G. Dallenbach-Hellweg

Histopathology of the Endometrium

Third Revised and Updated Edition

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English Translation by F. D. Dallenbach

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With 147 Figures and 2 Colored Plates

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Dr. med. GISELA DALLENBACH-HELLWEG
Professor for General Pathology and Pathological Anatomy, Head of the Department of Gynecological Morphology and Morphological Research of the University Hospital for Women of Mannheim (University of Heidelberg)

Translator:
Dr. med. FREDERICK D. DALLENBACH, M.D.
Professor for General Pathology and Pathological Anatomy, Department of Experimental Pathology, German Cancer Research Center, Heidelberg

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Preface to the Third Edition

Although the purpose and scope of this monograph remain unchanged, I have been obliged to revise and rewrite many sections to keep pace with the recent growth in knowledge of endometrial pathology and physiology.

New knowledge emanates from every quarter, engendered by improved methods of study in virtually every subspecialty, by exemplary cooperation between disciplines, and especially by the exchange of ideas internationally. On the other hand, the catalogue of diseases is everchanging. Some, once common, become rare or even disappear. Others suddenly appear, unique and previously unknown. Increased longevity, modern ways of living and new methods of treatment have modified or augmented the clinical and diagnostic problems confronting us. Accordingly, therapy with hormones and intrauterine contraception receive special attention, commensurate with the importance afforded them today. Under the precept "nil nocere," the almost unlimited uses for these agents warrant that their effects be carefully monitored by precise morphological studies, a prerequisite that succeeds only when clinician and pathologist cooperate closely. The sections on procedures for obtaining endometrial tissue, on steroid receptors, on functional disturbances, and on spontaneous abortion have been changed or expanded to incorporate new facts from recent discoveries that now appear significant. Only time, however, will prove their true value. Much of historical interest in the text has been left intact, for "who wants to read into the future, must consult the past" (André Malraux).

To the correspondents and consultants who have contributed valuable suggestions and brought to my notice errors or omissions in the last edition, I gladly acknowledge my hearty thanks. To my daughter, Friederike, I am particularly grateful, for without her help and untiring support I could never have finished this revision so soon. Again, the Springer-Verlag has earned my deep gratitude for its patience, generosity, and skill in preparing this new edition.

Mannheim/Heidelberg, March 1981 GISELA DALLENBACH-HELLWEG

Foreword to the German Edition

During life form changes. From the form seen we can often interpret function. From such correlation *functional morphology* has developed. When applied to the endometrium it means we use histological features existing at the time of biopsy to diagnose functional changes. What we try to detect are the local reactions induced by hormones under control of higher centers. Correlation of form with function succeeds only when the clinician and morphologist work together. Of the many factors that are important, the time of biopsy is decisive, since the target tissues need time before they can react and change in response to the hormonal stimulus. In our interpretations we must always take such reaction-times into account. By using functional morphology as a method of study, we can determine what type of hormonal dysfunction exists, how intense it is, and how it changes with time. More important, we are able to evaluate the biological effects of the hormonal stimuli on the peripheral target tissues with greater accuracy than if we were to measure the hormones biochemically. Although the advantage may shift in favor of biochemical analyses, as our knowledge progresses in the practice of medicine today the morphological change in the target organ remains the basis by which we recognize disease processes and decide how to treat them.

Besides the changes of functional morphology, we must also evaluate other local changes we find in the histological sections, which, from present-day knowledge, may or may not be induced by hormonal stimuli. Whether certain morphological changes in target organs, particularly the precancerous or carcinomatous transformations, may be brought about by excessive hormonal stimulation or may become refractory to such influences, are questions of extreme importance in learning about the biology of these changes.

In gynecology every morphology must be functional morphology, a principle that particularly applies to the interpretation of the endometrium. My associate, Dr. DALLENBACH-HELLWEG, is an authority on the diagnosis of endometrial changes. Brought up in the HAMPERL school where she became familiar with both general and gynecological pathology, she finished her training under A.T. HERTIG in Boston. By coming to a women's hospital she finally found her way to applied gynecological pathology. Consequently, she is in the position to represent the interests of the clinician as well as those of the morphologist. In this monograph she has recorded her vast experience and thorough knowledge of both disciplines. Her book serves as a bridge between clinician and pathologist, its purpose—to facilitate an exchange of information and ideas in both directions. May the conditions prevail to encourage such trade, hopefully leading to collaboration and teamwork between these specialists.

Mannheim, November, 1969 PETER STOLL

Preface to the German Edition

The endometrium differs from all other tissues of the body in that it rhythmically changes its structure and function. For many years the meaning of these changes remained puzzling and obscure. At about the turn of the century some investigators held the physiological fluctuations of the menstrual cycle to be inflammatory changes. Later, when stricter criteria for the pathology of the endometrium were applied, morphologists misinterpreted pathological fluctuations in the cycle either as physiological variations, or they overlooked them entirely. Today as previously the pathologist is often confronted with the dilemma that he is unable to adequately diagnose the endometrium merely from the structural changes. Accordingly, the gynecologist finds the pathological report of little value. In like manner, if the clinical information given the pathologist is incomplete, then he cannot form a clear notion of the clinical problem.

Although the detection of focal lesions of the endometrium is important, of much greater consequence is the recognition of functional (hormonally controlled) variations and their cyclic course, for it is from these that the clinician is guided in deciding what therapy he should use. The ability to detect such functional changes requires not only that the morphologist possess a thorough knowledge of the physiological and pathological anatomy of the endometrium but also that he receive exact information about the patient's menstrual history and have insight into clinical problems. Prerequisites of that kind make it possible to relate morphology with function, a synthesis essential for the optimal diagnosis of the endometrium. Such a correlation is the purpose of this monograph. It attempts to bridge the gap between pathologist and clinician; it is designed for both. Should these pages stimulate the pathologist's interest for clinical problems or aid the clinician in understanding why the pathologist needs clinical information, thus fostering close cooperation between the two, then the book has achieved its purpose.

The numerous photographs depict most of the endometrial variations that one might encounter. I thank the publishers for accepting so many illustrations and particularly for reproducing halftones of such high quality. Although addressed primarily to the practicing pathologist, this book is intended as well for the gynecologist or research pathologist who, it is hoped, will find among its pages stimulating suggestions and information. May the numerous references cited facilitate further study of special problems. The bibliography, albeit comprehensive, is hardly complete. Every effort was made, however, to cull from the boundless wealth of literature precisely those works that have contributed significantly in their time to the solution of a specific problem.

My special thanks go to Professor Dr. med. PETER STOLL for his critical review of my manuscript, for his invaluable suggestions and advice, as well as

for his helpful and understanding support. I am most indebted to Mrs. G. SANKOVIC for her untiring and dedicated devotion in typing the manuscript and in preparing the bibliography. To Miss B. MERKEL I gladly acknowledge my gratitude for reading the manuscript and for her valued support in overcoming technical problems. Again, I express my sincere thanks to the publishers for their care and efficiency in preparing the text and illustrations, and their willingness to fulfill my many requests.

Mannheim/Heidelberg, November, 1969 GISELA DALLENBACH-HELLWEG

Contents

A. Methods of Obtaining, Preparing, and Interpreting the Endometrium

The diagnosis of changes in endometrium obtained by curettage depends not only on a thorough microscopic examination of the histological preparations; the diagnosis actually starts in the clinic. The close interplay between structure and function that is so apparent in the human endometrium requires we ask about or determine what the patient's hormonal state is. We need to know about her menstrual history, previous pregnancies, basal temperature, and any hormones she may have received. What we learn will help us in evaluating the microscopic sections and in detecting abnormal changes.

1. Indications for Curettage

Before a curettage is performed, two questions should be answered: Will the curettage contribute to the diagnosis? What dangers are there in the procedure? Although large statistics indicate the mortality rate for the operation is 0 per cent, in rare instances the uterus may be perforated. On the other hand, with well-founded indications a curettage is especially recommended after the menopause since it often leads to discovery of a carcinoma; or it may also be used to exclude with 100 per cent assurance the presence of such a tumor, thereby sparing the patient a more extensive operation (DAICHMAN and MACKLES, 1966).

Curettage of the endometrium for histological study is indicated:

a) *only rarely*, in conjunction with other methods of study (clinical history, measurement of basal temperature, cytological examination, determinations of hormones), *for diagnosing the functional state when the menstrual cycles are regular*, as for example, in sterility or in trial therapy with hormones. Instead, a simple ("single-stroke" or "strip") endometrial biopsy suffices here and may be carried out in the outpatient clinic or office without dilatation of the cervix.

b) most often *for the diagnosis and treatment of all types of abnormal bleeding*, where the functional (hormonal) or morphological cause needs to be clarified. Here, a complete curettage including the tubal recesses is desirable. To perform it the cervix must be dilated under anesthesia.

c) *when a carcinoma is suspected with or without bleeding*: a complete curettage should be made including the tubal recesses. To insure a thorough and accurate examination the endocervical canal should be curetted separately from the endometrial cavity, and the fragments from each region collected separately. Only enough tissue should be scraped away as is needed for diagnosis if a possibility exists of perforating the uterine wall.

d) in an *abortion* with bleeding and a patent endocervical canal. A complete curettage is indicated here, usually carried out with a large blunt curette. If it can be easily inserted into the endocervical canal, anesthesia is not required.

It becomes apparent that a curettage sometimes serves to supplement or complete a functional diagnosis. At other times, however, curettage becomes necessary as a life-saving procedure. When used for purely diagnostic reasons, then it should be performed at a time optimal for histological study, insuring that the most information will be gained.

2. Selection of the Proper Time for Curettage

The best time depends on the *functional disturbance* presented by the patient and on the diagnosis that the gynecologist anticipates from the histological study. For example, if the clinical signs and symptoms suggest an anovulatory cycle, then a curettage during the proliferative phase would be of little value. A diagnosis of an anovulatory cycle is possible only during the secretory phase, by recognizing that the typical secretory changes have failed to appear in the epithelial cells and stroma. Since the proliferative phase may be prolonged, even normally, and since the first secretion by the glandular cells can be detected with routine stains at best thirty-six to forty-eight hours after ovulation, the curettage should be performed shortly before menstruation. It should certainly be done no earlier than twelve days before the last date for onset of menstruation, as calculated from the clinical history. A diagnosis that ovulation took place can readily be made during the last days of the secretory phase or even on the first day of menstruation, not however directly after ovulation. For most of the other functional diagnoses, particularly for evaluating the function of the corpus luteum and for diagnosing sterility, the late secretory phase is the best and occasionally the only time for curettage to insure a useful histological diagnosis. Admittedly, in patients under study for sterility the danger exists that a pregnancy might be interrupted by curettage in the secretory phase (ARRONET *et al.*, 1973). Such a risk, however, may be circumvented by postponing the curettage until the basal temperature falls; that is, from two days before to just before menstruation starts, provided the basal temperature has been elevated indicating ovulation had probably occurred. In rare instances an endometrial biopsy taken during the "conception cycle" may not disturb the implanting blastocyst and may in fact promote a better decidual reaction (KAROW *et al.*, 1971; ROSENFELD and GARCIA, 1975). Another advantage of curettage in the late secretory phase or just before menstruation, even though the menstrual cycle is irregular, is that the secretory changes should be maximal by then.

Intense hemorrhage but also even *mild atypical bleeding* represent exceptions to the rule of late curettage. Such hemorrhages are an indication for prompt curettage, not only from a clinical standpoint but also from that of the pathologist, since the longer the bleeding continues, the less the amount of tissue to be found in the uterus. Consequently, the chances the histological study will prove worth while diminish with the duration of the hemorrhage. Because of the greater danger of cancer after the menopause, if appropriate clinical signs exist, it is highly advisable to perform a curettage promptly. WINTER (1956) was able to make a pathologic diagnosis in 74 per cent of his patients when the endometrial curettage was performed during the period of abnormal bleeding. When he per-

formed the curettage after the bleeding had ceased, he was able to make a diagnosis in only 34 per cent.

Waiting until bleeding has stopped is justifiable in only a few instances: a) When irregular shedding is suspected. The histological changes typical of that condition are difficult to recognize in curettings obtained on the first day of menstruation. Rather, the histological diagnosis here depends on finding fragments of involuted, though well-preserved endometrium several days after bleeding starts. b) For diagnosing a hypomenorrhea, the curettage is best performed shortly before or three to five days after the onset of menstrual bleeding. If the endometrium is still highly secretory before the bleeding begins, or if only superficial fragments of endometrium are discharged after bleeding has commenced and these reveal involution, then there is no ovarian insufficiency. The changes described more likely represent scanty menstrual shedding with intense shrinkage within normal limits (HINZ, 1953). In rare instances menstrual bleeding fails to occur although ovarian function apparently is normal (PHILIPPE *et al.*, 1966). Since amenorrhea may have various causes, if the endometrium discloses no characteristic changes it is advisable to repeat the curettage; a single strip biopsy suffices.

In summary, the following guide lines (based on HINZ, 1953) are valid:

Clinical diagnosis	*Best time for curettage*
Sterility with suspicion of a corpus luteum insufficiency or an anovulatory cycle:	shortly before or at the onset of menstruation
Hypomenorrhea:	shortly before or three to five days after onset of menstruation
Oligomenorrhea:	on the first day of menstrual bleeding
Menorrhagia with suspicion of irregular shedding:	according to clinical history of bleeding, from five to ten days after onset of menstruation
Amenorrhea (pregnancy must be excluded):	endometrial biopsy repeated at short intervals
Metrorrhagia:	best done without delay

Equally as important as selecting the most favorable time for curettage is the **reporting to the pathologist** about the patient's menstrual history and any hormone therapy she may have received. Besides the patient's name and age, the clinical report sent with the curettings should include: the date of curettage, the date on which the last menstruation started, a schema describing the menstrual cycles, an account of the menstrual flow, details of previous hormonal therapy, a statement about the patient's constitution including any endocrine disturbances, the clinical diagnosis, and questions to be answered (LAU and STOLL, 1963). The pathologist can make an accurate functional diagnosis only if he is sent the pertinent clinical information. For example, it is self-evident why an anovulatory cycle or a shortened or prolonged cycle can be diagnosed only when the phase of the patient's cycle is known, or why secretory change of the endometrium

can be interpreted as deficient only when the day of the cycle is stated. Lack of information about previous therapy with hormones may lead to false interpretations of histological changes and to false conclusions about the patient's ovarian function. Consequently, a purely morphological description of endometrial structure is worthless without correlation with clinical information. Some clinicians maintain that only they are in a position to interpret the histological diagnoses made by the pathologist. I regard such a viewpoint to be wrong. The close interplay between form and function becomes apparent only during the study of a histological preparation, not a posteriori from a histological report. Clinicians and pathologists should endeavor to work together (LETTERER and MASSHOFF, 1941; STOLL 1949; HINZ, 1953; LAU and STOLL, 1963).

3. Procedures for Obtaining Endometrial Tissue

From the pathologist's standpoint it would be ideal to have a *complete curettage* performed lege artis in every patient, since an examination of only all endometrial tissue will insure that no important changes will be overlooked. If the slightest suspicion of carcinoma exists, then the entire endometrial cavity should be curetted. In doing so, it is often advisable to collect the tissue from the corpus separately from that of the endocervical canal, making it possible to localize the tumor. On the other hand, if the purpose of the curettage is to determine the changes brought about by hormonal therapy, that is, to make a functional diagnosis, then a "fractionated" curettage should be employed. Such a study involves repeating an *endometrial biopsy* (strip or single stroke) during a menstrual cycle; it provides more information than a single, complete curettage. In addition, a simple biopsy is usually enough if only a functional diagnosis of the mucosa is sought, for example, in the diagnosis of sterility (SILLO-SEIDL, 1967). Although the amount of tissue obtained with a strip biopsy is relatively scanty, that does not compromise the accuracy of the diagnosis made from it, since the endometrium of the uterine cavity usually develops homogeneously. NOYES (1956) was able to prove that fact by comparing biopsies of the right and left anterior and posterior walls. The decision of what type of procedure to use as well as when to perform the operation will depend upon the patient and the problems involved. If the curettage is indicated for therapeutic reasons, then only a complete curettage will suffice.

Whether a complete curettage is decided upon, or only a biopsy, what is important is that tissue be removed from the endometrial cavity, since all important normal and pathological changes take place in the endometrial cavity, not however (or only very slightly) in the isthmic portion (of the lower uterine segment). A careful curettage of the tubal recesses (cornua) is important, since these are sites of predilection for carcinoma and benign polyps, and they often shelter the last remnants of placental tissue. When the mucosa of the cornua is normal it is particularly high and well-developed, superbly suited for diagnosing functional changes.

In the last few years the histological study of endocervical curettings has become more important for two reasons: 1. Gynecologists have learned the

value of collecting endocervical curettings separately from endometrial curettings, and are practicing the procedure with increasing frequency, especially for the exact localization of a malignancy; 2. therapy with progestational agents, especially certain potent oral contraceptives, induces changes in the endocervix that are characteristic and should be recognized as such.

The Technique of Endometrial Biopsy

The procedure may be carried out in the doctor's office without anesthesia. Preparation: The patient's temperature, leukocyte count and sedimentation rate should be normal. Those with localized or systemic illnesses must be excluded as well as those with a pregnancy as strongly suggested by careful questioning and serological tests. The patient should empty her urinary bladder. After the speculum is inserted and the portio inspected, colposcopy may be done and cytological smears prepared, including wet-mount preparations for phase-contrast microscopy (STOLL, 1970). The uterus is palpated to determine its position and size, attention being paid to adjacent structures.

The portio vaginalis (ectocervix) is cleansed with disinfectants. Under direct inspection and without the need of a tenaculum to stabilize the cervix, the biopsy-curette is inserted into the endocervical canal and up into the fundus. The biopsy of the endometrium is made with a single stroke, usually along the anterior wall, and the curette is withdrawn.

The Technique of Complete Curettage

The procedure is performed best under a brief general anesthesia with an intravenous agent. Preparation of the patient is the same as for the endometrial biopsy (see above). After the pubic hair is trimmed away with scissors, the vulva is cleansed with disinfectants. The portio vaginalis is grasped with a tenaculum and pulled lightly to stretch the uterus. A probe is inserted and the endometrial cavity carefully explored and evaluated. The endocervical canal is then enlarged with Hegar dilators up to size No. 10. A sharp curette is inserted into the endometrial cavity and strips of endometrium gently scraped from the anterior, posterior, right and left uterine walls. The strips of tissue are collected on a linen cloth on the instrument table, examined, and promptly placed in an appropriate fixative. A more thorough curettage may be made by ensuring the strokes of the curette parallel one another and reach the tubal recesses.

When a carcinoma is suspected the endocervix should be scraped first before the curette is inserted into the endometrial cavity; the fragments of endocervical mucosa should be collected separately and fixed. If friable, soft, gray-white tissue is removed from the corpus, highly suggestive of a carcinoma, then the curettage should be discontinued to insure the uterus is not inadvertently perforated by additional scraping.

Emptying the endometrial cavity in an incomplete abortion. If the products of conception have not been discharged it is best to wait until they are spontaneoulsy expelled if the patient's condition permits. Premature intervention requires dilatation of the endocervical canal and the subsequent danger of a cervical insufficiency. In addition, the physician may be accused of having performed an abortion. If the cervical os is found dilated a finger's breadth, permitting insertion of a curette, then no anesthesia is required unless to spare the patient possible psychic trauma. After shaving off the pubic hair, the vulva is cleansed with disinfectants. The urinary bladder is emptied by catheter and the vagina cleansed. The position, size, and consistency of the uterus and neighboring structures are determined by careful palpation. A speculum is inserted and the portio carefully inspected, paying special attention to evidence of disease. The cervix is seized and held fast with a tenaculum and the endometrial cavity explored with the largest blunt curette possible. To stimulate uterine contraction three I.U. of oxytocin are injected i.v. before the curettage is begun. The curettage is performed gently to make sure the soft trophoblastic tissue is removed but not the underlying basal layer of the endometrium or the myometrium. Curettage is completed when the uterus contracts well.

Procedure with a hydatidiform mole. Occasionally with a hydatidiform mole two curettages become necessary, the first being limited to partial removal of the mole to allow the uterus to contract. Later, a second and complete curettage is performed. The procedure used depends on the severity of bleeding. It is advisable to inject oxytocin during the curettage.

Besides biopsing the endometrium with a curette, *biopsy by suction* (vacuum aspiration) can also be used. It has proved ideal for office practice because it is so simple to perform.

For such a suction-biopsy NOVAK (1935, 1937) and RANDALL (1935) employed a thin, hollow probe with a saw-toothed rim. The instrument can be inserted without dilatation of the endocervical canal or anesthesia, and used to detach and aspirate fragments of endometrium from the uterine cavity. NOVAK's probe has subsequently been modified in various ways by numerous other investigators. NUGENT (1963) compiled the results of several series of studies made with the suction-biopsy and calculated that among 1434 biopsies cancer was overlooked in 7.9 per cent (for further literature see NUGENT, 1963). With the probe designed for suction-biopsy by FREISCHÜTZ and JOPP (1964), however, the use of vacuum-suction and sharp excision with a retractable ring-knife within the hollow probe make it possible to remove larger pieces of endometrium. The jet-washer introduced by GRAVLEE in 1969 combines suction with a system for flushing the uterine cavity with physiological saline. The method has proved fairly popular. Since then, further technical improvements have been described and introduced for collecting endometrial tissue suitable for diagnosis (HALE *et al.*, 1976; INGLIS and WEIR, 1976; FERENCZY *et al.*, 1979); their value, however, has not been proved as yet by statistical analyses. Numerous investigators have tested the reliability of many of these methods, especially those used for detecting carcinoma, by comparing the histological diagnoses of them with those made of an ensuing complete curettage or a hysterectomy specimen. When suction biopsy was compared with complete curettage, the histological diagnoses agreed in 81% of the patients (GREENWOOD and WRIGHT, 1979, with 891 patients) or in 96% (KAHLER *et al.*, 1969, with 160 patients; see also DENIS *et al.*, 1973; COHEN *et al.*, 1974; HATHCOCK *et al.*, 1974; MUENZER *et al.*, 1974; LIU *et al.*, 1975; WALTERS *et al.*, 1975; WEBB and GAFFEY, 1976). In contrast, reports indicate agreement with the jet-wash method varies greatly. With that method HENDERSON *et al.* (1975) were able to collect enough tissue for diagnosis in only 58% of their studies but increased the diagnostic accuracy to 92% when they performed simultaneous cytological studies of the perfusion fluid. LUKEMAN (1974) found that agreement in diagnoses for his patients was 89.8%. According to many authors, the diagnostic reliability of the suction and jet-wash methods is equally good (DOWLING *et al.*, 1969; SO-BOSITA *et al.*, 1970; HIBBARD and SCHWINN, 1971; KANBOUR *et al.*, 1974; RODRIGUEZ *et al.*, 1974). Generally the suction biopsy is recommended for patients who are in poor general health or are anesthetic risks (HALLER *et al.*, 1973), and for functional diagnoses in young women (ENGELER *et al.*, 1972; MATHEWS *et al.*, 1973).

From our experience the diagnostic value of the tissue obtained either by suction or by jet-washing depends primarily on the amount of intact tissue that can be collected. Because the interrelationships between gland and stroma are so important in evaluating the quality of neoplastic and preneoplastic hyperplasias, without these interrelationships important distinctions cannot be made. Consequently, we prefer the suction method to the pure washing methods (cf. also VASSILAKOS *et al.*, 1975). For diagnosing endometrial *function*, the strip or suction biopsy is adequate in most instances and well recommended as a method that saves time and expense (see alo ANSARI and COWDREY, 1974). Although a complete curettage performed afterwards may at times contain polyps which escaped the suction biopsy, these contribute no information needed for the functional diagnosis.

Despite all the encouraging reports about the diagnostic reliability of detecting endometrial cancer by suction biopsy, a warning should be issued against placing too much reliance on that method. As a method, it has the same limitations as does endometrial strip-biopsy with the curette. Certainly under optimal conditions a carcinoma may be diagnosed with both methods. Failure

to find carcinoma in the tissue removed with these two methods, however, does not prove that there is no carcinoma in other parts of the endometrium. That holds true especially for the early stages, since endometrial carcinoma generally develops in the basalis or in tubal recesses which are difficult to reach by suction.

For purposes of thoroughness we should mention the use of *whole uteri* in the study and diagnosis of the endometrium. For the pathologist, whole uteri represent ideal specimens for study. When properly examined, they present no problems in diagnosis, nor do they require such detailed diagnoses as do curettings, except when a carcinoma is present.

Besides providing tissue for histological studies, freshly extirpated uteri are a source of material for *cytological smears* and tissue culture. Desquamated, viable epithelial and stromal cells may be examined in wet-mount preparations under the phase-contrast microscope, or in fixed smears stained after the Papanicolaou method or other techniques (SCHÜLLER, 1961; DALLENBACH-HELLWEG and JÄGER, 1969). In some respects the study of living cells with phase-contrast yields information that histological sections cannot provide; for example, knowledge about ciliary motion of the columnar epithelium, or about motility of bacteria or protozoa.

Cytological studies alone are unsuitable for evaluating endometrial function or for diagnosing carcinomas. They fail to provide the cellular interrelationships of the tissue so important for making a definitive diagnosis. Since the study of material obtained by sponge and brush techniques is based on cytologic criteria, these techniques have proved unsatisfactory. The "strip" or suction biopsy are preferred, particularly because they are easiest for patient and physician.

4. Preparation of the Endometrial Specimen

a) Fixation

Since the endometrium is exceedingly soft and undergoes rapid autolysis, it should be carefully handled and promptly fixed. Before fixation, however, it is best to remove clots of blood and mucus. These may be separated either by rinsing the fragments of tissue gently in physiological saline or by spreading them on a fine-meshed sieve or fabric, from which they may be transferred into the fixing solution with one arm of a blunt forceps, exercising care to avoid squeezing or pinching them. If the curettings are left in the gauze or tampon for delivery to the pathologist, then subsequent drying and squeezing will make it difficult for the pathologist to remove the now sticky fragments from the meshes of the gauze. Consequently, we recommend that endometrial curettings never be wrapped in fabric.

In selecting a fixative one should be guided by the principle of trying to preserve intravital structures as completely as possible. To obtain the finest preservation, however, it would be best to forgo a fixative entirely, and instead prepare *sections of unfixed, rapidly frozen tissues* with the *cryostat*. Such sections preserve