

GYNECOLOGIC ONCOLOGY

LARRY MCGOWAN

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Preface

The diagnosis and treatment of cancers of the female reproductive organs have always been an integral part of the obstetrician's and gynecologist's education and medical practice. The many individuals who devoted their lifelong energies to the field of gynecologic oncology have left a rich legacy to the discipline of obstetrics and gynecology. Today, the gynecologic oncologist is recognized as the primary physician responsible for treatment planning, treatment, follow-up, rehabilitation, and terminal care of the woman with cancer of the female reproductive organs. This evolutionary process has been a logical response by the medical profession to centralize responsibility for the care of women with gynecologic cancers in those individuals who by training, experience, and current practice are most proficient. There is also a need to bring together sufficient clinical material to develop better diagnostic aids and therapies for several gynecologic cancers. Perhaps the most pressing demand for education and certification in gynecologic oncology is in the area of delivery of health care. No longer is it acceptable to make a patient fit into a fixed therapeutic modality or schedule; rather, the

treatment—whether it be surgery, irradiation, or chemotherapy—must be individualized to the particular patient's needs.

The team approach in caring for the gynecologic cancer patient is desirable, and several disciplines of medicine are required to develop reasonable plans. The contributors to this edition are thus representative of several disciplines and, in an attempt to achieve balance, are drawn from a number of institutions with a wide geographic distribution. We have tried to present the current consensus in diagnosis and therapy of gynecologic cancer. Where opinion remains divided, we have given the rationale for each suggested form of management. At times the experience of the contributor has been extensive and consistent, which permits a particular form of treatment to be outlined. The objectives of this edition have been the creation of a gynecologic oncology text of sufficient scope to meet the needs of medical students, residents and fellows in gynecology, practicing obstetricians and gynecologists, physicians in closely allied fields, and gynecologic oncologists.

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Gynecologic Cancer: The National Problem

LARRY MCGOWAN, M.D.

Cancer of the female genital tract has been subjected to more study over a longer period of time than any other major cancer in humans. Historical documentation of the compilation of knowledge regarding cervical cancer and its diagnosis and treatment is familiar.^{1,2} There is no other major cancer in which more is known about the disease pattern and methods to markedly reduce morbidity and eliminate mortality than cervical cancer. The Papanicolaou cytosmear was one of the first broadly used cancer screening laboratory aids available to physicians to detect early cancer and remains today as one of the better screening aids.

Malignancies of the female genital organs are second in frequency only to breast cancer among women, and, if in situ carcinomas are included, they are the most frequently seen cancers.³ Although it has been estimated that there are 387,000 women alive following a history of uterine cancer (excluding carcinoma in situ) in the United States,⁴ a distressing figure is that in one year an estimated 248,927 person years are lost due to death from uterine cancer.⁵ The American Cancer Society's estimation of cancer deaths and new cases in 1978 for the genital organs⁶ is listed in Table 1-1. Cramer and Cutler, presenting data from the Third National Cancer Survey, noted that 6 of 10 newly diagnosed cancers of the female genital organs were invasive malignancies, and the remainder were in situ carcinomas. Of the invasive malignancies, 38 percent originated in the corpus, 30 percent in the cervix, and 25 per-

cent in the ovary; 94 percent of the in situ carcinomas originated in the cervix.³ Carcinoma in situ of the cervix peaked at ages 25 through 34 and decreased rapidly thereafter. The age-specific incidence of invasive cervical cancer in whites increased more slowly than that for in situ carcinoma and plateaus at ages 45 through 49, though the rates at ages 65 through 80 are slightly greater. Cancers of the corpus are relatively infrequent until age 40, but increase rapidly, reaching a peak at 65 to 74 and declining thereafter. In all women younger than 45, cervical cancers, both in situ and invasive, are predominate. In black women, cancers of the cervix remain the most common cancers of the female reproductive organs throughout life. In white women, cancers of the corpus and ovary increase rapidly in the 45 to 50-year age group, and the incidence of cancers of the cervix, corpus, and ovary is similar in this period. After age 55, cancers of the corpus and ovary are more numerous than those of the cervix in white women.³

The average age of patients with epidermoid carcinoma (51.4 years) was significantly less than the average age of patients with adenocarcinoma of the cervix (56.2 years).³ Sarcomas of the corpus also appeared at younger ages than adenocarcinoma of the corpus (56.5 versus 60.7 years). Cramer and Cutler observed that patients with germ cell malignancies of the ovary had a mean age of 37.5 years compared with the overall age of 57.7 years for women with ovarian cancer. Sar-

Table 1-1. ESTIMATED CANCER DEATHS AND NEW CASES FOR ALL SITES—1978

<i>SITE</i>	<i>ESTIMATED TOTAL DEATHS</i>	<i>ESTIMATED TOTAL NEW CASES</i>
Genital organs	22,500	69,200
Cervix, invasive	7,400	20,000*
Corpus Uteri	3,300	28,000
Ovary	10,800	17,000
Other female genital	1,000	4,200

Incidence estimates are based on rates from NCI Third National Cancer Survey 1969-71.

*Invasive cancer only.

comas of the vulva occurred at a younger age than that for all invasive malignancies of the vulva (32.9 versus 65.3 years). For cancers of the corpus, blacks showed a proportionately greater number of sarcomas and fewer adenocarcinomas than whites.

For ovarian cancer, blacks had a proportionately greater number of gonadal stromal and germ cell cancers, and fewer serous cystadenocarcinomas. Basal cell carcinomas and melanomas of the vulva were rare among blacks.³

Cramer and Cutler attached great importance to the observation that the crude rate in women 20 years of age and older for all invasive cancers of the genital organs had decreased from 118 cases per 100,000 in 1947, to 89 cases in 100,000 in 1969 and 1970. While the cervix accounted for one-half of the invasive malignancies in 1947, it now accounts for less than one-third of the cases.

The percentage of malignancies of the corpus has doubled, while ovarian cancers increased 40 percent.³ The decrease in deaths due to uterine cancer is partly related to improved diagnostic methods for detecting cancer of the cervix, but the death rates were already on their way down when cervical cytology programs were being implemented, therefore, this decline cannot be totally explained by these programs.⁴ A trend toward larger numbers of in situ carcinomas of the cervix is being observed in the United States.

The most common multiple primary cancers within the female reproductive tract were of the corpus and ovary. Cramer and Cutler report that the dominant malignancy in women is breast cancer, and, among women with multiple primaries, breast cancer was frequently found with cancers of the corpus and ovary.

REDUCTION OF MORBIDITY AND MORTALITY FROM GYNECOLOGIC CANCERS

There are only three avenues by which the toll of cancer illness and death can be controlled and reduced: prevention, earlier detection, and improvements in treatment. In women with a history of coitus, regular examinations that would include visualization of the cervix, a cervical cyt smear, prompt biopsy of an obvious lesion, and pelvic examination would have an even greater impact on the immediate reduction in cervical cancer morbidity and mortality. Visualization and more frequent biopsy of persistent lesions of the vulva and vagina would also reduce morbidity and

mortality from vulvar and vaginal cancer. Endometrial tissue aspiration in perimenopausal or postmenopausal women who are at risk for developing endometrial cancer (obese, hypertensive, diabetic, few to no children, or taking oral estrogens in high dosages over long periods of times) performed in the doctor's office will detect endometrial cancer at an earlier stage and reduce morbidity and mortality.

Although there should be very few deaths due to cervical cancer today, the fact remains that over 7000 occurred last year and with an overall five-

year salvage that is only slightly better than 60 percent. Cervical cancer should serve as our model for delivery of cancer health care. Every physician's office should be a cancer detection center. Each obstetrician and gynecologist should be able to perform appropriate diagnostic procedures and basic surgical operations to establish the diagnosis of cervical cancer.

Screening for cervical cancer, whether it takes place in a physician's office or through a federal, state, or local program, must be intimately associated with the health delivery system (Fig. 1-1). An isolated or freestanding screening program can result in women with suspicious or positive cytoscans for cancer having a low percentage of follow-up and histologic study. These women then have a false sense of security that they are cancer free when, in fact, the opposite is true. Also, Schmitz and associates have documented that haphazard therapy for cervical cancer must not occur if women are to have the best chance to be cured of their disease.⁷

Three perceptions must be held before women will seek screening services for a gynecologic

cancer: (1) The disease must be recognized as being serious, (2) a woman must believe herself to be susceptible to the disease, and (3) she must be convinced that early detection will lead to prevention of serious illness or that treatment will be effective. The absence of one or more of these beliefs in a group of women would indicate a need for cancer education.

In 1973, approximately three-fourths of all civilian, noninstitutionalized females 17 years and older had at least one Pap smear. Approximately 61 percent who had ever had a Pap smear had the examination during the preceding year. A higher proportion of females 25 to 44 years of age had a Pap smear than other ages (90 percent). Proportionately fewer females 65 years of age and over had ever had a Pap smear compared to other age groups, and these women were less likely to have had a recent examination.⁸ This is an important observation, as the woman at age 65 today has an expected 17 more years of life and at age 55 about 25 more years of life.⁹ The value of a complete physical examination, which must include a pelvic examination, cannot be too strongly stressed.

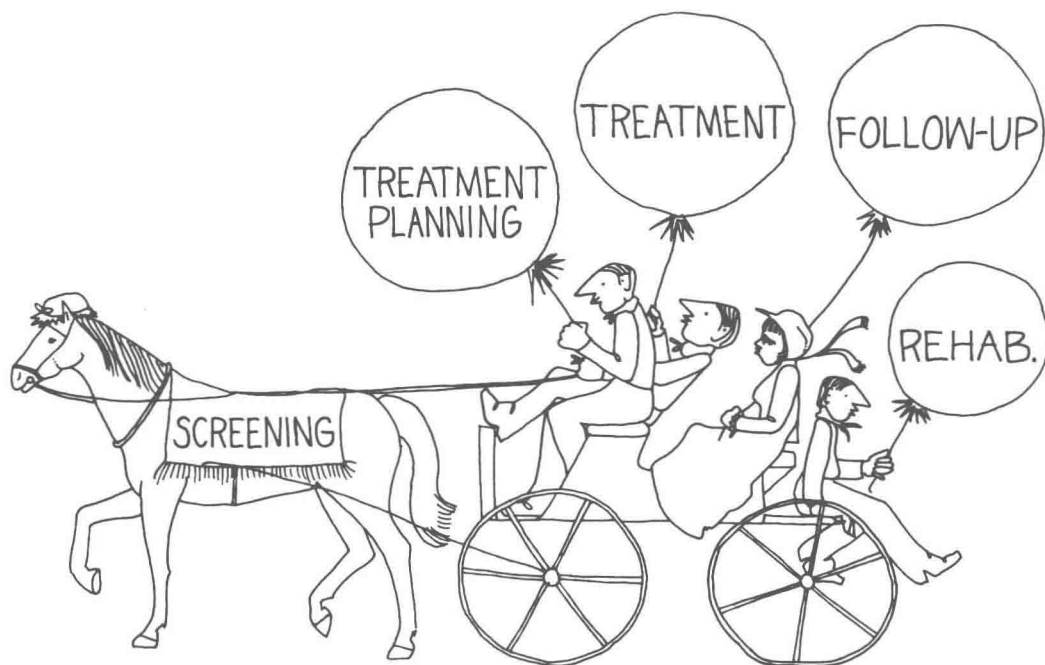


Figure 1-1. Screening for cervical cancer must be coupled with treatment planning, treatment, follow-up, and rehabilitation programs.

DELIVERY OF GYNECOLOGIC CANCER HEALTH CARE

The interaction between medicine and society, physicians and their patients are undergoing changes in several areas. Patients are becoming increasingly aware of their rights as consumers of health care and more commonly are exercising these rights. Costs of delivery of gynecologic cancer health care are under increasing public scrutiny, as well as the medical profession's concern as to who should deliver cancer care and where.

Informed Consent

Physicians must reveal the risks which, to a reasonable woman, would enable her to make her decision as to whether or not to undergo treatment. She has the right to have all the information that is necessary and relevant to give an informed consent. The physician must relate to his patient her medical problem in language that she can understand and be prepared to answer relevant questions. Areas to be covered in diagnosis are (1) what her condition is called, (2) how it affects her body, and (3) what her prognosis is with and without treatment.

Patients expect to be concisely informed on diagnostic and treatment procedures by knowing what the procedure is called, how it is performed, by whom, and where, what are the chances of it helping her and will it need to be repeated, and how long do these procedures take. If hospitalization is required, the patient should know how long will she be in the hospital, how painful the procedure is and will it limit her activity afterward, what are the possible side effects, complications, or risks and how often do these occur. Also, are there alternates to your suggested procedure and why is the one you have chosen better, is the treatment you are suggesting generally accepted or is it an experimental procedure, and if it is experimental, how often have you performed it. If surgery is to be used, will the anesthesiologist be available to visit your patient before operation and explain to her the type of anesthesia, risks, and how she will feel postoperatively.

With the use of drugs, particularly chemotherapy, patients need to know the name of the medication, how it is given, in what dosage and how often, and what does it do. Any side effects, restrictions, or limitations should be explained to the patient in terms she will understand. The risk

involved in taking the medication and the frequency of these risks, as well as alternative medications and whether it is a generally accepted drug or an experimental one should be stated.¹⁰

The role and image of the physician in American society is changing. There is a suggestion that the physician is more of a technician than ever before, more likely to work as part of an institutionalized health care system, and subject, like other experts, to recurrent debunking of his once unquestioned authority. In our morally pluralistic, aggressively participatory society, physicians must first of all do no harm and respect the rights of patients in medical decision making beyond the strictly scientific level.

Costs

The costs of a catastrophic illness such as gynecologic cancer are significant. There are increasing professional and public concerns with the continued deaths from cervical cancer, which are almost universally preventable as are most endometrial cancer deaths. With approximately 7500 deaths due to cervical cancer last year in the United States⁶ and a conservative estimate of \$16,000 representing all expenses related to the disease and the death process,¹¹ a national figure of \$120,000,000 each year is impressive.

All patients wish to know the costs of various diagnostic and treatment procedures in relation to the adequacy of their insurance coverage. Many people today would place national health insurance against catastrophic illness as an urgent demand. Over 96 percent of all women with gynecologic cancer are admitted to a hospital at some time during their illness to receive care.⁴ Medicare and other "government" funds now finance about half of all hospital costs of all cancer patients.¹²⁻¹³ Doctors must pay greater attention to governing themselves and particularly to overseeing the quality and costs of medical treatment.

Gynecologic Oncology

Every physician's office is a cancer detection center. Burkons and Willson, in a recent study in Michigan, found that 44 percent of women have no primary care physician and 86 percent see only their obstetrician-gynecologists for regular

periodic examinations. Also, 41 percent of the women reported that their obstetrician-gynecologist either had treated them for non-gynecologic conditions or had decided that no treatment was necessary.¹⁴ The U.S. Department of Health, Education and Welfare has defined obstetrics and gynecology as one of the disciplines of medicine included in primary care. The American Board of Obstetrics and Gynecology feels that the first year of graduate study should help prepare the physician to serve as the initial contact for entry into the health care system.

For at least the past two decades, there has been thoughtful inquiry within the field of obstetrics and gynecology, as to who should treat pelvic cancer,¹⁵ where should gynecologic cancer be treated,¹⁶ the need for advanced specialization,¹⁷ and the responsibilities and training of the gynecologic oncologist.¹⁸⁻²¹ Gynecologists have been involved for many years in formal education in gynecologic oncology, international collaboration in staging and end-result reporting, definition of uterine cancer precursors, devising combinations of surgical, irradiation, and chemotherapeutic regimens, and currently establishing standards for certification in gynecologic oncology.

The gynecologic oncologist today is the primary physician responsible for treatment planning, treatment, rehabilitation, follow-up and terminal care of the gynecologic cancer patient. No longer is it acceptable medical care to treat gynecologic cancer in an environment where there are not personnel and facilities to permit a team approach. On that team, to mention a few, are the obstetrician and gynecologist, cytopathologist, clergy, family or general practitioner, internist, medical oncologist, nurses, pharmacist, radiotherapist, social worker, surgical pathologist, and urologist. The public's demand for integrated medical care as well as the demand for identification of a coordinating physician has been met by the discipline of obstetrics and gynecology for cancers of the reproductive tract by the recognition and certification of the gynecologic oncologist. No woman with gynecologic cancer should be fitted into a treatment regime; rather, the treatment should be adapted to her particular needs and her disease. For example, she should not be referred to an institution or an individual who carries out only a surgical procedure or to another institution or individual who solely performs irradiation therapy for cervical cancer.

Although the gynecologic oncologist is the central figure to bring together treatment plan-

ning, treatment, follow-up, rehabilitation, or terminal care of the cancer patient, the obstetrician and gynecologist must be able to carry out basic diagnostic procedures and perform basic surgical operations for the diagnosis of gynecologic cancer. The obstetrician and gynecologist, along with the radiation therapist, family, or general practitioner, internist, or medical oncologist must share in the follow-up, rehabilitation, and terminal care of the gynecologic cancer patient.

The overall survival for most gynecologic cancers reflects a serious need for improvement. It is universally acknowledged that *in situ* carcinoma of the cervix is 100 percent curable. The overall survival for all cases of invasive cervical cancer is slightly better than 60 percent^{4,22} and of all invasive cervical cancers 20 to 30 percent of them are in stages II to IV at the time of diagnosis. This latter figure has not changed in over 20 years. The survival rate for ovarian cancer has not changed in 30 years, with 70 percent of patients dying in 5 years.²² Since there are approximately 17,000 new cases of ovarian cancer each year in the United States, it is obvious that more concentrated study of these women must be carried out. Epidemiologic studies, development of diagnostic aids, and improved therapies for this disease which now is the fourth leading cause of cancer deaths in American women are necessary. An overall five-year survival of 75 percent for endometrial cancer also reflects the need for more purposeful screening of women for endometrial cancer and an integrated team approach to therapy. The less frequent cancers, such as vulvar, vaginal, fallopian tube, as well as sarcomas of the female reproductive organs certainly could have an improvement in their generally poor prognosis by more organized medical care.

As the team approach for primary and continuing care of gynecologic cancer gives the patient a better chance for cure, it becomes readily apparent that increased training programs in gynecologic oncology must be developed so that there are sufficient health care delivery team leaders for all invasive gynecologic cancer patients in the United States.²³ Obstetrics and gynecology, with the support of the American Medical Association, has been a leader in the concept of regionalization of medical care. In 1971, both organizations supported centralized community and regionalized perinatal intensive care, and in 1976, they approved the concept of regionalization of obstetric care. Regionalization of gynecologic cancer care would seem to be the next logical step.

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Current Problems in Gynecologic Pathology

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Communication of accurate, meaningful information between clinicians and pathologists is essential in providing optimal care for patients with gynecologic cancers. A deficiency in communication between clinician and pathologist may compromise the management of patients. Technical problems in the handling of tissues can reduce the accuracy and reliability of pathology reports, and

problems in histologic interpretation and classification of tumors must be appreciated in order to make meaningful comparisons of data from different institutions. Each of these problem areas is examined below in anticipation that all members of the oncology team, and ultimately the patient, may benefit from an appreciation of the pathologist's viewpoint.

CLINICIAN-PATHOLOGIST COMMUNICATION

Pathology reports may contain so little information that planning of therapy is compromised. Examples of lapses in communication abound. For example, a diagnosis of "adenocarcinoma of the endometrium" is far from adequate. The pathologist should state the location of the tumor within the corpus, degree of differentiation, depth of myometrial penetration, and length of endometrial cavity, as prognosis and additional therapy often depend on these factors. It is as if the pathologist were unaware of the factors relating to the prognosis of endometrial carcinoma when he omits the essential information. Recognition of the prognostic factors is the key element of modern pathology and radical departure from prior decades when the pathologist was expected only to "pin a label" on the process. Now, a label is not enough and can be misleading. Our understanding of most histologic aspects of gynecologic

cancer has progressed to the point that now the pathologist is required to identify not only the process but also its subtype, extent of growth, grade, and any unusual aspects or factors relating to prognosis, so far as the specimen is able to provide them.

The terms chosen to characterize a neoplasm should be current and their meaning unmistakable to the clinician reading the report. Certain diagnoses require explanation or amplification to avoid misunderstanding. If the diagnosis "adenocarcinoma in situ" is used, the pathologist must make clear what he means by that diagnosis, as it has had several meanings in the past. When reporting "microinvasive carcinoma" in a cervical cone, the pathologist must make clear to the clinician the specific characteristics of the lesion in question, since a uniform definition of this term has not been established. He should specifically