THE EARLY DETECTION OF PELVIC CARCINOMA — METHODS AND THEIR LIMITATIONS

JAMES S. KRIEGER, M.D.
Department of Obstetrics and Gynecology

EARLY detection of pelvic carcinomas is not a guarantee of the eradication of such tumors, but nevertheless is highly desirable. The effectiveness of treatment is dependent not only on the stage of the disease when treatment is instituted, but also on the response of the tumor to varieties of treatment, and the invasiveness or ability of the tumor to replace normal host tissues. Some tumors already have metastasized when the primary lesion is small and otherwise would be considered favorable for treatment.

Because early diagnosis generally will improve survival rates, the American Cancer Society and other interested agencies have conducted intensive educational campaigns directed at the layman as well as at the physician. A great quantity of literature directed at the public, points out the desirability of frequent and regular examinations for cancers. The medical literature contains a multitude of reports pertaining to various methods of detection. As a result, many women are having yearly pelvic examinations. Despite these efforts there are many misconceptions regarding the whole problem of cancer detection. The laity is prone to look on the diagnosis of cancer as a problem with a precise answer, and to expect all physicians to have the facilities for full and complete detection of cancer. In some instances, people seem to regard the detection process as simple as dropping a coin in a penny scale and obtaining a weight and fortune. The answer to malignant disease is not so easily obtained.

It is unfortunate that physicians in some regions do not have adequate facilities available for pathologic study. Consequently, cytologic or histologic reports may be incomplete or misleading. Incorrect diagnoses may result, and some patients may be treated for cancers they do not have, or may be given clearance for cancers that actually are present. In view of this confusion, it is well for the physician to reconsider what can be expected from various available detection methods and to recognize the limitations in their use.

Defining the Problem

What is the relative incidence of the several types of gynecologic cancer? In terms of survival rates, which anatomic sites present the most favorable prognosis following treatment? Randall and Gerhardt[1] have estimated that gynecologic malignancy can be expected to develop in approximately 10 per cent of all women. The occurrences of cancer of the cervix and the body of the uterus are three and one-half times more frequent than are the combined occurrences of ovarian and of vulvar carcinoma. The incidence of vaginal and of tubal carcinoma is small.

The early detection of malignancy is dependent upon the site of involvement, since, if lesions can be visualized and specimens can be easily obtained, diagnostic studies are more easily performed. The cure rate does not necessarily follow this pattern, since there are variations in individual tumors: though the cervix is visible, carcinoma of the body of the uterus is more amenable to treatment than is cervical carcinoma. Randall[2] reported cancer mortality rates, covering a period of 20 years according to specific age groups and to anatomic sites, in females in New York State. Over this period, the mortality rates for cancer of the breast remained unchanged. Mortality rates for uterine cancer decreased 10 per 100,000 women, and ovarian cancer mortality rates increased 4 per 100,000 women.

Although the ovary is less accessible for diagnosis, it also may represent neoplastic behavior similar to that in the breast. In spite of the accessibility of the breast for examination, survival rates from cancer of the breast have not improved in a considerable number of years. It is probable that even if the ovaries were superficially located, mortality rates would be unchanged. The increase in incidence of ovarian carcinoma in large part is due to better diagnosis and a population with increasing longevity.

Present detection methods may be grouped into clinical and pathologic phases. The clinical methods are confined to evaluation of history, inspection, and palpation. These procedures do not establish the diagnosis, but are helpful in indicating the need for histologic examination. Pathologic examination of cell (cytology) and of tissue specimens is of the utmost importance; the former in screening patients and the latter in establishing diagnoses.

History

The importance of the patient's history depends upon the particular site where cancer might be found. The history is of maximal value in endometrial carcinoma and of the variable value in vulvar and cervical carcinoma. The history is of practically no value in detecting ovarian carcinoma, because this tumor generally is silent, producing no distinct symptoms until it is extremely far advanced.

Sporadic bleeding or mucous vaginal discharge generally will occur in the presence of carcinoma of the endometrium at a time when the tumor may be completely controlled by available methods of treatment. This is in large part due to the fact that cancer of the body of the uterus remains localized for a considerable period of time and bleeding occurs secondary to local overgrowth and necrosis of neoplastic tissue.

A history of long-standing vulvar pruritis, a painful lesion that has failed to heal, or a remote history of irradiation treatment for vulvitis certainly should arouse the suspicions of the examining physician as to the presence of vulvar carcinoma.

In years past, the symptoms of cervical carcinoma were thought to be of great importance. These symptoms consist of bleeding that is painless, progressive, and prone to follow trauma. New and unusual vaginal discharge may also be important. Unfortunately, these symptoms may occur only when a tumor is in an advanced stage, and it is for this reason that regular pelvic examinations are of great importance even in the absence of symptoms.

Inspection

Inspection is of value only in the detection of vulvar and cervical lesions. It is of less importance in cervical lesions, since, if inspection were to be depended upon, approximately 90 per cent of the cervical carcinomas in situ, which are microscopic, would be overlooked. Inspection of the vulva is of great importance, and should constitute the first step in a well-ordered pelvic examination. Unfortunately, the physician oftentimes overlooks the vulva and proceeds directly to the examination of the cervix and the vagina. Greater attention to the vulva on routine examinations would improve the rate of early detection of vulvar lesions.

Carcinoma in situ and invasive carcinoma of the cervix are often associated with otherwise benign cervical lesions; consequently, the presence of a cervical erosion, polyp, laceration, eversion, or chronic cervicitis indicates the need for establishing histologically the presence or the absence of invisible carcinoma in situ or of invasive carcinoma.

Colposcopy has been suggested as an aid to better evaluation of the cervix. Scheffey, Lang, and Tatarian[3] have reported that in 168 patients colposcopy did not result in the primary diagnosis of a single case of malignancy nor did it result in differentiation between carcinoma in situ and early invasive carcinoma. It is true that colposcopy may complement cytologic examination by indicating the sites where biopsy specimens should be taken. Colposcopy is a research tool and seems unlikely to become widely used or necessary for early detection of cancer.

Palpation

Palpation is of importance in diagnosing ovarian caricinoma, but it is of little or no value in identifying malignant lesions at sites other than the ovaries. Unfortunately, when suspicious ovarian enlargements are found, they may represent far-advanced cancer. A cyst 7 cm. or larger in size, which persists in a young woman, should be investigated. In women at or near the menopause, considerable caution is indicated. Any persistent ovarian enlargement should be investigated promptly. A good precept is that a palpable ovary in a postmenopausal woman denotes the presence of carcinoma until proved otherwise.

Cytologic Studies

Cytologic studies have become widely used in the last 10 years and patient

demand for them is increasing. This demand has occurred despite an original concern by clinicians in regard to the cost of cytologic studies, and because of the high rate of reliability, as confirmed by well-controlled and large series that have been reported. Unfortunately, there is considerable variability in results and accuracy in many parts of the country. When accuracy is not dependable, it is better not to carry out such studies; standard quadrant biopsy of the cervix is preferable. A high rate of false-positive reports leads to needless alarm and to many unrewarding diagnostic studies. A high rate of false-negative reports may lead to an unwarranted sense of security and to the clinician's overlooking of lesions that should be found.

The methods of obtaining cytologic specimens vary considerably over the country. These have consisted of a great variety of implements and materials ranging from applicator sticks, tongue blades, spatulas and aspirating pipets, to Gelfoam and tampons. Most pathologists have preferences that should be observed by the clinicians. It is our procedure to use a single cotton applicator stick that is rolled over the surface of the cervix and into the external os.[4]

Four people are involved in cytologic accuracy: the patient, the clinician, the technician, and the pathologist. Patients are prone to take douches just before having a pelvic examination unless advised not to. Such a practice may be responsible for false-negative results, since diagnosis is dependent on exfoliated cells. The clinician is responsible for providing a well-prepared slide or slides for interpretation by the pathologist. The technician must be well trained in staining and in screening specimens, and the pathologist must have a breadth of experience enabling him to interpret the slides properly. The clinician is ultimately responsible for making a clinical application of the information obtained. When numerous persons handle specimens there is a continuing chance that wrong identifications may occur.

Several principles are important in the interpretation and clinical application of cytologic studies. First, these studies are screening in nature and serve to indicate those patients who require more complete investigation. These studies are not diagnostic, and therapy should not be started without a histologic diagnosis. Secondly, a positive cytologic report should not be ignored. Cytologic studies may be likened to the sport of fishing: when no fish is caught, it does not rule out the presence of fish, but when a fish is caught, we are generally convinced that other fish are present. When abnormal cells are found, we must assume that there is a source for them and efforts should be made to find that source. If a second cytologic study is done and is negative for neoplastic cells, it does not negate the first result.

Cytologic studies may be of value in detecting any gynecologic malignancy; however, its greatest value lies with the early detection of cervical abnormalities. When the standard cervical technic is used for the detection of endometrial

carcinoma, the accuracy drops to about 80 per cent as opposed to a better than 90 per cent accuracy in the detection of cervical carcinoma. Endometrial-aspiration spreads are of value only when they are positive for atypical cells. A negative cytologic report is of no value, particularly when clinical symptoms are present. An occasional ovarian carcinoma can be detected by either cervical or endometrial cytologic technics.

Biopsy

Biopsy is the only available method of confirming clinical impressions derived from the application of any of the above-outlined technics. Excisional biopsy should be performed on any suspicious vulvar lesions, such as those that are ulcerated or that fail to heal in a short time under active medical treatment. When a cervical lesion is present it should be biopsied before cauterization or any other treatment. This generally can be performed in the office, causing little or no pain to the patient and minimal inconvenience to the doctor.

Endometrial biopsies obtained in the office are of value only when the specimens are positive for carcinoma. Biopsies may be desirable if frozen-section diagnosis is not available, or if radium is not used as part of the treatment of endometrial carcinoma.

An ovarian biopsy requires laparotomy, and the clinician must be well versed in the gross pathologic features of ovarian carcinoma and be ready at the time of operation to make a decision regarding appropriate therapy. Under ideal circumstances, a pathologist is available for providing frozen-section diagnoses. An evaluation of diagnostic aids is summarized in *Table 1.*

Table 1.—*The early detection of pelvic malignancy—evaluation of diagnostic aids*

	Site of carcinoma			
Diagnostic aids*	Cervix	Corpus uteri	Ovary	Vulva
History	±	+	0	±
Inspection	±	0	0	+
Palpation	0	0	±	±
Cytology	+	±	0	+
Office biopsy	+	+	0	+
D and C	+	+	0	0

* + means generally helpful; ± of variable help; 0 of no value.

Specific Application of Cytologic Technics

Our cytologic results are reported according to the original Papanicolaou classification with various subgroupings. Diagnostic methods depend on the gross appearance of the cervix and the cytologic classification: classes I and II are essentially normal and require no treatment. A gross cervical lesion should be biopsied. If the biopsy specimen is negative for carcinoma, cautery or conization should be performed to eliminate the cervical lesion. When the cervix is clean, a yearly cytologic study should be done. Spreads of cytologic class III represent findings that are too important to disregard but not serious enough for immediate concern if the cervix is clean. Another spread should be obtained in three months. If the cervix presents a gross lesion, biopsy and cautery or conization should be performed for more complete diagnosis and treatment. The cervix should be examined periodically (including cytologic studies) after the completion of healing.

Classes IV and V spreads demand intensive diagnostic study. In both of these classes, a biopsy is done if there is a visible cervical lesion. If the biopsy reveals no invasive carcinoma, a sharp-knife and cautery conizations *(Fig. 1)* with incidental dilatation of the cervix and curettage (D and C) are performed. When no lesion is visible, sharp-knife and cautery conizations are done without further study. Conization specimens are subjected to step-block examination *(Fig. 2)* so that the whole specimen is examined as thoroughly as is feasible.

A random or quadrant biopsy that reveals chronic cervicitis, rules out nothing. Scott and Reagan[5] have demonstrated the high incidence of endocervical carcinoma in situ when the squamocolumnar junction is negative for this lesion. On the other hand, a biopsy that reveals carcinoma in situ does not rule out the presence of invasive carcinoma. We know that these two lesions coexist and that finding one does not rule out the presence of the other. Therapy for carcinoma in situ is grossly inadequate for invasive carcinoma.

When histologic examination fails to demonstrate the source of abnormal cells, it may mean that the lesion has been removed but was not found in the examined tissue, or, more importantly, the lesion may have been overlooked completely and still be present. Thus, when the cervix has healed, follow-up cytologic study should be carried out. If negative for abnormal cells, these studies should be done at three-month, at six-month, and thereafter at yearly intervals. If cytologic studies are persistently positive, a second conization and dilatation and curettage should be performed. If the lesion is still not demonstrated, cytologic follow-up is indicated. If positive spreads persist, exploration and hysterectomy should be advised because abnormal cells may be produced by the ovaries or the tubes. The percentage of false-positive cytologic reports largely depends on the persistence of the clinician and the pathologist. Our false-positive incidence is 4 per cent in 22,716 cytologic specimens. Thus, when a positive report is obtained, there is only one chance in twenty-five of its being unexplained. Patients having

unexplained positive cytologic reports before D and C and conization, and normal reports thereafter, may either have had a micro lesion removed or, if none was present, be spared future trouble because of the prophylactic benefit derived from conization.

The technic of conization is of great importance. It has previously been detailed.[6] In summary, the procedure should always be done under anesthesia. The vaginal preparation should be gentle with as little trauma to the cervix as possible. A No. 10 Bard-Parker blade is used for the conization, employing a sawing motion in a Scanzoni-like maneuver. Care should be taken to avoid

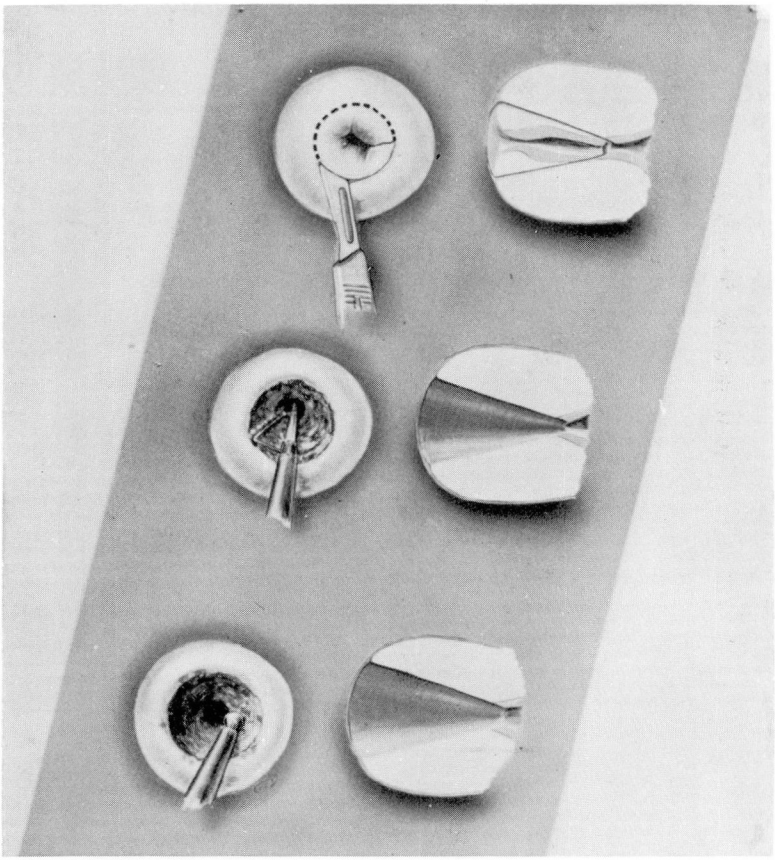

Fig. 1. Drawing showing sharp-knife conization (top), cautery conization (middle), and ball-point cauterization (bottom). In each series the end-on view is left, the longitudinal section is right. (From Krieger, J. S., and McCormack, L. J.: Surg. Gynec & Obst. 109: 328-332, Sept. 1959; by permission of SURGERY, GYNECOLOGY & OBSTETRICS.)

needless laceration of the cervix and to obtain as large a specimen as is practicable. Efforts should be made to extend the conization as close to the internal os as possible. A Heyman loop is used for cautery conization immediately after the sharp-knife procedure. It is believed that this improves the appearance of the healed cervix and is of value in controlling bleeding. Final hemostasis is obtained with a ball-point cautery.

Fig. 2. Conization specimens reduced to serial blocks. (From Krieger, J. S., and McCormack, L. J.: Surg. Gynec. & Obst. 109: 328-332, Sept. 1959; by permission of SURGERY, GYNECOLOGY & OBSTETRICS.)

Summary

The early detection of pelvic carcinoma depends on the co-operation of the patient, the clinician, and the pathologist. Women are being educated to have regular pelvic examinations. Detection methods comprise both clinical examination and pathologic studies. The diagnostic methods available in the detection of pelvic malignancy are tabulated briefly. Our most encouraging results, in early diagnosis, occur when multiple diagnostic methods are available, particularly for the cervix and the endometrium; ovarian carcinoma can be detected early only by chance. Vulvar carcinoma can be diagnosed earlier and more frequently than occurs now, if physicians will look for such lesions.

References

1. Randall, C. L., and Gerhardt, P. R.: Probability of occurrence of more common types of gynecologic malignancy. Am. J. Obst. & Gynec. **68:** 1378-1388; discussion 1388-1390, 1954.

2. Randall, C. L.: Ovarian carcinoma; risk of preserving ovary. Obst. & Gynec. **3:** 491-497, 1954.

3. Scheffey, L. C.; Lang, W. R., and Tatarian, G.: Experimental program with colposcopy. Am. J. Obst. & Gynec. **70:** 876-885; discussion 885-888, 1955.

4. Krieger, J. S., and McCormack, L. J.: Use of cervical spread in cancer detection; effective method and evaluation. Cleveland Clin. Quart. **24:** 137-140, 1957.

5. Scott, R. B., and Reagan, J. W.: Diagnostic cervical biopsy technique for study of early cancer; value of cold-knife conization procedure. J. A. M. A. **160:** 343-347, 1956.

6. Krieger, J. S., and McCormack, L. J.: Individualization of therapy for cervical carcinoma in situ. Surg. Gynec. & Obst. **109:** 328-332, 1959.