

# Meetings

## Cytology

Twenty years ago, in an article in *Science* [95, 438 (1942)], Papanicolaou described abnormal cells in vaginal secretions of women with cancer of the uterine cervix. This paper had a tremendous influence on the scientific and practical aspect of cancer and raised the hope of eradication of a dreadful disease which kills in this country over 20,000 women every year.

Vast educational campaigns by the American Cancer Society propagated the "cytological cancer test" so successfully that the response of the public was overwhelming. In most laboratories the volume of such tests has surpassed by far the conventional method for cancer diagnosis, namely, the microscopic examination of tissue removed from suspicious lesions.

The tenth annual meeting of the American Society of Cytology convened at St. Louis, 8-10 November 1962 as a memorial to Papanicolaou who had died the same year. Its purpose was to learn of past accomplishments and of future goals of cytology, 20 years after Papanicolaou's epochal discovery. Most of the scientific papers had originated in the pathology departments of medical schools and were almost all presented by pathologists. In analyzing the subjects of discussion one felt the contrast between the dearth of basic cytological research and the wide range of papers on clinical, statistical, and technical aspects of cytology.

Topics on basic research were discussed by A. G. Foraker who studied the properties of cervical squamous mucosa in normal, metaplastic, dysplastic, and carcinomatous conditions by using interference microscopy combined with photometry. Normal mucosa gave higher transmission than any of the varieties of abnormal squamous mucosa, but there were no significant differences found between the various kinds of atypia and carcinoma. Other studies were described by Patten, Hughes, and Reagan who inoculated suspensions of trichomonas into the

vagina of mice and observed cellular changes consistent with dysplasia as early as 3 weeks after inoculation. These changes persisted but did not progress to malignant tumors during the duration of the experiment.

Comparisons of the behavior of alveolar epithelium from cases of diffuse fibrosis of the lungs have been made with those of alveolar carcinoma. According to H. Grunze (West Germany) the most reliable criterion of malignancy was lack of dust phagocytosis. Nuclear atypia of alveolar cells may be present also in benign conditions; in alveolar carcinoma, on the other hand, uniform cuboid cell types may predominate and present great diagnostic difficulties. Focal pools of lymphocytes have been found in sputum from patients with lung carcinoma. In eight of 12 cases studied by E. M. Tassoni, these pools of lymphocytes appeared before cancer cells were detected. However, the mechanism of this phenomenon is not clear. Photomicrographs of cervical smears from patients treated with contraceptives (norlutin or dimethisterone) have shown many cases of marked cytologic atypia. A. I. Cole advised long-term followup studies before these steroids become widely used as oral contraceptives. In a study of the normal exfoliation of endometrial cells in premenopausal women, W. Liu found endometrial cells in vaginal smears in 7 percent of her patients. No endometrial cells were present except in the first 10 days of the cycle. An abnormal rate of exfoliation of normal endometrial cells rather than exfoliation of abnormal endometrial cells may be a sign of endometrial pathology. Liu pointed out that asymptomatic cases of endometrial carcinoma have been discovered in menopausal women by the presence of normal endometrial cells in smears leading to diagnostic curettage.

The statistics gleaned from various studies show how this cytology has aided in the diagnosis of cancer. A. Sedlis contended that routine cytological screening of all prenatal patients is an effective means of cervical cancer

control. Since March of 1950 in the hospital where he practices about 10,000 prenatal patients have had cytological smears regardless of the stage of gestation. Cotton applicator and dry smear technique, without fixative, was used. In the smears, atypia was found 453 times; there were suspicious findings 69 times; and positive findings 4 times. Histologic examination revealed atypia in 25 cases, carcinoma *in situ* in 23, and invasive carcinoma in 2. In another study patients were followed in whom cytology and colpomicroscopy had revealed dysplasia or carcinoma during pregnancy. No biopsy or curative therapy was employed. In no instance was the lesion found to regress after the pregnancy period.

W. L. Williams and co-workers reported on a large series of patients studied in a general hospital. In 4 years vaginal and cervical tests were made on almost 94,000 cases. Of the total tests, 664 smears (0.7 percent) were diagnosed as suspicious or positive. In 160, or 24 percent of the positive smears, carcinoma *in situ* was confirmed histologically.

Thirteen VA hospitals and clinics participated in a survey for the detection of mouth carcinoma by the smear method. During 3 years, 90,000 male patients were screened. All lesions were scraped with applicator whether cancer was suspected or not. H. C. Sandler reported that early primary oral cancer was often found to be asymptomatic. In 20 percent of the positive cases, no suspicious lesion was present.

Statistical results of cytological examination using esophageal washings were presented. In 16 of 18 patients with esophageal cancer, the smears after lavage with physiological salt solution were positive. Material obtained during esophagoscopy directly from the lesion proved to be less reliable. Cytologic examinations of 10,000 samples of urine showed that *in situ* carcinoma of the bladder usually yielded a high percentage of malignant cells while invasive bladder tumors often failed to produce diagnostic cells because of necrosis. Atypical cells were often found in systemic diseases such as diabetes mellitus, blood dyscrasias, and infection of the intestinal tract. Similar atypical cells were noticed in patients with malignant tumors involving other than urinary organs.

In another screening procedure H. E. Knoernschild took mucosal smears during sigmoidoscopy from more than 17,000 patients. There were 132 cancers



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visible by sigmoidoscope and 96 patients in whom the tumor could not be seen. Of the former, 79 percent yielded positive smears, while in cancer which could not be reached by the sigmoidoscope only 5 percent positive smears were obtained. The accuracy of the colonic mucosal smear depended therefore on actually seeing the tumor and so the method was of little value in the diagnosis of cancer of the colon.

S. B. Gusberg, the only gynecologist on the program, reported on his results of cervical biopsy. Punch biopsy missed carcinoma (after positive smear) in 14 percent, while conization failed only in 3.4 percent. Gusberg performs, instead of the conventional complete conization, a narrow ring biopsy at the squamocolumnar junction. Sixty percent of the patients with final diagnosis of carcinoma *in situ* were asymptomatic. During the last few years he has performed 224 total hysterectomies for carcinoma *in situ*. In 52 percent of the uteri removed after conization, carcinoma *in situ* was still present. The recurrence rate after hysterectomy was 1.9 percent.

The accuracy obtained by W. Kaufman after using colpomicroscopy in almost 1500 cases was 84 percent in early carcinoma. He feels this method is so superior that it can often replace biopsy. However, from his photomicrographs this opinion appeared to me somewhat optimistic.

As routine office procedure, King and his associates performed cytological smears on urine for the purpose of detecting unsuspected bladder tumors. The method involved triple strength methylene blue on dry, fixed urine sediment. The results of this simple staining method compared well with preparations made by Papanicolaou's method or by the millipore filter technique.

The final session of the symposium was a cytology seminar moderated by von Haam. The panelists stressed that the purpose of cytology was not only to make a diagnosis of "positive" or "negative" smears, but to use the cytological findings to supplement clinical data and physical findings and to arrive at a final clinical diagnosis of the whole case. The comparison of tissue sections with the cytological findings demonstrated the value of the cytological method, if used as a preliminary screening test or adjunct, but never as a substitute for histological study and thorough clinical evaluation.

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