, accurate and complications of the complications are very uncommon, if they are occurred that could be relatively mild. In accordance with the imaging techniques, the fine needle aspiration evaluation is done at the spot .Pain and patient discomfort is very

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

mild and can be prevented and tolerated by local anathesia, if necessary. Infections are very rare due to the test under sterile conditions.

The advantages of the cytological methods:

- Simple: Almost all the health care providers are well-known to the cytological techniques and the procedure was very simple to perform by the pathologist.
- Quick: The procedure can be done within in the 24-28 hours.
- Cost effective

Branches of the cytology:

i. Exfoliate cytology:

- Gynaecological samples: In the exfoliate cytology the Pap smear /papanicolous smear are the first samples to examine.
- Discharge cytology: nipple discharge is the one of the clinical manifestation of the breast tumour, breast lump and malignancy .During the category nipple discharge is used as the screening method for detection of the mammary carcinoma.
- Respiratory samples: Includes sputum, bronchial brushing cytology. Commonly used for the detection of the pulmonary malignancies and infections.
- Body –fluid cytology: pleural fluid, pericardial fluid, peritoneal fluid, and cerebrospinal fluid (CSF) cytology to detect the malignancies and infections.
- Gastrointestinal tract cytology: mucosal smears collection is the routine procedure during the endoscopy and to detect the lesions of neoplasia cells, viral and fungal infections.
- Scrape cytology: skin smears are common samples in the scrape cytology.Dectection of the cancer cells at any surface can be quick and accurate.
- Urinary cytology :predictive anaplastic lymphoma kinase gene (ALK).rearrangements.

In the urinary tract cytology, atypical urothelial cells are the equivocal for the malignancy cells .FISH is the valuable objective for the ancillary diagnosis (supplementary diagnosis). Fluorescence insitu hybridisation is the morphology based technique and reliable FISH result in a targeted evaluation of the cells in question (cancer /atypical cells).

ii. Fine needle aspiration cytology:

Fine needle aspiration cytology (FNAC) is a quick, simple, pain free and cost effective .It is widely used method to investigate the lymphoadenopathy. It is the first line technique with differential diagnosis.

- This technique is the based on the fact that the tumour cells are cohesive and are easily aspirated.
- Used in the diagnosis of the breast lumps, thyroid nodules, liver disease, subcutaneous soft tissue.

During the FNAC , a thin small needle is inserted into the lump to remove the cells that are then examined under the microscope to make a diagnosis. Ultrasound examination is suggested to find out the spot of the lump for the perfect incision of needle to draw out the cells

During the collection of the mucosal sample from the oral cavity and that biopsy is called open biopsy. During the open biopsy it leads to the lot of bleeding which is difficult to control.

ADVANTAGES	DISADVANTAGES
Simple technique.	**Loss of architecture of tissue.**
Quick procedure within the 24-28 hours.	**Possibility of false negative and false positive results.**
Cost effective.	**Specific training is needed for the accurate interpretation.**
Painless, no anaesthesia .	**Experience is necessary for the interpretation.**
Accurate.	**Definitive diagnosis is not always possible.**
Small size of needle avoids damages on the head and neck.	**Difficult to differentiate the non-invasive and invasive cancers.**

Fine needle aspiration cytology:

Two procedures are:

1. Fine needle aspiration cytology with aspiration.
2. Fine needle aspiration without aspiration.

Procedure of FNAC with aspiration:

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

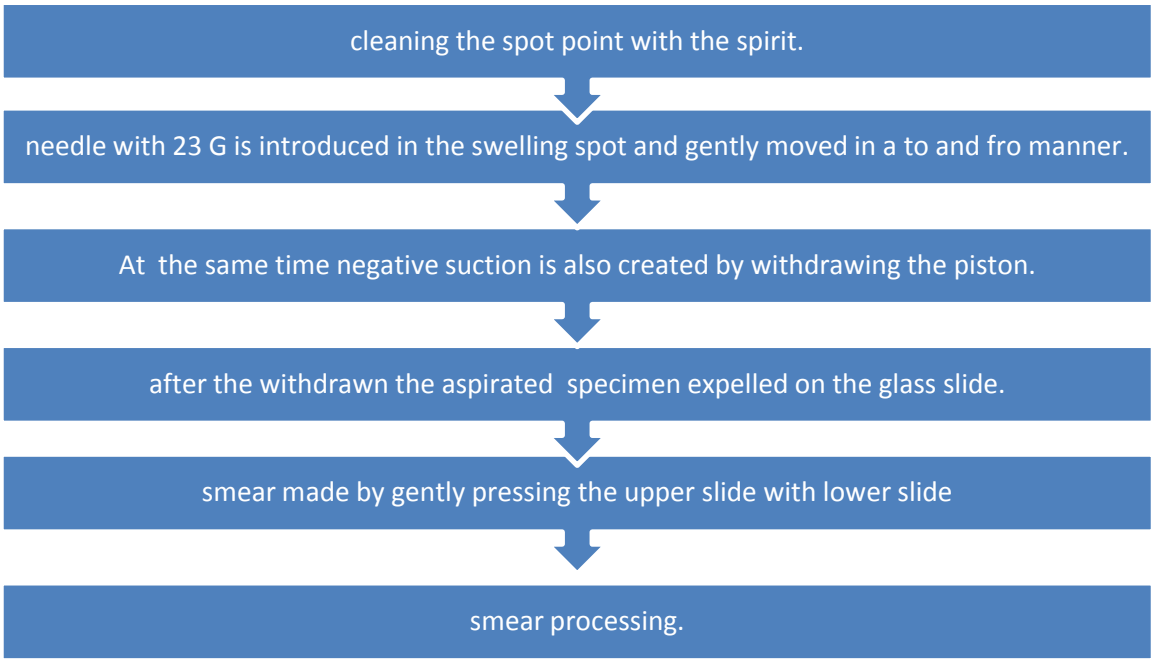

Fig 2.1 fine needle aspiration cytology with aspiration procedure

Procedure of FNAC without aspiration:

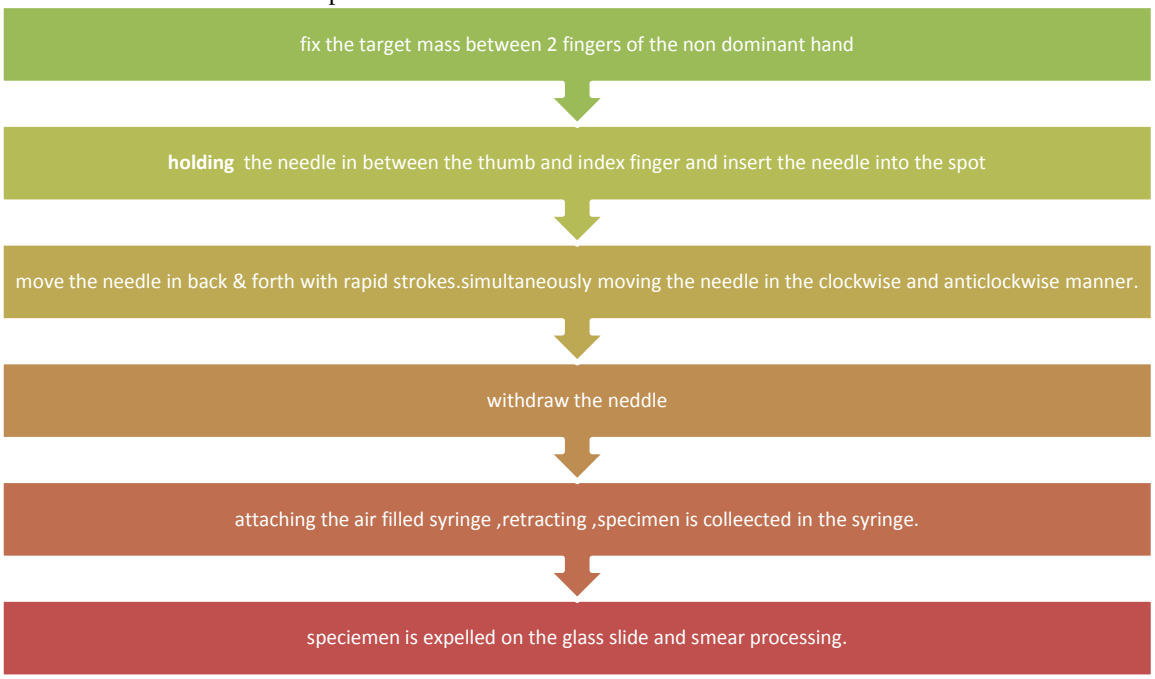

Fig 2.2 Fine needle aspiration cytology procedure without aspiration

Smear processing –

- Smear is expelled on the glass slide by using the air in the syringe.

1. DIRECT - dry and wet

Dry -smear with numerous cells and suspended in tissue fluid .
Wet -smear with smaller number of cells in fluid or blood .

2. Indirect –

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

Thin fluid samples with processed by centrifugation.

- Fixation and staining :

Two methods of fixation are –
Air drying followed by staining with a haematological stain such as MAY GRUNWALDGIEMSA STAIN, Jenner-Giesma, and Diff-Quick.
Alcohol fixation and staining according to PAP / H&E.

- **Papanicolaou stain :**

It contains Harris's haematoxylin, orange G6, EA 50 and results are nuclei with blue/black, cytoplasm with blue/green.

- **Romanowsky stain:**

The contents present in it are -Methylene blue /azure B and eosin, dissolved in acetone –free methanol, include Jenner,Giesma, May Grunewald and Lesihman stain.
Results are nuclei –purple/blue, cytoplasm – pink/blue, esionophils –pink and red.

- MAY GRUNWALD –GIESMA STAIN :

Commonly used for staining of blood smears.
The contents present in it are ethylene blue, azure are both basic dyes and eosin is an acid dye.
Results are the nuclei of the white blood cells and granules of basophiles granulocytes –blue, red blood cells and esinophils –red, cytoplasm of WBC –light blue.
These are some of the stains used in the procedure of the fine needle aspiration technique.

3. HISTOCHEMISTRY AND CYTOCHEMISTRY:

Histochemistry and cytochemistry are the other diagnostic tools of cancer .They used in the study of visualization of biological structures of the cells .The techniques are involved in the study of the chemical compositions of the cells, their constituents and their products by special staining techniques.

Name of the **Staining procedure**	**Detection**
Lipids staining	Lipid staining showing the normal distribution of the lipids in the cell. Stains include- • ORO (oil red O) solution, glycerine jelly mounting medium. • Nuclei –blue • Lipid – red colour
Feulgen's reaction	Stains used are methyl green pyronin and acridine orange Staining nucleic acids in the cells.
Periodic Acid –Schiff (PAS)	Detects the saccharides mainly glycogen. Stains used are lithium, ruthenium red and Alcan blue.
Milton's reagent	Used for the detection of the amino acid tyrosine Components are mercuric nitrate and mercurous If the smear is stained with the Milton's reagent it turns red in colour do to the presence of the tyrosine .

Fig 3.1 histochemistry and cytochemistry staining techniques.

4. IMMUNO HISTOCHEMISTRY (IHC) :

- The theory of immunohistochemistry is to spot out the antigens present in the tissue smears by the use of the labelled antibodies as specific reagents through the antigen and antibody interactions that are visualized by a marker such as the fluorescent dye, enzymes, radioactive elements or colloidal gold.
- In the IHC the tissue smears are fixed by the paraffin .The antigen and antibody complex is visualized microscopically under the fluorescent dyes.
- Utilization of the monoclonal and polyclonal antibodies localizes the antigens in the tissue smear.
- Using the specific tumor markers ,physicians use the IHC to diagnose the cancer as benign

Well as malignant and determining the stage and grade of the tumour and helps in identifying the cell type and origin of a metastasis to find out the site of the primary tumour

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

Iummunohistochemical markers are polyclonal and monoclonal antibodies are used to identify the proteins in the tissues .The antibodies binds to the specific proteins that are being accessed by the colour reagent stain, in fact, if the protein which is expressed by the tumour. The proteins that are identified are helps in the differentiation of the tumour and help us in render diagnosis.

Prediction of the proteins of often required for tumours that cant readily classified on the routine sections.

1. CYTOKERATINS – which are molecules expressed by the carcinomas and adrenocarcinomas.
2. VIMENTIN – it is an intermediate for the connective tissue tumours and melanomas.
3. LCA or LEUKOCYTE COMMON ANTIGEN – it is an antigen in the lymphomas and leukaemia's.
4. CD20 – This is a protein on the B-lymphocytes.
5. CD3 – which is protein found on the T-lymphocytes.
6. CD34 – which are expressed on the vascular tissue and by the angiomas and angiosarcomas and some types of fibroblastic neoplasm's.
7. SMA or SMOOTH MUSCLE ACTIN – stains the actin filaments in the smooth muscle cells and myofibroblastic, myoepithelial cell tumours expresses these types of the filaments.
8. DESMIN – which protein muscle marker.
9. S-100 – which is an intermediate filament that stains the neural cells as well as other cells types such as cartilage .melanocytic lesions are express these markers.
10. HMB -45 – some types of the melanomas, but not all.

- IHC methods give out the approaches to diagnose the tumour s uncertain origin, benign as well as metastatic from unknown primary tumor.
- Immuohistochemical stains for intermediate filaments which are expressed by the tumour cells (keratin, glial fibillary acidic proteins, and neurofilaments).
- IHC widely used to predict the therapeutic activity in two important tumours are carcinoma of breast and prostate. These tumours are under growth regulation hormones are located on respective tumour cells .These are basically from the endogenous hormones perspective tumours shows the high level receptor positivity.
- To lower their levels hormonal therapy is suggested such as oestrogen therapy for the prostate cancer and androgen therapy for breast cancer.

5. TUMOR MARKERS:

A substance produced by a tumour or by the host in response to the tumours presence and can be detected in the blood, body fluids or tissue of the host.

Ideal tumor marker:

- Highly selective and highly specific.
- Accurate differentiating between the healthy individuals and patients.
- Detectable neoplastic and non –neoplastic diseases.
- Detectable at early stage of tumor.
- Cost effective.

But every tumour marker is not a ideal marker.

Tumour markers are not the key diagnostic tool, but can be a supplementary to the other diagnostic techniques.

Most of the tumour marker levels alone are often the standard tool of investigation

- Levels can be elevated in benign situations.
- Levels are not elevated in the every person with cancer
- The level of the tumour marker can be elevated more than one type of the cancer.

Tumour markers play a limited role in the tumour screening, because of low sensitivity & lack of specifity.

For example:

- Alfa feto protein (APF) in the liver cancer.
- Prostate specific antigen (PSA) for prostate cancer.

- Level of the certain tumour marker can contributes as prognostic factor.

E.g.:

High PSA reflects the high grade of the tumour progression.

The serum levels of the tumour marker reflect the success of the treatment.

Even after the surgery the elevated remains the same that indicates the incomplete removal of the tumour, recurrent or the presence of the metastasis.

Examples:

- PROSTATE CANCER :

Prostate specific antigen (PSA) is commonly used to detect the prostate cancer at the early stage.

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

Levels above the 4ng/ml suggest the cancer where as levels above 10ng/ml indicates the cancer presence.
A subsequent rise in the PSA after the treatment could indicate the relapse.

- Colorectal cancer CEA CA 19-9

Carcinoma embryonic antigen (CEA) should return to normal levels in about the 4 to 6 weeks of the treatment.

- OVARIAN CANCER :

In the ovarian cancers the APF levels are rise in the levels.

HORMONES	
Human chorionic gonadotrophin	Trophoblastic tumours
Calcitonin	Medullary carcinoma of thyroid
Catecholamine metabolites	Phechromocytoma and related tumours
ONCO -FETAL ANTIGENS	
Alfa- feto protein (AFP)	Liver cancer, germ cells of testis related cancers.
Carcino-embryonic antigen(CEA)	Colo-rectal cancers
ISOENZYMES	
Prostatic acid phosphotase (PAP)	Prostate cancer
neuron-specific enolase	Pulmonary related cancers and neuroblastoma
SPECIFIC PROTIENS	
Immunoglobulin's	Multiple myelomas
Prostate specific antigen (PSA)	Prostate cancer
MUCINS AND OTHER GLYCOPROTEINS	
CA -125 (cancer antigen)	Ovarian cancer
CA-19-9	Colon cancer and pancreatic cancer
CA-15-3	Breast cancer
NEW MOLECULAR MARKERS	
APC ,p53,RAS mutants in stool and serum	Colon cancer
RAS and p53 mutants in stool and serum	Pancreatic cancer
RAS and p53 mutants in sputum and serum	Lung cancer
P53 mutants in urine	Bladder cancer

Fig 5.1 Selected Tumour Markers

6 OTHER DIAGNOSTIC TECHNIQUES:

FLOW CYTOMETRY:

Flow cytometry measures the count of the cells, percentage of the living cells, morphology of the cells through the samples of the blood, tissue fluids, bone marrow. The technology involves in the study of the tumour cell progression.

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 321-332 www.ijprajournal.com ISSN: 2249-7781

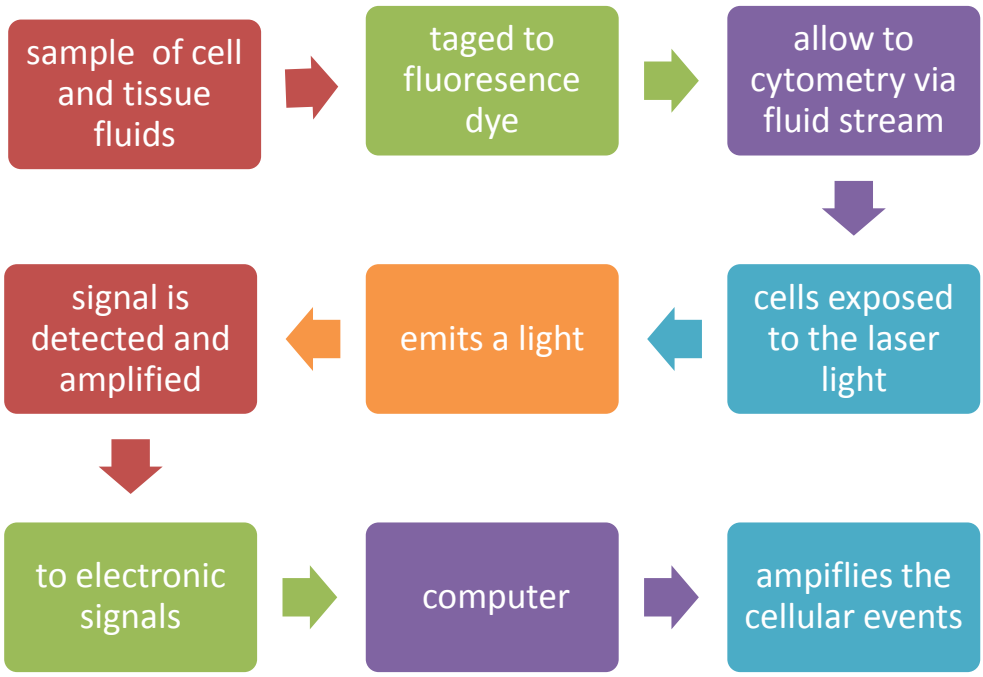

Fig 6.1 flow cytometry procedure and analysis of the cellular events.

Here, due to the presence of the fluorescence probe so cells emits the light when exposed to the laser light.

OVERVIEW:

- Histological image analysis differs from radiology images in having the larger amounts of the interests like (cell morphology, cell boundaries, nuclei & stroma around the cells).
- While, the radiology techniques provides information on the image analysis of the organs.
- A histology image is usually size (~10^9 pixels) much larger than radiology images (~10^5pixels).

On the other hand cytological studies shows the intracellular cell structure but the histology complexity reveals not only the tissue boundaries ,type of overlapping tissues around ,structure of the cells, abnormalities in the morphology of the cell and tissues.

PARTICULARS	TISSUE BIOPSY	FNAC
1. **SAMPLE REQUIRED**	TISSUES	CELLS
2. **COST**	EXPENSIVE	NOT MUCH EXPENSIVE
3. **ERRORS**	RARELY	POSSIBLE
4. **SCARS**	ALWAYS	NEVER
5. **ANASTHESIA**	SOMETIMES NECESARY	NOT MUCH NECESSARY

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