TREATMENT OF CANCER AND ALLIED DISEASES

SECOND EDITION

VOLUME VI

Tumors of the Female Genitalia

BY TWENTY-SEVEN AUTHORS

Edited by **GEORGE T. PACK,** M.D., F.A.C.S.

and **IRVING M. ARIEL,** M.D., F.A.C.S.

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TREATMENT OF CANCER AND ALLIED DISEASES

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I: Principles of Treatment

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VII: Tumors of the Male Genitalia and the Urinary System

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Dedicated to the late

GÖSTA FORSSELL

a pioneer in cancer research and an early and important contributor to the scientific application of irradiation in the treatment of cancer

and to

MAUD WILCOX

who dedicated her energies and time over a long and productive lifetime to the advancement of cancer education and research

Science is at the same time the motivating force of society in the campaign against cancer and the eagle eye searching to discover weapons.

—GÖSTA FORSSELL

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Preface

This volume describes and critically evaluates all methods currently employed in the treatment of neoplasms arising from the female genital tract. Each therapeutic method—surgical, radiologic, chemical, or hormonal—is considered as to technic, accomplishments, and complications.

Neoplasms of the female genital system have served as the proving ground for testing new methods of treating cancer. The surgical attack upon intra-abdominal organs began with an ovariectomy for a cyst of the ovary (Ephraim McDowell, 1809). Some of the first attempts to utilize x-rays and radium (Zowers, 1906) were for cancer of the uterus. Since these pioneer efforts, each new development in surgical practice and in the science of radiotherapy has been applied to the treatment of tumors of the female genitalia. There has developed a healthy competition between surgeons and radiotherapists as to the relative efficacy of each of these sciences in curing gynecologic cancers. This competition reflects attempts by all interested in treating this group of neoplasms to improve their methodology, striving ever for an increased number of cured patients.

The surgical era in the treatment of gynecologic cancer received its impetus in 1898 when Ernst Wertheim began his series of radical hysterectomies for cancer of the cervix, an operation developed experimentally by Ries of Chicago in 1895 and performed clinically, in the same year, by J. G. Clark of the Johns Hopkins Hospital and by Howard A. Kelly of Baltimore and E. T. Thring of Sydney. Radical hysterectomy was gradually extended to include resection of the inguinal and iliac lymph nodes (Taussig, 1930; Nathanson, 1932) in selected instances.

With the development of improved radiation equipment and refinements of technic, this modality enjoyed increasing popularity in the treatment of gynecologic cancer and was employed extensively during the 1920's and 1930's. Technics of intracavitary radium irradiation of cervical cancer were devised by the Stockholm group, who applied an intensive course of radium at weekly intervals, and, simultaneously, by the group at the Curie Radium Institute in Paris, who utilized a continuous, low intensity radium source. In the United States, high voltage x-radiation and the vaginal radium applicator were extensively used by William P. Healy. Dosimetry was improved, and in 1938 the Tod and Meredith Manchester dosage system was devised in order to obtain more uniformity for radium distribution.

Improvement in surgical technic then led to a resurgence of the surgical attack on these neoplasms which has continued to the present. Pelvic exenteration for cervical cancer was first performed by Brunschwig in 1946 and by Parsons in 1947. The present ability of surgeons to remove practically any pelvic organ and to construct artificial conduits for elimination demands careful evaluation to determine which patients are suitable candidates for these extensive procedures.

Paralleling this renascence of interest in the surgical treatment of gynecologic cancers there

has been continued progress in the development of radiation apparatus, dosimetry, and the clinical application of radiation to these cancers: rotation therapy, supervoltage x-ray therapy (1932), the betatron (Kerst, 1941), the cyclotron (Lawrence, 1932), with the associated radioactive isotopes, the proton beam, the neutron beam, and the deuteron beam. At present, both surgery and radiation therapy are extensively utilized, either singly or in combination, in the treatment of cancer of the female genital tract.

It has been the Editors' aim to present the current status of each therapeutic modality employed in the treatment of gynecologic cancer. Included are a chapter on high energy irradiation of pelvic cancers and separate chapters on the surgical and radiation treatment of neoplasms arising from each organ of the female genital system.

The chapters on vulvar cancer indicate why this neoplasm responds poorly to irradiation and describe the technics and accomplishments of radical vulvectomy and bilateral groin dissection, an operation based on the routes of spread of this neoplasm as originally shown by Basset in 1912.

Vaginal cancer—considered by Way to be the most difficult gynecologic cancer to treat successfully and concerning which Taussig in 1935 stated, "We acknowledge our total inability to do anything effective for primary cancer of the vagina"—is now responding to modern methods of treatment. The radiation treatment of this cancer is critically evaluated; and the more radical surgical procedures (e.g., radical hysterectomy and vaginectomy), which are curing a significant number of vaginal cancers, are described and illustrated.

Similarly, the volume includes a critical analysis and detailed descriptions of all technics (surgical and radiologic) utilized in the treatment of cancer of the uterine cervix, corpus uteri, fallopian tubes, and ovaries.

Additional chapters are devoted to such problems as precancerous lesions of the vulva; the treatment of myomas of the uterus as they pertain to uterine sarcoma; the treatment of endometriosis; hydatidiform mole and choriocarcinoma; sarcoma of the uterus; and the treatment of neoplasms of the female genital organs when complicated by pregnancy.

The female genital system continues to be the testing field for the clinical application of new methods of cancer control. One gynecologic neoplasm, choriocarcinoma, is the only cancer which, at this writing, has apparently been cured by an anticancer drug (Methotrexate). Similarly, the detection and treatment of early cervical cancer, the carcinoma-in-situ, represents a dramatic advance in the control of a frequent form of cancer in women. The roles of such relatively new disciplines as hormonal therapy, chemotherapy, and radioisotopic therapy in the management of gynecologic cancer are discussed. The indications, technics, accomplishments, and complications of radical exenteration of extensive pelvic cancer, and the treatment of pelvic radiation reactions following the irradiation of uterine neoplasms are considered at length.

The treatment of cancer of the female genitalia is in a state of dynamic development, and every effort has been made to present in this volume all aspects of the present-day therapy of these common neoplasms. Great strides have been made in this field of oncology. Many patients are being cured; but despite these successes, approximately thirty thousand women will die in the coming year in the United States from cancer arising in organs of the female genital system. It is the hope of the Editors and each of the contributing authors that the procedures described in this volume, which have as their aim the earlier diagnosis of gynecologic cancer and improved treatment by means of precision irradiation and well-planned, often radical surgery, may contribute to a precipitous decline in the mortality from these neoplasms.

G. T. P.

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INTRODUCTION

Neoplasms of the Female Genital System: An Appraisal

Daniel G. Morton

INCIDENCE

Cancer affecting the female genital organs constitutes one of the principal causes of death in women and thus is a subject of great importance. In 1962, approximately 30,000 women in the United States will die because of it. Actually, the number of deaths from this cause per 100,000 women in the population has declined significantly during the last fifteen to twenty years, principally because of earlier diagnoses of cervical cancer, the most frequent cancer of the female pelvic organs. While cancer of the lung has been increasing shockingly as a killer, cancer of the cervix has been decreasing significantly. Public Health reports reveal that between 1940 and 1954, deaths from uterine cancer decreased in New York State 36 per cent and in California 41 per cent, to rates of 19.1 and 14.8 per 100,000, respectively. These rates are somewhat lower than those for cancer of the breast and for cancer of the digestive organs, but still are of great moment. The high death rate in women from pelvic cancer is particularly tragic because it is so often needless; many of the deaths could be avoided by carrying out simple diagnostic measures currently available. Much has been accomplished in this respect in the last two decades, and it seems likely that progress will continue.

ETIOLOGIC CONSIDERATIONS

The specific causes of pelvic cancers remain obscure although a great deal has been learned regarding predisposing conditions and etiologic factors.

VIRUSES AS CARCINOGENIC AGENTS

The suspicion that one of the potent carcinogenic agents is viral in nature has gained ground steadily in recent years, although there is no definite evidence to substantiate this belief in the human at the present time. Indeed, there are many similarities between cancer and infection, particularly with respect to the manner in which the body reacts to these two harmful stimuli. However, it seems highly probable that there is no specific relation between ordinary bacterial infection and cancer. On the other hand, it is known that viruses can cause cancer in fowl, and inclusion bodies have been found on occasion in the epithelial cells of the uterine cervix of women. Speculation regarding a relationship between nucleic acid and viruses has appeared in the literature of the last few years and further research should soon reveal whether the speculation is justified. Should there be such a relationship, the kind of evidence that could tie viruses and cancer together might well be forthcoming.

Additional observations bearing on a possible relationship between cancer and infection are: (1) When cancer of the cervix has been treated successfully, even though the lesion may have been a minimal one, the patient's general health frequently improves astonishingly, just as it does when a focus of infection has been removed. (2) Tumors of equal extent often react in diametrically opposite ways to the same treatment. Why? Differences in bodily resistance seem to be the most logical reason. Ruth Graham has attempted to show

that differences in bodily resistance to cancer of the cervix are reflected in the character of the normal cells shed into the vagina and the tabulations of her results are convincing (Table Introd.-1). (3) It is known that individuals sometimes remain alive and clinically well for many years with live cancer cells in their systems that then become active and the patients die of recurrence at some remote period after treatment. This, too, suggests a body resistance. Late recurrences of breast cancer are notorious. Although late recurrences, ten or more years after treatment, of cervical cancer are possibly less common, they do occur in a not inconsiderable number.

TABLE INTROD.-1.—CANCER OF THE CERVIX: FIVE-YEAR SURVIVALS IN RELATION TO SENSITIZATION RESPONSE*

	Poor sensitization response				*Good sensitization response*			
	Surgical treatment		*Irradiation*		*Surgical treatment*		*Irradiation*	
Stage	*Number*	*Per cent*	*Number*	*Per cent*	*Number*	*Per cent*	*Number*	*Per cent*
I	49/71	69	7/24	29	8/15	53	9/14	64
II	19/28	68	9/41	22	5/15	33	22/29	76
TOTAL	68/99	69	26/65	24.6	13/30	43	31/43	72

* *From* Ruth Graham [12], *courtesy American Journal of Obstetrics and Gynecology.*

INFLUENCE OF CELIBACY AND OF PARITY

Very striking are the findings of Gagnon and also of Janet Towne in their studies of nuns. These celibate women had a practically negligible incidence of cervical cancer although the incidence of other pelvic neoplasms, including endometrial cancer, was similar to that of the general population.

On the other hand, mere childbearing seems not to be specifically related, because the incidence is no greater in women who have borne six children than it is in those who have had one; or, indeed, who have simply been married, if we take into consideration the fact that most women have married and had children by the time they reach forty-five years, which is the age of greatest incidence for cervical cancer. What is the explanation? Does coitus initiate an infection that sometimes has dire results? There is, indeed, a definite correlation between cervical cancer and noncelibacy.

SMEGMA

Attempts to correlate the development of cervical cancer with smegma have not been completely successful, although a relationship has long been suspected. While Jewish women have fewer cervical cancers than do non-Jewish women, in some parts of the non-Jewish world where the men have all been circumcised, as in the case of Jewish men, the women develop cancer of the cervix as frequently as do women of other groups. So, while smegma *may* play a role, it is not an exclusive one.

ENDOCRINOLOGIC RELATIONSHIP

Hormones certainly have marked effects upon the cellular growth of some tissues and have been suspected of playing a part in carcinogenesis. The production of mammary cancer in certain strains of mice by the administration of large doses of estrogens is well known. However, it is also known that this susceptibility exists only in certain strains of these animals, many other strains being virtually immune to such action. Although heredity definitely plays a role in mice, no such definite correlation has been established in humans.

So far as the female genitalia are concerned, the relationship between endometrial carcinoma and excessive estrogen production and/or long-maintained estrogenic activity is the most suggestive piece of evidence that hormones can be responsible for carcinogenesis. That there is an increased incidence of endometrial carcinoma in women with feminizing tumors of the ovary, particularly thecoma, seems to be well established. In addition, hyper-