

Steven G. Silverberg

**Surgical Pathology
of the Uterus**

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Surgical Pathology of the Uterus

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NEW CONCEPTS IN SURGICAL PATHOLOGY OF THE SKIN

Richard J. Reed, M.D.

SURGICAL PATHOLOGY OF THE UTERUS

Steven G. Silverberg, M.D.

to Kiyoe

Series Preface

Surgical pathology has been through a revolution! Although conceived by surgeons (one of many areas that can be ascribed to the genius of William S. Halsted), by the participation and leadership of pathologists, it has evolved from a subdivision of surgery to become a discipline of its own. Like all disciplines, its tools need definition. Of its many tools, the basic one is the approach to a specimen. This requires an understanding of tissue handling and is addressed to the solution of at least two questions: (1) What and where is the lesion for which surgery was performed? and (2) What is the best way to demonstrate this lesion on a slide? These questions are basic to our profession. The approach to their answers is not only the fundamental skill of a surgical pathologist, but will, in fact, determine how well the surgical pathologist discharges his responsibilities to his colleagues, his trainees, himself, and his profession.

The concern of the surgical pathologist for diagnostic and experimental endeavors is documented in the literature. We have excelled in these endeavors. We are better equipped than our professional forefathers, but may have faltered in the use of our equipment. This series was conceived to improve our “bench” job and to make this basic approach available to trainees and practitioners.

The why’s and how’s of specimen handling in surgical pathology are our primary concern. Experts in a given anatomic area will address specimen handling and, having done so, will have the opportunity to discourse on a subject or subjects in their area of expertise and interest.

It is our intent that these volumes fill a void that has existed in surgical pathology literature since Joseph Colt Bloodgood, the first American surgical pathologist. We do not intend them to become compendia of diagnostic criteria. Our success will be measured by how completely we answer the two basic questions. The usefulness of our undertaking will be measured by the physicians, surgeons, and pathologists in practice and training. If this is a successful and useful series, they will know, and the patients they serve will benefit.

WILLIAM HARTMANN, M.D.

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Preface

The classical textbooks on the surgical pathology of the female genital tract are all basically disease-oriented in that the disease processes involving an organ such as the uterus are presented in a logical sequence, usually on the basis of etiology. Each is then discussed in terms of causation, clinical manifestations, gross and microscopic pathology, and differential diagnosis. This approach is an excellent one for learning systemic pathology, but it often fails to answer the basic specimen-oriented questions that confront the surgical pathology resident (or the medical student or clinical resident rotating through a surgical pathology service) every day. This book and others preceding and following it in this series attempt to answer these very practical questions of technique.

The approach described herein emphasizes the specimen and the clinical situation in which it has been obtained from the patient and submitted to the pathologist. The patient–surgeon–specimen–pathologist chain is the cornerstone of this approach, since it is through the specimen, not the disease, that the pathologist actually makes contributions to the surgeon, and in turn the patient. This approach can enable even the neophyte resident on the first day in the surgical pathology service to learn to treat the specimen in such a way as to obtain maximal diagnostic information, and to transmit this information in its clearest and most practical form back to the clinician for the ultimate benefit of the patient. Since this, in essence, is what the practice of surgical pathology is all about, the lessons gained from these monographs should be important to pathologists in every stage of their professional development, as well as to those clinicians who sincerely seek a better understanding of the problems facing their pathologists.

This book, as might be expected, is clearly a distillation of my own personal experience, and represents both the wisdom and the ignorance I have acquired and passed on to my own residents in the course of the past ten years. It contains many of my own personal prejudices. I do apologize if these are occasionally stated as fact rather than opinion, for I have tried my best to distinguish between the two and to present them in the proper context.

Since the book is meant to be specifically a handbook of technique rather than an encyclopedia of diseases, many of the rarer lesions of the uterus are discussed only briefly or not at all. Those readers wishing more intensive disease-oriented discussions should refer to the standard textbooks: Gompel and Silverberg, *Pathology in Gynecology and Obstetrics*, Second Edition, J.B. Lippincott Company, 1977; Dallenbach-Hellweg, *Histopathology of the Endometrium*, Second Edition, Springer-Verlag, 1975; and the International Academy of Pathology monograph entitled *The Uterus*, edited by Norris, Hertig and Abell, published by Williams & Wilkins in 1973. Readers desiring Kodachrome collections illustrating various aspects of uterine pathology can choose, among others, from the

OB/GYN Pathology Learning Program of the Council on Resident Education in Obstetrics and Gynecology (1 East Wacker Drive, Suite 2700, Chicago, Illinois 60601), prepared by Dr. Frank Vellios, and my own collection on *Hormonal Pathology of the Endometrium* (MEDCOM, 2 Hammar skjöld Plaza, New York, New York 10017).

Finally, although the defects in this work are undeniably my own, the values, such as they may be, are due in part to the efforts and encouragement of many others. I can mention only a few of these, but they certainly include the Series Editor, Dr. William Hartmann; the Associate Series Editors, Drs. Saul Kay and Richard Reed; and Ms. Ruth Wreschner, Editor at John Wiley & Sons, all of whom provided ideas, encouragement, criticism, and far more patience than I deserved. Dr. Edgar L. Makowski served as my clinical sounding board and procured clinical specimens for photography. Dr. Robert H. Fennell helped me select photomicrographs for the final illustrations, and he and many of our residents advised me on subjects to be included in and excluded from the text. The photographs were developed and printed by Howard Mitchell, who also produced the diagrammatic illustrations. LaVonne King and Shirley Grayson typed and retyped the manuscript with much enthusiasm and few complaints. To these and many others I offer my sincere gratitude.

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Surgical Pathology of the Uterus

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1

Introduction to Gynecologic Pathology

It is quite fitting that the skin and the uterus should have been chosen as the subjects of the first two volumes in this series of monographs on surgical pathology, since in most surgical pathology laboratories (including our own) specimens from these two organs comprise more than half of all accessioned material. Dermatologic specimens are in general fairly simple to deal with grossly, but often extremely complicated microscopically. On the other hand, uterine specimens run the gamut from the fairly routine and increasingly frequent therapeutic abortion to the complex histologic interpretation of hormonal abnormalities to the extremely complex gross orientation, description, and sectioning of a total pelvic exenteration specimen. Thus, the problems that may be faced in dealing with the surgical pathology of the uterus are in many respects a microcosm of all the problems encountered in general surgical pathology. Accordingly, I will attempt to deal in this first chapter with at least some of the principles and guidelines that are important in the surgical pathology of all organ systems.

The fields of dermatopathology and gynecologic pathology are also closely related in another way, namely the “love/hate” relationship that may exist between clinician and pathologist. I have long maintained that we who are interested in gynecologic pathology are extremely fortunate in being able to deal with a cadre of extremely well-informed and competent clinicians, who pride themselves on their knowledge and interest in the pathology of their cases. It is extremely gratifying when the pathologist is able to “speak the same language” as the clinician, and to find a clinician who is willing to cross the “paraffin curtain” and actually venture into the pathology laboratory to review the slides from his own cases. On the other hand, the spectre of the so-called “clinician-pathologist”—whom I prefer to call a pseudopathologist—continues to haunt the practice of both dermatopathology and gynecologic pathology, particularly in major academic centers.

This peculiar phenomenon appears to be a throw-back to the day (within the lifetime of many of us) when most pathologists were neither interested nor well trained in the interpretation of specimens from either gynecologists or dermatologists (not to mention nephrologists, gastroenterologists, and other subspecialists), since the field of surgical pathology was interpreted literally as deal-

ing with pathologic specimens submitted by general surgeons. As proof of the old adage that Nature abhors a vacuum, a number of clinicians in these neglected specialties began to take a particular interest in the pathologic interpretation of their own material and indeed performed a great deal of the pioneering work in these fields. However, the present generation of pathologists includes many who are actively interested in these areas, and the vast majority of pathologists in practice today have been trained adequately in these fields. These facts would seem to presage a decline in the number and influence of clinician-pathologists, but in fact in several areas quite the reverse has been true. The reasons for this are extremely complex and no doubt include factors relating to tradition and prestige as well as those that are purely economic. There is little doubt that the only thing more difficult than the building of an empire in academic medicine is the dismantling of one.

Nevertheless, there are highly compelling reasons for the practice of pathology by pathologists. Perhaps the major one of these is the increasingly important area of quality control and peer review. When the clinician who makes the decision that surgery is to be performed is also the surgeon who performs the operation and the pathologist who interprets the product thereof, there is little room in the process for the question of error to be raised. This is not meant to be an accusation of venality but merely to suggest that it is difficult to relinquish a preconceived notion. Furthermore, the clinician-pathologist often lacks the grounding in fundamental principles of basic pathology that the well-trained first year resident in pathology possesses; thus, although the gynecologist-pathologist may easily be able to distinguish the various forms of endometrial carcinoma, he may have a harder time telling a metastasis from a granuloma.

Finally, one of the most compelling arguments against the continuance of the tradition of the clinician-pathologist is the simple fact that the vast majority of medicine in this country is not practiced in academic centers. The pathologist in the community hospital needs to be familiar with material from all organ systems because there simply will not be any clinician-pathologist in his hospital to deal with the interpretation of these specimens. If the pathologist has not been exposed to this material during his training because it was sequestered in some other department, he obviously will be unqualified to practice pathology as it is practiced in the real world outside academic centers. The proliferation of subspecialty Board certifications in pathology simply serves to encourage this fragmentation and eventual inadequacy. There is no reason for the pathologist who is Board-certified in anatomic pathology to be less than competent in dermatopathology, gynecologic pathology, morphologic hematopathology, or any similar subspecialty area. I fervently hope that the ill-conceived Board of Dermatopathology will not serve as a model for similar follies in other subspecialty areas.

PRINCIPLES OF GENERAL PATHOLOGY

Having established that the surgical pathology of the uterus is and should be a subdivision of the general field of surgical pathology, it seems pertinent at the present time to consider some general principles of that field that will continue to be applicable throughout the later chapters of this work. Probably the most

important single general principle of surgical pathology is that of respect for the specimen. This is really the mirror of respect by the pathologist for both the clinician and the patient, without which the pathologist hardly can be said to be engaged in the practice of medicine. We must remember at all times that there is no such thing as an insignificant or unimportant surgical specimen—even the lowly hernia sac is far more important to the patient who has just been relieved of it than is an embryonal rhabdomyosarcoma belonging to someone else.

A corollary is the statement that the pathologist should treat each specimen as if he were the clinician—or better yet the patient—awaiting the surgical pathology report. Thus, such questions as “What gross measurements should I make?”, “How many sections should I take?”, or “What negative findings should I list in my microscopic description?”, are all answerable when one asks the basic question, “Were I the clinician or the patient, what information would I need about this specimen?” Unfortunately, as the performance of a clinical internship prior to entering the pathology residency continues to be discouraged, and as the period of acquisition of basic clinical skills in medical school continues to be truncated in favor of “electives,” it becomes more and more difficult to find a pathology resident who is capable of answering this basic question. Indeed, since the surgical pathologist deals not only with the general surgeon, as we have previously mentioned, but also with the gynecologist, the pediatrician, the internist, and numerous other specialists and subspecialists as well, an important part of the surgical pathologist’s basic and continuing education is an understanding of the basic principles and current developments in each of these fields. In order to further this goal, this monograph is divided into chapters emphasizing the types of specimens that may be received from the uterus, and each specimen is further identified by the clinical indication for its removal and submission.

Another principle based on that of the respect of the surgical pathologist for the specimen concerns the maintenance of the specimen after the initial gross description has been made and sections taken. It is always a possibility that additional gross information will be required on the basis of either microscopic findings or additional clinical information, and it is an even more likely possibility that additional sections will be needed for microscopic examination. Thus, the specimen should be left as intact as possible, consistent with the performance of an adequate initial examination. In those instances in which it is anticipated that extensive disruption of architectural landmarks will be necessary, a gross photograph, or at least a carefully drawn diagram, should be made before such disruption takes place. This principle usually is stressed in the university hospital, where teaching is one of the major functions of the pathologist, but it should be remembered that every community hospital pathologist is also a teacher and every surgical pathologist bears the responsibility of providing adequate information to the clinician in his final report on each and every specimen.

In his quest to maintain the specimen relatively intact, the pathologist may, on occasion, feel like a knight in rather rusty armor protecting his chosen damsel against the onslaught of a horde of ferocious dragons. The more interesting or unusual the case may be, the more of these dragons are attracted to it, each demanding a portion of the specimen for ultrastructural examination, viral cultures, chromosomal analysis, and the like. Often, the pathologist himself may be one of the petitioners, inasmuch as he may be interested in applying his favorite

research tool to the study of the specimen. Again, it must be remembered that the surgical pathologist's primary responsibility is to the patient and the clinician and involves the provision of an accurate and complete diagnosis. Thus, the specimen must proceed directly from the operating room or clinic to the surgical pathologist, who may then apportion it as he sees fit, being careful to retain adequate material to provide the necessary diagnostic and prognostic information. The receipt by the surgical pathologist of a specimen that has been mutilated by others is inexcusable and should be dealt with in the strongest possible terms.

On occasion, the primary mutilator of specimens turns out to be the surgeon, who is interested less in research than in instant gratification concerning the major gross findings. It is the duty of the surgical pathologist to point out to such a surgeon the importance to the surgeon himself and to his patient of the receipt of the specimen in an intact condition. The pathologist should indicate his willingness to come to the operating room to examine the gross specimen with the surgeon in those cases in which the surgeon deems this necessary. Indeed, in many instances, the complexity of a specimen may be such that the pathologist will profit considerably by such a collaborative initial examination.

Finally, one of the most formidable problems facing the neophyte surgical pathologist is the writing of the final report. The actual mechanism thereof differs from institution to institution, but the general principles remain the same and are founded on the duty of the surgical pathologist to provide optimal useful information to the clinician on each specimen submitted. Thus, the question "What would I want to know if I were the clinician?" should be the guideline in each and every case. Both the gross and microscopic description, as well as the final diagnosis, should be dictated or written with this in mind. In many instances, a microscopic description may not even be necessary, but in those cases in which one is rendered, it should be clear, concise, and complete. The gross description always should begin with the identification of the specimen, including reference to how it is labeled and in what condition (in formalin or saline or unfixed) it is received. The necessary measurements (including weight, if applicable) should then be recorded, followed by a complete description of the macroscopic characteristics of the specimen. It must be remembered that the pathologist is describing the specimen, not his own activities in the examination thereof; thus, phrases such as, "After I opened the uterus, I noted the presence of a tumor on its posterior aspect," should be avoided. Descriptions should proceed from the general to the specific—thus, the presence of a tumor must be noted before its characteristics can be described, and certainly before the condition of the resection margins can be noted.

The same rule should be applied to both the microscopic description and the final diagnosis. A carcinoma of the endometrium should precede the chronic cervicitis both in the microscopic description and diagnosis sections of the report, even if the cervix was processed grossly before the corpus. As a general rule, what is visible with the scanning lens of the microscope should be described before what is visible only with the high-power objective. Thus, the degree of circumscription or invasiveness of a tumor should always appear in the description before a characterization of its nuclear pleomorphism or mitotic activity. Information included in the microscopic description should be as specific as

possible—it takes no more effort to write “lymphocytes and plasma cells” than “a chronic inflammatory infiltrate,” and in the endometrium, for example, the distinction is an important one, since lymphocytes are a normal finding while plasma cells are pathologic.

The final diagnosis, like all other information, should be written with a view to its clinical relevance. For example, the histologic grading that is so important in adenocarcinoma of the endometrium is relatively unimportant for squamous cell carcinoma of the cervix, in which the tumor should be classified as keratinizing, large cell nonkeratinizing, or small cell, rather than Grade I, II, or III. If there is any doubt about the clinician’s comprehension of a term, a synonym also should be used—for example, when signing out an endometrial carcinoma as adenoacanthoma, I always also include the synonym, “adenocarcinoma with squamous metaplasia.” The final diagnosis always should include reference to all parts of the specimen received. Grossly and histologically unremarkable structures such as ovaries or fallopian tubes can be identified as “normal,” “unremarkable,” “no diagnostic features,” and the like, but always should be identified somewhere in the final diagnosis. Finally, the use of comments or notes to clarify certain points that may not be immediately apparent from a quick perusal of the final diagnoses is commendable, as is the judicious use of an instrument that too often is excluded from the armamentarium of the surgical pathologist—the telephone. The clinician always should be contacted for more information in any case with unexplained findings, and should be notified of any important unexpected pathologic findings.

Many of these points will be commented on in much greater detail in subsequent chapters. I hope that their applicability, not only in the study of the uterus but in all fields of surgical pathology, will be apparent.

2

Infertility: The Endometrial Biopsy

In 1925, Kelly⁵⁰ suggested outpatient diagnostic curettage without anesthesia as a method of providing histologic samples of endometrium. In 1935, the Novak⁷⁶ and Randall⁸³ curettes were described as tools for the performance of this procedure. Since Schroeder in 1915,⁸⁸ and Meyer in 1920,⁶¹ had correlated the cyclical changes in the endometrium with the changes of ovarian hormonal function, it quickly became apparent that the technique of endometrial biopsy should be of value in the study of infertile patients. Although numerous newer techniques have been devised for cytologic and histologic study of the endometrium, the Novak and Randall curettes remain the instruments in use in the great majority of clinics for the study of infertility, while other techniques are used more often in the evaluation of abnormal vaginal bleeding or screening for endometrial carcinoma and its precursors.

It should be emphasized that endometrial biopsy is just one of many investigations to be performed in the work-up of an infertile couple, and actually should be performed only after other procedures have not proven fruitful. For example, in addition to the male portion of an infertility work-up, Behrman and Kistner list the following as the minimal diagnostic procedures for the female partner: history and physical examination, serology, blood count and sedimentation rate, urinalysis, T-3 or T-4 by column, postcoital tests including sperm penetration tests, tubal insufflation, and miscellaneous tests including a Papanicolaou smear, fern test, serial vaginal cytology, a hanging drop preparation for *Candida* and *Trichomonas*, and an incompatibility test for cervical mucus and semen.⁷

As mentioned above, the endometrial biopsy in an infertility work-up usually is performed as an outpatient procedure, using either a Novak or Randall curette (Fig. 2-1). The Novak curette has serrated edges surrounding its biopsy aperture, while the Randall curette lacks serrations and is shaped like a small scoop. The curettes range from 15 to 20 cm in length and 5 to 6 mm in diameter. The biopsy usually causes only minor discomfort and requires neither local nor general anesthesia. Exceptions to these statements obviously exist, and in such cases different sampling techniques may be required, occasionally including hospitalization with general anesthesia and formal dilatation and curettage. Outpatient biopsy usually is not used when the diagnosis of endometrial car-