

# Role of Cytology in Modern Medicine

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Cytology or Cytopathology is morphological study of cells. By the definition it has to be microscopic as cells can't be visualized by naked eye examination. The cells are structural and functional units of our body. The diseases start at cellular level and usually impart some cellular morphological alterations. Proper recognition of these findings leads us to the correct diagnosis of the disease. Cytology is the morphological study of the cells. Peripheral smears and bone marrow aspirates are also examples of cytology and the same is true for gram and Ziehl-Neelsen stain for Acid Fast bacilli. Cerebrospinal fluid (CSF) examination is another form of cytology. In a way we are all used to cytology. Various cytological examinations had been tried for years<sup>1-4</sup>; however the new era of cytology ushered by Papniacolaou's introduction of cervical smear cytology to detect various stages of dysplasia and carcinoma<sup>5</sup>.

Cytology is one of the most fascinating disciplines of pathology. It has remarkable swiftness, grace, humane and simplicity on one hand and tremendous usefulness on the other hand. It saves patients, relatives and the treating physicians from unnecessary, delayed, painful, traumatic and costly procedures. Cytology usually causes no pain and no fuss. Collecting samples of sputum, urine and cervical smears are totally painless. Touch cytology of the removed specimen of course does not cause any additional pain. Fine Needles Aspiration Cytology (FNAC) is remarkable as it can avoid many unnecessary surgeries. Needle albeit painful is far more acceptable than a knife!

And where knife can't reach this majestic fine needle can reach with ease and poise. It fetches out the precious pearls of diagnostic material from liquid as well as from solid organs. Closed cavities e.g. pleural, peritoneal and peri-spinal cord spaces can be penetrated and liquid containing diagnostic cells can be easily obtained. In many cases even this needle is not required; you just have to pick the floating flowers (cells) while sitting at the bank of a stream. Thus diagnostic cells can be obtained from urine, sputum and cervical secretions. From solid rocks, superficial or deeply seated lesions, pearls and diamonds may be obtained with ease. And where it is difficult to palpate the lesion, the CT, MRI and Ultrasound enlighten the path! And even the disease itself helps us in aspiration. The infections and tumors may melt the bones to let us collect the cells and arrive at diagnosis. At other times with a tender and affectionate touch numerous cells come rushing on the slides showing their enormous beauty and patterns. The touch cytology, no doubt is a touch of a class.

Cytology is more of an art than a science. One has to have considerable dexterity along with thorough knowledge of pathology and medicine to interpret those cells. It is a liquid biopsy, yielding hot from oven, fresh, distortion free bright and gorgeous cells. One has to have eyes to appreciate and understand the fine changes in these cells. It requires considerable patience and love for the cells. The cells narrate their story through the fine tunes and rhymes of subtle changes. Not only the cells but also the environment is very important.



The latter; on glass slides speaks its own language and provides useful hints and directions.

Apart from the diagnosis of benign and malignant lesions, the cytology is used for hormonal assessments, infections, ultrastructural and the genetic studies. There is remarkable uniformity amidst variability in morphological alterations. As there is no such thing as random in the universe, we must try our level best to understand and correlate findings. At times we will fail but that is understandable.

The shape of the cells, the number of the cells, the shape and size of the nuclei, the chromatin density, distribution & clearing, the nuclear membrane's folds and breaks, the shape and contours of nucleoli and inter cellular relationships all have solid chemical and physical basis.

Cytology procedures are easy and can be carried out rather conveniently in the outpatient setting. They should constitute the first line of tests in most diseases. Their utility, usefulness, scopes and limitations must be understood by every modern physician. It should be noted clearly contrary to the common belief. Cytology is not merely a screening test but indeed it is a definite diagnostic test in most cases. Without proper understanding of cytology and its full utilization, precious hours and energy of the physician and surgeons and hospital resources will be wasted, not to talk about the miseries of patient and his/her relatives. It is therefore essential to include cytology as part of pathology in early sections of medical curriculum and then reinforce throughout as the student passes through steps. For pathology residents who are the main audience of the book, a solid and firm understanding of cytology is absolutely essential. With all this one must bear in mind the immense importance of history and clinical data without which making a diagnosis is comparable to

shooting blindfolded.

## **Types of Cytology**

**Exfoliative:** The cells fall themselves like the leaves from tree branches in autumn. You have to just pick them;

- Without assistance: These can be picked without assistance e.g. sputum, urine and cervical pap smear

- With some assistance: For example the form of piercing the barriers would be required e.g. pleural effusion, ascitis, bronchial lavage and cerebrospinal fluid

**Touch Imprint Cytology:** When you touch the tissue on the slide, cells will come out and touch the slide which you can stain and see microscopically. Here again:

- Without assistance: No assistance may be required. Just touching the tissue on the slide is sufficient and brings out good number of well preserved cells.

- With some assistance: Some sort of assistance may be required e.g. scraping with blade etc.

Touch imprint cytology brings out fresh from oven well preserved cells; sometimes with good histological architecture. Touch cytology smears can be stained for variety of stains in addition to routine H & E stain, Giemsa or Wright stain and special stains. We may use these smears for estrogen progesterone and other cytochemical and immunological stains<sup>6-8</sup>.

As a matter of fact Touch Impression Cytology or simply touch cytology has replaced frozen sections in most cases and at many places.

Touch impression Cytology is especially



useful for Pakistan where electricity is problem and where cryostat equipment for frozen section may not be available<sup>8</sup>.

### **Fine Needle Aspiration Cytology (FNAC):**

Fine needle aspiration cytology is an elegant and simple technique which performs wonders. As a matter of fact not doing is almost a sin and a great disfavor to both the patient and his relatives as well as to the hospital particularly where money making is not the priority<sup>9</sup>. Various types of needles can be used for FNAC<sup>10</sup>. These include routine 5 cc syringes with needle, needles alone without active aspiration, butterfly needles and even insulin syringes with 29 gauge needles. Using fine needle of 21 or higher gauge (thinner than 21) one can aspirate the cells using negative pressure. The smears are spread on the slides which are then stained and microscopically examined. FNAC or FNAB are synonymous terms. These can be performed:

- 1) In the Laboratory
- 2) In Outpatient
- 3) In the wards
- 4) Intraoperatively
- 5) Endoscopically
- 6) As part or in place of autopsy

### **Types of Tissues Frequently targeted by FNAC:**

Let me say here plainly that every tissue in the body may be targeted by FNAC; may it be bone, brain or testis. Palpable lesions generally don't require ultrasound, X-Ray, CT or MRI guidance. Deep seated lesions and hard to palpate swellings may required radiological guidance. Most frequently organs sampled by FNAC include lymph nodes, salivary glands, breast, soft tissues,

liver, spleen and intra abdominal tumors. Infrequently we are doing FNACs on testes for azoospermia as well as for testicular tumors, bones and rarely we have done brain FNAC; later we have done on autopsy cases only. For many diseases surgery and other traumatic procedures may not be required for establishing a firm diagnosis at all; for example tuberculosis, lymphoma, metastases and adenomatous goiter in its early stage etc. The FNAC has avoided about 70% surgeries in adenomatous goiter in several countries. Some tissues such as spleen are usually not biopsied due to fear of hemorrhage. FNAC brings good diagnostic material almost equivalent and sometimes even better than biopsy material. We found FNAC of spleen and liver quite useful for both neoplastic and non neoplastic diseases<sup>11</sup>.

In Lung pathology, generally the very first step should be sputum examination. It should be real sputum and not saliva and as much free from contamination as possible. At least three specimens should be obtained on different days.

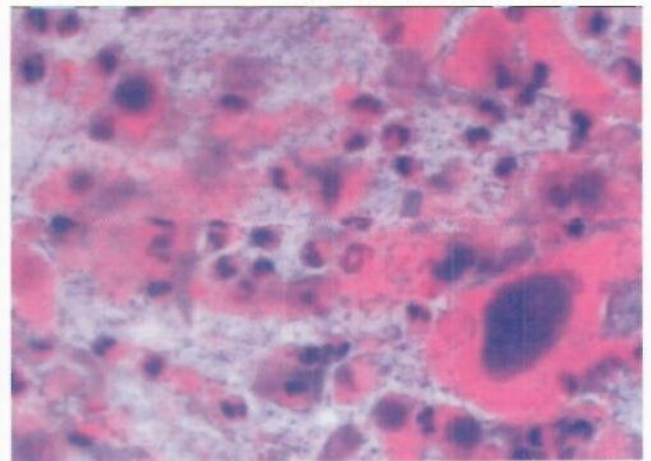


Figure 1: Lung squamous cell carcinoma in Sputum cytology (H & E X 400)



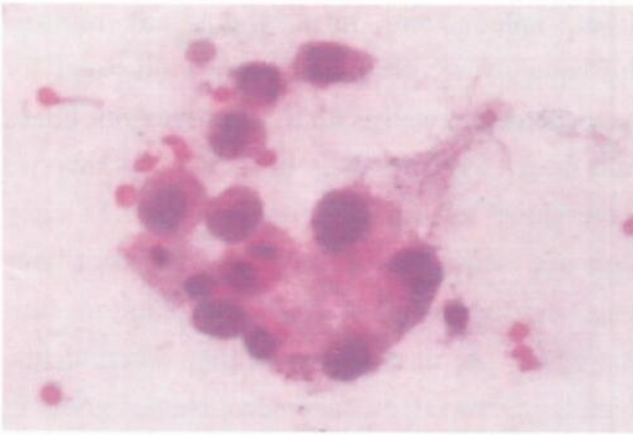


Figure 2: Lung adenocarcinoma on FNAC (H & E X 400)

If there is strong suspicion of malignancy the number can be extended to five. The next step would be FNAC of the lung lesion. Bronchial lavage cytology can be used if there is a central lesion<sup>12,13</sup>.

Sputum, bronchial washings and lavage can be helpful in diagnosing a number of benign and malignant conditions of lung. At first sputum cytology was mainly used in diagnosis of tuberculous and benign lesions<sup>14</sup>.

With increasing recognition of bronchogenic carcinoma, however, sputum and bronchial secretions were used in diagnosing malignant cells. Since 1980s there has been an increase in use of FNA for investigating localized lung lesions<sup>15</sup>. The main indication for FNAC of intrathoracic lesions is to investigate the nature of a mass of unknown origin or to confirm suspected malignancy. FNA material can be obtained by transbronchial or transthoracic route, usually the later. FNAC of lung masses entails radiology assisted or radiology guided insertion of 23-24 gauge fine needles in the mass. Although sputum cytology or bronchial lavage is generally preferred cytological methods for centrally located lesions, FNAC of these lesions is equally reliable.

Why do a brain surgery if we can make the

diagnosis of glioblastoma multiforme, tuberculosis or metastatic tumor on aspirated material through FNAC of the brain via very tiny Burr hole under radiological guidance? Is the need to do a Whipple procedure justified to find out that patient has lymphoma justified? Certainly not; the diagnosis could be easily made by FNAC of the enlarged lymph nodes. Bacterial, fungal, protozoa and viral infections can also be diagnosed on cytology. Several viral infections show characteristic nuclear inclusions and other changes. Similarly sarcoidosis and several other non infectious diseases could also be diagnosed on simple FNAC.

Interestingly FNAC of bone is also quite useful for osteomyelitis and neoplasms; both primary and secondary<sup>14</sup>. Bone gets soft in these pathological processes and needle easily pierces into the lesions. For spermatogenesis evaluation FNAC of testis is quite good modality.

In Pakistan where autopsies are infrequent and relatives may not grant permission for autopsies on their beloved ones, FNAC can be performed on multiple sites in the light of the history and clinical findings!<sup>15</sup>

Brain FNAC can be performed on the stereotactic radiological guidance in multiple clinical settings such as primary and secondary malignancies as well as in infections like tuberculosis etc. However there are large areas of brain which need to be explored. These include metabolic and diseases of uncertain origin. Currently their management is almost purely empirical and lack solid microscopic evidences. FNAC of brain will insha Allah not only provide the microscopic morphological features of the diseases processes but also their progression and treatment effects.

Brain FANC is waiting for exploration and evidence based journeying in the areas of such



disease as multiple sclerosis and Alzheimer's disease<sup>16,17</sup>.

In conclusion FNAC and other cytological modalities are widely used in all sorts of pathology. Each and every organ can be targeted; at times with active collaboration of our radiology colleagues. FNAC diagnosis could be rendered in minutes as opposed to histopathological examination. The cytology tests are quite quick, less painful, easily tolerable, and inexpensive and hence should be the very first test in most investigation. These may avoid unnecessary operations along with their complications. We at Pakistan Institute of Medical Sciences (PIMS) are routinely performing FNAC for neoplastic as well as non neoplastic conditions of lymph nodes, breast, pleural fluid, lung, liver, spleen and soft tissues. In non neoplastic conditions infections, storage diseases, biliary atresia, gout and endocrine lesions are included. The FNAC saves patients and surgeons from undue anxiety and delays in diagnosis. It saves patients from unnecessary trauma and expenses. The FNAC also helps in optimal utilization of hospital resources e.g. through eliminating unnecessary surgeries. Less unnecessary surgery means availability of operating theaters, blood and blood product and surgeons for more needy and necessary surgeries. There is definite and dire need to teach cytology and its importance to both pathologists and non pathologists. Its importance must be highlighted in the medical curriculum. Its proper use will insha Allah go a long way to improve the health care of our patients.

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