

## Role of Cytology in Cancer Screening (The Citiscreen Experience)

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Received: December 04, 2021; Accepted: December 12, 2021; Published: December 19, 2021

### **INTRODUCTION**

Papanicolaou (PAP) smears revolutionized the cytopathology field. Recently, gynecologists are moving to fluid-based technology that provides more accurate interpretation and allows for molecular testing for the HPV infection [1-3].

Besides PAP smears, cytology is successfully used for the detection of other malignancies, including the following:

1. Respiratory/exfoliative cytology, (bronchial washing, sputum, bronchoalveolar lavage, and bronchial brushing). Those are used to detect lung cancer.
2. Urinary cytology (Urine cytology, bladder washing, and brushing cytology). Kits utilizing the Fluorescent In Situ Hybridization (FISH) are already in use [4-6].
3. Body cytology: (Pleural fluid, pericardial fluid, peritoneal fluid, and cerebrospinal fluid (CSF) cytology). Those are used mainly to detect malignancies.
4. Gastrointestinal Tract: Sampling the mucosa is a routine procedure during endoscopy.
5. Discharge cytology: The most common example is nipple discharge used to screen for breast cancer.

The detection of premalignant oral lesions improves the survival and the morbidity of patients. The cytological study of oral cells is a technique that is an attractive option for the early diagnosis of oral cancer [7,8].

The advantages of cytology are fourfold: Cheap, quick, safe, and simple. Advances in cytology research led to the development of more sophisticated techniques which may be summarized as follows [9].

1. Regular smears.
2. Cyto centrifuge smears. This method concentrates cells and is advantageous when few cells are present.
3. Centrifuge smears using membrane filters. This method utilizes a paper filter with small pores to trap contaminating material.
4. Monolayer liquid-based cytology. The smears are superior to the conventional ones and also allow testing for viral DNA 69-72.

### **DIAGNOSTIC PITFALLS**

No single cell characteristic is pathognomonic of malignancy. The following are cytological signs of possible premalignant or malignant disease: High cellularity, increased nuclear/cytoplasmic ratio, nuclear hyperchromasia, prominent and large nucleoli, increased mitotic activity, nuclear membrane abnormalities, cellular and nuclear pleomorphism among others. As a rule, cytological assessment, if abnormal requires confirmation via definite histology. Technical problems (inadequate sampling, poor fixation, etc.) make cytological diagnosis challenging at times. Cellular changes (inflammation, necrosis, atypical appearances, etc.) may be due to non-neoplastic conditions (infection, trauma, infarction, hemorrhage, etc.) and require an experienced cytologist.

**Citation:** BM Petrikovsky, Role of Cytology in Cancer Screening (The Citiscreen Experience). *Cancer Med J* 5(2): 70-72.

## **SMEARS IN GYNECOLOGY**

The most popular and well-recognized screening technique is PAP smear in cervical cancer prevention. Very few in the medical community, let alone in the general public, knows that the pioneering authors (Papanicolaou and Traut) targeted endometrial rather than cervical cancer. [10,11]. Since 10%-15% of uterine cancers are detected in premenopausal women, we suggested a new screening test based on the endometrial cell's evaluation. The endometrial cells were obtained from the menstrual content of menstrual pads, cups, and intravaginal tampons [12,13]. This technique was later expanded to include smears obtained from the content of post-menopausal bleeding [13]. Studies have suggested that endometrial cells on cytology in women over 40 years of age may be correlated with a greater risk of endometrial pathology [14,15]. In 2001, the Bethesda System for cervical cytology recommended reporting endometrial glandular cells identified in the PAP tests of women  $\geq 40$  years of age [16].

Endometrial cells are shed throughout the menstrual cycle but are more common in the first 12 days. These cells can be found in the cervical smear [17,18]. A thin-layer Pap test has a sensitivity of 88.3% and a specificity of 87.5% for the detection of endometrial carcinoma [19]. The cytological distinctions among normal endometrial cells and adenocarcinoma are well established: enlarged nuclei and presence of nucleoli in abnormal endometrial cells, variation of nuclear size, coarse chromatin, and irregular nuclear membranes [19]. In the absence of abnormal cells, the presence of normal endometrial cells did not increase the risk of endometrial malignancy. Adding the results of the PAP smear to endometrial thickness helps detect endometrial cancers that are missed by transvaginal sonography [20]. Citiscreen incorporates a number of smears (urine, cervical, dental, etc.) into its screening protocols [21]. Further advances in cytology will allow for more accurate utilization of these safe and reliable technologies for cancer screening algorithms [22].

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