Arrest and cure of cervical cancer may be achieved in many cases by recognizing malignant cells before they become invasive. Described is the exfoliative cytology technique of screening patients for early and unsuspected uterine cancer.

Uterine Cancer Case Finding by Vaginal Cytology

—Memphis and Shelby County, Tennessee—

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EXFOLIATIVE CYTOLOGY as a technique for recognizing cancer cells shed or abraded from epithelial surfaces has greatly facilitated the recognition of carcinomata before they become invasive, particularly carcinoma of the uterine cervix. Such a carcinoma is not apparent by its mass or by its surface, and on visual inspection, it is not distinguishable from normal or benignly altered epithelium. Discovery, therefore, at this stage is largely dependent on recognizing suspicious cells sampled from epithelial surfaces. Blind sampling of larger surfaces can be accomplished more efficiently by smear than by biopsy, although this fact has no bearing on the relative merits of the two procedures for establishing a final diagnosis.

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The cytological technique in finding cases of cervical carcinoma presents some practical difficulties, but these are not insurmountable. In Memphis and Shelby County, Tenn., an area with a population of about 165,000 adult females, a uterine cancer case-finding study was begun in August 1952 to be continued for a 3-year period, or until all women who are participating have had an opportunity to have three successive examinations at yearly intervals.

One of the objectives of the study is to determine age-specific incidence and prevalence rates for carcinoma in situ and for presymptomatic carcinoma of the cervix. Because carcinoma in situ of the cervix is frequently present in younger women, all females aged 20 years and over are offered the opportunity for cytological examination.

Although the original technique for cytological examination was based on examination of the exfoliated cells in vaginal pool specimens (*1*), most cytology laboratories find it expedient to examine a specimen taken directly from the cervix only or a cervical specimen in conjunction with the vaginal pool specimen. In this study, vaginal pool specimens are used exclusively in initial screening, since they can be taken by personnel who are not physicians.

Organization of the Study

Specific plans for implementing the project were developed after the Memphis and Shelby County Medical Society had endorsed preliminary plans. The cytology laboratory is equipped and staffed by the National Cancer Institute of the Public Health Service. The division of pathology and bacteriology of the University of Tennessee furnishes space, supervises the operation of the project, and examines biopsy specimens from indigent patients. With the cooperation of the other pathologists in this region, this division sees all other biopsies recommended because of cytology findings.

A policymaking committee composed of the organizations participating and cooperating in the study includes representatives of the divisions of pathology and bacteriology and of obstetrics and gynecology of the University of Tennessee, the Memphis and Shelby County Health Department, the Shelby County Medical Society, the Bluff City Medical Society of Negro Physicians, the Shelby County Unit of the American Cancer Society, and the Public Health Service. The general plan of the study was approved by this committee, and in July 1951 preparations were begun to put the project into operation. A year was allowed for establishment of the cytology laboratory and the training of personnel.

Cytology Laboratory

Staffing the cytology laboratory and training technicians to handle the anticipated volume of 400 cytology specimens a day was the first step in organizing the project.

The laboratory staff is composed of a pathologist, a chief technician, 3 secondary screeners, and 12 primary screeners. The primary screeners work in groups of 4 under a secondary screener, who is responsible for supervising and checking their work. The 3 secondary screeners are supervised and their work is checked by the chief technician. Final review and interpretation of suspicious and positive slides are the responsibility of the pathologist.

One additional technician examines all cervical specimens when these are requested as repeat examinations. We believe that this is important, since a smear from the cervix has so many more cells than a smear from the vaginal pool that a technician shifting from the examination of one type of specimen to the examination of the other is likely to become inefficient in both procedures.

Training of the staff was begun in July 1951. Three technicians who had had experience in cytology screening in a Public Health Service laboratory and one technician who had had training in the division of pathology and bacteriology of the University of Tennessee formed the nucleus of the staff. A physician with some training in pathology and with experience in cytology was also available for training and eventual supervision of the cytology laboratory.

Because additional technicians were not available, recent college graduates were interviewed, and 12 were selected as trainees. After a period of preliminary training, three of the best qualified technicians were sent to the cytology laboratory of the Vincent Memorial Hospital in Boston for additional training for supervisory positions. This laboratory uses vaginal pool specimens exclusively.

The cytology laboratory supplies the physicians of the community with materials for taking specimens from their private patients, collects the specimens periodically, and replenishes supplies of materials.

The amount of information which physicians are requested to submit to the laboratory with specimens is kept to a minimum: name, age, race, and home address; age at marriage; pregnancy history—age at first and at last pregnancy, number of pregnancies, and date of last menses; history of vaginal bleeding; history of surgery or radiation therapy in the pelvis; and name and address of physician or clinic submitting the specimen.

Since the cytology examination serves as a screening procedure, the laboratory report to the physician or clinic either indicates that the findings are negative or recommends further study—additional cytology specimens or biopsy, depending on the judgment of the pathologist—without specifying a provisional diagnosis. Because the initial cytology examination is made on a single vaginal pool specimen, slides containing abnormal but not definitely suspicious cells warrant, in addition to a second vagi-

nal pool specimen, a repeat examination with a specimen taken directly from the cervix.

A negative report is accompanied by a stamped postal card addressed to the patient, informing her that the results of her test are negative and urging her to repeat the examination in a year. The private or clinic physician signs the card and mails it to the patient.

Record Unit

The record unit of the laboratory keeps a record of all women for whom cytology specimens are examined, the results of this examination, and a record of tissue examinations up to the point of final diagnosis. Space is provided on the back of the record card for recording the cytology findings and the report of biopsy when this is recommended and completed.

The unit is staffed with a supervising clerk, 2 record clerks, and 1 coding clerk, who codes the recorded material for preparation of punchcards to be used in the mechanical tabulation of data for analysis. The coding clerk also assists with routine recordkeeping when necessary.

The record unit keeps a tickler file of all patients for whom additional diagnostic study has been recommended. If the initial examination indicates a need for additional cytology specimens, the arrival of such specimens in the laboratory indicates that followup has been successful. If no specimens are received, further followup is carried out.

Followup

The physician is responsible for contacting private patients for whom the cytology report indicates the need for further study. Two weeks after the report is sent to the physician, the cytology laboratory makes a telephone inquiry to him concerning the patient's response. If a biopsy has been taken, the name of the pathologist who examined the specimen is noted, and his findings are recorded on the patient's card in the record unit. If a biopsy has not been taken, the laboratory contacts the physician's office periodically until the patient returns for further study and a report of the results of examination is available. For both private and clinic patients, if cancer is found the case is closed as far as the cytology laboratory is concerned. Therapy becomes the responsibility of the private physician or the gynecology clinic.

The followup services of public health nurses are available to private physicians, although most physicians prefer to assume this responsibility themselves.

Clinic patients for whom further study has been recommended are followed up by the division of public health nursing of the Memphis and Shelby County Health Department. The cytology laboratory sends referral slips to the health department to be given to the general public health nurse who serves the area in which the patient lives. The nurse contacts the patient personally and makes clinic appointments for further examination.

The health department nurse responsible for supervising cytology referrals periodically checks with the record unit of the cytology laboratory to determine which patients are not responding to followup, and when necessary, she sees that additional visits are made by a general public health nurse. If repeated followup visits are unsuccessful, the supervising nurse makes a home visit in a final effort to persuade the patient to come in for further diagnostic study.

Clinics for Indigents

After the vaginal cytology study was organized, all adult female patients at the clinic for indigents in the Gailor Out-Patient Clinic of the City of Memphis Hospitals and the women who accompanied them to the clinic were informed that cytology examinations were available in the clinic newly established for that purpose. The large attendance, chiefly Negroes, and the response of the patient to the cytology service made this clinic a very productive source of material for study. Since the gynecology clinic is held in the same building as this cytology clinic for indigents, the latter has become the central clinic for indigent patients who come for repeat smears and for referral for further study.

In the clinic for indigents, vaginal pool speci-

mens are used exclusively. A trained nurse, who has had considerable experience in cancer clinics and several years' experience in taking specimens for a cytology laboratory, supervises the personnel who take the specimens.

In the interest of economy and efficiency, nonprofessional personnel take the specimens. They are supervised directly by the nurse in charge until she is satisfied that they are capable of working under general supervision. These employees also clean and sterilize vaginal pipettes and see that the kits furnished to physicians are equipped with slides, pipettes, and record forms.

These personnel were recruited through local employment sources from a group of intelligent but untrained young women. They were given some background information on genital anatomy and the symptoms of uterine cancer and instruction in the method of obtaining information for the record form, handling of patients, and the technique of obtaining a vaginal smear.

Two senior members of the resident staff of the division of obstetrics and gynecology are responsible for the clinical study of indigent patients with suspicious and positive cytological findings. All patients in this category are seen by these two physicians and are kept under their observation until tissue studies have been completed and a final diagnosis has been established. Patients who have cancer are hospitalized for treatment by the staff of the division. All tissue examinations of these patients are made in the division of pathology and bacteriology of the University of Tennessee. For uniformity of tissue interpretation in connection with the study aspects of the project, other pathologists of the area who examine biopsies from patients found to have suspicious cytology as a result of the project have cooperated by allowing these biopsies to be reviewed.

As the technicians taking specimens became sufficiently experienced, cytology clinics were opened in two other locations in the city where facilities for indigent patients are available. These are largely prenatal and well-baby clinics, and most of the patients are Negroes. The hope was that the publicity given the program would attract well women to the clinics, as well as women attending the other clinics operated in these facilities, but the response has been disappointing. The cytology examinations are largely made on the regular clinic patients and on the relatives and friends who accompany them to the clinic.

Other Cytology Clinics

Parent-teacher organizations were informed about the project through publicity in the newspapers, over the radio, and through talks given at their regular meetings. Offers were made to open clinics in school buildings at hours which would be convenient for the women interested. A number of clinics were opened on this basis and attendance has been excellent.

In these clinics, each patient is asked for the name of her family physician, and the report of cytology findings is sent to him. If the patient has no physician, she is referred to the Memphis and Shelby County Medical Society for a list of recommended physicians. The results of the examinations are reported to the physician she chooses; no report is ever made directly to the patient.

Industrial organizations are another source of cytology specimens from well women. The management of a number of industries was informed of the nature and purposes of the project, and an offer was made to conduct cytology clinics for female employees. The response to this offer has been gratifying, and many industrial organizations in the study area have had the benefit of this service.

The usual plan for industrial organizations is to have two clinic sessions about 2 weeks apart. At the second session, patients whose examinations were unsatisfactory are reexamined, and women who were menstruating when the first clinic was held have an opportunity to take advantage of the service. Reports are sent to the family physician or to the plant physician, never to the patient.

Publicity

The mechanics of the cancer case-finding project makes public acceptance and cooperation crucial to its success. The project was initiated with a minimum of general publicity by newspapers and radio, for, with no previous experience in cancer case finding to draw upon,

there was no way of anticipating what the public's response would be. A widespread general response by the 165,000 women in the area who were eligible for the examination would swamp the available facilities. Therefore, it was necessary to work for an even flow of patients on a long-term, continuing basis. Also, to test the flow, processing, and reporting of specimens and reports, a "shakedown" period was considered necessary.

It soon became evident that the public was not overly conscious of cancer as a personal problem, and that more aggressive educational measures were needed. Yet it was necessary that publicity should not antagonize practicing physicians since their cooperation is a necessary part of the project.

The chairman of the policy committee is responsible for the supervision and direction of publicity. Facilities of the university are used to carry on the publicity, and regular announcements and descriptions of the project in local newspapers and on the radio are supplemented by donated space in store windows, billboards, advertising on buses, and pamphlets. Soon after the project began, an exhibit was presented at the local fair. Opportunities are sought to discuss the project before women's organizations and parent-teacher and church groups.

In the beginning, the publicity staff consisted of one full-time person, who devoted most of her time to working with Negro groups. Negro women are less inclined than white women to obtain the cytology examination voluntarily, although they are quite willing to have the examination when they are attending a clinic for another purpose. Added to the staff a few months later was a second person, who had gained considerable experience in public relations in the health field as a result of working with voluntary organizations.

Any apprehension about the public's overconsciousness of cancer has been completely dispelled. Enlightenment and motivation have become the leitmotivs of the publicity program in the effort to reach women individually through every possible medium, until they accept the fact that they can have cervical cancer, and that the cytology examination is a means of detecting this cancer in a curable stage.

Discussion

Progress of the study of vaginal cytology as a means of finding cases of uterine cancer has been very satisfactory. Only occasionally have the laboratory facilities been taxed to capacity. However, it is doubtful whether the laboratory as presently staffed could maintain the pace required by the original estimate of a maximum of 400 smears a day. Each primary screener can process 25 to 30 slides daily, a laboratory total of about 300, but personnel turnover, need to recruit and train new technicians, illness, and vacations make this potential difficult to meet. Nevertheless, the cytology laboratory has been able to provide the service demanded of it.

A preliminary report on the results of the study has been published elsewhere (*2*). It is sufficient to say that, in general, in the first 30,000 women examined, 90 percent of the smears have been negative; 6 percent have been unsatisfactory and a repeat examination has been requested; and 4 percent have been recommended for further study. Of these 4 percent, a little less than half have been recommended for biopsy after initial or repeat cytology study. Epithelial changes warranting a diagnosis of carcinoma in situ or invasive carcinoma of the cervix have been found in about half of the biopsy specimens.

Since vaginal smears are used exclusively for initial screening, records of cases of cervical cancer in the Memphis hospitals are checked against the records of the cytology clinic to determine whether these cases were missed by cytology examination. A few such cases have been observed. As a further check, the morbidity survey conducted prior to the beginning of the project is to be repeated (*3*) and known cases of cervical cancer will be checked against the cytology file to identify additional missed cases.

In a few instances, skeptics have put the cytology program to the test by submitting specimens from known or clinically obvious cases. There are no known instances in which the cytology examination has failed under these circumstances.

As stated earlier, repeat smears from the cervix as well as from the vaginal pool are requested when the original pool specimen cannot be classified as negative. The smear from the

cervix is examined by the technician trained in the examination of cervical specimens, and the new vaginal pool smear is studied by another technician. Each technician makes a report to the chief technician, who studies both report and slides and makes a final evaluation for the review of the pathologist in charge of the laboratory. In this project, cytology is used for screening; it is not competing with the tissue study for relative accuracy in final diagnosis.

Pelvic examinations are not an essential feature of the project. Private physicians use their own discretion in this matter. Indigent patients are not given pelvic examinations but are queried as to symptoms suggestive of cancer. If they have any questionable complaint, they are urged to go to the gynecology clinic without waiting for the report of the cytology findings. If smears contain unexplained microscopic blood, the patient is referred to the gynecology clinic for examination, regardless of the cytological evidence.

Because of staffing and other requirements, it is not feasible at this time to determine minimum costs per examination in this study, but we feel that the cost of cytology examination is not prohibitive when it is compared with the cost of other laboratory procedures. Cost estimates of cytology examination in other studies have ranged from 90 cents (*4*) to $3.00 per smear (*5*), but it is difficult to determine what fixed costs, such as rent, are included in these figures.

Final judgment of the value of vaginal cytology will depend on the following considerations:

1. Can the periodic use of such a simple procedure as vaginal cytology in a population of women result in the diagnosis of cervical cancer sufficiently early so that it will become predominantly a curable disease?

2. Can the interval between examinations be safely extended to more than a year?

3. Will the public accept the cost of finding cancer in a curable stage by this method as a substitute for prolonged treatment that is often only palliative and all too frequently hopeless?

Summary

A 3-year cytology screening program for cervical cancer in a general female population was organized in Memphis and Shelby County, Tenn., in 1951 and was put into operation in 1952.

The goals of the study are:

1. To determine whether periodic vaginal exfoliative cytology as a screening procedure can be used to diagnose cancer in the preinvasive stage.

2. To accumulate data for determining age-specific incidence and prevalence rates for both preinvasive and invasive cervical cancer.

3. To estimate the frequency with which vaginal cytology needs to be applied to be effective as a case-finding procedure.

4. To determine whether, through this case-finding procedure, cervical cancer can become largely a curable disease.

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