

larly the military officer, hearing about new weapon possibilities, may see new possibilities for their tactical use or how they could be adapted to new situations. The idea that the function of the military is to tell the scientists what weapons they need—and that the function of the scientists is to deliver them without argument—is as obsolete as the idea that the scientist can toss new weapons at random at the military services and expect them to find a use for them.

Weapon development is a tough business and requires the best combined talents we can muster at all stages of the enterprise. If military secrecy is interfering with this intimate meeting of minds, then secrecy is working against national security, and it is time that *real security* considerations come first.

If I were to express a hope for the future of the Johns Hopkins Applied Physics Laboratory, it would be that, as it maintains and develops the spirit of research that I have been discussing, it also becomes a meeting place where scientists and military men meet together to discuss broadly and intimately and vigorously the problems of the military defense of this country. Out of such discussions will come new and important concepts in the field of military weapons and their uses. For your business and my business is not just a better device for this or that purpose, it is, rather, nothing less than the safety of this nation. And it is your responsibility and mine—not someone else's—to insure that each of us is making his most effective contribution to that end.



New Horizons in Cancer: Cytology in Research and Practice*

John R. Heller, Jr.

National Cancer Institute, U.S. Public Health Service, Bethesda, Maryland

GENERALLY speaking, the early diagnosis of cancer offers the most hope for successful treatment. This doctrine has been the principal theme of efforts by the National Cancer Institute, the American Cancer Society, and other cooperating groups to improve case-finding. Educational programs to alert the public and to aid the physician in cancer diagnosis and treatment are yielding valuable dividends. Education alone, however, is not enough. Urgently needed to ease the cancer case-finding burden are practicable screening methods. An ideal solution to this problem would be a simple, inexpensive chemical or blood test as useful as the Wassermann test for syphilis. Over the years, many attempts have been made to devise a laboratory procedure that would show whether or not an individual is harboring a cancer. Altogether, hundreds of such tests have been proposed.

Since 1948 a program to evaluate the old tests and to develop new ones has been conducted, with financial and technical assistance from the National Cancer Institute, by investigators at the medical schools of Tufts College and the universities of Washington, Alabama, Tennessee, and Kansas. Much good work has been done by these and other workers in this field and reported in the literature (1, 2). None of the tests evaluated so far has been found sensitive and specific enough for clinical use. However, the approach seems hopeful. The fact that certain tests are effective to some extent is an indication that tangible changes do occur in the body of the cancer patient, and that these changes may be measurable in a diagnostic procedure. For instance, it is known that there are changes in

the body chemistry of cancer patients. In some patients with cancer of the prostate the acid phosphatase level is increased. Measurement of prostatic acid phosphatase has been developed to the point where several laboratories are evaluating it as a means of diagnosing prostatic cancer. Other promising procedures being investigated include a serum flocculation reaction, the use of radioactive tracers, and means of detecting abnormal steroid in the blood or urine (1).

Although a practical general diagnostic test for cancer appears to be still in the future, considerable progress has been made in the development of tests to aid in detecting cancer of specific sites. The most useful of these is the cytologic examination developed largely by George N. Papanicolaou (3). In the past few years, Papanicolaou's "baby" has come of age. Today it is established as a valuable complement to other clinical procedures in early diagnosis of cancer, particularly of uterine cancer. Many qualified persons have been trained in the cytologic test, and numerous clinics and physicians in general practice are employing it routinely in cervical cancer diagnoses. Variations of the original cytologic technique have been developed to aid in the detection of cancer of the lung (4) and of gastric cancer (5). These variations show considerable promise when used in combination with other procedures. Cytology is being evaluated as a screening test for cancer of the genitourinary tract, the rectum, and the colon. Also under study are applications of the cytologic examination to breast secretions and spinal fluid.

The value of vaginal cytology as a detector of early

cervical cancer has been indicated in many clinical investigations (6). One of the most recent studies concerned more than 5000 women who received cytologic examinations by private physicians (7). The study reported that the examinations had revealed 48 definitely curable asymptomatic cervical cancers. The study also pointed out the economic feasibility of this screening procedure, estimating that its cost per private case is within the keeping of many other laboratory procedures.

Cytology provides not only a means of detecting cervical cancer in its incipency but also material for study of the development of the disease. Research of this type is underway which may answer questions that bear directly on the problem of controlling uterine cancer, questions such as: Do the intraepithelial or "early" cancers progress invariably to invasiveness? How frequent is "early" cervical cancer? How many of these cancers regress spontaneously?

A number of studies seeking the answers to these questions have yielded significant preliminary findings. The University of Tennessee College of Medicine, with the support of the National Cancer Institute and other groups, is applying vaginal cytology in a mass-screening survey for uterine cancer and intraepithelial cancer among 165,000 women in Memphis and Shelby County, Tennessee.

The results obtained in the screening of the first 70,000 women are very encouraging. The cytology findings were suspicious or positive in 1327, or 1.9 percent, of the women. Tissue biopsy studies have been completed in 1076 of the 1327 cases. The biopsy diagnoses were positive in 51 percent of the cases; borderline, suspicious, or inconclusive in 15 percent; and negative in 34 percent. Vaginal cytology resulted in false positives in only 369 cases, or one-half of 1 percent, of the 70,000 women screened. From the point of view of cancer control, it is especially significant that 88 percent of the 282 confirmed cases of

intraepithelial cancer of the cervix were unsuspected prior to cytology, and 29 percent of the 245 confirmed cases of invasive uterine cancer were unsuspected.

Also of particular interest is the age distribution of these cancers among the cases screened in the Memphis cytology study. On the average, the women with intraepithelial cancer are about 20 years younger than the women with invasive uterine cancer. The median age of the women with early cervical cancer is 33, while the median age of those with invasive cancer is 52. This suggests that preinvasive lesions are present for a long enough time to allow for their eradication.

The Memphis study was begun in July 1952. Cytologic examinations of the women will be repeated at yearly intervals, and the study will be continued until the incidence of intraepithelial cancer and its relationship to the incidence of invasive uterine cancer are determined.

References and Notes

- * Based on an address before the Southern Society of Cancer Cytology in St. Louis, Mo., 8 Nov. 1954.
1. J. E. Dunn and S. W. Greenhouse, "Development and evaluation of cancer diagnostic tests," *Public Health Repts. (U.S.)* **68**, 880 (1953).
2. *Proceedings of the First Conference on Cancer Diagnostic Tests, 1950*, U.S. Public Health Service Publ. No. 96 (GPO, Washington, D.C., 1951).
3. G. N. Papanicolaou and H. F. Traut, *Diagnosis of Uterine Cancer by the Vaginal Smear* (Commonwealth Fund, New York, 1943).
4. S. M. Farber *et al.*, "Evaluation of cytologic diagnosis of lung cancer," *J. Am. Med. Assoc.* **144**, 1 (1950).
5. F. G. Panico, G. N. Papanicolaou, and W. A. Cooper, "Abrasive balloon for exfoliation of gastric cancer cells," *ibid.* **143**, 1308 (1950); M. Rosenthal and H. F. Traut, "Mucolytic action of papain for cell concentration in the diagnosis of gastric cancer," *Cancer* **4**, 147 (1951).
6. Emerson Day, "Cytological techniques in screening uterine and lung cancer," *CA-Bull. Cancer Prog.* **2**, 57 (1952); R. B. Nelson and A. W. Hilberg, "Diagnosis of unsuspected cancer of the cervix," *J. Natl. Cancer Inst.* **11**, 1081 (1951).
7. J. E. Ayre, "Frequency of early cancer of the cervix. Results of cytologic screening in the private physician's office," *Am. J. Obstet. Gynecol.* **3**, 111 (1954).

News and Notes

Events Related to Differentiation of Cells

A conference on *Molecular Events in Differentiation Related to Specificity of Cell Type* was held under the auspices of the New York Academy of Sciences at the Barbizon Plaza Hotel in New York, 8-9 Oct. Among the many informative papers given was one by J. D. Ebert *et al.* (Indiana) who reported: (i) The major synthesis of cardiac myosin is initiated during formation of the primitive streak; this protein can first be detected (by immunological methods) at the midstreak stage; (ii) in the definitive primitive streak stage embryonic cardiac myosin is distributed throughout the ectoderm; it has not been detected in the entoderm; (iii) the restriction in distribution of cardiac myosin coincides with the initiation of synthesis of at least one antigen of the cardiac actin com-

plex, which is already limited in distribution to the heart-forming areas at the time it is first detected. C. L. Markert (Michigan) recounted the use of various substrates for melanogenesis in tissue culture, including C¹⁴-labeled tyrosine, dopa, tryptophan, glucose, glycine, and unidentified oxidation products of tyrosine. Of these, only uniformly labeled tyrosine and its oxidation products were differentially incorporated into melanin granules as shown by autoradiograms. He reported that since tyrosine with a C¹⁴ in the side chain did not serve as a melanin precursor, doubt is cast upon the generally accepted scheme for melanogenesis. C. E. Wilde, Jr., (Pennsylvania) reported that the differentiation of the cells of the Urodela neural crest in tissue culture appears to be controlled by a special metabolism concerned with phenylalanine