In Volume 7, Number 1, 1963, of Acta Cytologica, a review article with original contributions on the cytodiagnosis of lung cancer was published. The article (below) was written by Drs. William O. Russell, Heinrich W. Nedhardt, Clifton F. Mountain, Kenneth M. Griffith and Jeffrey P. Chang from the departments of pathology and thoracic surgery of the M. D. Anderson Cancer Center, Houston, Texas, U.S.A. The article consists of 44 pages, scores of black-and-white illustrations and tables, and 102 references.

It is perhaps of interest that this was the first review article on the state of the art of pulmonary cytology as it was in 1962 and the first prospective study on early detection of lung cancer, supported by the National Cancer Institute of the United States.

Dr. Russell was cofounder of the Anderson Cancer Center and the first chairman of pathology, from 1948 to 1977. He was a student of George Papanicolaou. In 1961 he introduced the membrane filter technique in diagnostic cytology. (For more on William O. Russell and his contributions, see American Journal of Clinical Pathology 1998;109:492–493).

CYTODIAGNOSIS OF LUNG CANCER

Cancer of the lung has shown such a remarkable increase in incidence over the past 25 years that it is currently recognized as a serious world health problem. It is estimated that, in 1962, 39,300 people will die from this disease in the United States alone; an estimated 45,000 new cases of lung cancer are expected by the end of 1962. In the United States and many western European countries, lung cancer is now a leading cause of
death among men over 50 years of age. This increase has been attributed to various factors such as cigarette smoking, urban residence, and various occupational hazards.

With bronchogenic carcinoma had an average survival of 6.2 months from the time of diagnosis. The reported short survival time may be significantly influenced by the fact that the disease is generally discovered in a terminal, inoperable stage. It has been estimated that the survival rate could theoretically be increased to 34 per cent if the presently employed methods of treatment were applied earlier.

Exfoliative cytology has contributed so greatly to the early detection of cancer of the uterus that it seems reasonable to expect that exfoliated cancer cells in sputum could make an equally significant contribution to the detection and early treatment of lung cancer. In recognition of this problem, the National Cancer Institute of the United States Public Health Service, in conjunction with The University of Texas M.D. Anderson Hospital and Tumor Institute, initiated a program in Houston in 1957 to study various aspects of the application of exfoliative cytology to the early diagnosis of lung cancer.

The material reported in this communication consists of two parts. Part I contains a review of the literature significant to pulmonary exfoliative cytology and the lung cancer problem. This review includes an analysis of 12,217 cases of bronchogenic carcinoma reported in 22 publications from 1945 to 1962 as to incidence of histologic types, distribution by sex, propensity for exfoliation in the bronchial tree, and prognosis. Studies indicate that the exfoliated cancer cells in sputum can provide a positive morphologic diagnosis of cancer in nine of ten cases when five or more sputum specimens have been examined: the exfoliated cells can indicate the presence of cancer two to three times more accurately than punch biopsy. And they can provide a more accurate diagnosis of early lesions than any other method. Most tumors yielding identifiable cancer cells in smears were centrally located. Peripheral tumors usually yielded negative results. Squamous cell carcinoma is the histologic type of pulmonary neoplasm most often diagnosed by the cytologic technic.

Pulmonary cytology is more difficult than uterine cytology. There are usually fewer malignant cells; the cells generally show more degenerative changes because they must travel a longer distance and cannot be removed directly from the respiratory tract as are the cells from the vaginal tract. When utilized, however, as a screening test for pulmonary malignant disease in a large, unselected population, reports of the efficacy of the method have varied widely and are not altogether encouraging.

In Part II of the communication, the organization of this program, the over-all objective was concerned with enhancing the application of the test by practicing physicians. For these studies, 10,024 specimens of sputum and bronchial washings were collected from 3,662 patients, and more than 30,000 slides were stained and screened. Of the 438 primary lung cancer patients, only one or more positive cytologic reports (Class IV or V), 11 per cent had one or more suspicious cytologic reports (Class III) but no positive reports, and 38 per cent had only atypical (Class II), negative (Class I), or unsatisfactory cytologic reports. Of the 3,002 patients who had no malignant disease in the lungs, only five had positive cytologic reports for a false positive rate of 0.2 per cent. The greatest influence on the diagnostic efficacy of pulmonary exfoliative cytology are:

1. Persistence in obtaining multiple specimens is more important than the specific collection method chosen.
2. The screening of two slides prepared from two separate portions of the specimen produces substantially better yields of positive diagnoses than the screening of two slides prepared from a single portion of the specimen.
3. Specimens collected directly in fixative and smeared after fixation were found to have diagnostic accuracy equal to specimens smeared immediately on collection before fixation.
4. Substantial loss of diagnostic accuracy can occur in specimen processing and microscopic screening as a result of human error; factors related to personality and attitudes appear to deserve more emphasis than education and experience in the selection of cytotechnologists. Much of the source of error would appear to be controllable. If reasonable work loads are maintained, human error can undoubtedly be kept at a minimum level through careful personnel selection, training, and supervision.
5. A comparison of pulmonary exfoliative cytology with the other objective diagnostic methods in current use reveals substantially higher diagnostic yields by cytologic methods than by bronchial biopsy or scalene node biopsy either singly or combined. Sputum cytology has
probably the greatest potential of the currently available diagnostic methods for development as a means of early detection of lung cancer by the screening of susceptible populations.

The data obtained in this study indicate that sputum cytology, when properly applied, is a highly useful, in fact indispensable, instrument for diagnosis of lung cancer, providing detection rate far superior to any other diagnostic method in current use.

The method is clearly one for which there is a need and one which warrants the further development required to achieve its maximum diagnostic efficacy. The study, and microscopical examination, of the sputum in pulmonary diseases ought thus to be as much a matter of routine on the part of the physician, as the practice of auscultation and percussion, or the examination of the urine in vesical and renal diseases.

Edited by Steven I. Hajdu, M.D., F.I.A.C.

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