

ROBB (Hunter)

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and of Excised Pieces as an  
Aid to Diagnosis.*

*Based upon the Analysis of One Hundred Cases.*

BY

HUNTER ROBB, M.D.,

PROFESSOR OF GYNÆCOLOGY, WESTERN RESERVE UNIVERSITY,  
CLEVELAND, OHIO.

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*presented by the author*



FROM

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES,

JANUARY, 1897.



THE IMPORTANCE OF A SYSTEMATIC MICROSCOPICAL EXAMINATION OF UTERINE SCRAPINGS AND OF EXCISED PIECES AS AN AID TO DIAGNOSIS, BASED UPON THE ANALYSIS OF ONE HUNDRED CASES.

BY HUNTER ROBB, M.D.,

PROFESSOR OF GYNÆCOLOGY, WESTERN RESERVE UNIVERSITY, CLEVELAND, OHIO.

THE object of the present paper is to call attention once more to the advantages to be derived from a systematic microscopical examination of tissues removed from patients at gynæcological operations. It has for some time been a matter of routine with me to preserve for microscopical examination all structures so removed, the findings in each case being recorded regularly in a systematic way. The results thus obtained have been by no means without interest. While it is true that in perhaps a majority of instances the microscopical examination simply verified more or less completely the diagnosis which had been previously arrived at from a careful clinical study of the case, it has not infrequently brought to light evidences of the presence of a malignant tumor whose existence had by no means been suspected. On the other hand, in several instances the microscope has proved a suspicion of malignancy to be unfounded, and in ordinary benign cases has thrown much light upon the exact nature of the existing process. And, lastly, in a small number of cases the microscopical examination has proved of the utmost importance in that it has placed us in a position to recognize a malignant process in its very earliest stages, and while it was still possible to remove the growth completely by operation, before it had given rise to metastases, or had spread by contiguity or continuity to such a degree that all attempts at complete removal would have been useless.

The importance of a microscopical examination of scrapings from the uterine or cervical cavity, and in distinctly suspicious cases of deeper portions of the cervix, or, indeed, of the uterus itself, excised for purposes of diagnosis, does not, in this country, seem to have been as yet sufficiently appreciated. The difficulties in the way of a general application of the method, it is true, are somewhat formidable. Thus, in addition to the technique and experience necessary to make the results of the examination of value, the question of time has to be considered, so that the majority of busy surgeons will be compelled to delegate the work to a well-trained assistant or to a pathological colleague. In Europe, and especially in Germany and Austria, attached to the best



clinics are a number of competent men whose duties as assistants include the making of such examinations, and gynecologists in this country have long been in the habit, in doubtful cases, of submitting specimens for microscopical examination to pathologists in whom they have confidence. The tendency to make these examinations as a matter of routine is gradually growing, and the aid to be derived from the microscope in apparently simple as well as in doubtful cases is becoming more and more appreciated.

There has existed in the past an idea, now, fortunately, becoming less prevalent, that the result of the pathological examination in a clinically doubtful case is never certain. This, I think, grew out of the unreasonable demand of the clinician that, when his own methods failed in establishing a diagnosis, the pathological appearances should always be pathognomonic. While, however, the most enthusiastic supporters of the microscope as an aid to diagnosis are the most ready to admit their inability to give a positive statement as to the malignancy or non-malignancy in every case, this much at any rate can be asserted: in cases which are doubtful clinically the microscope will sometimes clear up the diagnosis absolutely, and were such instances met with only once in a dozen, or even in a hundred patients, the results obtained would more than repay us for the time and trouble spent in the systematic microscopical examination of every case. The technical procedures employed in this branch of work are simple and can be easily carried out by anyone who has been trained in the ordinary histological and pathological technique. The experience necessary to form a satisfactory judgment as to the evidence concerning the presence or absence of a malignant growth in a given case, or as to the nature of inflammations, hyperplasias, and other changes, is indeed considerable; but we may safely assume that modern gynecologists will not grudge time spent in preparing themselves for this work. The field for original studies in this direction, in which all modern histological and micro-chemical methods are applicable, is very wide and attractive; but, leaving out all such considerations here, it is my aim in this paper rather to lay stress upon the importance of the more simple work and that which is done for purposes of diagnosis alone. For the sake of clearness it may be well to outline briefly the routine followed in my own work, in which I have the help of a pathological assistant.

*The Obtaining of the Material; its Preservation and Preparation for the Microscope.* In the majority of cases the material which is to be examined is that which is brought away by curetting the uterus. For purposes of examination this material possesses decided disadvantages as well as advantages.

The two main advantages are (1) the ease with which such material can be obtained, even from regions, such, for example, as the fundus

of the uterus, from which a portion of tissue can be excised only with difficulty; and (2) because it gives an opportunity to study portions of the mucous membrane from many different areas. The chief disadvantages that may be mentioned are: 1. In only a few of the cases does one obtain any of the muscular tissue from the body of the uterus, and scarcely any of the tissue, whether mucous membrane or muscular tissue, from the cervix. 2. The sections are necessarily made up of very small pieces, thus rendering it possible to miss just the tissue for which we are searching. 3. Examination of the material removed by curetting from the cavity of the uterus is frequently less satisfactory than the examination of tissues excised directly from the wall. This objection, as will be mentioned presently, applies even more strongly to scrapings from the cervical canal. 4. In curetted particles one necessarily loses almost all idea of the topographical relations of the tissue under examination.

With reference to the cervix, I am of the belief that it is almost an impossibility to obtain with the curette suitable material for microscopical examination. The mucous membrane adheres so closely to the underlying fibromuscular layer that it is almost impossible to separate it satisfactorily with any of the ordinary curettes. In order to examine the mucous membrane of the cervix it is always much better to excise a small wedge-shaped piece of tissue, which should include an appreciable portion of the suspicious growth, and, whenever possible, together with it a small portion of what is apparently healthy tissue. The piece excised should be of sufficient size to enable us to handle it readily and to recognize macroscopically its former relations. The incisions should be made sufficiently deep into the tissues of the cervix to include the bottoms of the glands, and should be carried some distance up the cervical canal. After the required portion has been removed the edges of the wound can be brought together by means of interrupted silk or catgut sutures.

If an immediate microscopical examination of the tissue is not demanded, the scrapings may be satisfactorily prepared as follows: 1. They are washed quickly in salt-solution or in cold water to free them from blood as thoroughly as possible. We have found that the addition of a small amount of sodium bicarbonate to lukewarm water facilitates this procedure very much. The tissues should not be permitted to lie in water or in salt-solution, however, as they will soon become macerated and unfit for examination. 2. The specimens are then placed in 50 per cent. alcohol for several hours. 3. They are transferred to 97 per cent. or to absolute alcohol. The former, as a rule, is sufficiently strong, and, although absolute alcohol is perhaps better, it has the disadvantage of being much more expensive.<sup>1</sup>

The more solid excised portions should be allowed to remain for from

twenty-four to forty-eight hours in the stronger alcohol until they are perfectly free from water. If, however, they are comparatively large, it will be necessary to pass them previously through a number of alcohols graded from 50 per cent. to absolute alcohol, since it has been found that the transference of too large pieces directly from the 50 per cent. alcohol solution to absolute alcohol will cause them to shrink extensively, so that the various relations may be distorted. Thus, for example, we have found that the epithelial cells often become detached from their base of support. 4. The specimens are then usually placed in a mixture consisting of equal parts of commercial ether and alcohol, in which they are allowed to remain for twenty-four hours. They may then be placed in ether for twenty four hours. This step, however, in our experience has proved to be unnecessary and may be omitted. 5. They are next transferred to a thin solution of celloidin (of about the consistency of milk), in which they are allowed to remain for twenty-four to thirty-six hours. 6. They are then placed in thick celloidin (of the consistency of treacle) for from twenty-four to forty eight hours or even longer. By employing a solution of a consistency about midway between that of the thin and that of the thick solution we have often succeeded in preparing sections of endometrial scrapings with a single solution; but with portions excised from the cervix, or with pieces of relatively large size—over one centimetre square, for instance—it is advisable that they should be thoroughly saturated in both solutions. Instead of the ordinary celloidin, an excellent home-made substitute can readily be prepared by making ether-alcoholic solutions of photographers' fibre-cotton, which costs from about fifty cents to one dollar an ounce. 7. The specimens are next to be placed on small blocks made from wood, cork, paper, or glass. When dealing with uterine scrapings we usually place ten or twelve pieces on one block. 8. The "blocked" specimens are then allowed to remain for about fifteen minutes exposed to the influence of the air, until some setting and contraction of the superficial part of the celloidin have taken place. The blocks are then placed in 50 or 75 per cent. alcohol, and after several hours are ready to be cut with the microtome. When on the blocks and kept in the alcohol the specimens remain comparatively good for an indefinite length of time, although after some months, as a rule, sections which are taken from them do not stain so well as when they are cut shortly after the specimens have been prepared.

This "celloidin-embedding method" is in general use in the preparation of pathological specimens, and is for ordinary work preferable to all others. For "ribbon-sections," or serial sections in continuous bands, the "paraffin-method" must be employed. It may besides be objected

<sup>1</sup> The ordinary 97 per cent. alcohol may be converted into nearly absolute alcohol by the addition of sulphate of copper from which the water has been dried off by heat, the alcohol being afterward decanted off as required.

that the celloidin-sections are also somewhat thicker; but certainly the after-handling of them is much easier and the method itself is simpler. Serial sections, though not in continuous bands, of course, can be made by the celloidin-method.

Some of the European gynecologists prefer to employ paraffin in preparing tissues for microscopical examination. The method is somewhat as follows: 1. The specimens are first hardened in absolute alcohol. 2. They are then placed for twenty-four hours in some solution in which paraffin is soluble. Chloroform, xylol, or an ethereal oil may be used for this purpose. 3. They are then saturated with paraffin, either directly by placing them in paraffin melting at 50° C. for twenty-four hours, or indirectly by permitting them to remain in an open vessel in a solution of paraffin in xylol at a temperature of 50° to 55° C., the xylol being gradually volatilized. 4. A small paper cell is prepared of sufficient size to hold the preparation and at the same time to allow considerable free space, which is first filled with melted paraffin of a slightly higher melting-point. The specimens are then taken from the paraffin and placed in the cell in the desired position, hot needles being used for this purpose. The cell is then cooled either by exposing it to the air or by pouring cold water around it, after which the paraffin, which has now become a solid block, and which holds the preparation firmly imbedded in it, is removed from the cell and the sections can be cut with the microtome.

Besides alcohol for hardening and preserving tissues may be mentioned formalin, corrosive sublimate, and Müller's fluid. Formalin acts very quickly indeed in solutions even as dilute as 2 per cent., except in the case of mucous membranes, where even very strong solutions do not seem to harden tissues nearly so well as alcohol. It is especially good in dealing with gross specimens, and preserves the blood-cells in the sections. Formalin-tissues do not, however, stain satisfactorily in hæmatoxylin and eosin. The fumes are irritating and may produce an unpleasant and persistent coryza. With some individuals even in weak solutions it produces a peculiar dryness of the skin if allowed to come in contact with it for any length of time. The sensation which is thus caused is somewhat comparable with that following exposure to strong solutions of carbolic acid, but the effects are probably much more decided. Dr. Cullen, of the Johns Hopkins Hospital, advocates a formalin-method for rapidly preparing permanent sections.<sup>1</sup>

His method in brief is as follows: 1. The tissues are cut by means of the freezing-microtome. 2. The cut sections are placed in a 5 per cent. aqueous solution of formalin for from three to five minutes. 3. They are then placed in 50 per cent. alcohol for three minutes. 4. Then in abso-

<sup>1</sup> The full description of this method, which is one of the most valuable recently introduced is to be found in the Johns Hopkins Hospital Bulletin, No. 49, April, 1895.

lute alcohol for only one minute. 5. Further treatment is carried out as with the ordinary celloidin-sections. Cullen advises that when possible the tissue should be hardened in a 10 per cent. formalin-solution for two hours before it is frozen and cut. He believes that this is of special value in preparing scrapings from the uterine cavity. The first method occupies about fifteen minutes, while the second consumes an additional two hours. Cullen says that by the latter method the blood in the tissues is partially retained and will stain to some extent, but not wholly satisfactorily. Personally we have not had any experience with this second method, but we propose to employ it in the near future. As was said before, the rapidity with which it penetrates and hardens the tissues makes formalin of special value in the preparation of gross specimens.

*Corrosive Sublimate.* A saturated solution in normal salt-solution fixes tissues well, if minute particles only are used. After being fixed the tissues are further hardened in alcohol. The metallic deposits may be removed from the sections with tincture of iodine, and this in turn with 80 per cent. alcohol.

*Müller's Fluid.* The action of this fluid upon tissues is so slow that in the preparation of small tissues it is advisable to use other agents for fixing and hardening. It requires several weeks to harden small objects in Müller's fluid, and the fluid must be frequently changed.

When it is necessary to make an immediate examination of tissues it is best to cut the tissues into sections by means of the freezing-microtome, or better still, perhaps, to follow out Cullen's suggestion. It is to be remembered that only thin fragments are suitable for the freezing-microtome.<sup>1</sup> It is hardly necessary to mention that alcoholic specimens will not freeze unless the alcohol is first removed from them.

Although in normal histological work it is especially desirable to make thin sections, moderately thick ones can, as a rule, be utilized for pathological examinations. We have been able to obtain at times very thin celloidin-sections by properly diluting or strengthening the alcohol which is employed in keeping the knife and specimen moist. We find, however, that absolute alcohol is not to be recommended, as it will render the celloidin sticky, and may even dissolve it. About 85 to 90 per cent. is the limit of strength which should be employed for this purpose. The sections which are cut away may be removed from the knife-blade either with the flat of the finger, or, better still, by means of a moderate-sized camel's-hair brush, which may also be employed to keep the knife and specimens wet. These sections when cut are put into the 75 per cent. alcohol, and are now ready for staining.

*Staining of Sections.* A great variety of staining-methods are in use,

<sup>1</sup> An excellent description of the technique of the freezing-microtome will be found in Friedländer's *Microscopische Technik* or Kahlden's *Histologische Untersuchung*.

but for ordinary pathological work in gynæcology a few simple stains suffice. Much can be learned as to "form-relations" from the study of unstained specimens; but for finer histological changes staining with one or more dyes is highly desirable. Delafield's hæmatoxylin alone or in conjunction with eosin as a counter-stain yields excellent results, especially if acid alcohol be used as a differentiating fluid. Carmine, picro-carmine, and Van Giesen's mixture are valuable general stains. For demonstrating bacteria in specimens the four following methods<sup>1</sup> are the most common in use for purposes of diagnosis: 1. Gram's method, either simple, or Gram's method with previous staining with picro-lithium carmine. 2. Weigert's fibrin-stain, which stains many forms of bacteria, fibrin, hyaline, and sometimes elastic tissue. 3. Carbol-fuchsin. 4. Methylene-blue.

#### *The Clinical Records of the Cases.*

In order to enhance the value of the microscopical examinations I have made it a rule to keep parallel clinical protocols of the cases, paying particular attention to the following points:

Name, age, social condition, residence, color, occupation.

Number of labors, whether instrumental or not. Age of oldest and youngest child; character of puerperia.

Miscarriages or abortions; at what period of pregnancy. Any possible sequelæ.

Menses. Age at first appearance. Regularity; amount; duration; whether painful or not. Date of last menstrual period.

Leucorrhœa; whether present or not. Character of discharge, whether irritating or not; color and amount.

Micturition; any disturbance noticed by patient.

Bowels. Usual condition; general effects of laxatives and purgatives.

Family history.

Personal history.

Patient's chief complaints; *i. e.*, those subjective symptoms which led the patient to present herself for treatment or diagnosis.

Present condition, embracing a thorough physical examination.

Examination of urine, chemical and microscopical.

Results of the examination: (1) without anæsthesia, (2) under anæsthesia.

#### *The Histological Protocols.*

In studying the sections particular attention is paid to the following points, and the results are recorded:

1. *The superficial epithelium; i. e.*, the layer of epithelium lining the cavity of the uterus.

<sup>1</sup> These methods are fully described in the books on microscopical technique.

Character of cells :

Ciliated or not.

Single layer or multiple layers, etc.

2. *Utricular glands* :

Course.

Length.

Size.

Lumina.

Shape.

*Glandular epithelium.* Character of cells :

Ciliated or not.

Single layer or multiple layers.

3. *Stroma.* Size of cells. Physical characteristics.

*Different sorts of cells* :

Lymphoid.

Ovoid or round.

Fusiform or spindle.

Peculiarities in arrangement of cells.

4. *Vessels.* Those near the superficial mucous membrane, and those further away from the surface.

5. *Muscular tissue.* If present or not ; and if any peculiarities noted.

6. *Cervical tissues.* If present or not ; and if any peculiarities noted.

7. *Histological Diagnosis.*

8. *Notes or Remarks.*

In this way it will be seen that the careful clinical history which is taken of the cases and the histological findings are made to supplement one another. A discussion of the many different points to be considered in the diagnosis of the specimens is impossible in the present paper. Fortunately, however, we now have at our disposal a rich literature upon the subject, and especially worthy of mention in this connection are the work of Ruge and Veit on *Uterine Carcinoma*, Abel's *Technik und Diagnostik in der Gynäkologischen Praxis*, and the section of Orth's *Pathology*, entitled "Weibliche Geschlechtsorgane."

CONCLUSIONS. A study of the appended tables, in which the results of the parallel examinations of 100 cases have been systematically arranged, reveals a number of interesting points.

Thus, in Table I, it will be seen that of 100 cases the question of malignancy or benignancy could be settled in 95. In 2 cases which clinically appeared to be benignant, positive and timely evidence was given of malignancy by the microscopical examination. In 2 cases in which the clinical symptoms pointed to malignant disease the microscope enabled us to confirm the clinical diagnosis beyond all doubt. In 1 case in which there was clinically at least a warrantable suspicion of malignancy the microscope changed the condition of suspicion to one of

certainty. In 26 cases in which the clinical symptoms rendered the suspicion of malignancy at least warrantable the microscopical examination proved the absence of malignant disease. In 63 cases in which the clinical symptoms pointed to a benign disease the microscopical examination confirmed the clinical diagnosis or showed a normal endometrium.

In Table I.(a) the clinical symptoms met with in different conditions of the endometrium and in some few malignant conditions have been tabulated.

*Pain.* In 22 cases in which the microscope showed normal or approximately normal endometrium pain was absent in but 3 cases. This is a point we think worthy of some emphasis, inasmuch as it proves the possibility of the existence of painful affections referable to the uterus, in cases in which histological changes, at least by the methods ordinarily employed, are not demonstrable. In 31 cases of endometritis glandularis pain was absent in but 1 case. In 24 cases of endometritis interstitialis pain was absent in only 2 cases. In 5 cases of endometritis glandularis et interstitialis pain was absent in but 1 case. In 8 cases of endometritis post abortum sive partum pain was absent in but 2 cases. In the 5 malignant cases it was not absent in a single instance, and was generally continuous. In 30 cases of endometritis glandularis dull pain occurred in 21 and sharp pain in 9. In 19 cases of endometritis interstitialis dull pain occurred in 9; sharp pain in 10. In endometritis

TABLE I.

	100	22	31	24	5	8	2	3	0	5
	Normal endometrium,	Endometritis glandularis,	Endometritis interstitialis,	Endometritis glandularis et interstitialis,	Endometritis post partum sive post abortum,	Adenocarcinoma,	Squamous carcinoma,	Sarcoma,	Material insufficient, or diagnosis doubtful, or malignancy doubtful.	
Total cases . . . . .	100	22	31	24	5	8	2	3	0	5
a. Cases in which clinical symptoms pointed to benign disease. Microscope showed absence of malignant disease . . . . .	67	17	20	15	4	7	...	...	...	4
b. Cases in which clinical symptoms pointed to benign disease. Microscope showed presence of malignant disease . . . . .	2	...	...	...	...	...	...	2		
c. Cases in which clinical symptoms pointed to malignant disease. Confirmed by microscope . . . . .	2	...	...	...	...	...	1	1		
d. Cases clinically suspicious as to malignancy; microscope showed undoubted malignant disease . . . . .	1	...	...	...	...	...	1	...		
e. Cases clinically suspicious as to malignancy; microscope showed absence of malignant disease . . . . .	28	5	11	9	1	1	...	...	...	1

TABLE I.(a)—CLINICAL SHEET.

	Normal endometrium.	Endometritis glandularis.	Endometritis interstitialis.	Endometritis glandularis et interstitialis.	Endometritis post partum sine post abortum.	Adenocarcinoma.	Squamous carcinoma.	Sarcoma.	Material insufficient, or diagnosis doubtful, or malignancy doubtful.
Pain absent . . . . .	3	1	2	1	2				
continuous . . . . .	3	2	4	...	...	2	2		
intermittent . . . . .	15	27	15	4	4	...	1	1	5
worse at periods or on exertion . . . . .	11	19	11	3	5	1	1	...	5
lancinating or sharp . . . . .	4	9	10	2	1	1	2	...	4
dull or boring . . . . .	10	21	9	3	3	1	1	...	1
limited to pelvis . . . . .	17	29	19	4	4	1	2	...	5
headache . . . . .	3	6	2	...	...	...	...	...	1
backache . . . . .	12	21	11	5	5	1	1	...	5
Discharge, moderate . . . . .	7	13	11	4	5	1	...	...	2
absent . . . . .	2	8	5	...	...	2	2	...	2
profuse . . . . .	13	10	8	1	3	1	1	...	1
Menses, amenorrhœa . . . . .	2	...	1	...	1	1	...	...	1
too frequent . . . . .	3	6	6	2	...	1	1	...	...
too infrequent . . . . .	2	3	4	1	1	...	2	...	1
regular . . . . .	15	22	13	2	6	...	...	...	3
scanty . . . . .	5	6	6	1	1	...	2	...	1
profuse . . . . .	9	17	8	3	3	1	1	...	2
normal in amount . . . . .	6	8	9	1	3	...	...	...	1
normal in duration . . . . .	10	18	12	1	2	...	1	...	2
too long in duration . . . . .	6	10	6	3	5	1	1	...	1
too short in duration . . . . .	4	3	5	1	...	...	1	...	1
painless . . . . .	10	13	7	1	2	...	2	...	2
painful . . . . .	10	18	16	4	5	1	1	...	2
with clots of blood . . . . .	3	5	3	2	3	1	1	...	1
Metrorrhagia . . . . .	2	3	...	1	5	2	1	...	1
O-parous women . . . . .	10	16	12	4	3	1	...	...	3
Parous women . . . . .	12	15	12	1	5	1	3	...	2
Abortion diagnosed clinically . . . . .	...	...	...	...	2	...	...	...	...
Results of treatment :									
cured . . . . .	1	...	...	...	...	...	1	...	...
benefited permanently . . . . .	14	20	18	1	8	...	1	...	2
temporarily . . . . .	7	10	6	3	...	2	1	...	3
unimproved . . . . .	...	1	...	1	...	...	...	...	...
died . . . . .									

glandularis et interstitialis, 5 cases, dull pain occurred in 3 and sharp pain in 2. This would seem to show that in cases of glandular endometritis dull or boring pain is more frequently met with than sharp or lancinating pain, while to a somewhat less extent the reverse is true in cases of interstitial endometritis. The pain complained of is in the great majority of instances limited to the pelvis or to the lower portion of the abdomen. We found this to be true in about 80 per cent. of cases. Headache is a rather infrequent symptom, being met with but 12 times. Backache is much more frequently met with, being recorded 61 times.

*Discharge.* In 22 cases in which the microscope showed normal endometrium discharge was absent in but 2 cases, and in 20 cases it was considerable in amount. In these cases the discharge probably originated from the cervix, and not from the body of the uterus; that is to say, the cases, or the majority of them, must have been instances of "cervical" endometritis. In 31 cases of definite glandular endometritis discharge was

TABLE I.(b)—HISTOLOGICAL SHEET.

	Normal endometrium.	Endometritis glandularis.	Endometritis interstitialis.	Endometritis glandularis et interstitialis.	Endometritis post partum sive post abortum.	Adenocarcinoma.	Squamous carcinoma.	Sarcoma.	Material insufficient, or diagnosis doubtful, or malignancy doubtful.
<b>Superficial epithelium :</b>									
wanting, or insufficient for diagnosis . . . . .	2	3	...	1	1	2	2	...	2
single layer . . . . .	20	26	24	4	7	...	1	...	3
multiple layers . . . . .	...	2	2	...	...	...	...	...	...
high columnar . . . . .	16	19	15	2	...	...	...	...	3
medium columnar . . . . .	3	8	6	1	3	...	1	...	...
low columnar or cuboidal . . . . .	1	1	4	...	4	...	...	...	...
ciliated . . . . .	17	24	15	3	2	...	1	...	3
cilia not demonstrable . . . . .	3	4	9	...	5	...	...	...	...
character of epithelium undetermined (not sufficient to judge from) . . . . .	...	...	...	1	...	...	...	...	1
<b>Utricular glands :</b>									
wanting or material insufficient . . . . .	...	...	...	...	1	...	1	...	1
course, tortuous or zig-zag . . . . .	1	31	9	4	6	...	...	...	...
straight or nearly so . . . . .	21	...	15	1	1	...	1	...	2
number, increased . . . . .	...	18	4	1	2	2	...	...	...
normal . . . . .	22	6	6	1	2	...	1	...	1
diminished . . . . .	...	1	10	2	3	...	...	...	1
size of lumina, regular . . . . .	17	...	4	...	...	...	1	...	1
irregular . . . . .	5	31	20	5	6	2	...	...	3
shape of lumina regular . . . . .	20	...	21	1	...	...	1	...	2
irregular . . . . .	2	31	3	4	7	2	...	...	2
invaginated glands . . . . .	8	21	13	2	...	...	...	...	...
<b>Glandular epithelium :</b>									
wanting or insufficient to judge from . . . . .	...	...	...	...	1	...	1	...	...
single layer . . . . .	22	28	24	5	6	1	1	...	5
multiple layers . . . . .	...	7	3	2	3	2	...	...	...
high columnar . . . . .	19	18	20	3	2	...	1	...	4
medium columnar . . . . .	3	10	4	1	1	1	...	...	...
low columnar or cuboidal . . . . .	...	3	...	1	5	2	...	...	1
ciliated . . . . .	20	22	23	5	3	...	1	...	4
cilia not demonstrable . . . . .	1	9	1	...	4	2	...	...	1
undetermined . . . . .	1	...	...	...	1	...	...	...	...
<b>Stroma :</b>									
small round and ovoid cells with fusiform cells around gland lumina . . . . .	20	27	13	3	5	1	1	...	4
round or oval cells, varying in size, some large, some small . . . . .	1	4	7	2	2	...	...	...	1
bands of spindle-cells running through stroma . . . . .	...	...	18	2	1	...	...	...	...
spindle-cell element in excess . . . . .	3	1	23	3	2	1	...	...	...
cells crowded closely together . . . . .	4	11	6	1	1	...	1	...	...
cells not closely packed together . . . . .	1	4	4	...	1	...	...	...	1
lymphoid cells . . . . .	12	13	12	1	6	1	2	...	2
polynuclear leucocytes . . . . .	13	14	10	...	6	2	...	...	3
regularly distributed grouped in spots . . . . .	3	6	3	...	2	...	...	...	...
free red blood-cells numerous . . . . .	14	18	12	3	3	...	...	...	1
few . . . . .	4	5	4	...	1	...	...	...	2
decidual cells . . . . .	...	...	...	...	8	...	...	...	1
<b>Vessels, numerous . . . . .</b>									
scanty or none found . . . . .	14	20	15	3	8	2	...	...	1
dilated . . . . .	8	11	9	2	...	...	...	...	4
collapsed . . . . .	10	16	13	3	8	1	...	...	2
muscle-tissue, present . . . . .	6	8	4	...	...	...	1	...	4
absent . . . . .	4	4	5	...	1	1	1	...	3
Cervical tissue, present . . . . .	18	27	19	5	7	1	2	...	2
absent . . . . .	1	2	1	...	2	...	2	...	2
Placental villi, chorionic or amniotic remnants . . . . .	21	29	23	5	6	2	1	...	3
	22	31	24	5	8	2	3	0	5

absent in 8 cases, or in nearly 25 per cent. This shows that leucorrhœa is by no means always present in such cases. In 24 cases of interstitial endometritis leucorrhœal discharge was absent in 5 cases, or in about 20 per cent. This is also interesting when considered together with the immediately preceding statement. In 8 cases of endometritis following abortion or labor a leucorrhœal discharge is noted in every case. In 2 cases of adenocarcinoma, one of the cervix, the other of the fundus of the uterus, a leucorrhœal discharge was present in both cases. In 3 cases of squamous carcinoma leucorrhœal discharge was absent in 2 cases, and was profuse in 1 case. In the two cases the disease being incipient, there were, in fact, no well-marked clinical symptoms such as would have rendered one even suspicious of a malignant condition. It was only in the course of the routine examination of all tissues that the presence of a malignant growth was demonstrated. In the third case carcinoma could be diagnosed clinically, but the condition unfortunately had progressed too far to admit of a removal of the uterus.

*Menses.* Regularity: in the majority of cases the menses are noted as being regular. It is interesting to note that in 8 cases of endometritis after abortion, or after labor, the menses are noted as being regular in 6. Amount: in 31 cases of glandular endometritis the amount was scanty in 6; profuse in 17; normal in 8. In 24 cases of interstitial endometritis it was scanty in 6; profuse in 8; normal in 9. We shall watch with interest the results in such cases in the future in order to see if the relations here presented be characteristic in these diseases. The table shows that in over 50 per cent. of cases of glandular endometritis profuse menstruation was met with, but in only 33 per cent. of cases of interstitial endometritis was the same condition found. In 8 cases of endometritis post abortum sive partum menstruation is recorded as profuse in but 3. In only one of the eight cases is amenorrhœa noted. Five of these eight patients are recorded as having the menstrual period of too long duration. Of the 2 cases of adenocarcinoma, one patient was past the menopause, being about sixty or sixty-five years of age. She had had a very trifling hemorrhage from the uterus previous to her admission into the hospital. This was the only symptom that the patient complained of; but she had been further told by her attending physician that there was no malignant disease of the uterus, and on physical examination alone nothing could be made out suggesting such a condition. As regards painfulness or painlessness of menses, pain seems to be more constantly present in the interstitial form of endometritis than in that of the glandular type; in endometritis interstitialis, 23 cases, the menses were painful in 16, painless in 7, with clots of blood noted altogether 18 times. Out of 8 cases of endometritis post abortum sive partum pain was present in 3 cases.

*Metrorrhagia* was noted twice in 22 cases in which the endometrium

appeared to be normal on microscopical examination; three times in 31 cases of endometritis glandularis; in no instance in 24 cases of endometritis interstitialis; five times in 8 cases of endometritis post abortum, sive partum; twice in 2 cases of adenocarcinoma; once in 3 cases of squamous carcinoma. It is interesting to observe that in 8 cases of endometritis post abortum sive partum abortion had been diagnosed in but 2 cases. Exactly what proportion of these 8 cases were post abortum and what post partum I was unable to say, but three of the 8 cases are recorded as occurring in nulliparous women. In 1 case placental villi were found in a fairly well preserved condition nine months after the abortion was said to have taken place.

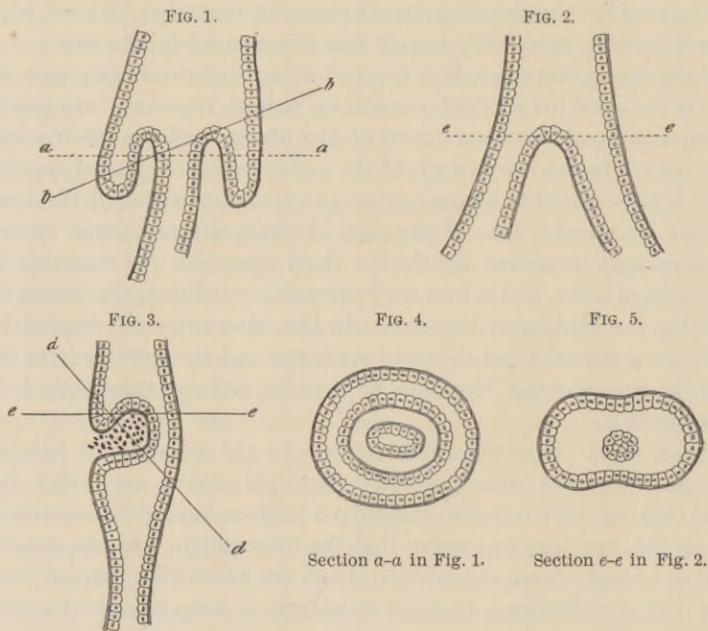
*Results of Treatment.* No deaths are recorded. 2 cases are classed as unimproved. In the majority of cases, 64, treatment effected a permanent benefit; temporary benefit was experienced in 32 cases.

Of the malignant cases, in 2 cases of adenocarcinoma temporary benefit was recorded. In one of these cases radical treatment was impossible on account of the local extent of the disease and the occurrence of metastases. In one case the age of the patient and her general condition compelled the writer to advise against any operation, although the disease was not advanced. One of the cases of squamous carcinoma reported as temporarily benefited has had a third operation for curetting and cauterization since, and is in a very precarious condition, the disease now involving the bladder and rectum. In the other two cases vaginal hysterectomy was performed over two years ago and the patients have been up to the present time free from any return, and are apparently in excellent health.

TABLE I.(b).<sup>1</sup> *Superficial epithelium.* In the majority of instances a single layer was demonstrated. Multiple layers are noted in 2 cases each of endometritis glandularis and endometritis interstitialis. We should say here in passing that the determination of the question whether a single layer or multiple layers are present is attended with a great deal of difficulty. One has constantly to keep in mind the readiness with which the appearance of multiple layers is produced by oblique section and by thick sections, so that considerable experience in interpreting the microscopical image is demanded. We cannot agree with some authors that a multiple layer of epithelium, either of the superficial or glandular type, is of itself a sign of malignancy. The appearance may be accounted for in several ways; it may be due, for example, to shrinkage and distortion of the specimen during preparation, to oblique and thick sections, and possibly to other causes. We believe also that, in the majority of instances where these external causes may be excluded, multiple layers denote merely a hyperplasia of the cells.

<sup>1</sup> From the Pathological Laboratory of the Western Reserve University.

With regard to the height of the cell, Abel has pointed out that low or medium columnar cells are suspicious of pregnancy. Now, in eight of our cases of endometritis post abortum sive partum low or cuboidal epithelium is noted in four cases and medium columnar in three. This effect of flattening out the cells, which may indeed go so far that the superficial epithelium becomes changed into a sort of endothelial membrane with cells having more breadth than depth, and resembling endothelial cells very closely, is probably, though not entirely, the result of pressure. We have noticed similar flattening of cells in cases of ectatic glands and in cases of hydrosalpinx, where the pressure of the contents must have been greater than the usual pressure which is exerted upon the cells.



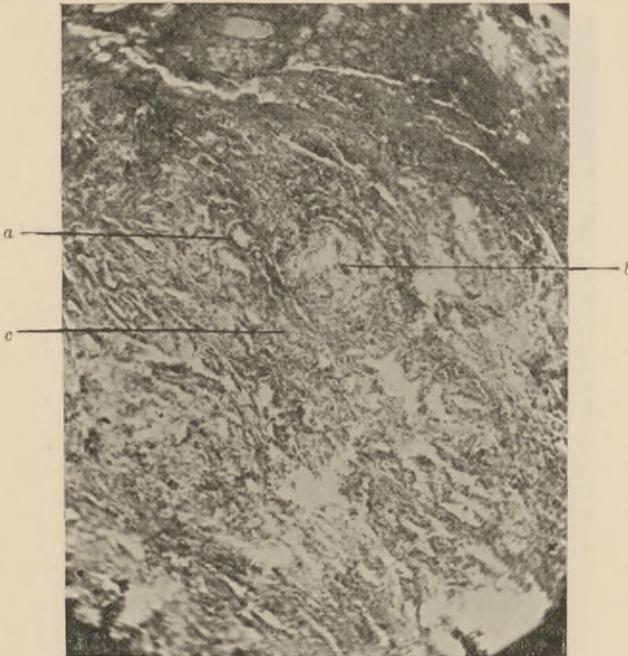
*The presence or absence of cilia.* In the majority of cases cilia were found, their absence being recorded only 21 times. In 8 cases of endometritis post partum or post abortum they were demonstrated in but 2 cases and not demonstrated in 5 cases.

*Utricular glands.* A tortuosity of the glands, probably in the lower layer of the mucous membrane, seems to be an almost constant finding in cases of endometritis post abortum sive partum. There is also some irregularity in the size and more especially in the shape of the glands in these cases. Invaginated glands were found 8 times in 22 cases, where the endometrium had to be designated as normal; 21 times in 31 cases

of endometritis glandularis; 13 times in 24 cases of endometritis interstitialis; twice in 5 cases of endometritis glandularis et interstitialis.

Invaginated glands or sections of lumina within lumina, or rather the appearance of such things in the microscopical section, may be produced in a variety of ways. A pictorial representation will illustrate this to better advantage than can be done in other ways. Fig. 1 represents a true intussusception or invagination of a utricular gland. Fig. 2 shows

FIG. 6.



Adenocarcinoma of the cervix uteri.

a. Gland-ducts, but little changed. b. Alveolus filled with flat cells. c. Atypical gland-duct.

a uterine gland dividing dichotomously. Fig. 3 shows a papillary projection into the lumen of gland. The lines *aa* to *ee* represent sections. If these be made perpendicular to the plane of the paper, we should have somewhat the result pictured in Figs. 4 and 5. The papillary projections in Fig. 3 may appear somewhat diagrammatic, but we have seen just such a condition under the microscope.

*Glandular epithelium.* What has been said of the superficial epithelium holds true also for that of the glandular type. Multiple layers, however, are more frequently met with in the glands.

*Stroma.* The typical normal stroma may be said to consist of small

round or oval cells, almost, but not quite, as small as lymphoid cells, all of about one size, with a single layer of fusiform cells round the gland lumina. These fusiform cells make the membrana propria for the glandular epithelium. They show the fusiform shape under the microscope, but they are probably flat endothelial-like cells. We can readily understand this when represented pictorially. These cells which appear to be fusiform are in all probability only endothelial like cells, through which perpendicular sections have been made. In 20 of the 22 cases of nor-

FIG. 7.



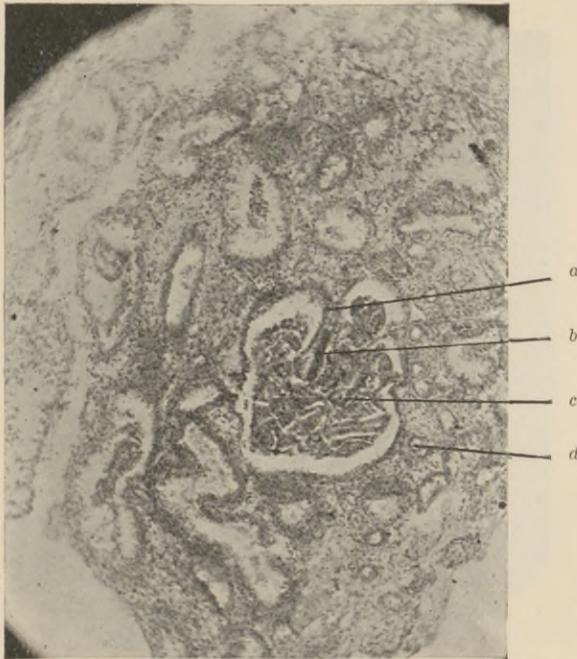
Decidual remnants and placental villi.

a. Placental villus. b. Large piece of decidua showing large decidual cells.

mal endometrium and in 27 of the 31 cases of endometritis glandularis this condition was found. In 13 of the 24 cases of endometritis interstitialis, in 3 of the 5 cases of endometritis interstitialis et glandularis, and in 5 of the 8 cases of endometritis post abortum sive partum these structures could easily be made out. In all of these last 8 cases, however, decidual cells were also found. It is interesting to note in this connection the behavior of the stroma-cells to staining with the different dyes. It was found when using the picro-carminic method that the nuclei of the small round and oval cells stained intensely with the carmine, while the cell-bodies, though taking on faintly the same stain, did not stain at all with the picric acid. In other words, unless they are undergoing

some degenerative process, no yellow tint could be seen in them. Blood-cells, on the other hand, whether free in the stroma or inside the vessels, stained intensely with the picric acid. The cell-bodies stained with eosin, however, but faintly. Decidual cells took on the eosin-stain deeply, and one could recognize them even with low powers by the peculiar pinkish tinge of the section whenever they were present in sufficient numbers. In 7 cases of endometritis interstitialis out of a

FIG. 8.



Papillary growth encroaching upon lumina of glands.

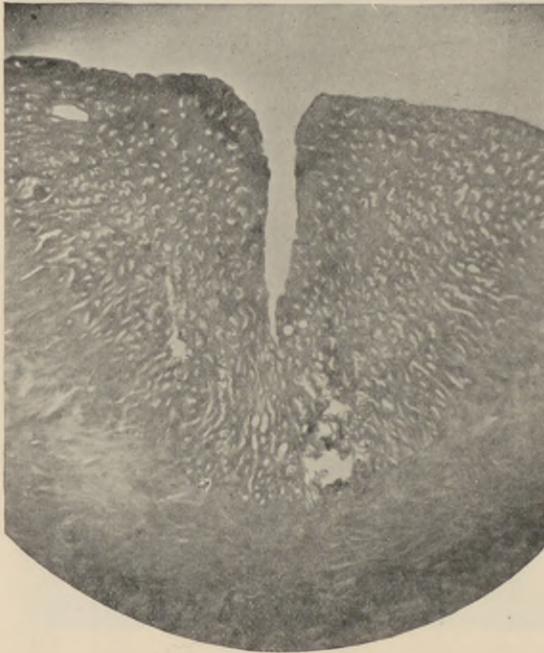
*a.* Pedicle. *b.* Foreign body. *c.* Complicated papillary growth. *d.* Bloodvessels.

total of 24, and in 4 cases of endometritis glandularis out of 31 cases the stroma-cells are noted as varying much in size, some being larger, some smaller than normal. Giant cells with many nuclei were seen in quite a number of the cases of endometritis post abortum sive partum. The exact record of the number of times of their occurrence, unfortunately, has not been noted, but I can recall three instances in which they were found. In one case they were so numerous as to give rise to a suspicion of giant-celled sarcoma, there being at the time no clinical history of abortion or miscarriage, and the fetal structures not being positively demonstrable. The answers of the patient, however, upon being closely questioned as to the occurrence of an abortion, previous

to her applying at the clinic, went to show that she had miscarried. Histologically the picture presented by the section under the microscope resembled closely that of a myosarcoma.

*Bands of spindle-cells in the stroma* were observed 18 times in 24 cases of endometritis interstitialis, while the spindle-cell elements were found in excess 23 times. Very characteristic pictures in endometritis interstitialis are the concentric whorls of spindle-cells which form around the gland lumina. Instead of the normal single layer of spindle or fusi-

FIG. 9.



Muscularis.

Endometritis glandularis hyperplastica.

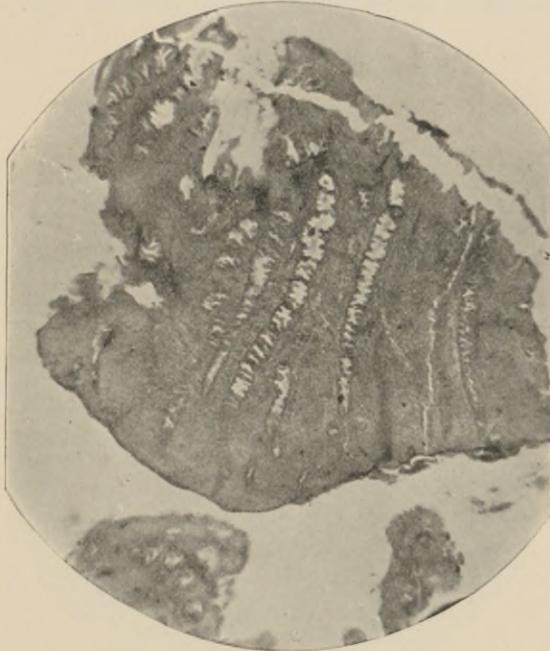
The cleft in the middle of the section is part of the cavity of the uterus.

form cells, sometimes as many as ten layers may be seen. In many places these cells are seen to be compressing the gland, and the gland-epithelium is undergoing degenerative changes, sometimes of the nature of simple atrophy, while sometimes active degenerative changes—*e. g.*, cloudy swelling or necrosis—have taken place.

*Polynuclear leucocytes* were found free in the stroma as follows: in 22 cases of normal endometrium, 13 times; in 31 cases of endometritis glandularis, 14 times; in 24 cases of endometritis interstitialis, 10 times; in 8 cases of endometritis post abortum sive partum, 6 times. Just what their presence signifies it is hard to say. In most of the cases they were found sparsely, but more or less regularly distributed, not being present

in great numbers and evidently not representing inflammatory infiltration. Their almost constant presence (in six out of eight cases) in cases of endometritis post abortum sive partum would seem to indicate that they are perhaps playing some rôle in the involution of the mucosa. It is evident, however, that their presence in the uterine mucosa (when sparsely and regularly distributed) is of no great pathological significance.

FIG 10



Endometritis glandularis hypertrophica. Specimen obtained by curetting.

*Free blood-cells* were also frequently met with; in 22 cases in which the endometrium has been classed as normal, 18 times; in 31 cases of endometritis glandularis, 23 times; in 24 cases of endometritis interstitialis, 16 times; in 5 cases of endometritis glandularis et interstitialis, 3 times; in 8 cases of endometritis post abortum sive partum, 4 times. The explanation of their presence in such a number of cases with normal endometrium does not seem clear. What their rôle is, apart from the phenomena of menstruation, we do not understand.

*Decidual cells* were found in all the 8 cases of endometritis post abortum sive partum. True decidual cells were not found in any of the other conditions, though cells approaching them closely in size were often found in cases of interstitial endometritis.

*Vessels.* No true arteries or veins are found in the superficial layers of the mucosa. Here the bloodvessels are all venous or arterial capillaries,

the latter far outnumbering the former. In all 8 cases of endometritis post abortum sive partum the vessels were found dilated.

*Muscular Tissue and Cervical Tissue.* We desire to call attention especially to the infrequency with which muscular tissue and cervical tissue were met with. Muscular tissue is recorded as being present in but 19 cases. Cervical tissue is recorded as being present in but 11 cases.

The above table includes several cases in which sections were made from the cervix, so that cervical tissue really was obtained by curetting even fewer times than would at first appear from the table.

FIG. 11.



Endometritis interstitialis. Specimen obtained by curetting.

*Placental villi, chorionic or amniotic remnants,* were found in 5 cases of endometritis post abortum sive partum. We are inclined to the opinion that, lacking a clinical history of abortion or pregnancy, it is impossible in many instances to make an absolute diagnosis of a foregoing pregnancy unless such fetal remnants be demonstrated. Their presence, however, must be considered, of course, as proof positive of a preceding pregnancy.

In conclusion, I wish to thank my assistant, Dr. Walter R. Lincoln, for valuable aid in the preparation of the tissues and in the laborious analysis of the cases.

The several micro-photographs illustrate typical microscopic findings in some of the cases to which we have referred.



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