CHAPTER XII

DISEASES OF THE OVARY AND PAROVARIUM

Tumors constitute the principal lesions occurring in the ovary, and of these about 95 per cent are cystic. There occur also infections, mostly secondary inflammation, and endocrine disturbances with important functional and structural results.

Classification of Diseases of Ovary and Parovarium

- Prolapse of Ovary and Circulatory Changes.
- Infections
  - Inflammation (gonococcus, streptococcus, staphylococcus, colon bacillus)
  - Tuberculosis, Syphilis, and Rarer Infections
- Disturbances of Follicular Function
  - Follicular Atresia
  - Follicular Cysts ("cystic ovary")
  - Corpus Luteum Cysts
- Embryologic Rests
  - Undifferentiated Sex Cells
    - Endocrine Influence
      - Feminizing
        - Granulosa-Cell Tumor
      - Masculinizing
        - Arrhenoblastoma
        - Adrenal Adenoma
    - No Endocrine Influence
      - Dysgerminoma (Seminoma)
      - Brenner Tumor
      - Hypernephroma
  - Undifferentiated Somatic Cells
    - Dermoid Cyst
    - Teratoma
  - Embryologic Remnants
    - Parovarian Cyst
    - Gaertner's Duct Tumor
- Transplantation or Heteroplasia or Embryologic Rests
  - Endometrial Cyst
  - Pelvic Endometriosis
  - Adenomyoma
- Changes Dependent on Endocrine Disturbances in Distant Organs
  - Theca-Lutein Cysts
    - Hydatidiform Mole of Uterus
    - Chorioepithelioma of Uterus
    - Adenoma of Pituitary
  - Follicular Atrophy
    - Adrenal Adenoma
    - Adrenal Hyperplasia
    - Pituitary Atrophy (by tumor or otherwise)
- Other Benign Growths
  - Proliferating Cysts
    - Pseudomucinous Cyst
    - Serous Cyst (Papillary Cyst)
  - Solid Growths
    - Fibroma
    - Myoma and Adenomyoma
- Miscellaneous Rare Tumors
  - Lymphangioma
  - Mesonephroma
  - Ganglioneuroma
- Ovarian Cancers
  - Carcinoma
    - Primary
    - Secondary
  - Sarcoma
    - Primary
    - Secondary

Satisfactory classification of ovarian pathologic changes has long been one of the problems of systematic gynecologic teaching. The reason for this lies in the complexity of the organ's structure and physiology and the resulting

complexity of its pathologic activities. The principal difficulty is with the great variety of benign growths and near-growths, some of which are real neoplasms and others only retention cysts.

It is hoped that the above working classification may help some toward clarifying the situation. In classifying these pathologic changes it seemed best to base the classification on *cause,* as far as the cause is known. This brings at once to the student a rational grouping of the confusing variety of pathologic changes with which he must deal. Also, it puts him in touch promptly with the etiologic factor, which is one of the first items to be considered in connection with any lesion, and which is also usually helpful in understanding the microscopic picture and the clinical progress.

PROLAPSE OF OVARY

A large heavy ovary is likely to sink low in the pelvis, especially if its supporting attachments are weakened through subinvolution after labor or through congenital deficiency. The enlargement is often due to the formation of numerous follicular cysts, giving the enlarged "cystic ovary" described later.

Prolapse of the ovary does not ordinarily become of clinical importance unless it drops into the peritoneal cul-de-sac back of the uterus. In this situation it may give rise to pressure symptoms, especially during the menstrual congestion or at the time of ovulation. The principal disturbance comes in those cases in which the ovary becomes adherent in this location, and cannot move on pressure as it normally does.

In most cases giving trouble, the principal complaint is dyspareunia, with the discomfort located high inside rather than at the vaginal entrance. Occasionally there is pain on bowel movement or pressure discomfort when the rectum is filled. In some retrodisplacement cases, the ovary is found low in the cul-de-sac under the corpus uteri, and the disturbance from its fixation there may furnish the principal symptoms.

As to treatment, there may be prolapse and fixation of one or both ovaries without any symptoms. Consequently, when the condition is found in the course of an examination, question the patient carefully to determine if there are symptoms due to it before disturbing her with knowledge of its presence.

When there are troublesome symptoms, the knee-chest posture may aid by gravitating the tender ovary out of the cul-de-sac or by lessening circulatory disturbance in it. If movable and pushed out of the cul-de-sac during examination, it may stay in the improved position. Occasionally a retrodisplacement pessary will keep it up out of the way comfortably.

If the ovary is adherent, it may be possible to stretch light adhesions by digital pressure or by use of the mercury pressure bag. If there is persistent discomfort despite conservative measures, operation is advisable to correct the painful condition. Very often there are more important associated lesions requiring operation, and the prolapsed ovary is taken care of incidentally, by removal or fixation, as conditions indicate.

Circulatory Changes

Interference with the circulation to the ovary causes it to become edematous and occasionally cystic. Retrodisplacement of the uterus, with a consequent prolapse of the ovaries, is a common etiologic factor in this condition. Other causes are pressure on the vessels by tumors of other organs, varicose veins, a chronic twist in the pedicle not sufficient to cause a gangrenous ovary, and trauma (operative or otherwise). These ovaries are usually a little larger than normal, and the chief microscopic finding is edema and chronic passive congestion.

INFECTION OF THE OVARY

Infections include inflammation which may be due to contagious disease or to ordinary pus bacteria (gonococcus, streptococcus, staphylococcus, colon bacilli), and tuberculosis and syphilis.

Inflammation of the ovary is usually secondary to salpingitis or other adjacent inflammation. There may be one or more points of infection with the usual infiltration and swelling—the inflammation involving both the follicles and the interfollicular connective tissue. It may or may not progress to the stage of abscess formation. When an ovarian abscess forms, it is usually in connection with tubal suppuration, hence it was considered along with salpingitis.

The ovary, instead of becoming infected, may simply become surrounded by exudate, which compresses it, damaging it and causing cellular infiltration of the connective tissue (both the capsule and stroma). In time this round-celled infiltration forms scar tissue, and as it contracts it further interferes with the graafian follicles, so that they atrophy or form small cysts. From this process the functionating part of the ovary becomes reduced in size, and the organ may come to consist simply of a mass of fibrous tissue with small cysts scattered through it. This condition is called cirrhosis, and ovaries thus affected are designated as "cirrhotic ovaries."

The other type of inflammation of the ovary is that in which the infection comes by way of the blood stream. This is seen at times in various general infectious diseases, particularly mumps and scarlet fever. The fact should be kept in mind that pelvic symptoms during the course of acute infectious diseases may be due to oophoritis, which may require additional rest and care during convalescence.

The pathologic findings are the same as those seen in acute inflammation elsewhere in the body. There is edema with dilated capillaries and leucocytic infiltration.

Chronic Inflammation.—The acute inflammation may resolve leaving no permanent damage or it may result in a chronic inflammation with adhesions and permanent damage to the tissue. The common finding in these cases is a mass composed of ovary, tube, and exudate, with or without abscess. In tubo-ovarian abscess either a tubal abscess ruptures into the ovary or an ovarian abscess ruptures into the tube and the two become fused. Microscopically there is a marked round cell infiltration. Later there may be destruction of the follicular apparatus and sclerosis of the remaining stroma.

Tuberculosis of Ovary

Tuberculosis of the ovary is almost always secondary to tuberculosis elsewhere. Direct extension is the usual method of infection, and it is commonly secondary to tubal tuberculosis. According to the statistics of Orthmann, in 307 cases of genital tuberculosis the ovary was involved in 33.9 per cent. In the gross the ovary is usually embedded in adhesions and studded with tubercles. In the late cases there are areas of caseation surrounded by thick, ragged walls. Cases of tuberculosis of the ovary associated with ovarian cysts have been reported.

Microscopically discrete tubercles are found in the superficial layers of the ovary. When a follicle or corpus luteum is involved, tubercles are found in the wall of the structure.

The symptoms and treatment are the same as for the more frequent tubal tuberculosis, the details of which are given in the preceding chapter.

Syphilis of Ovary

The protean manifestations of syphilis no doubt affect the ovary in structure and function, and this is to be kept in mind when pelvic symptoms or disturbance appear in patients who have syphilis.

There are only a very few authentic cases of syphilis of the ovary in the literature. In the case reported by Gellhorn the gumma was centrally located, indicating its systemic origin. Microscopically it was a granulomatous mass containing a large number of plasma cells and eosinophiles.

DISTURBANCES OF FOLLICULAR FUNCTION

It is surprising how much structural change can be brought about in the ovary by mere disturbances of function. A slight misdirection of the endocrine influences which control normal ovulation may lead to follicular changes in the ovary of marked extent. The most common example of this marked structural change due to functional deficiency is "follicular atresia," in which the ovum dies and the follicle ceases growing and eventually shrivels. This occurs regularly on a large scale, for only a small percentage of the thousands of young follicles go on to maturity. Some of the follicles in which the ovum dies do not shrivel and disappear but fill with fluid which increases, resulting in the formation of small cysts (follicular cysts). Occasionally a corpus luteum instead of progressing normally will develop an increasing amount of fluid (corpus luteum cyst).

The above changes in the ovary occur without any causative lesion of other organs. Later, reference will be made to changes in the ovary brought about by lesions in other organs. Belonging to this class are the theca-lutein cysts, which may enlarge the ovaries till they fill the pelvis and lower abdomen, and follicular atrophy of the cortical functioning portion of the ovaries.

Follicular Cysts

Follicular cysts are simply unruptured graafian follicles which have become dilated. The increase in the fluid of the follicle and the consequent

formation of a small cyst are due to failure of the follicle to rupture. This failure to rupture may be caused by functional disturbance in the ovarian-pituitary endocrine cycle or it may be caused by mechanical difficulty due to deep situation or to thickening of the tunica albuginea or to peritoneal adhesions covering the surface of the ovary.

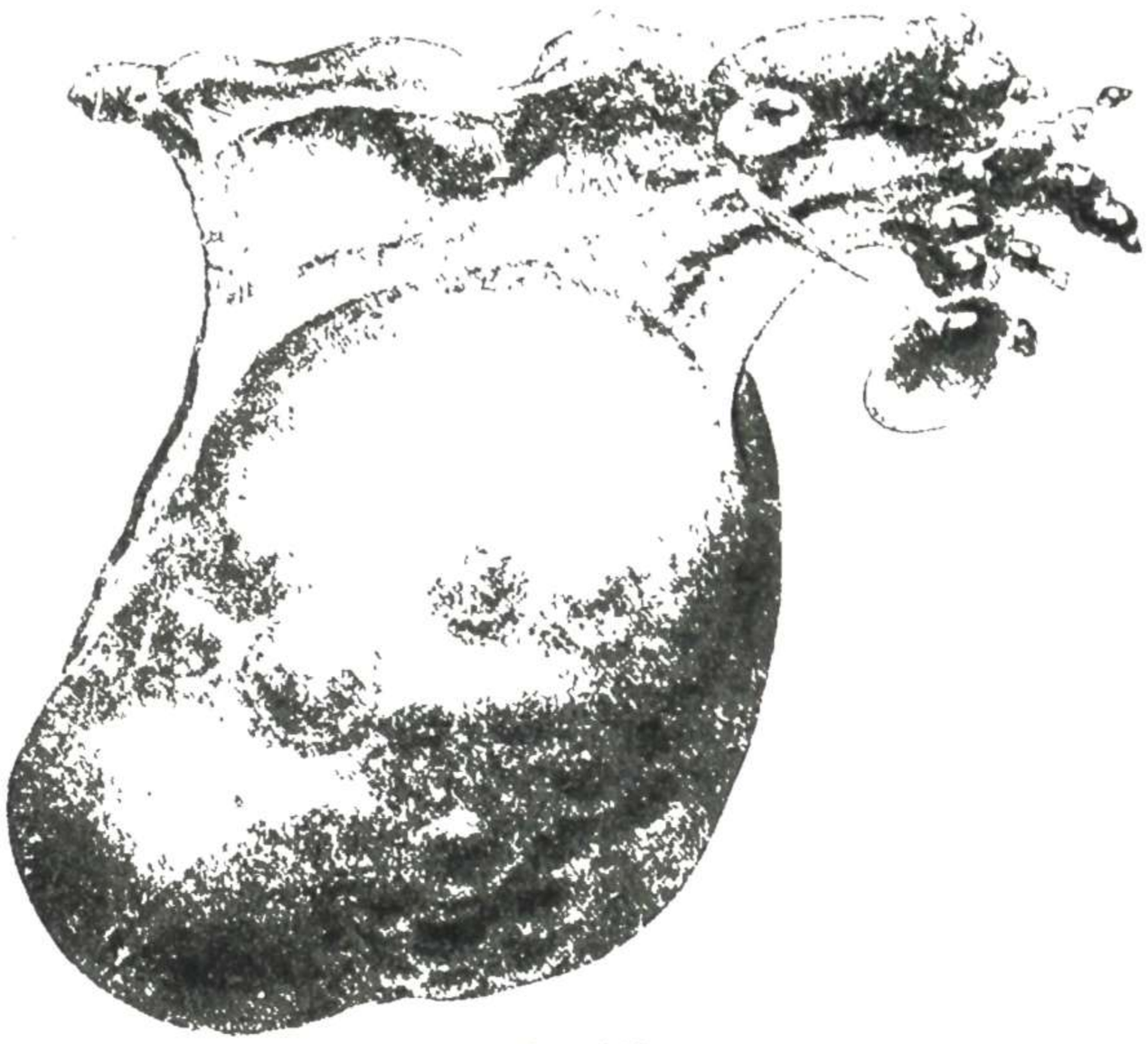


Fig. 945.

Fig. 946.

Fig. 945.—Follicular cysts of the ovary. (Kelly—*Operative Gynecology.*)

Fig. 946.—Polycystic ovary. Note that a major portion of the ovary is occupied by these follicle cysts. Gyn. Lab.

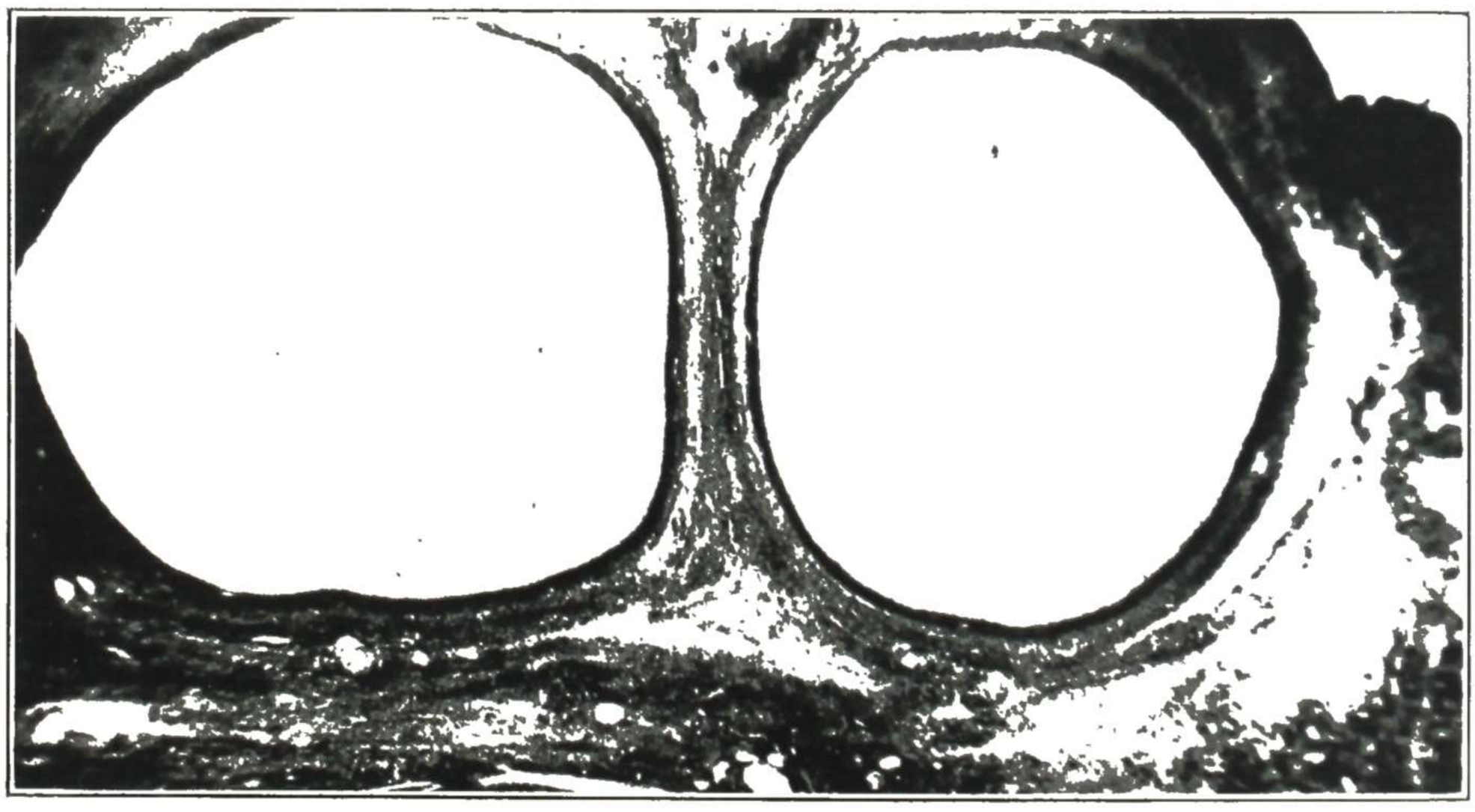


Fig. 947.—Polycystic ovary. Microscopic view of the upper cysts in Fig. 946. Note the lining of compressed granulosa cells. Gyn. Lab.

These cysts vary in size, the average size being that of a pea. When superficially placed the little cyst protrudes above the surface of the ovary as a translucent vesicle. In marked cases the ovary may be studded with these cysts. On cut surface they are usually seen in the cortex but occasionally are situated deeper. Sometimes there is a single large cyst.

The cyst wall consists of an outer fibrous layer containing blood vessels running parallel to the lining. In the younger cysts the lining may still show the granulosa-cell characteristics. In the larger older cysts the lining is usually missing; if present, it generally consists of a single layer of low cylindrical or cuboidal epithelial cells with central dark staining nuclei. Figs. 945 to 951 show the characteristics of follicular cysts.

Fig. 948.

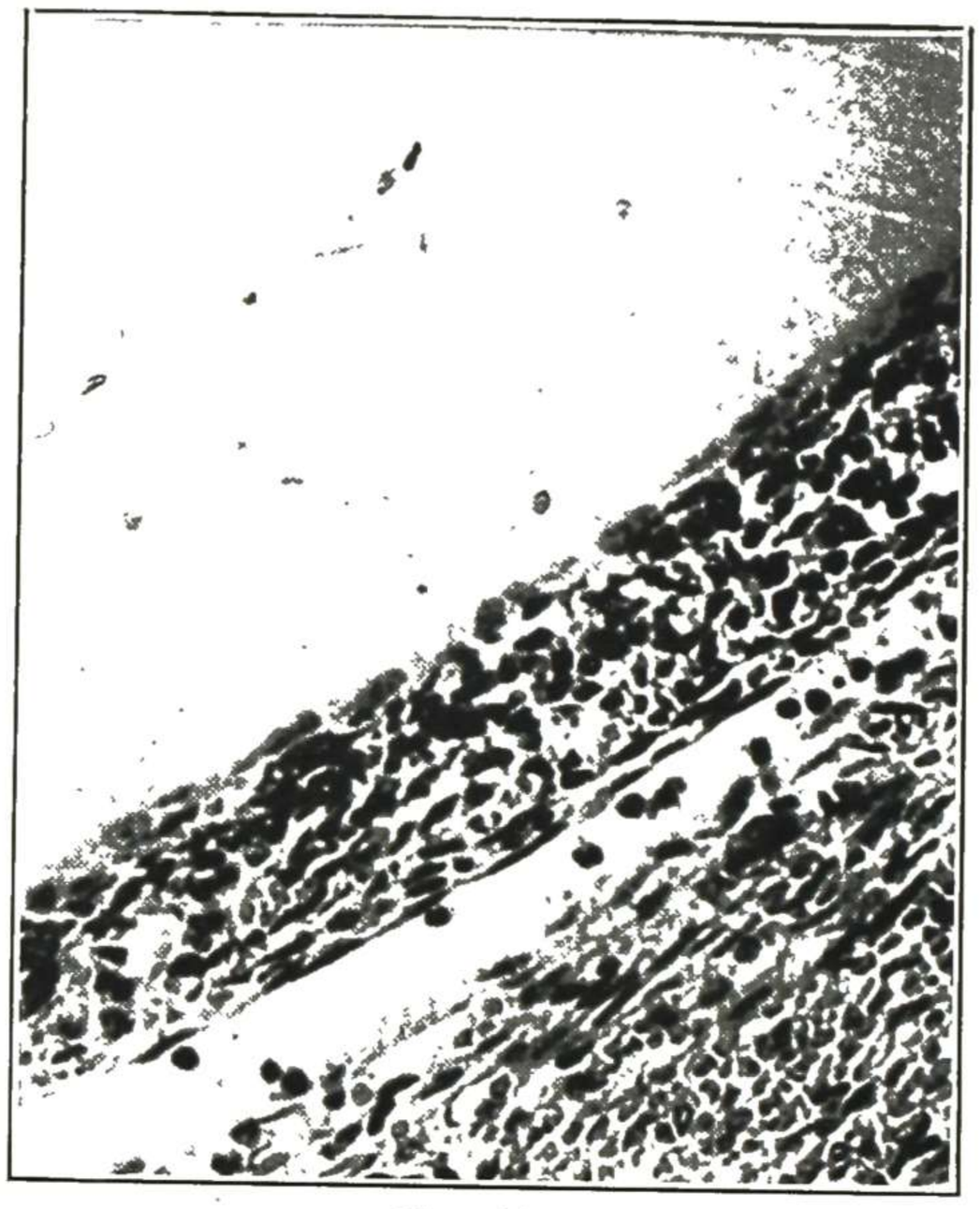


Fig. 949.

Fig. 948.—Lining of follicular cyst shown in Fig. 947. The membrana granulosa may still be recognized though it is markedly compressed by the increased intracystic pressure. Gyn. Lab.

Fig. 949.—Lining of a larger follicular cyst. The membrana granulosa is thinned out due to pressure, and there is evidence of beginning disintegration. Gyn. Lab.

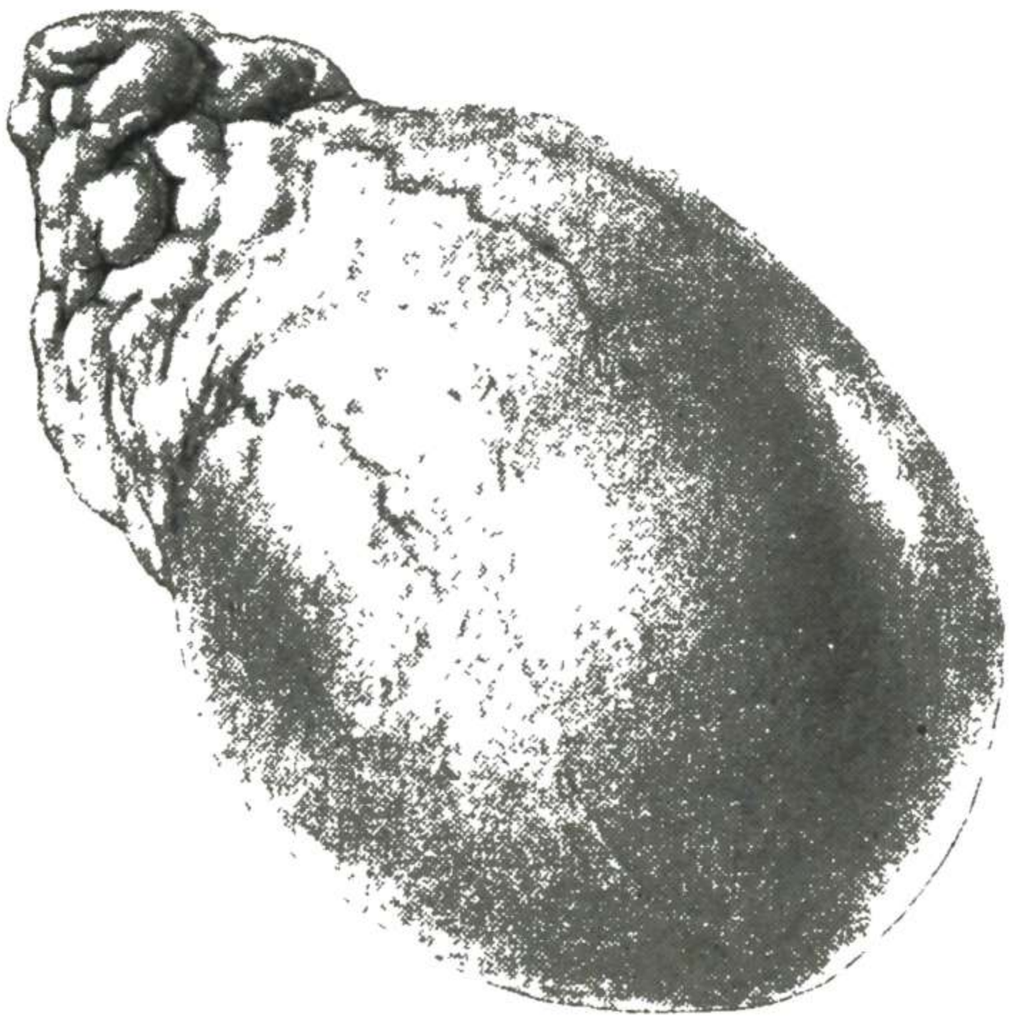


Fig. 950.

Fig. 951.

Fig. 950.—Single cyst leaving the larger portion of the ovary (left upper part in illustration) intact. Gyn. Lab.

Fig. 951.—In contrast to specimen shown in Fig. 950, this cyst formation involves the entire ovary, which had to be removed together with the tube. Gyn. Lab.

Symptoms and Treatment.—These follicular cysts are small and rarely produce serious symptoms. While a single cyst often involves only a part of the ovarian substance (Fig. 950), in other instances it may be found to affect the entire organ (Fig. 951). They are frequently found in chronic oophoritis, and an ovary may contain fifteen or twenty of them and still not be more than twice its normal size (Fig. 945).

Such a condition is designated by the term "hydrops folliculi" and also by the term "cystic ovary." This condition is not an indication for operation, unless there are serious complications or unusually severe symptoms. A marked cyst discovered in the course of an operation for some other pelvic lesion is ordinarily resected, with the minimum sacrifice of normal tissue.

The important point in treatment is to overcome the endocrine disturbance which interferes with ovulation and starts cyst formation.

In certain cases the failure to ovulate and the resulting cyst formation is due to old exudate or adhesions about the ovary or to thickening of the capsule.

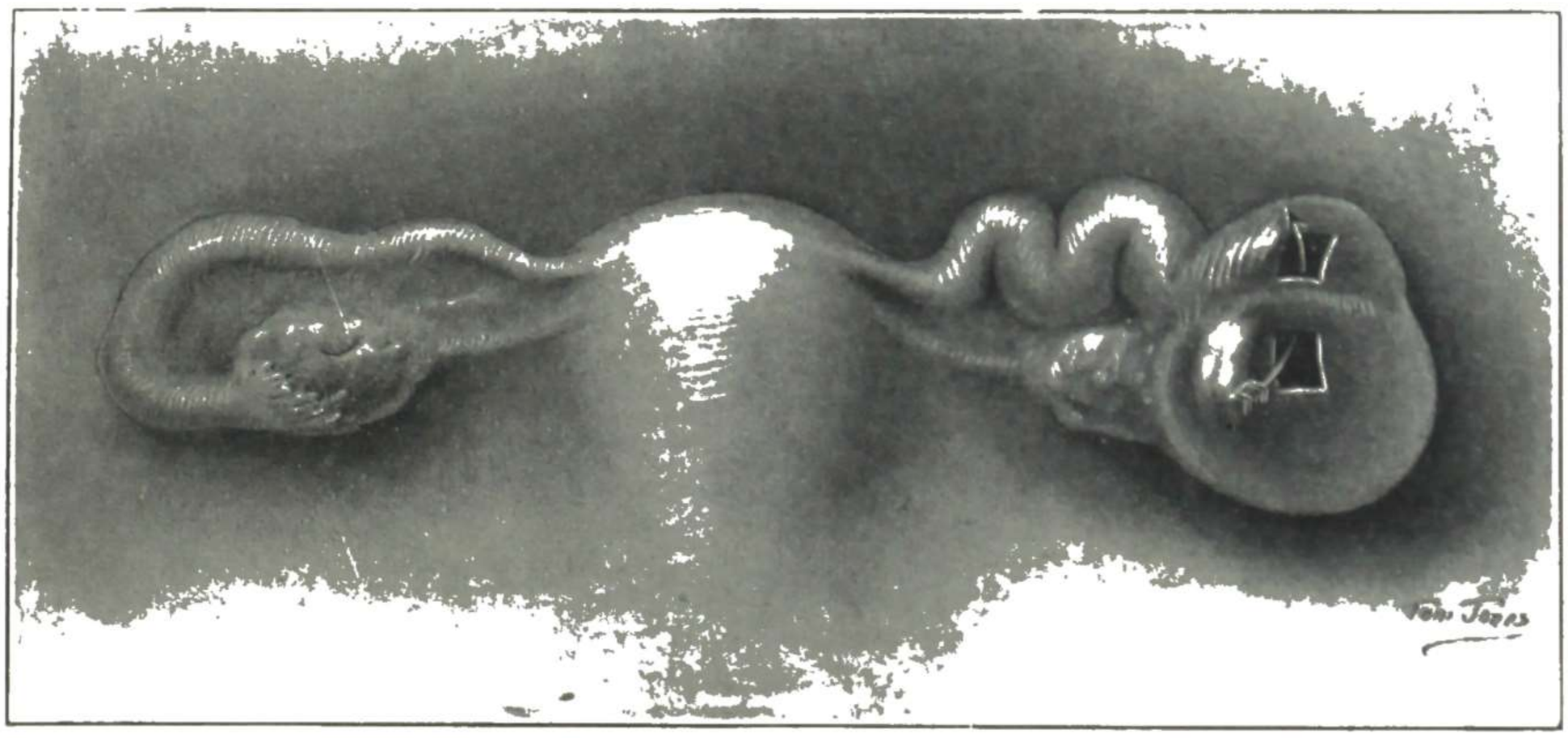


Fig. 952.—A tuboovarian cyst. The arrow, passing in one window and out of the other, indicates the communication between the ovarian and the tubal portion of the cystic mass.

This is an important factor in some cases of sterility, and when other factors are eliminated, operation to remove the thickened capsule is to be considered. The diagnosis and treatment of sterility cases of this type are taken up in Chapter XV.

Tuboovarian Cyst.—A simple cyst of the ovary may break into an adherent tube, or a dilated tube containing fluid (hydrosalpinx) may become adherent to an ovary and break into it. In either case the wall of the resulting cavity is formed by both the tube and ovary, and the resulting cyst is designated "tuboovarian" (Fig. 952). These cysts are usually small.

Corpus Luteum Cysts

Corpus luteum cysts are, as their name indicates, derived from corpora lutea, which, instead of undergoing the regular process of absorption and cicatrization, undergo a cystic change. Microscopic examination of the wall of such a cyst will show the lutein cells, characteristic of the corpus luteum. Corpus luteum cysts are usually not larger than an egg, but cases have been

reported in which the cyst was the size of a child's head. In cut section the striking thing is the lining membrane which is brownish yellow or orange yellow, depending upon the amount of lutein and blood pigment present. The lining separates easily from the connective tissue wall. Figs. 953 and 954 show lutein cells in the wall of a corpus luteum cyst. In the older cysts there is sometimes only a single layer remaining. The cells are usually covered over on the cavity side by a thin layer of connective tissue, but this may be absent. Occasionally the lutein cells have disappeared, and in these cysts there is usually marked hyaline degeneration of the wall. The central cavity is sometimes filled with an old blood clot.

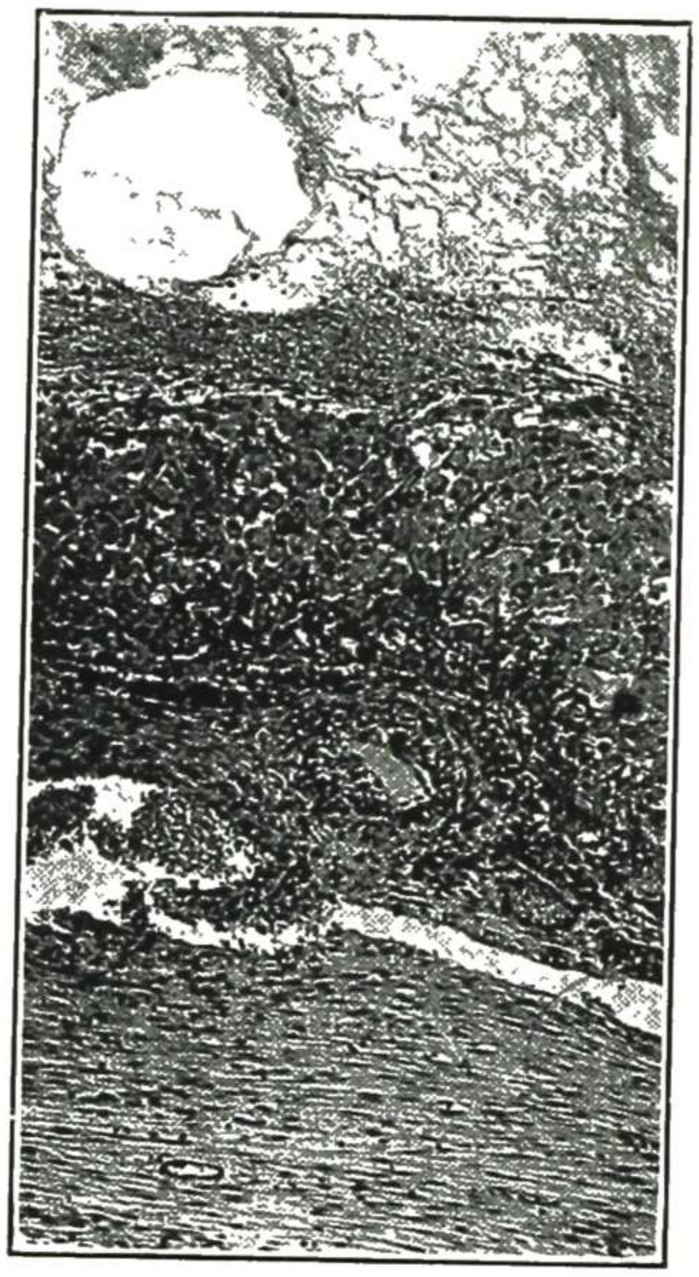


Fig. 953.

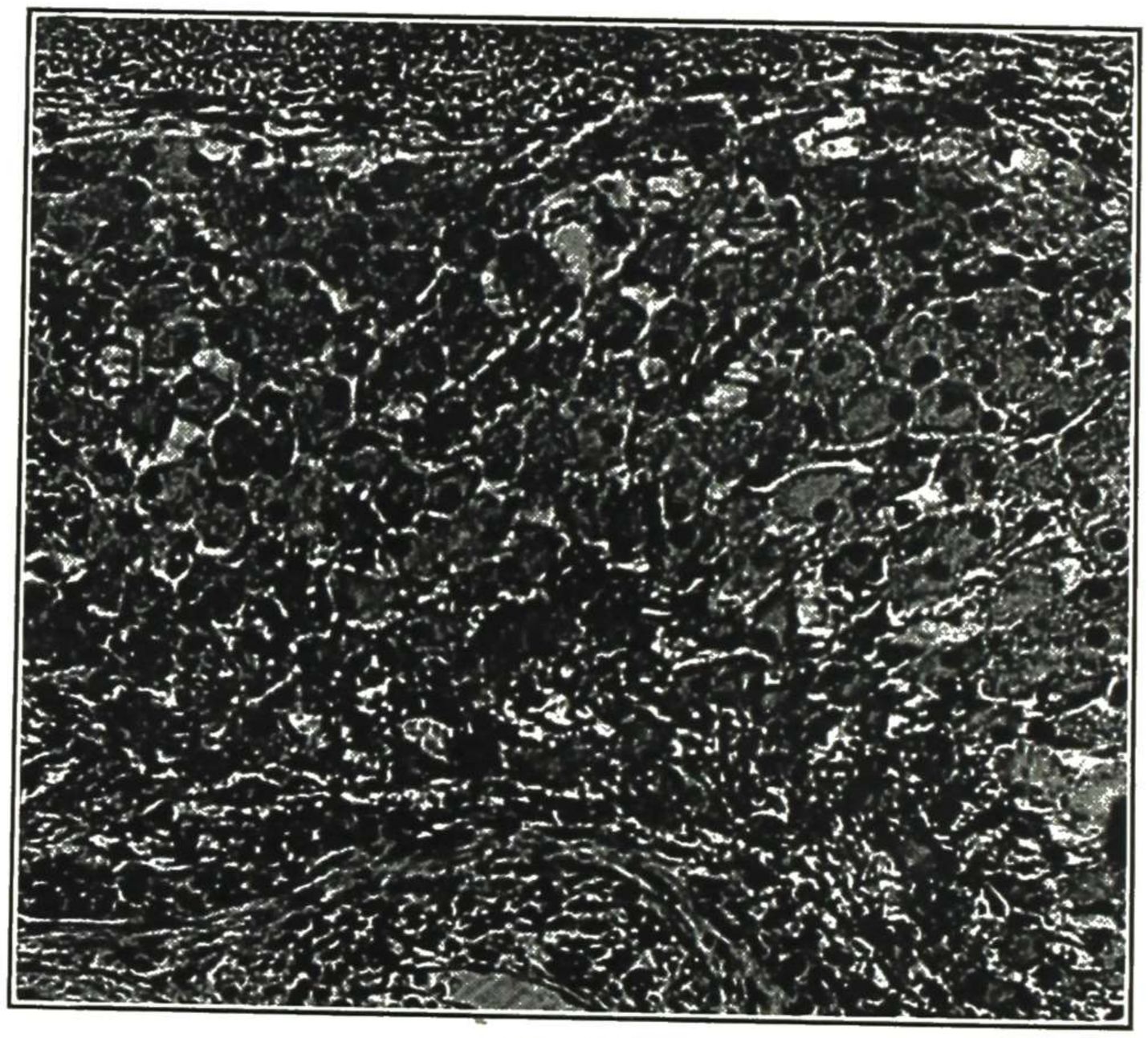


Fig. 954.

Fig. 953.—Section through wall of another corpus luteum cyst. Low power showing the cavity above, the three layers of the wall, and part of the surrounding ovarian stroma.

Fig. 954.—High power of Fig. 953, showing the lutein layer and the underlying theca interna and externa. Gyn. Lab.

Corpus luteum cysts, like follicular cysts, require removal only when giving trouble. It is possible that the luteum cells may multiply instead of degenerating, thus forming a neoplasm with exaggerated progesterone effect. Wheelon and Wilson reported a case of corpus luteum cystoma to which they attributed the patient's amenorrhea. But Novak questions the likelihood of the evanescent lutein cells alone forming a tumor. In discussing "luteoma" in connection with granulosa-cell tumors, he says that in most cases the so-called "luteoma" is really an adrenal adenoma of the ovary, the tendency of which is masculinizing rather than feminizing when it shows any definite endocrine effect.

EMBRYOLOGIC RESTS

In tumors developed from embryologic rests, three types may be distinguished, according to the character of the cells of the remnant from which the growth developed. Certain tumors develop from undifferentiated sex cells.

Some of these growths as they develop carry with them a certain amount of endocrine sex function—that is, they pour sex hormones into the system, in an erratic way and often with bizarre and striking results. The granulosa-cell tumor and the arrhenoblastoma belong to this class. Other tumors developed from undifferentiated sex cells seem devoid of any special endocrine influence, as in the dysgerminoma and the Brenner tumor.

Other tumors arise from undifferentiated somatic cells, and from the erratic cell development as the tumor grows there appear samples of various tissues, as in the dermoids and the teratomas. To the teratomas containing a considerable amount of thyroid tissue are applied the terms "strumous" or "ovarian struma."

A third class of tumors arise from remnants of developed embryonic structures, which formerly functioned but which largely disappear in the maturing of body growth. This class includes the parovarian cysts.

FROM UNDIFFERENTIATED SEX CELLS WITH ENDOCRINE INFLUENCE

In the past few years interest has been aroused in the study of a group of tumors arising from early oophorogenic structures in the sex gland area. There are two general groups: (1) those which function and produce hormones and in this way determine certain secondary sexual changes, for example, granulosa-cell tumors and arrhenoblastomas, and (2) those which exert no endocrine effect, such as Brenner tumors and dysgerminomas. We are indebted to Robert Meyer of Berlin for his clear-cut classification of these confusing pathologic pictures. The endocrine group will be considered here, and the second group under the next heading.

Granulosa-Cell Tumors

These tumors, according to Meyer, arise from dormant undifferentiated embryonic tissue situated in the medullary portion of the ovary. Such tissue can be found in the fetus and in infants and even into adult life, and occasionally in the ovaries of women far past the menopause. These cells persist without differentiation into late life. Under conditions still unknown they may at any age produce granulosa-cell tumors. These in turn produce estrin and can cause development of secondary sex characteristics in young children or enlargement of the uterus and uterine bleeding in elderly women. They have never been known to develop from mature follicles nor do they ever contain ova. Furthermore, they are found in women from sixty to seventy years of age, in whom the ovary no longer contains follicles.

Of course, much is still unknown about the granulosa cells of the graafian follicle and what they can do in the various stages of growth and retrocession. The studies by Gardiner on the normal and pathological cell activities in the follicles indicate that a variety of tumors may arise from the lining cells.

Structural Pathology.—Meyer gives the following three histologic classifications according to the structure.

1. It may occur as a folliculoma, often associated with small cysts. The cells are arranged about a central liquefied area so that they resemble somewhat small primordial

follicles (Figs. 955 and 956). The similarity to Call-Exner bodies found in rabbit ovaries is very striking. In the first few cases these were thought to be abnormal follicles, because the central cavity superficially resembled an ovum. Meyer stressed the fact that the cells around the small cystic cavities are arranged in a curious antipodal fashion, that is, the nuclei of the inner layer are placed close to the lumen while those of the outer layer are away from it, toward the periphery. Between these two layers there may be several layers of well-preserved cells, or only a thin zone of degenerated cytoplasm may remain. This so-called follicular type may contain small or large cavities.

2. The second and most common type is the cylindroid type, in which there are solid cords of cells or cylinders. Hyaline degeneration of the connective tissue stroma is commonly present. Many bizarre patterns are found, which have been compared by Novak to elaborate scroll work or rippled water or the pattern of moiré silk.

3. Some cases show a diffuse structure which cannot be distinguished from sarcoma. Figs. 957 and 958 show this type of tumor. Speaking of granulosa-cell tumors in general, Novak states that in some cases there seems to be a lutein-like transformation of some of the cells. Where this is found, the endometrial pattern in such cases indicates that there is a secretion of the corpus luteum hormone as well as of the follicular hormone.

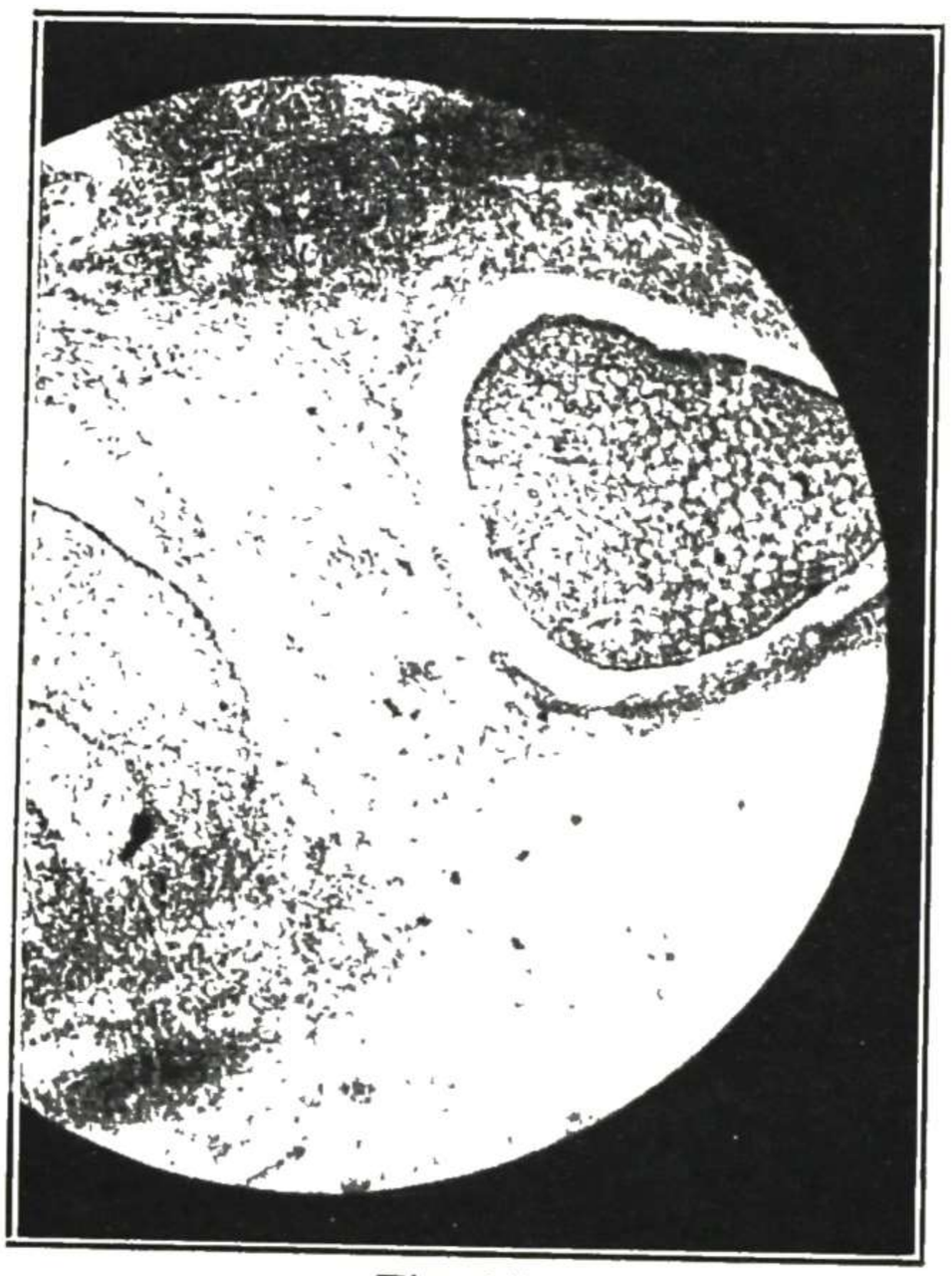


Fig. 955.

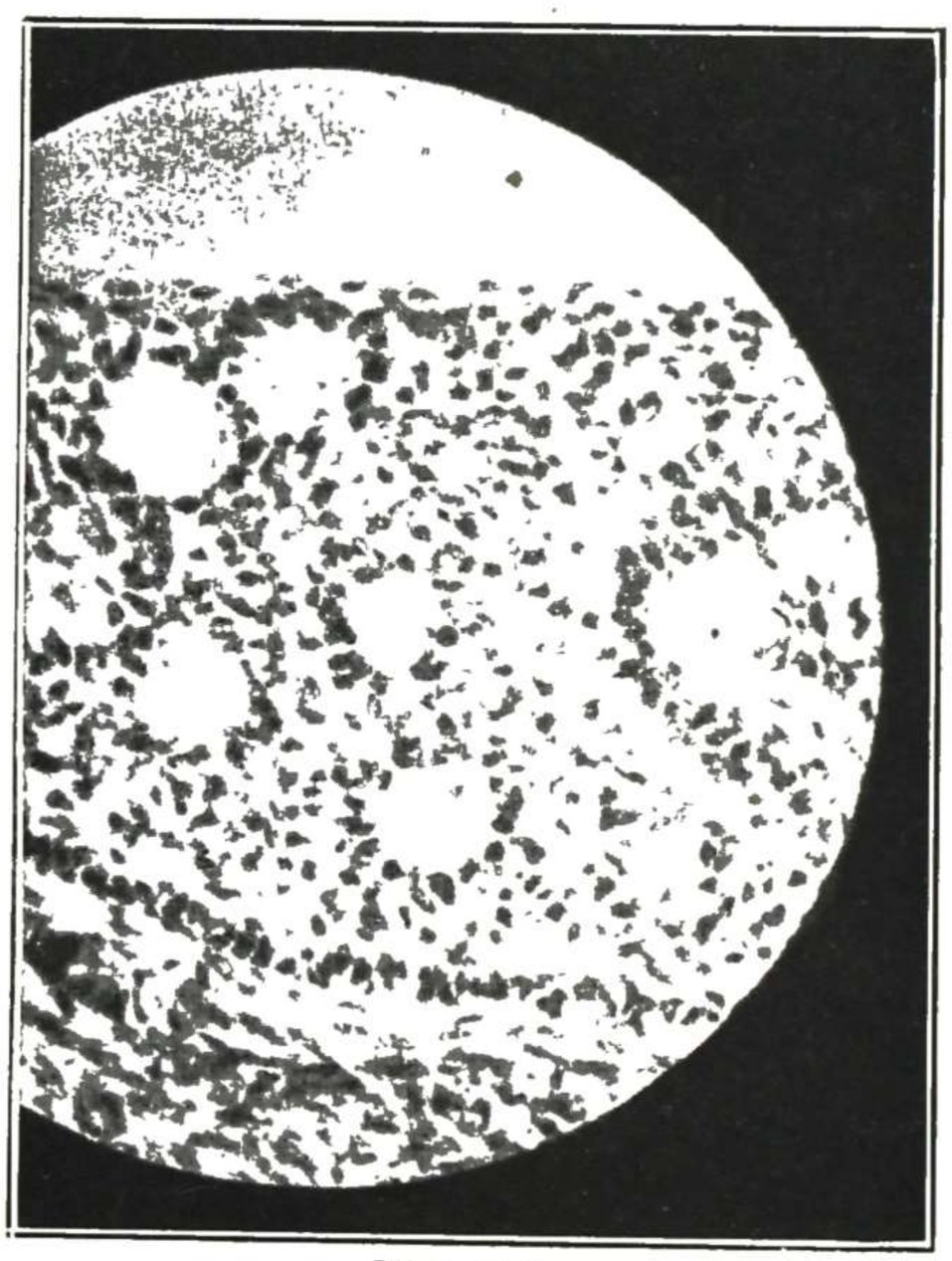


Fig. 956.

Figs. 955 and 956.—Small granulosa cell tumors in the otherwise normal ovary of a woman, aged forty. Fig. 956, Higher magnification of a special area in Fig. 955, showing the resemblance to Call-Exner bodies. (Meyer—*Am. J. Obst. & Gynec.*)

The three types are not infrequently found in different parts of the same tumor, merging into one another and giving the impression of having a common origin. In the recent work of Fischel strong evidence is produced in favor of this idea. Contrary to the generally accepted idea, that the follicular apparatus is the result of a downgrowth of the germinal epithelium covering the ovary into the mesenchyme beneath, Fischel believes that the granulosa cells are formed in situ from the ovarian mesenchyme, as are also the theca cells and stromal cells of the ovary. This theory of follicle development clarifies somewhat the confusing pictures seen in granulosa-cell tumors and seems to fit in much better than do the older theories.

In regard to the degree of malignancy this tumor is felt to be relatively benign, and Meyer emphasizes that it is only necessary in most cases to remove the involved ovary; the fact must not be overlooked, however, that from 5 to 10 per cent of the reported cases have run a malignant course, with recurrence and metastases and death.

These tumors are usually of a moderate size but may vary from very small tumors to huge growths filling the abdomen. On cut surface the small ones present a solid granular surface. In the larger ones cystic areas are seen.

Physiologic Pathology.—The usual picture of the endometrium in these cases is endometrial hyperplasia though this is not always present. In cases showing luteinization of the granulosa cells a premenstrual endometrium may be found. In children there is usually a premature development of the secondary sex characteristics and menstruation. In adult life there may be prolonged bleeding interspersed with periods of amenorrhea due to the inhibition of the pituitary by an excess of estrin in the blood. When such a tumor develops after the menopause, the atrophic uterus may return to normal size and begin to exhibit intermittent bleeding.

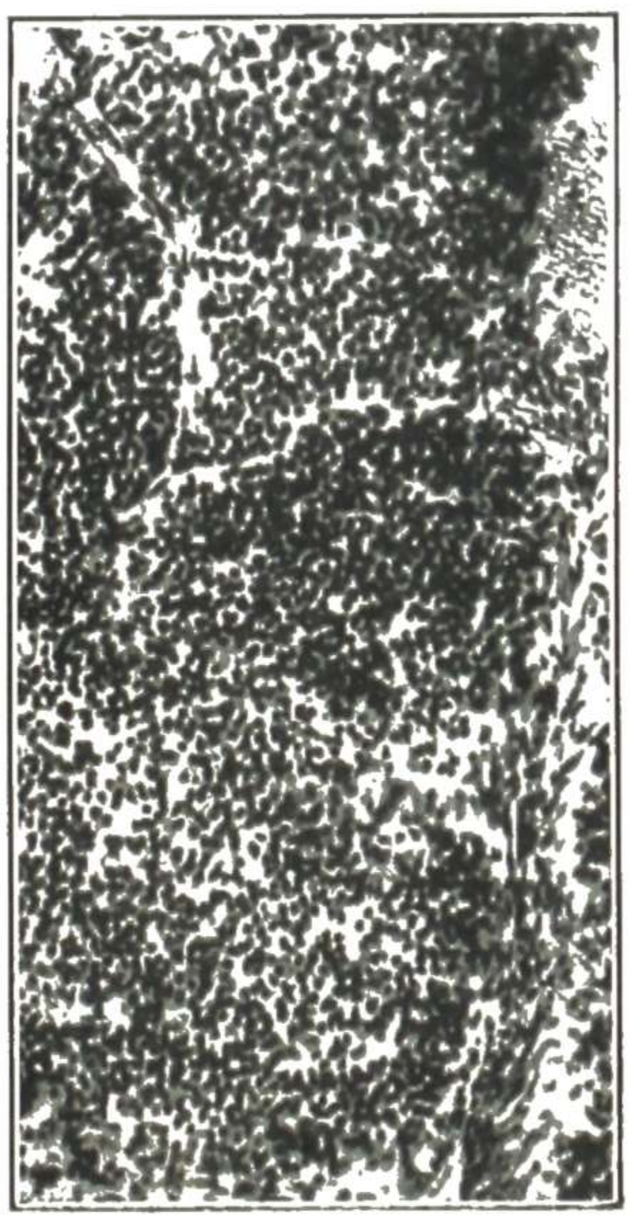


Fig. 957.

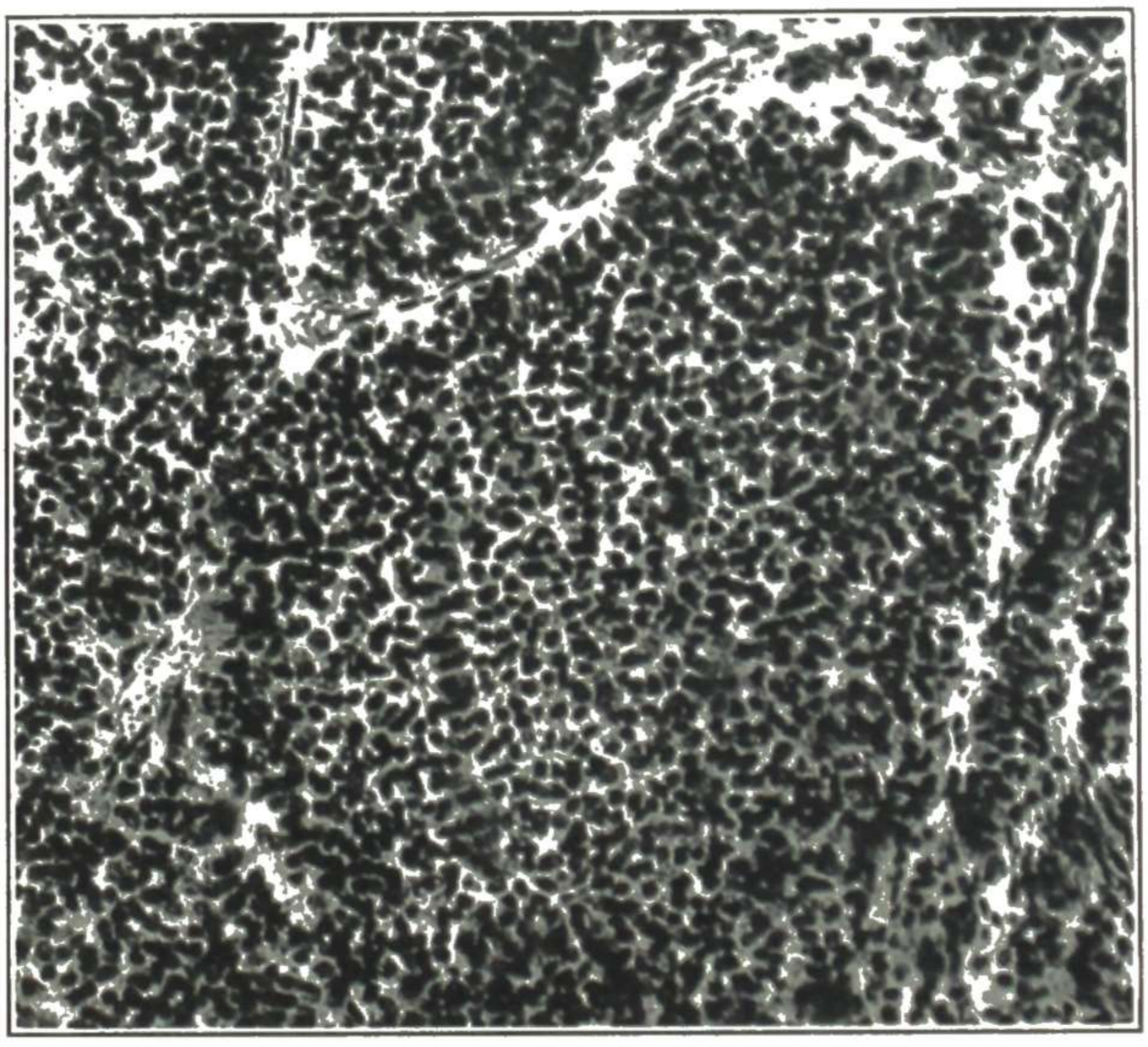


Fig. 958.

Figs. 957 and 958.—Granulosa cell tumor, Class III. Fig. 957, Shows a diffuse structure resembling sarcoma. Fig. 958, High power of Fig. 957, showing the character of the cells. Gyn. Lab.

Patients with these tumors have more estrin in the urine than do normal patients. The Aschheim-Zondek Type I reaction for prolan A is present in many of these cases and occasionally the Type II reaction is obtained when luteinization is present in the tumor. Extracts made from these tumors and injected into castrate mice cause estrus.

What stimulation causes these undifferentiated sex cells to grow and function is not known. It is probable that the stimulus is endocrine in character. The endocrine influence of the tumors themselves is evident from their cellular structure and from the resulting clinical manifestations. The islands of embryonic sex cells may at any age begin to grow and function, causing symptoms of excessive ovarian activity. The resulting clinical picture varies according to the age of the patient when the tumor cells begin to function.

In children, the excess estrin secreted by these tumors causes precocious puberty, the child maturing sexually at any early age. Menstruation may

appear at two or three years of age, with secondary sex characteristics, such as enlargement of the breasts and appearance of pubic hair. The mental age and activities of the child are not in advance of her years.

Certain cases of precocity reported in the older literature with pictures of patients can now be classified as cases of granulosa-cell tumor, and from these we can learn the life history of such individuals. Lenz in 1913 reported a series of 130 cases of precocious menstruation. In this series were a number of cases in which the flow occurred at birth or within a few days thereafter, which of course we know now may be due to the withdrawal of the maternal estrin at birth. He shows other cases, however, with the photographs proving early maturity, which leave little doubt as to the presence of a granulosa-cell tumor.

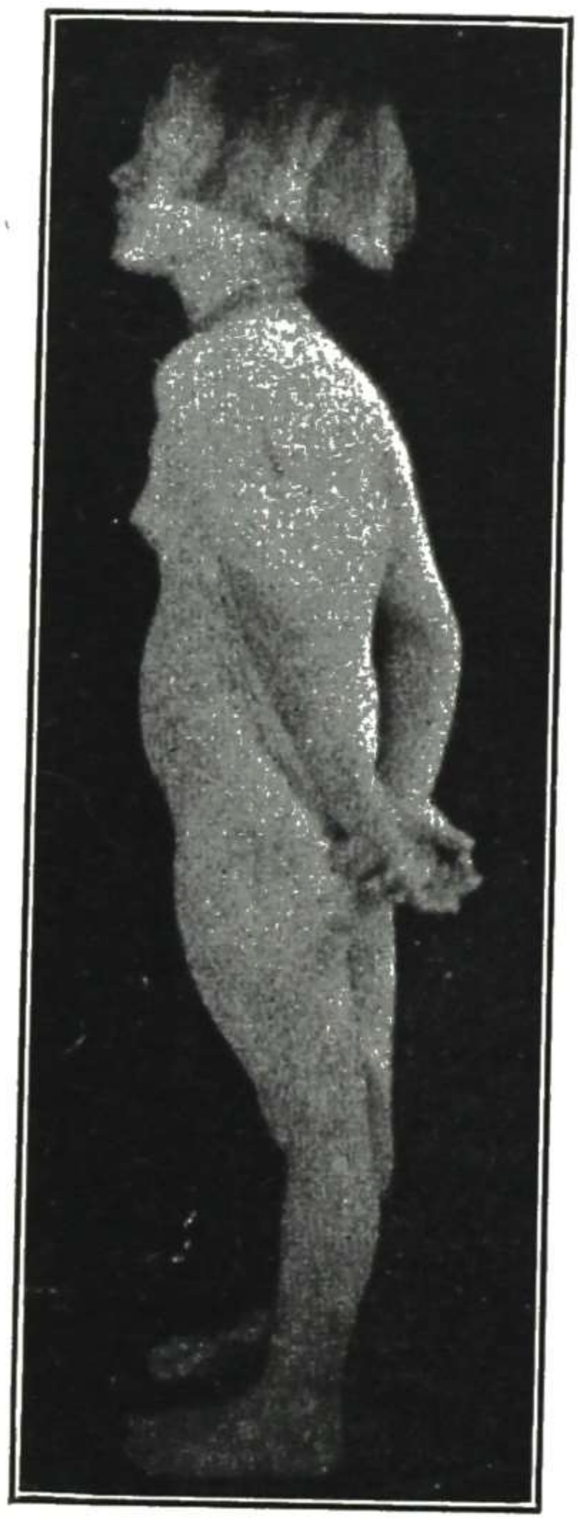


Fig. 959.

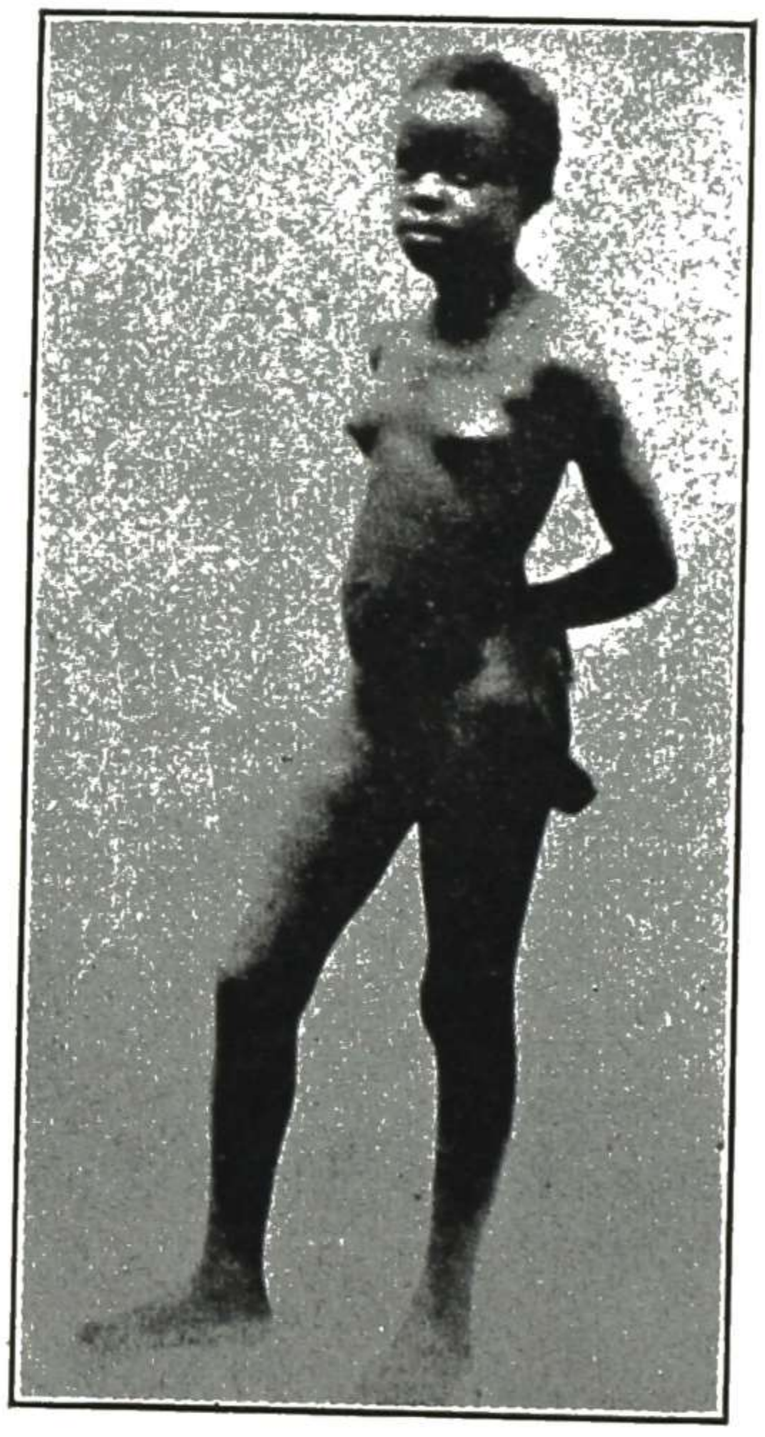


Fig. 960.

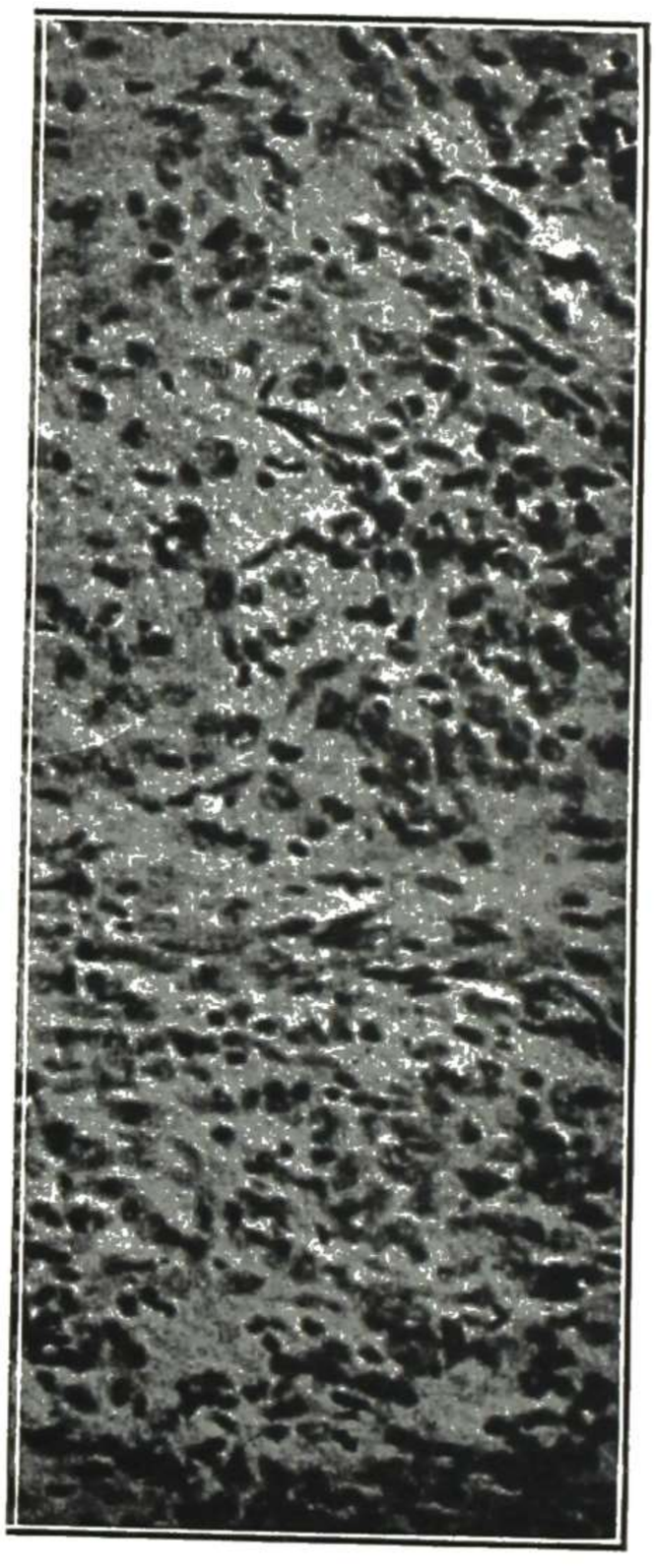


Fig. 961.

Fig. 959.—Patient, aged about four years, with a granulosa-cell tumor. Lateral view of patient at age of three years and eleven months. Menstruation had begun at three years and seven months. Note the hypertrophy of the breasts. (Novak—*Am. J. Obst. and Gynec.*)

Fig. 960.—Patient aged six years, with a granulosa cell tumor. General view, showing marked general development, the mammary overgrowth, and the broad hips. There is a heavy growth of axillary hair, though it is not seen in the picture. (Novak—*Am. J. Obst. and Gynec.*)

Fig. 961.—The microscopic structure of tumor shown in Fig. 960. (Novak—*Am. J. Obst. & Gynec.*)

That there is precocious development to real sexual maturity in these patients is hown by the fact of early pregnancy. Mandeslo reports the case of a girl who began to menstruate at three and gave birth to a son at six years of age. Lenz refers to the case, reported by von Haller in 1751, in which the patient began to menstruate at the age of two, gave birth to a child at nine, menstruated regularly until fifty-two years old, and lived to the age of seventy-five.

In the cases in which the tumor does not begin until adult life, when the person is already menstruating, the symptoms are frequently masked. There may be an increase in the amount of the menstrual flow, and nothing else to

indicate the tumor. Occasionally there are periods of amenorrhea interspersed with periods of menorrhagia. There have been so few of these cases diagnosed before operation that the number in which hormone tests have been run preoperatively is not sufficient to permit detailed deductions.

After the menopause, the tumor is likely to cause return of menstruation, or prolongation of menstruation if it becomes active before menstruation ceases entirely.

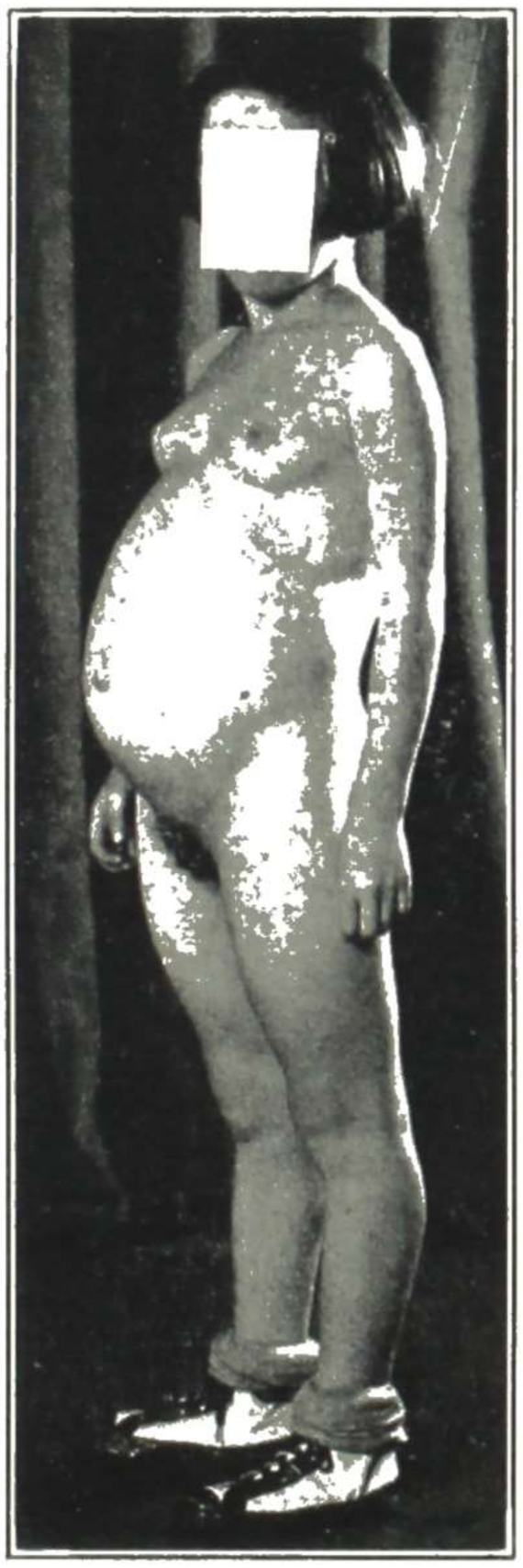


Fig. 962.

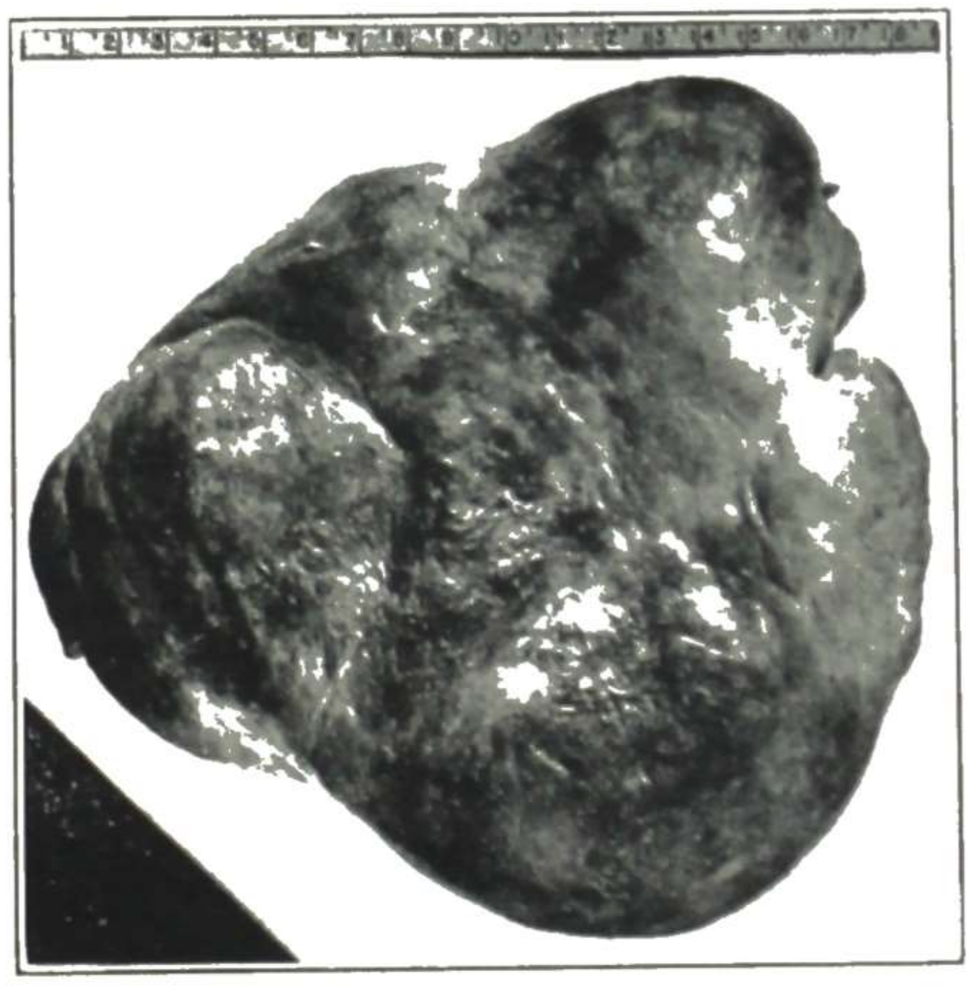


Fig. 963.

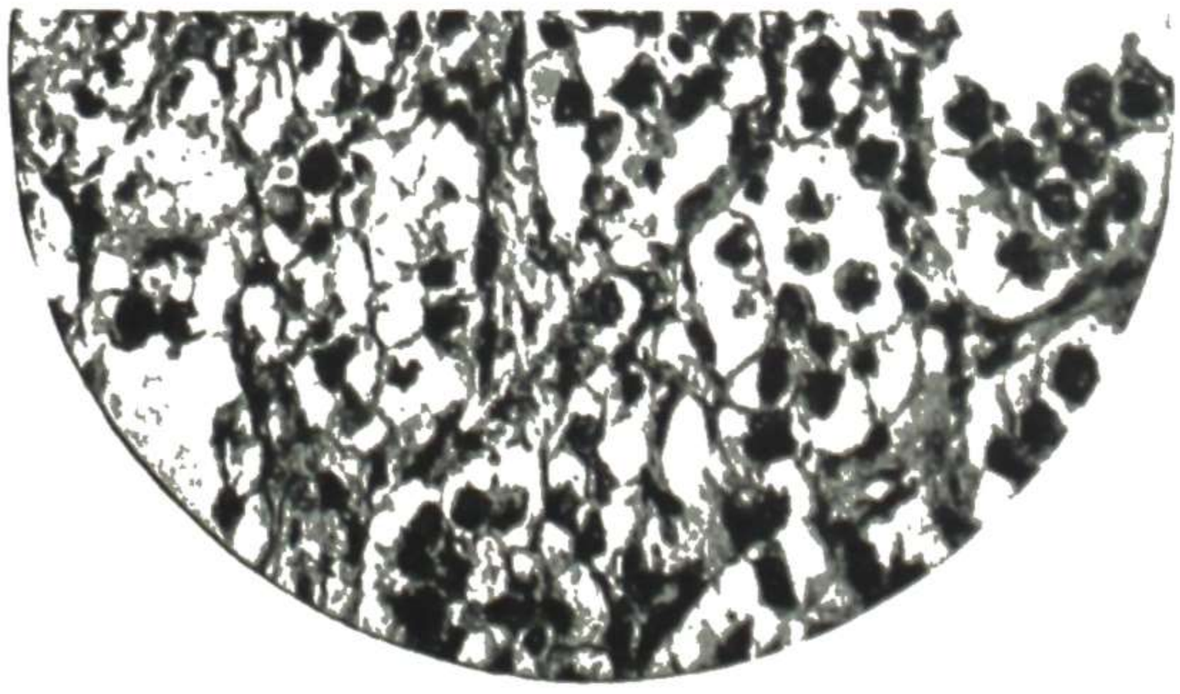


Fig. 964.

Fig. 962 to 964.—Patient, aged seven years, with a granulosa-cell tumor. Fig. 962, General view, showing the precocious sexual development, with marked growth of pubic hair and hypertrophy of breasts. In this case there is also marked enlargement of the abdomen from the tumor. Menstruation began four months before the patient was brought for treatment. Fig. 963, The large tumor removed in this case. It involved the left ovary. After the operation, the precocious menstruation ceased and the patient was well for eighteen months, when she came again with a similar growth of the right ovary, which seemed normal at the first operation. The Aschheim-Zondek test was positive before each operation, and was negative within two weeks after each operation. Fig. 964, The microscopic structure of the first tumor. The structure of the second tumor was the same. (Bland and Goldstein—*Surg., Gynec. and Obst.*)

The association of adenocarcinoma of the corpus uteri with granulosa-cell tumor has been more frequent than to be expected from mere coincidence, and this is an additional indication that excess estrin is a factor in the development of endometrial carcinoma.

Diagnosis.—In children, the diagnosis is made largely on the history and evidences of precocious sexual development. A child, aged four years, with such a tumor, from which menstruation began at three and a half years, is

shown in Fig. 959. Development of the breasts and pubic hair are marked in the child of six, pictured in Fig. 960. The microscopic type of this growth is indicated in Fig. 961.

Novak in a series of 33 cases of granulosa-cell tumors found the following age incidence: First decade 15 per cent, second decade 3 per cent, third decade 12 per cent, fourth decade 21 per cent, fifth decade (ages forty to fifty) 36 per

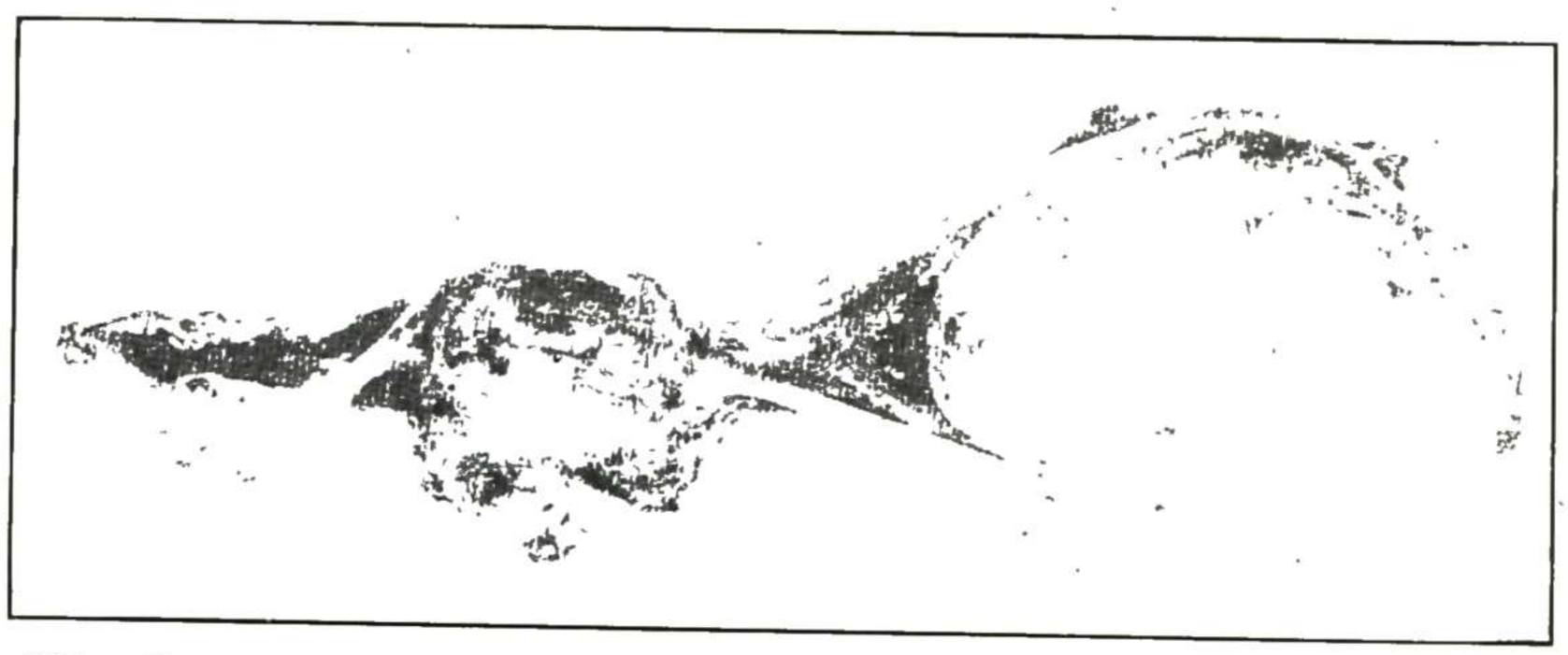
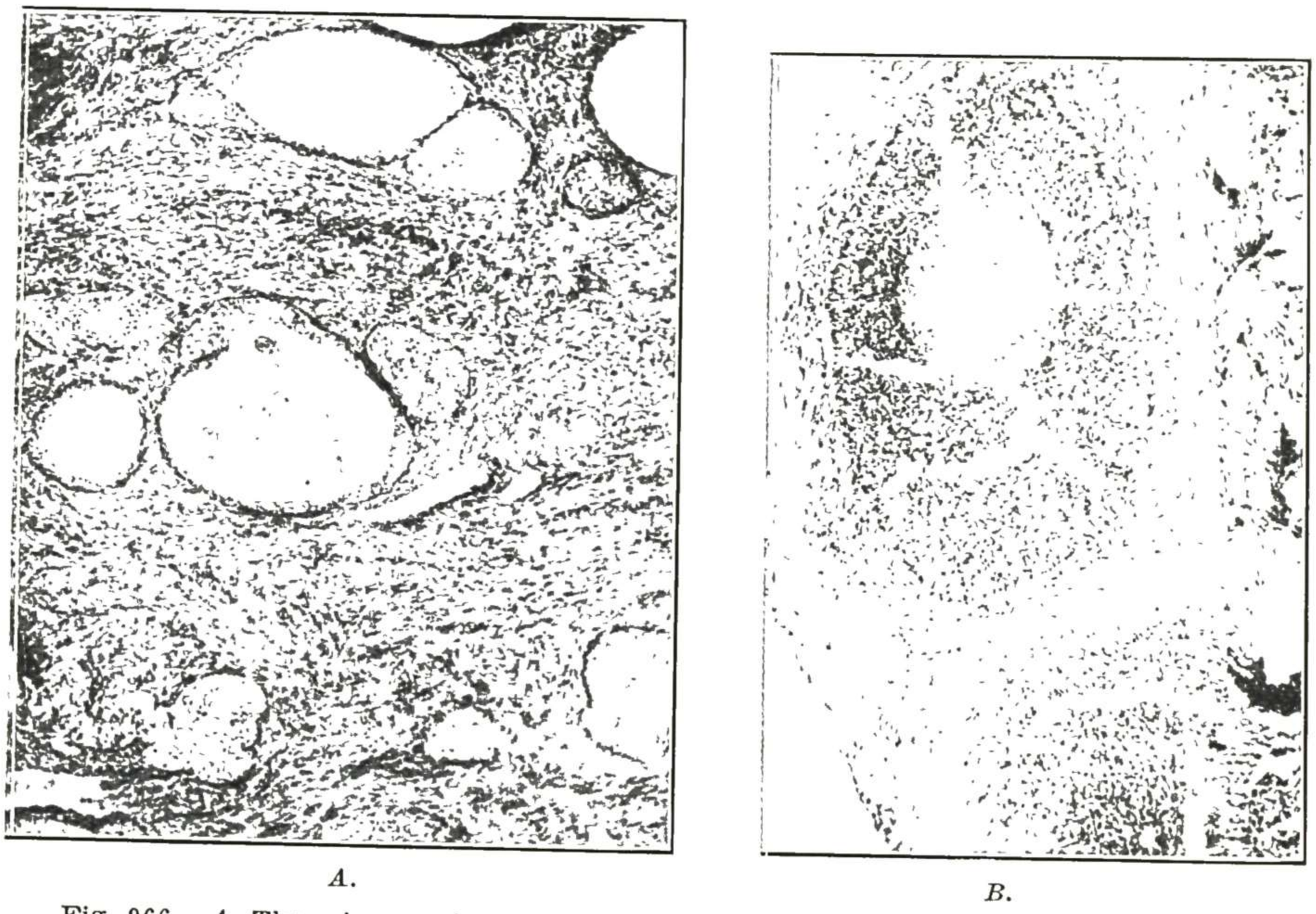


Fig. 965.—Granulosa-cell tumor from a patient, aged sixty-two years. Note well-encapsulated tumor large as a grapefruit, springing from the right ovary. The uterus was enlarged to the size of that of a woman during active menstrual life. (TeLinde—*Am. J. Obst. and Gynec.*)



A. *B.*

Fig. 966.—*A*, The microscopic structure of the tumor shown in Fig. 965. Note the follicle-like structure and the islands of solid tumor cells between which is an abundant fibrous stroma. *B*, Microscopic picture of another granulosa-cell tumor from a forty-three-year-old patient. It is composed of two portions, the one follicular, here shown, and a solid portion, part of which is shown in the lower edge of the photomicrograph. Note the lightly staining cells about the periphery of the follicle, resembling theca interna cells. (TeLinde—*Am. J. Obst. and Gynec.*)

cent, sixth decade 9 per cent, and seventh decade (ages sixty to seventy) 3 per cent. The tumors, while not common, are not nearly as rare as was formerly thought.

A girl, seven years of age, with abdominal prominence due to the large tumor and marked development of the breasts and pubic hair, is shown in

Fig. 962. The large tumor removed in this case is shown in Fig. 963, and the microscopic characteristics in Fig. 964. This patient had a similar tumor in the other ovary a year and a half later, and it was successfully removed. Along with the precocious sexual development there is precocious skeletal growth in these cases, so that the child is larger than normal.

Vaginal or rectal examination may or may not reveal an ovarian tumor. These growths are sometimes almost microscopic in size. In women during menstrual life, the diagnosis cannot be made with any degree of certainty, as there are so many other lesions that may give the same symptoms. It is to be considered especially in those patients with clinical symptoms of excess estrin associated with an ovarian mass. The hormone tests should be valuable in a suspected case, and should be run where facilities are available. An unusual elevation in the amount of estrin in the blood or urine in a series of tests, would add weight to the probability of a granulosa-cell tumor. Curettage in the premenstrual stage should show an endometrial hyperplasia in a high percentage of these cases, for it is known that excess of estrin tends to produce such hyperplasia. The diagnostic curettage should be made just before menstruation, because it is at that phase of the cycle that the curettings are most likely to be decisive as to the presence or absence of hyperplasia.

After the menopause, return of supposed menstruation is most likely to be due to endometrial carcinoma. If this be eliminated and there is an enlarged ovary, the lesion is probably a granulosa-cell tumor, though of course it might be a carcinoma of the ovary. A granulosa-cell tumor in the case of a patient, aged sixty-two years, is shown in Figs. 965 and 966.

Treatment.—The treatment consists in operative removal of the tumor.

In the case of a patient in the menopause or later, the question of malignancy must be settled. Though curettage for the abnormal bleeding may exclude malignancy in the uterus, it does not exclude ovarian malignancy. Consequently, if a definite ovarian mass can be felt, operative removal is advisable. In inoperable cases of advanced pelvic tumor, irradiation treatment for ovarian malignancy may be used.

Arrhenoblastoma

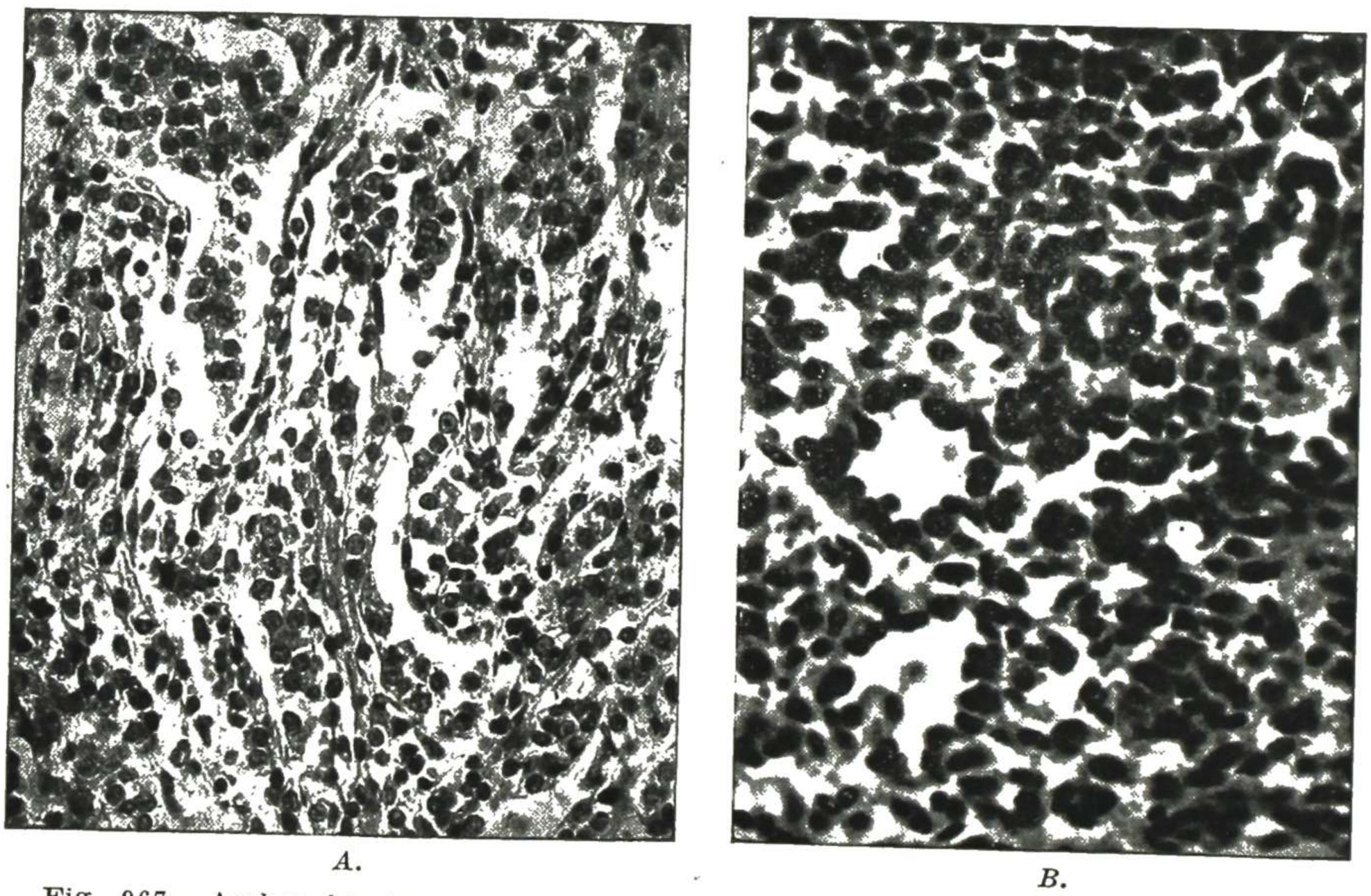
The second type of tumor producing endocrine effects is the arrhenoblastoma. According to Meyer, these tumors arise from undifferentiated germ cells which are not utilized during embryonic development but nevertheless retain their sexual potency. Under certain conditions they begin later in life to proliferate and then exert an influence toward maleness. Some types of this neoplasm exert no hormonal effects. The following quotations are from Meyer.

> In every embryonic sex gland undergoing development into an ovary, cells at the hilum remain for some time in an undeveloped state (blastema). This blastema under normal conditions later on produces the rete ovarii and some medullary cords or tubules which are homologues of the rete testis and tubuli efferentes of the testicle in the male. The future sexual character of the young embryo is not unalterably determined from the beginning, at least not in all instances, but does depend upon determining factors in the genes in the chromosomes. A priori every embryo and also every embryonic sex gland has the potential faculty of developing in either direction—male or female.

The rete ovarii and the medullary tubules, which do not exert any functional influence on the female sex gland, prove the normal bisexual anlage of the gonad. If these structures then persist in part in an undifferentiated state, and later for unknown reasons begin to proliferate, they may induce the male direction of development and thus change the sexual characteristics by creating bisexual stimulation like an ovariotestis.

In the hilum of the adult ovary, I found a small tubular adenoma in a very young stage attached to the rete, which proves this type of neoplasm may have its origin just in this location. Therefore, it is not the hormonal effect alone which justifies the name arrhenoblastoma but the fact that the resulting masculinization confirms the theory of the origin of this new growth.

Structural Pathology.—The tumors are usually unilateral and seldom get very large. On cut surface they have a soft consistency and are pale yellow in color. There are two distinct morphologic forms and a third which holds an intermediary position.



A. *B.*

Fig. 967.—Arrhenoblastoma, atypical group. *A*, Showing the irregular epithelial cord-like structures. *B*, Showing the sarcoma-like structure of these tumors. Some tendency to tubule formation is seen. (Taylor, Wolfermann, and Krock—*Surg., Gynec. and Obst.*)

1. The type described by Pick and named by him "adenoma testiculare ovarii" consists of an adenomatous structure made up of tubules resembling seminiferous tubules of the testis. It is not only similar to the adenoma developing in men but also contains some of the same structures. Masculinization occurs only occasionally in these cases.

2. The intermediary group shows sarcoma-like tendency but usually rudimentary cords or irregular tubules could be found (Fig. 967-*A*). Women with this type showed a little more tendency toward masculinization, amenorrhea, hirsutism, etc.

3. Atypical variety, resembling sarcoma with little to suggest its origin. Most of these patients showed marked masculinization. Fig. 967-*B* shows such a growth.

Physiologic Pathology.—In every woman there are rudimentary homologues of male structures. The one of importance in arrhenoblastomas is the rete ovarii which is the homologue of the male testis. Under certain unknown conditions this undifferentiated male tissue, near the medulla of the ovary, becomes active and produces a male endocrine influence which overrides the female influence, resulting in varying degrees of intersexuality.

In the first type there is very little tendency toward masculinization, in the second type there is a greater tendency that way, with amenorrhea and hirsutism or more marked changes if the cells are more nearly like Type III. In Type III, where the potential testicular tissue is extremely undifferentiated, the most marked masculinization occurs.

Diagnosis.—These tumors occur much less frequently than do the granulosa-cell tumors. There is no reported series large enough to estimate with any accuracy the age incidence.

Fig. 968.

Fig. 969.

Fig. 970.

Figs. 968-970.—Patient with an arrhenoblastoma of the ovary, showing the masculinity the tumor caused and its subsidence after removal of the growth. Fig. 968, Showing the development of hair on the face. Fig. 969, Showing the developing masculine type of pubic hair growing upward toward the navel, and the flatness of the breasts as compared with Fig. 970. Fig. 970, Six months after removal of the tumor. Note the return of the feminine type of breasts and hip-outline, and the lessening of the hypertrichosis on the face. (Taylor, Wolfermann and Krock—*Surg., Gynec. and Obst.*)

The patient usually becomes amenorrheic, hair appears on the face, and the pubic hair assumes a masculine appearance (extending upward in median line toward navel), the breasts become flattened, the voice deepens, and the clitoris enlarges. In long-standing cases the figure assumes a masculine character. The clinical features are shown in Figs. 968 to 972.

The diagnosis is made from the appearance of the patient, the history, and the finding of an ovarian tumor. In the differential diagnosis one must rule out basophilic adenoma of the anterior pituitary, adrenal cortex lesions, especially cortical hyperplasia, and pineal tumors.

In basophilic adenomas, the patients are usually very fat, and they have other symptoms referable to a pituitary lesion. Hirsutism is usually not a marked feature.

In adrenal disorders there is a marked hirsutism, and the breasts usually remain of normal size. A tumor may occasionally be felt in the kidney region, and there may be other adrenal symptoms.

Adrenal tissue may occur in the ovary and produce a tumor there. Such an ovarian tumor has much the same masculinizing influence as an arrhenoblastoma, so the differentiation has to be made by microscopic examination after removal of the growth.

In pineal tumors there is frequently calcification of the gland which can be seen in the x-ray. There is usually some evidence of increased intracranial pressure with an internal and external ophthalmoplegia and an impairment of the upward gaze. Secondary sex characteristics need not be changed.

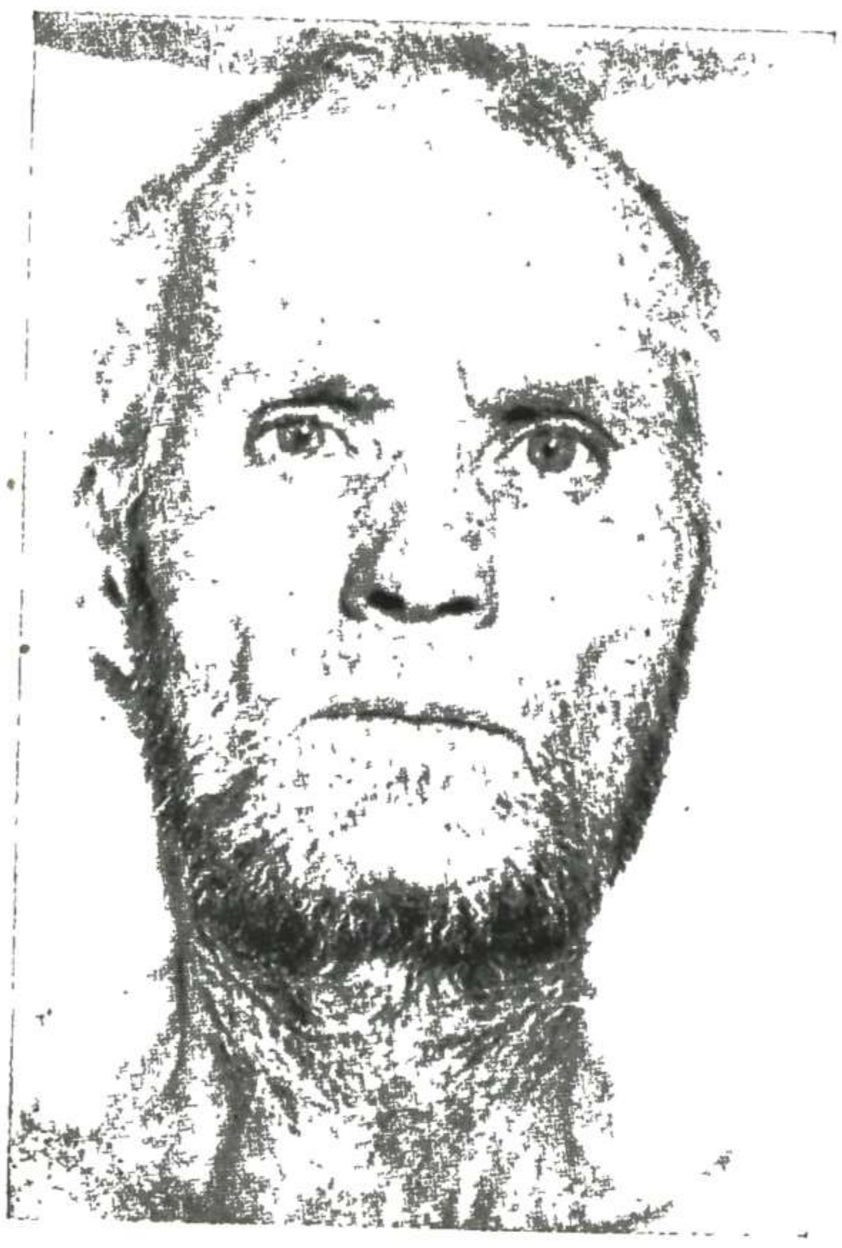


Fig. 971.

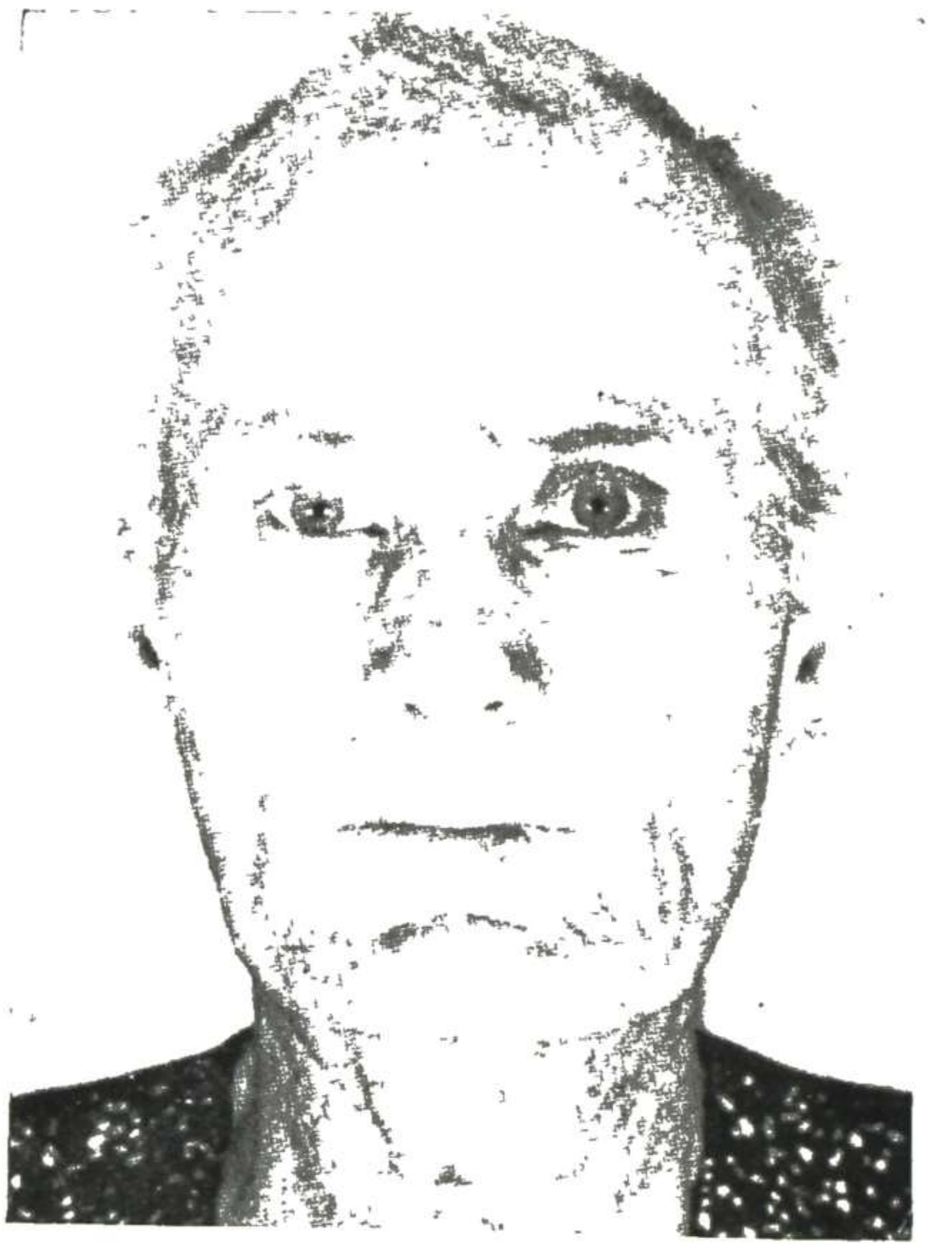


Fig. 972.

Fig. 971.—Facial hirsutism from an ovarian arrhenoblastoma in a patient age sixty-one years.

Fig. 972.—Three months after removal of the arrhenoblastoma, showing disappearance of the abnormal hirsutism. (Maxwell—*Western J. Surg.*)

The treatment for an arrhenoblastoma is removal. This causes a complete reversal to the feminine type. The abnormal hair drops out, the menses reappear, and the breasts assume the normal fullness. Figs. 968 to 970, show such a patient in the childbearing age, before and after operation, and Figs. 971 and 972 show one in the post-climacteric age.

Adrenal Ovarian Tumor

Novak, in his article on masculinizing tumors of the ovary, calls attention to the occasional occurrence of adrenal adenoma in the ovary and in the broad ligament. The endocrine effect, when present, is toward masculinization and hence the adrenal tumor may be mistaken for an arrhenoblastoma till removed and sectioned.

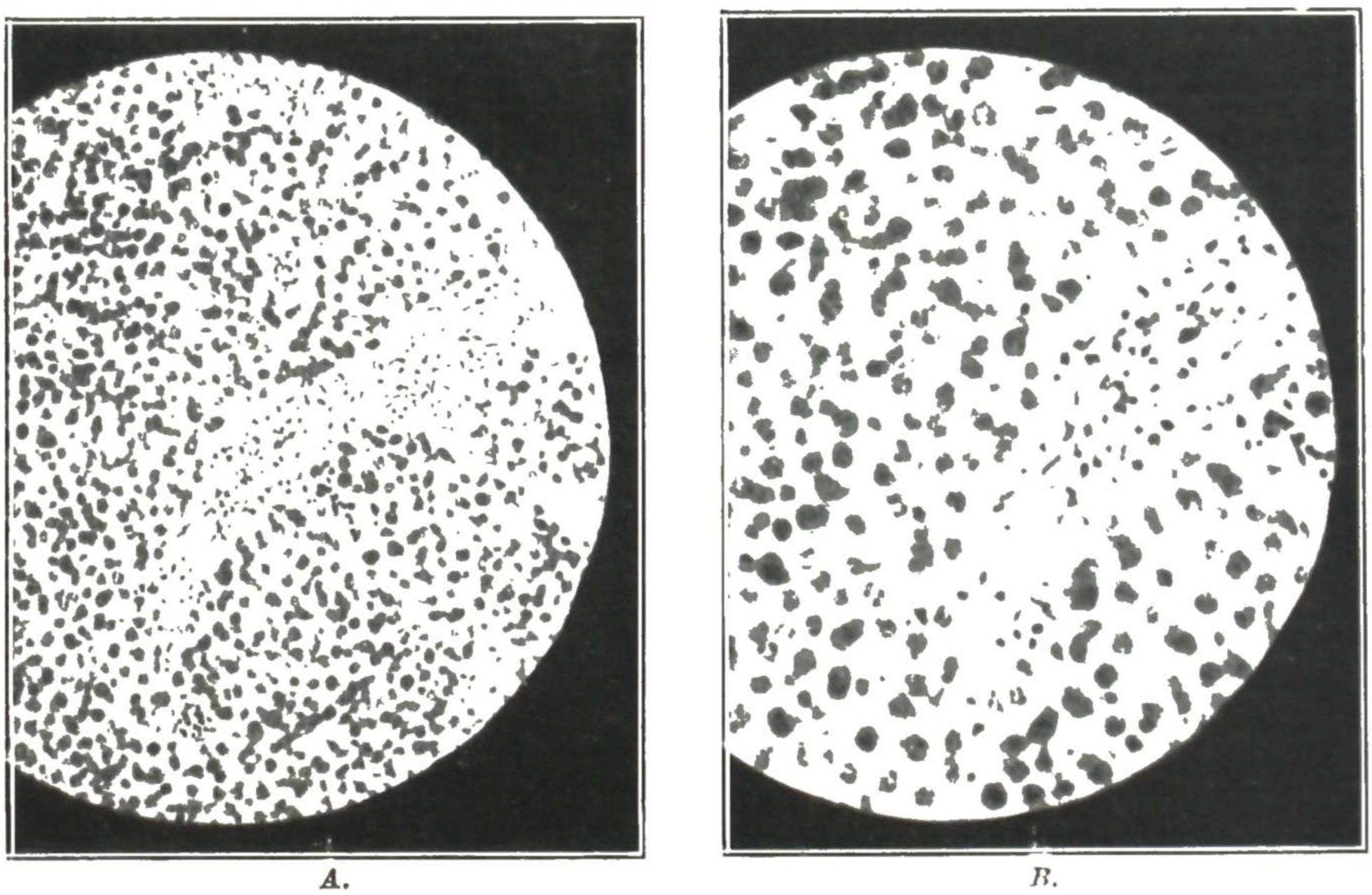
The microscopic picture, particularly the large lutein-like cells, has caused confusion with corpus luteum growths. Novak agrees with Schiller that most of the so-called luteomas of the ovary are really tumors of adrenal tissue. Rests of adrenal tissue occur in the ovary, and this fact must be taken into consideration in interpreting the microscopic pictures in uncertain conditions.

FROM UNDIFFERENTIATED SEX CELLS WITHOUT ENDOCRINE INFLUENCE

Certain tumors in this situation develop from undifferentiated sex cells which show no tendency toward specific male or female characteristics. They include the dysgerminoma and the Brenner tumors.

Dysgerminoma Ovarii (Seminoma)

The dysgerminoma arises according to Meyer from undifferentiated germinal cells which have lost their power of becoming either masculine or feminine, and therefore can develop into identical pathologic structures in either the



A. *B.*

Fig. 973.—Dysgerminoma of the ovary. *A*, Shows the resemblance to dysgerminoma of the testicle. *B*, High power of *A*. (Meyer—*Am. J. Obst. and Gynec.*)

testis or the ovary. They are very common in pseudohermaphrodites, in ovariotestis, and in poorly developed sex glands of otherwise normal persons. They are devoid of any specific sex influence and exert no hormonal action either toward masculinization or feminization.

The growths are rather rare generally but are common in pseudohermaphrodites. They usually appear in the second or third decade of life.

Meyer states that these tumors may attain enormous size, destroying the ovary and adjacent uterus. They are frequently bilateral. They are solid, grayish white, and doughy in consistency.

These tumors in the ovary have the same microscopic characteristics as they do in the testis, with the exception that there are no tubules present in the ovary. There is an alveolar arrangement of the large epithelial cells of the new growth. In some cases there is a cordlike arrangement of these large cells. There is a marked infiltration of the connective tissue. Fig. 973 shows a dysgerminoma of the ovary. These tumors are relatively benign.

Brenner Tumors

The Brenner tumors probably arise from the derivatives of the coelomic epithelium, as do the Walthard cell foci in the infantile ovarian cortex. If the Walthard cell foci retain their indifferent character in the course of their blastomatous development, the Brenner tumor results.

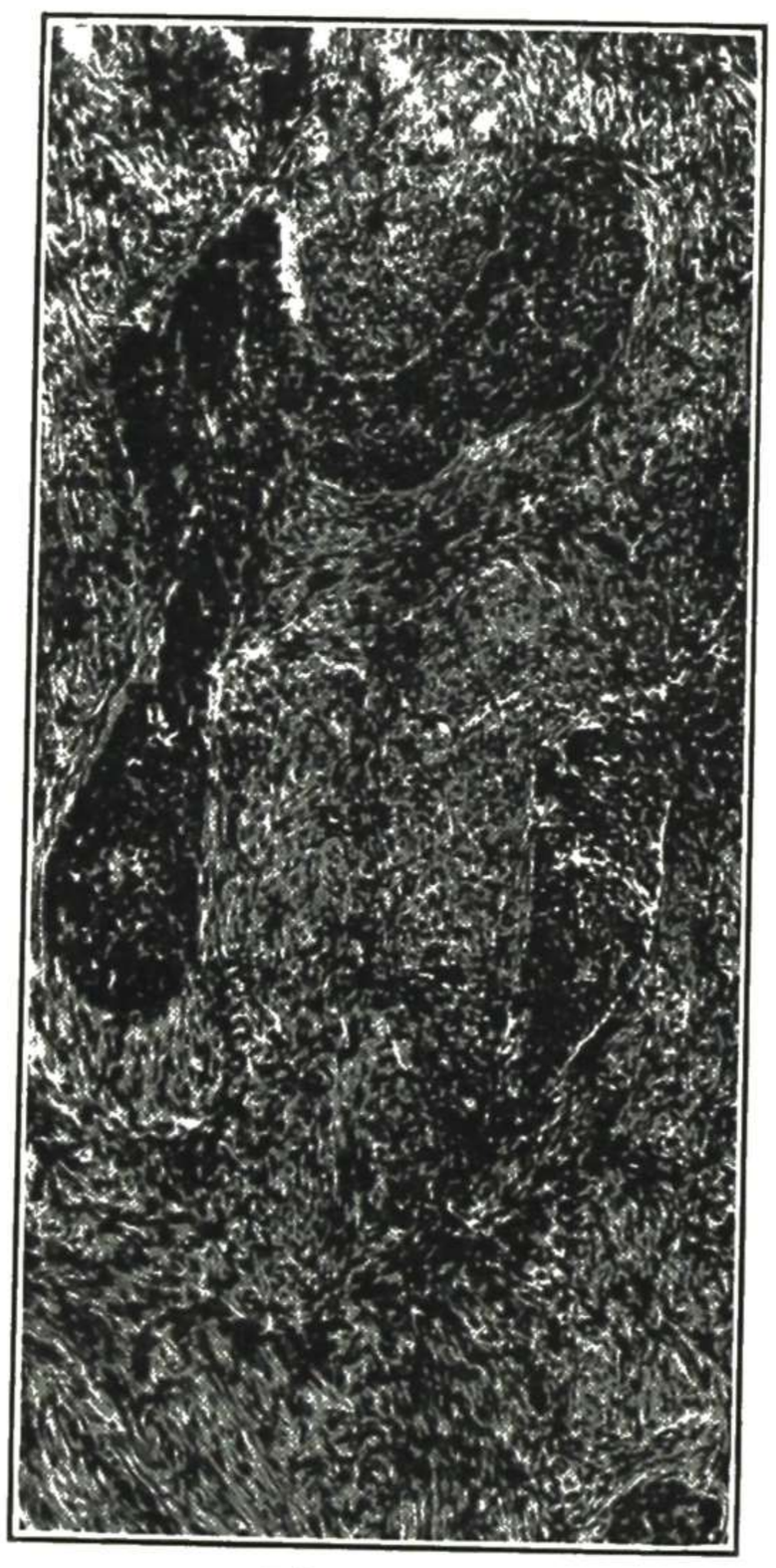


Fig. 974.

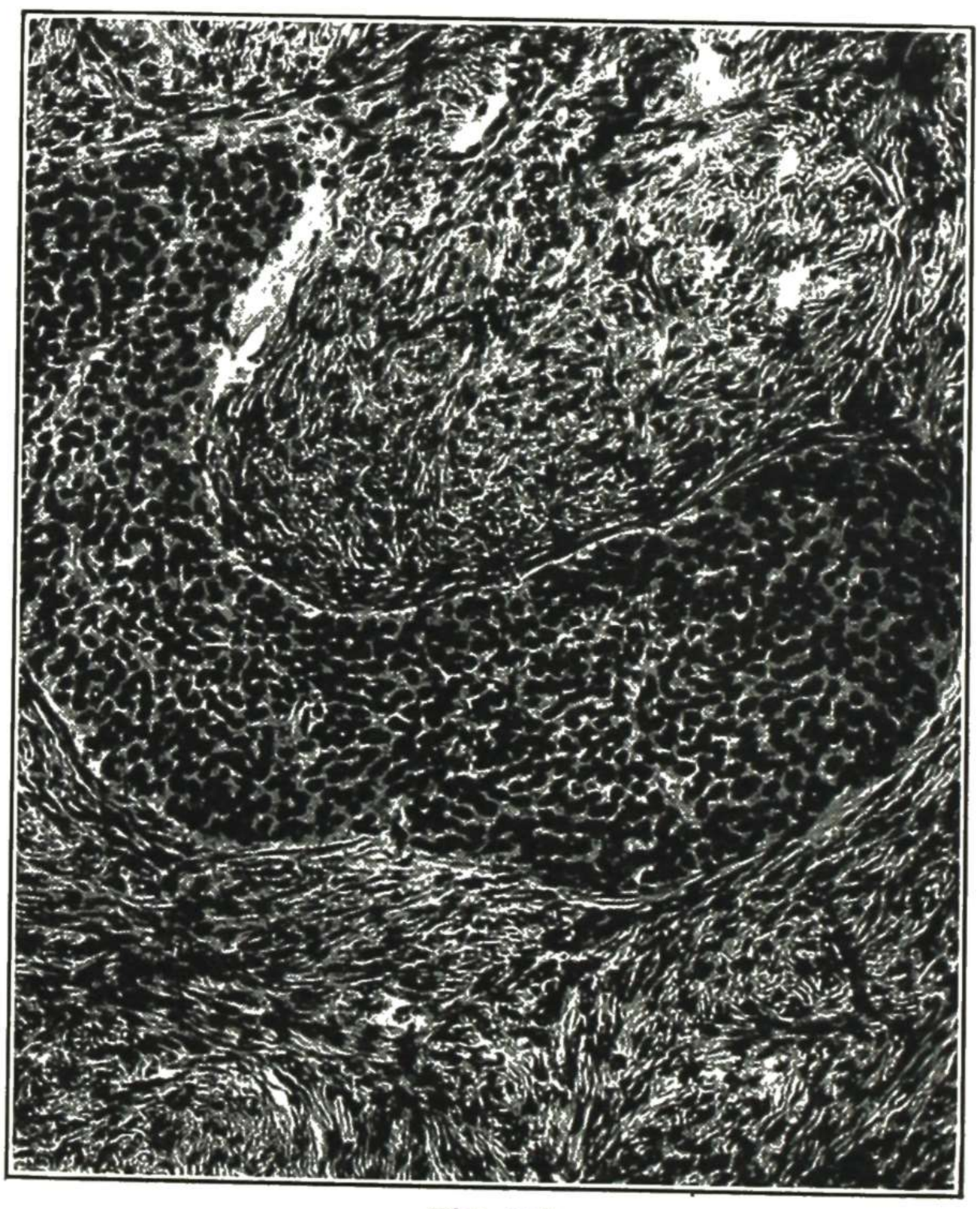


Fig. 975.

Fig. 974.—Brenner tumor, Type I. There are a few hollow spaces seen but no large cysts.

Fig. 975.—High power of the upper portion of the Y-shaped nest of cells seen in Fig. 974, showing the character of the cells. Gyn. Lab.

These tumors are usually unilateral and of moderate size. On cut surface, they are white in color and sharply defined and suggestive of a fibroma. The cystic type cysts usually contain pseudomucin.

Two types are described by Meyer: (1) solid tumors with or without small cysts, and (2) cystomas with or without pseudomucinous epithelium and containing nodules or Brenner cell tumors in the wall. A marked hyalinization of the stroma is characteristic, and there is a definite capsule present.

In the first type there are nests of epithelial cells embedded in the fibrous connective tissue. In the center of the nests there may be hollow spaces and cysts with indifferent cylindrical or mucous epithelium. Centrally, the cells are parallel to the long axis of the nodule while peripherally they are at right angles.

If the differentiation of the cell foci tend primarily in the direction of cyst formation, the second type of Brenner tumor is the result. In this type actual cystomas appear, and may or may not be lined by pseudomucinous epithelium. Maury and Schmeisser have reported a case of bilateral Brenner tumor in which the tumor in one ovary was of the first type and the one in the other ovary of the second type.

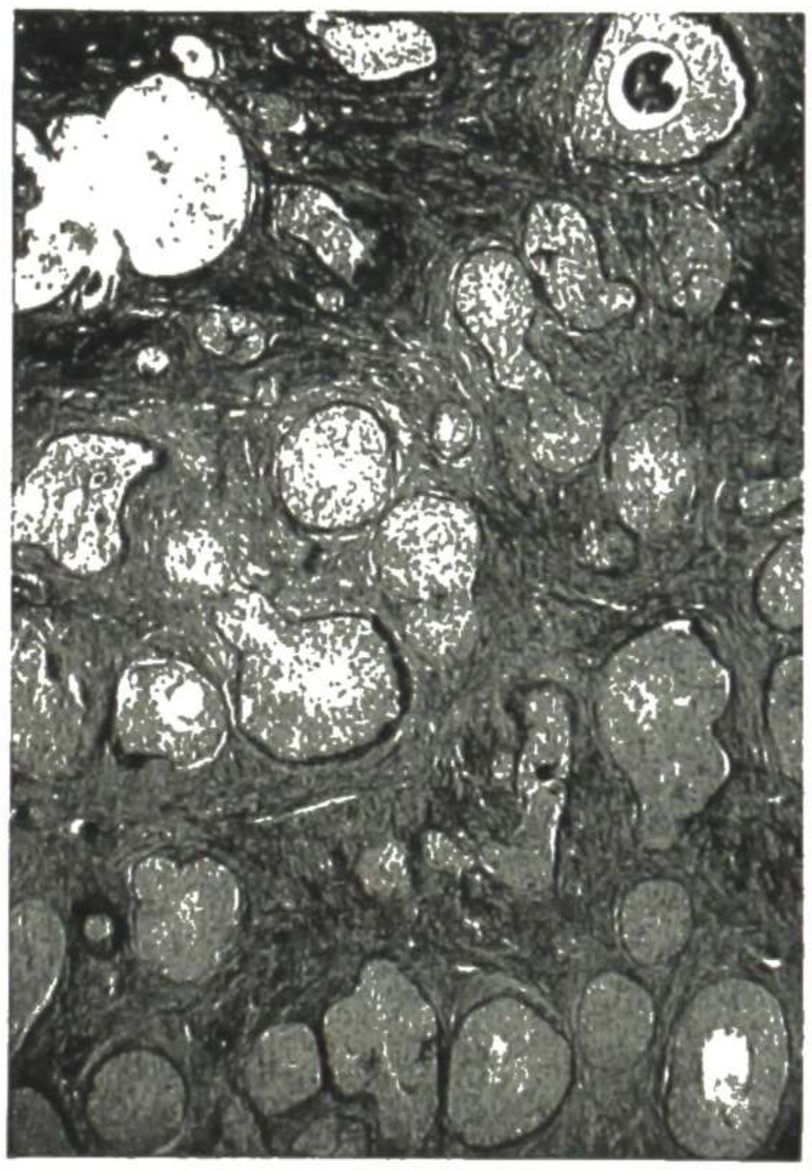


Fig. 976.

Fig. 977.

Figs. 976 and 977.—Brenner tumor. Fig. 976, Presents a characteristic picture at low power. Irregular stroma, epithelial masses varying in shape. They are partly hollow. They contain mucin. Narrow hyaline bands surround the epithelium. They are small cysts. Fig. 977, Partly hollowed out, pseudomucin containing epithelial mass. The outermost cells are conspicuous by their small, dark nuclei. (Plaut—*Surg., Gynec. and Obst.*)

Various microscopic characteristics are shown in Figs. 974 to 977. Proescher and Rosasco in reporting a case and discussing the subject state:

The epithelial part of the tumor does not develop from the ovarian parenchyma nor from the granulosa-cell islands, but from special cell elements which are not derived from the normal cells forming the ovary, but are abnormal cell inclusions which are found in Walthard's cell islands. According to R. Meyer, they originate from the celomic epithelium near the wolffian body, from which the epithelium of the müllerian duct is derived. The latter may form solid epithelial nodules, or larger formations of indifferent epithelium in abnormal locations, as in the tubes and ligaments. It may differentiate into mucous or columnar epithelium, like the surface epithelium of the ovary.

Walthard's cell islands are capable of forming tumors which not only contain mixtures of Brenner epithelium and pseudomucinous and serous cysts, but pure areas of these types of cells may occur side by side. Also pseudomucinous cysts may form without Brenner epithelium. The Brenner tumors are linked genetically with the majority of the serous, partially fibrous, and adenomatous and papillomatous cystomata, including the adenofibromas and the mixed seromucinous tumors. Only a small percentage of the pseudo-

mucinous cysts and cystomata originate from Walthard's cell islands. The majority constitute the endodermal part of a teratomatous anlage, which dates back to the early segmentation of the ovum.

The Brenner tumors have no clinical peculiarities save their frequency of occurrence at an advanced age, 50 per cent occurring after fifty years of age. They are benign and no metastases or recurrences have been observed. Malignant tumors arising from Brenner's epithelium are, so far, not known.

Novak, in reporting a series of cases, gives the following summary:

This paper is based upon the study of 17 cases of Brenner tumor of the ovary, including the 14 new cases herein reported. This brings the total of reported cases to 122, though new instances are being reported more and more frequently. The tumors are benign, and produce no characteristic symptoms. When small they are, therefore, likely to be found only accidentally in operations for other indications. They may, however, reach very large size, in which case they produce discomfort or pain, with perhaps the presence of a mass noticeable to the patient herself. The pathologic characteristics have been described in the paper. The essential elements are (1) the presence of nests or columns, often partially cystic, of rather uniform size and appearance embedded in (2) a matrix of fibromatous tissue which is sharply marked off from the surrounding ovarian stroma though there is no definite capsule. The tumors probably arise from the so-called Walthard islands of indifferent cells which may at times occur in the ovary, though other explanations have been suggested.

The most interesting histologic characteristic is the frequently observed transition of the cells into a cylindrical type identical with that characterizing the ordinary pseudomucinous cystadenoma, so that large tumors of the latter variety may be produced, with only small nodular Brenner tumor vestiges in the wall to indicate their origin. There is logic, therefore, in the subdivision of Brenner tumors into the solid and cystic varieties. Three such tumors are included in our series. On the other hand the fibromatous reaction may be so striking as to produce large fibromas of the ovary. In such cases, of which 2 are included in our group of cases, the origin is indicated by the finding of the typical cell nests scattered either sparsely or richly throughout the tumor. There is little or no evidence to indicate that Brenner tumors exert any such endocrine effects upon sex characters as those which characterize granulosa-cell carcinoma or arrhenoblastoma.

Because of the absence of any hormonal manifestations from these tumors, the diagnosis of the type of growth is made after removal.

UNDIFFERENTIATED SOMATIC CELLS

Tumor growth of embryonic rests of undifferentiated somatic cells gives rise to the dermoids and teratomas. The cystic dermoid tumor represents an adult type of growth and the solid teratoma an embryonal type.

Dermoid Cysts

Dermoid cysts, according to Ewing, constitute 10 per cent of all ovarian tumors. They are present at birth but are not discovered usually until later in life, between thirty and forty, when their growth begins to cause symptoms. Early in life they grow rapidly, but remain stationary after reaching a certain limit of development.

Rupture of dermoid cysts is a common occurrence, and the discharge of the irritating sebaceous material causes a marked peritoneal reaction and dense adhesions.

The origin of these growths is still an undecided question. Wilms feels that they are due to a parthenogenetic development of the unfertilized ovum. Goodall is in accord with this view.

Dermoid cysts are usually globular in shape and dull white in color. They contain structures associated with epidermal tissues, such as hair, teeth, bone, sebaceous material resembling fat. Specimens are shown in Figs. 978 to 980.

Occasionally on close inspection hair can be seen through the wall. They have a doughy consistency, with very hard areas where bony structures are present. When opened, a fatty, semisolid sebaceous material flows out. Hair and skin are nearly always present. The tumors contain elements of all three layers of the blastoderm as has been shown by Bonnet. The solid tissue is usually on one side of the tumor and is called the "dermoid plug."

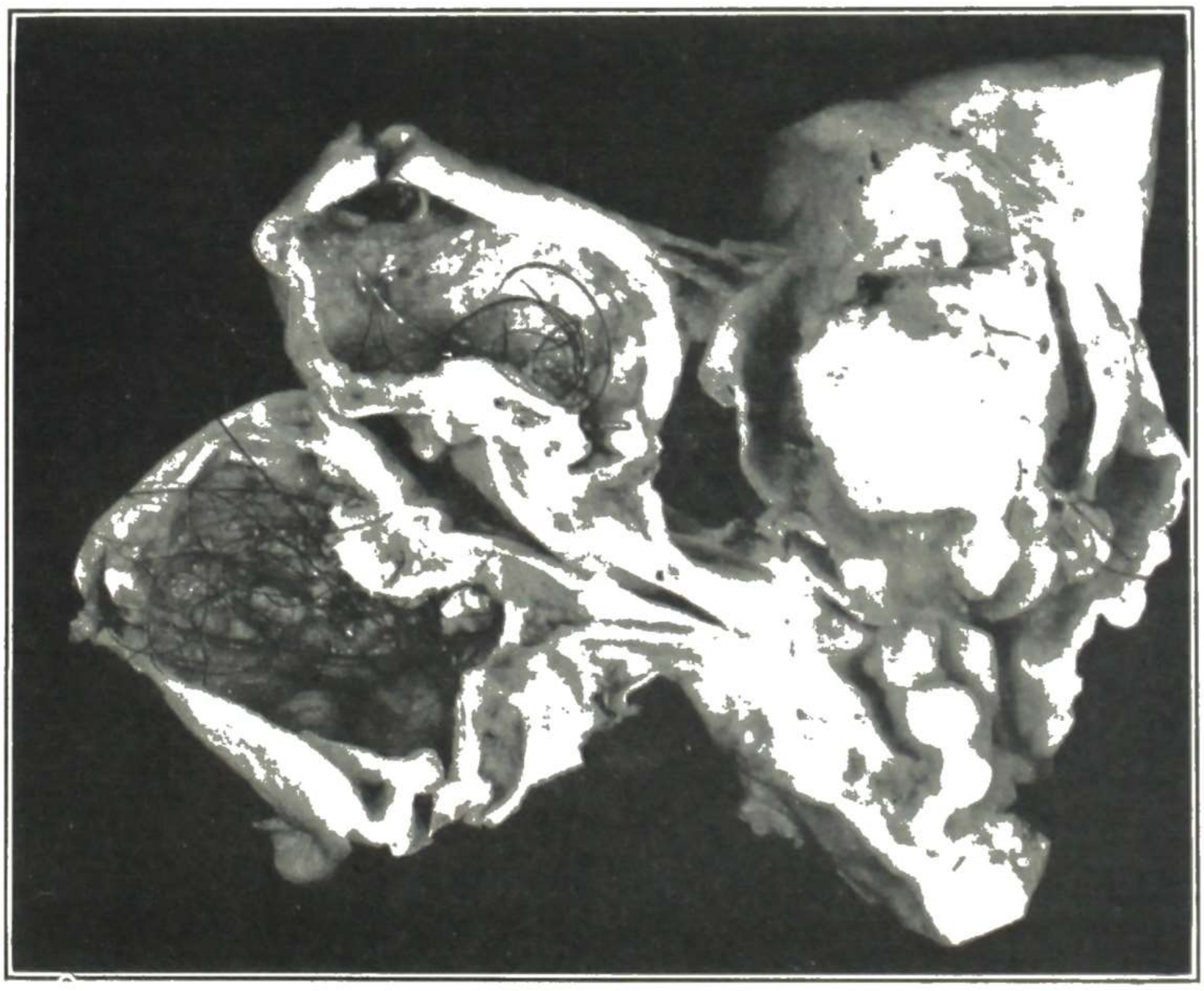


Fig. 978.—Dermoid cyst of the ovary. Gross specimen, showing several teeth in the lower right portion of the specimen and hair in the cystic portion on the left. Gyn. Lab.

The following is a partial list of tissues which have been found in dermoids: Skin and its derivatives, sebaceous glands, hair, sweat glands, and bone, especially the maxillae containing teeth. Up to 300 teeth have been found in one cyst. Rokitansky observed the eruption of permanent teeth after the discharge of the milk teeth. Milk teeth are more common in teratoma while the permanent teeth are usually found in dermoids. Long bones, digits, fingernails, and skull have been found. Brain tissue with its derivatives, intestinal loops, thyroid tissue, eyes, salivary glands, may occasionally be found. Even rudimentary fetuses have been described, such as a pelvis with hairy pubes and a vulva and clitoris. Brains with ventricles, spinal cord, and a few complete extremities, have been observed. Figs. 978 and 980 show opened dermoids in the gross, and Fig. 979 a microscopic picture of the wall structures.

Ewing states that dermoids become malignant in about 3 per cent of the cases and the type of malignancy is usually squamous-cell carcinoma of the contained epidermis. Fig. 1023 shows such a case.

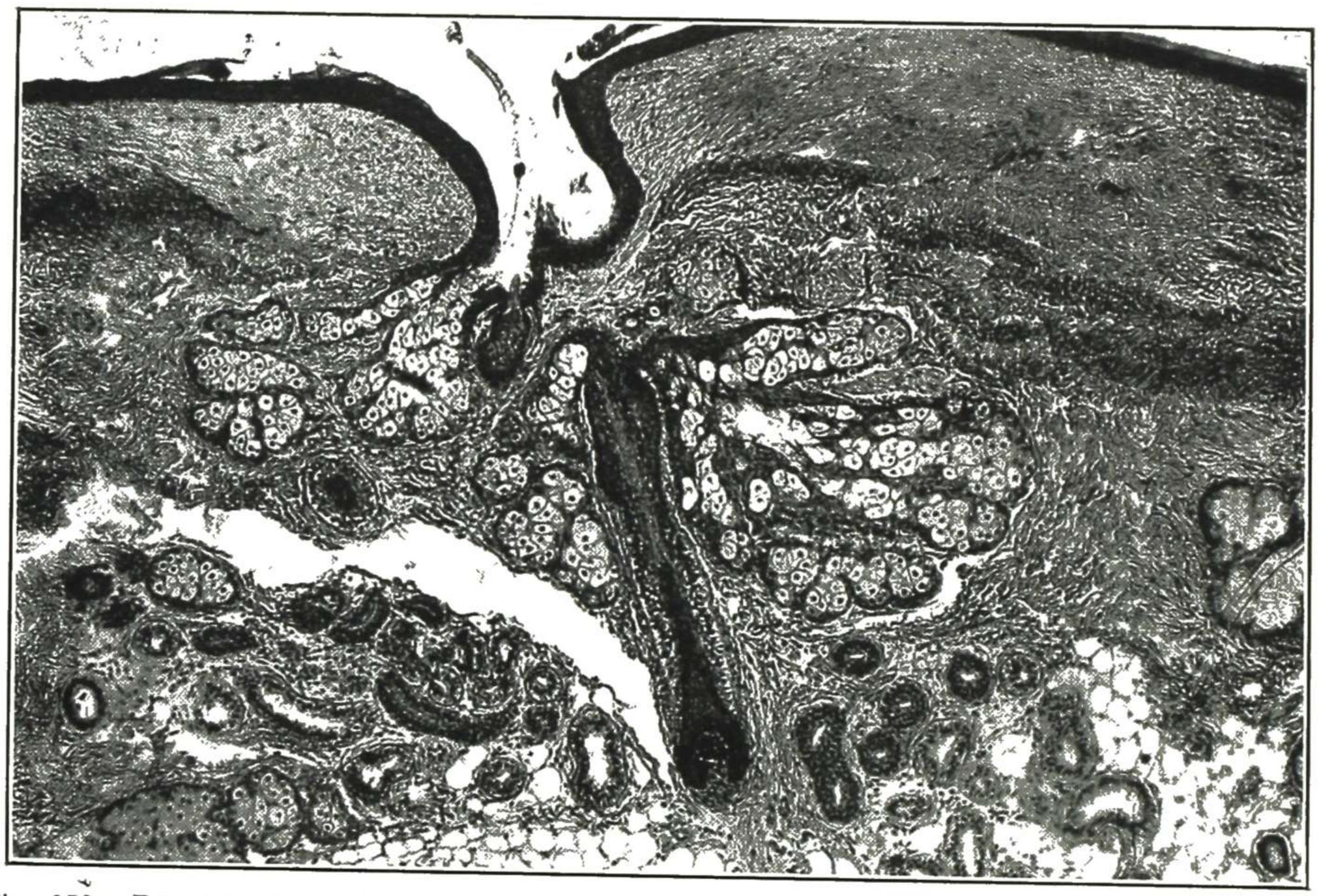


Fig. 979.—Dermoid cyst. Microscopic picture showing a hair follicle, sebaceous glands, sweat glands, and squamous epithelium. Gyn. Lab.

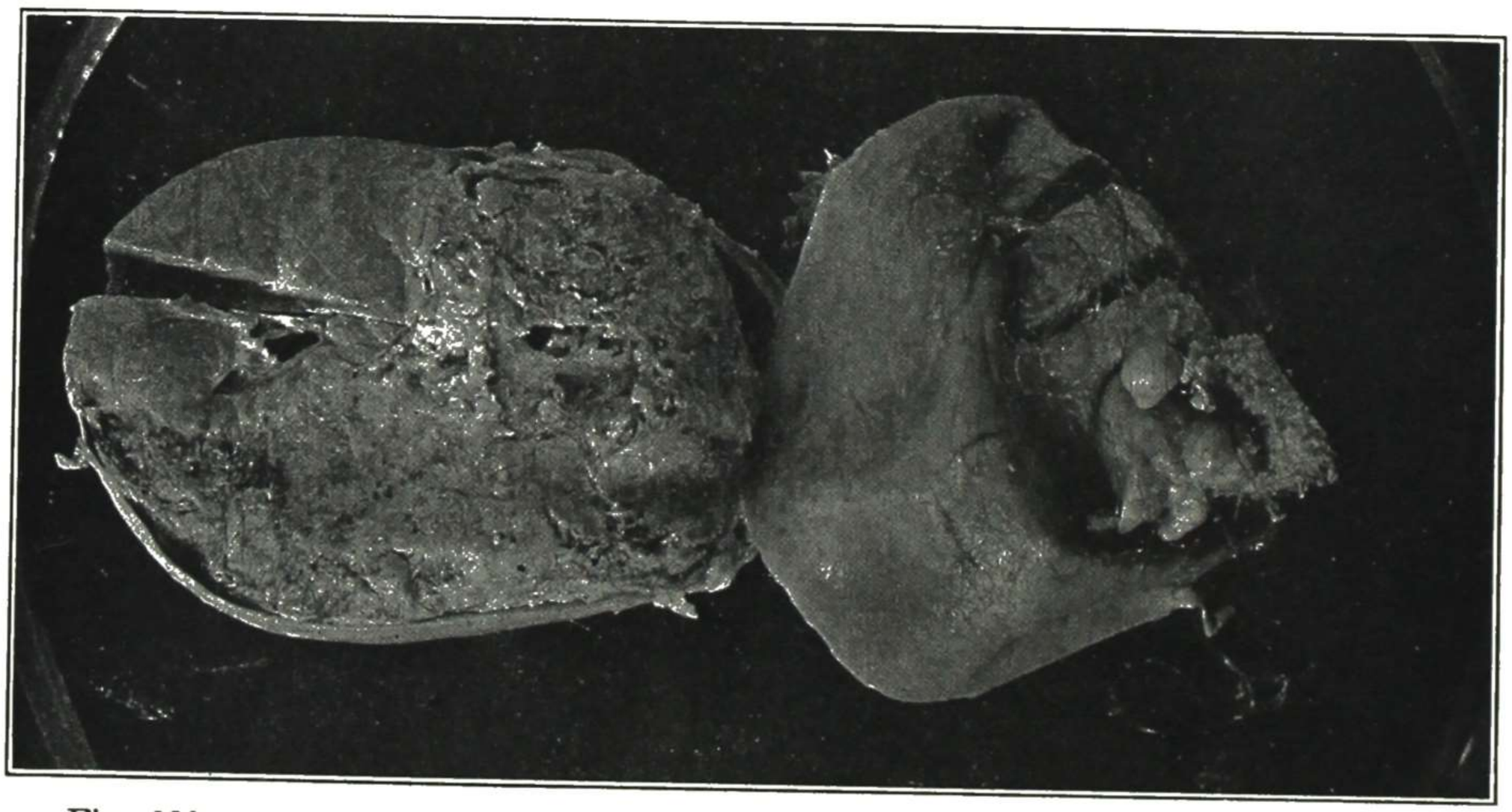


Fig. 980.—A small dermoid cyst, showing teeth, hair, sebaceous material and firm fat tissue. The teeth, shown in the right side, are unusually well developed and constitute a point of special interest in this specimen. (Courtesy of Dr. F. J. Taussig.)

Symptoms and Diagnosis.—Dermoid tumors may appear at any age. They have been found in children at birth and in women at ninety years. Dermoid tumors of the ovary are comparatively small, rarely getting larger than a child's head. But they are more dangerous than the ordinary large cysts, for the dermoid cysts usually present more and firmer adhesions, and their contents are

more irritating, so much so that the escape of any of the contents into the peritoneal cavity is likely to cause a peritonitis.

The symptoms of dermoids are about the same as for ovarian cysts in general, which are given in detail later in this chapter under Proliferating Cysts. In dermoid cysts there may be present a firmer surface on palpation. As they often contain bone or teeth, x-ray examination may assist in determining the character of the pelvic mass felt in pelvic palpation.

Morris and Rosenthal in studying a series of 79 cases, found teeth or bone alone or in combination, in 39 cases or nearly 50 per cent. They remark "Had x-ray been more frequently employed a high percentage of these tumors could have been diagnosed before operation."

Dermoids are more liable to suppuration and abscess formation than the ordinary cyst. Such abscess may rupture into the lower bowel, with discharge of bony material from the rectum. In such case differential diagnosis must be made between dermoid cyst and extrauterine pregnancy as the original trouble.

Quinby reports a dermoid which ruptured into the bladder. Carter, Thomas and Pearse reported a dermoid cyst which ruptured into the bladder and into the sigmoid, producing a very complicated condition. By means of pelvic, cystoscopic and gastrointestinal x-ray examinations the details were finally worked out.

Treatment.—The treatment of dermoid tumors which have become large enough to be appreciated and give trouble, is removal by operation, the same as for proliferating cysts. The fact that they may develop malignancy is an additional reason for prompt removal.

Teratomas

In certain of the tumors arising from undifferentiated somatic cells there is not so much development toward mature structures as in the dermoid cysts, but the growth is more solid and has more embryonic tissue. It is to such a tumor that the term "teratoma" is applied.

The cells being less developed and their activities more erratic than in the dermoid, there is a greater tendency to malignancy. There are usually small areas of partly mature tissue, such as bone, cartilage, hair, etc. There may be small cavities. Areas of hemorrhage are not uncommon. If the growth contains a considerable amount of thyroid tissue, it is designated "ovarian struma."

Clinically, on account of the tendency to malignancy, the teratoma is a very serious type of growth. Any tumor suspected to be of this character should be subjected to prompt operation, if the patient's condition will permit.

TUMORS FROM DIFFERENTIATED EMBRYOLOGIC REMNANTS

Growths of this class are represented principally by the tumors of the broad ligaments arising from the parovarium, which consists of remnants of structures which served their purpose during embryologic development and then largely disappeared.

Parovarian Cysts

The tumors of the parovarium (broad ligament tumors) are almost invariably cysts, and they are of two kinds: simple cysts and papillary cysts.

The **simple cysts** are single cysts containing clear fluid resembling water. On account of their confined position they produce very troublesome symptoms while still small. They arise from various parts of the remains of the wolffian body (parovarium, paroophoron).

The lining of these cysts consists, as a rule, of a single layer of flattened epithelium resting on a fibrous stroma. They rarely become malignant.

The **proliferating papillary cysts** arise also from the remnants of the wolffian body and their characteristic is the development of papillary growths in the interior of the cyst, which fill the cyst and grow through its wall, and spread to the peritoneal surface and the adjacent organs (uterus, ovaries, intestines). The whole pelvis may be filled with these warty cauliflower growths and, having spread to all the adjacent structures, they often give rise to an erroneous diagnosis of cancer.

In the majority of cases they are bilateral and usually rupture before attaining a large size. Though they grow rapidly and spread to adjacent organs, where they implant themselves on the peritoneal surfaces and grow freely, they do not have the fatal infiltrating and destructive tendency of malignant disease, and many patients recover when the abdomen is opened and the larger part of the growth removed. Later they may undergo malignant change, and then they present the usual characteristics of carcinomas.

These proliferating papillary cysts arise from the parovarium. As most parovarian tubules lie in the broad ligament, the papillary cysts are usually broad ligament cysts. But they may also arise from that part of the parovarium which is prolonged into the hilum of the ovary. It is from that location that the papillary cysts of the ovary arise. The papillary cysts of the ovary are usually bilateral and present all the characteristics of the broad ligament papillary cysts, except that they arise from the ovary instead of from the broad ligament.

Symptoms and Diagnosis.—In the clinical history and in the signs obtained by examination, broad ligament tumors resemble ovarian tumors very closely. Practically the same symptoms and signs which serve to distinguish an ovarian tumor from other diseases serve, also, to distinguish a broad ligament tumor from the same diseases. So that, as a rule, in this condition, when there is trouble in diagnosis, the difficulty is to tell whether the tumor present is a broad ligament tumor or an ovarian tumor.

The characteristics of the ordinary parovarian cysts, or "broad ligament cysts," as they are usually called, are as follows:

1. They grow into the broad ligament, separating its layers and displacing the adjacent organs. The uterus is pushed far to one side, and the tube is usually stretched over the cyst, being much lengthened and flattened (Figs. 981 to 984). The ovary also may be flattened out on the surface of the cyst. There is more or less fixation of the cyst and also of the displaced uterus. They may grow under the peritoneum and separate it from the rectum, bladder, and abdominal wall.

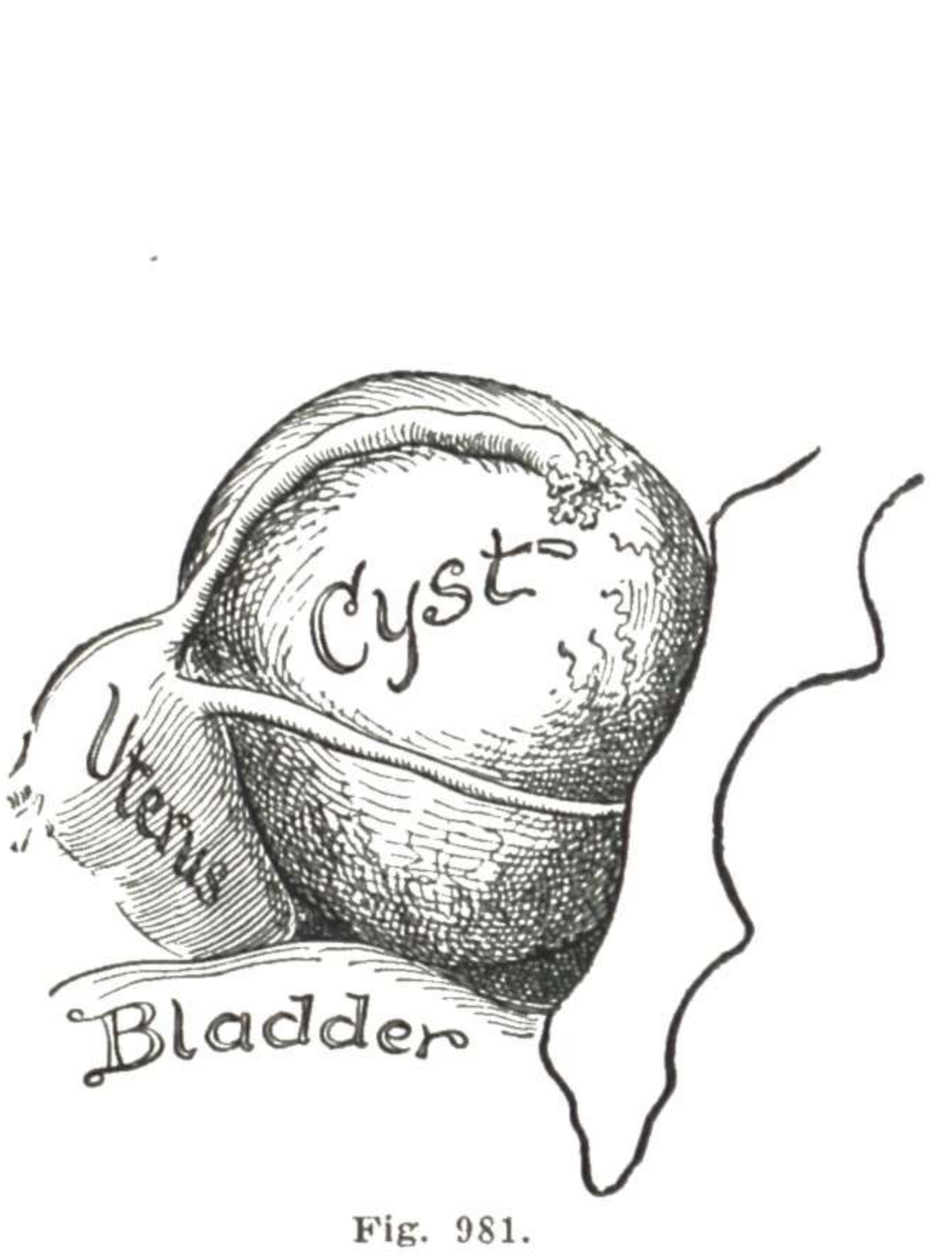


Fig. 981.

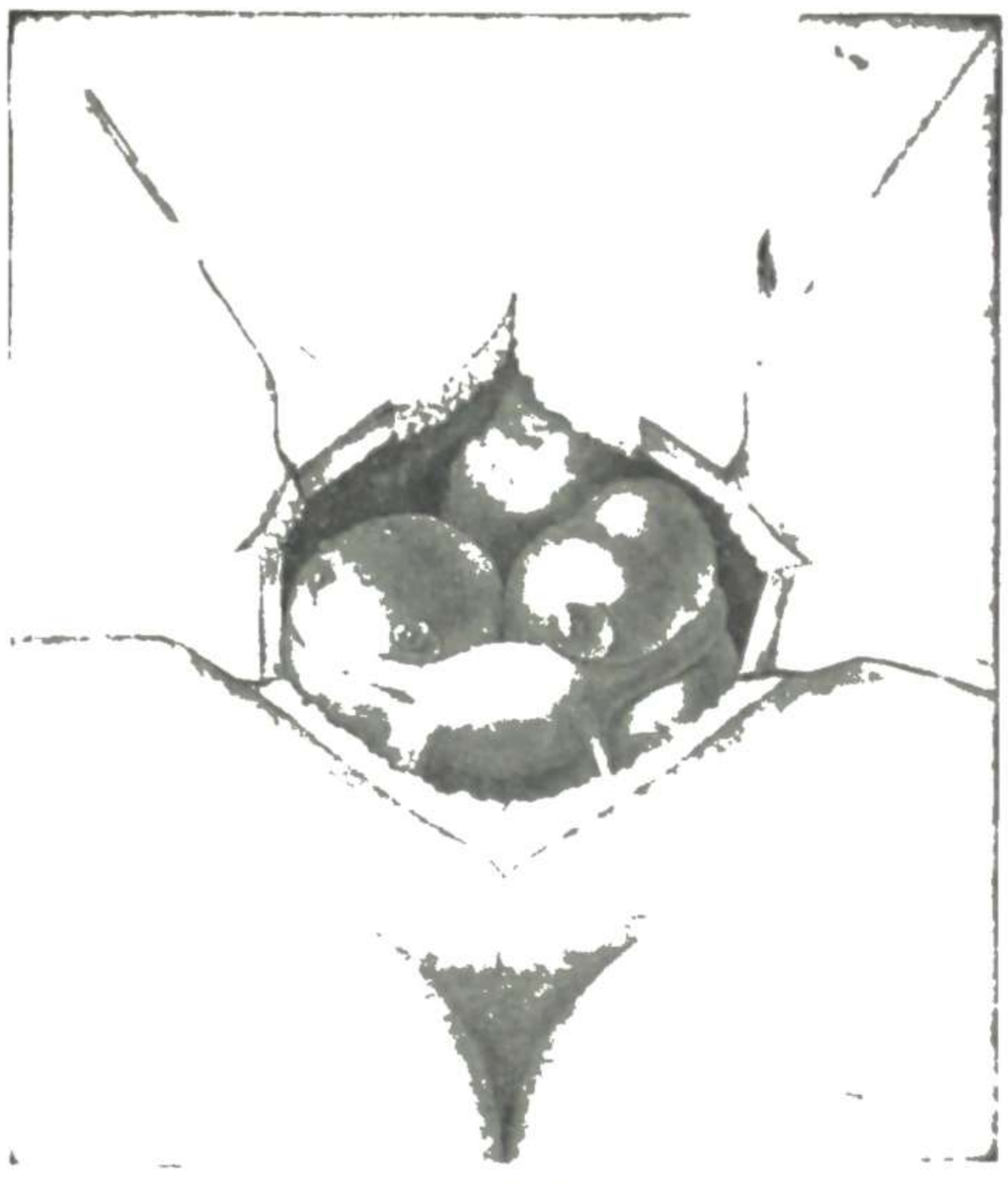


Fig. 982.

Fig. 981.—A parovarian cyst, forming a large mass and displacing the uterus. (Ashton—*Practice of Gynecology*, W. B. Saunders Company.)

Fig. 982.—Graafian-follicle cysts of the ovaries, which have become intraligamentary (Kelly—*Operative Gynecology*, D. Appleton-Century Company.)

Fig. 983.—Parovarian cyst from left side, view from above. The ovary is seen at the upper left portion. Just below it to the left is the severed uterine end of the tube, from which the flattened tube may be traced under the peritoneum to its fimbriated end near the center of the drawing. As the cyst grew in its situation between the layers of the broad ligament the sides of the ligament were spread apart, the ovary was raised, and the tube was stretched out and flattened. Gyn. Lab.

2. They produce serious symptoms much earlier than ovarian cysts. This is due to their being confined within the broad ligament and the pelvis, and hence making serious pressure on surrounding organs while they are still small. For this reason they cause more pelvic pain and more menstrual disturbance than ovarian cysts of the same size.

The papillary cyst, after rupture and spread of its papillary growths, may produce a clinical picture very much resembling tuberculous peritonitis or chronic pelvic inflammation. It then usually gives rise to marked ascites, and the fluid returns repeatedly after tapping.

The **rapidity of growth** of the broad ligament tumors depends somewhat on the character of the growth. Those of slow growth are usually simple cysts. The papillary cysts grow rapidly at the last, though the growth may be slow while confined within the broad ligament.

Treatment.—The treatment for broad ligament tumors is the same as for ovarian tumors—that is, removal by abdominal section. In some cases of simple cyst, very low in the pelvis, with the patient in bad condition, it is better to open the cyst from below, drain away the fluid and pack the cavity, keeping the wound open until the cavity is obliterated, the same as in the treatment of pelvic abscess. Some cases may be permanently cured in this way with much less danger than by abdominal section.

Ordinarily, however, the preferable operation is abdominal section. The operation for a parovarian cyst is somewhat more difficult than for an ovarian cyst owing to the fact that the parovarian growth lies between the layers of the broad ligament. This necessitates opening the broad ligament to extract the cyst and also necessitates careful closure of the remaining broad ligament cavity to prevent oozing or secondary hemorrhage.

Downing and Otoole in their study of parovarian cysts complicating pregnancy, collected sixty-two reported cases, but in only seven did the cyst produce dystocia. They report a case causing dystocia and requiring aspiration of the cyst to permit delivery.

TUMORS DUE TO TRANSPLANTATION OR HETEROPLASIA

This type of tumor is represented by the endometrial cyst of the ovary, so named because it contains tissue resembling the endometrium of the uterus.

Endometrial Cysts of Ovary (Pelvic Endometriosis)

Endometriosis is a serious pelvic disease concerning which little was known up to about two decades ago. The pathology has now been worked out very well, and we know that this process is responsible for the major portion of those dense adhesions found in patients without definite pelvic infection. The clinical significance, however, of this pathologic process—that is, its importance in everyday treatment and operative work—has not been sufficiently recognized.

The first thing that started the investigations which finally made clear the life history of this strange growth was the discovery that some uterine myomas contained glands, in addition to the muscle and connective tissue. This particular type of myoma, which

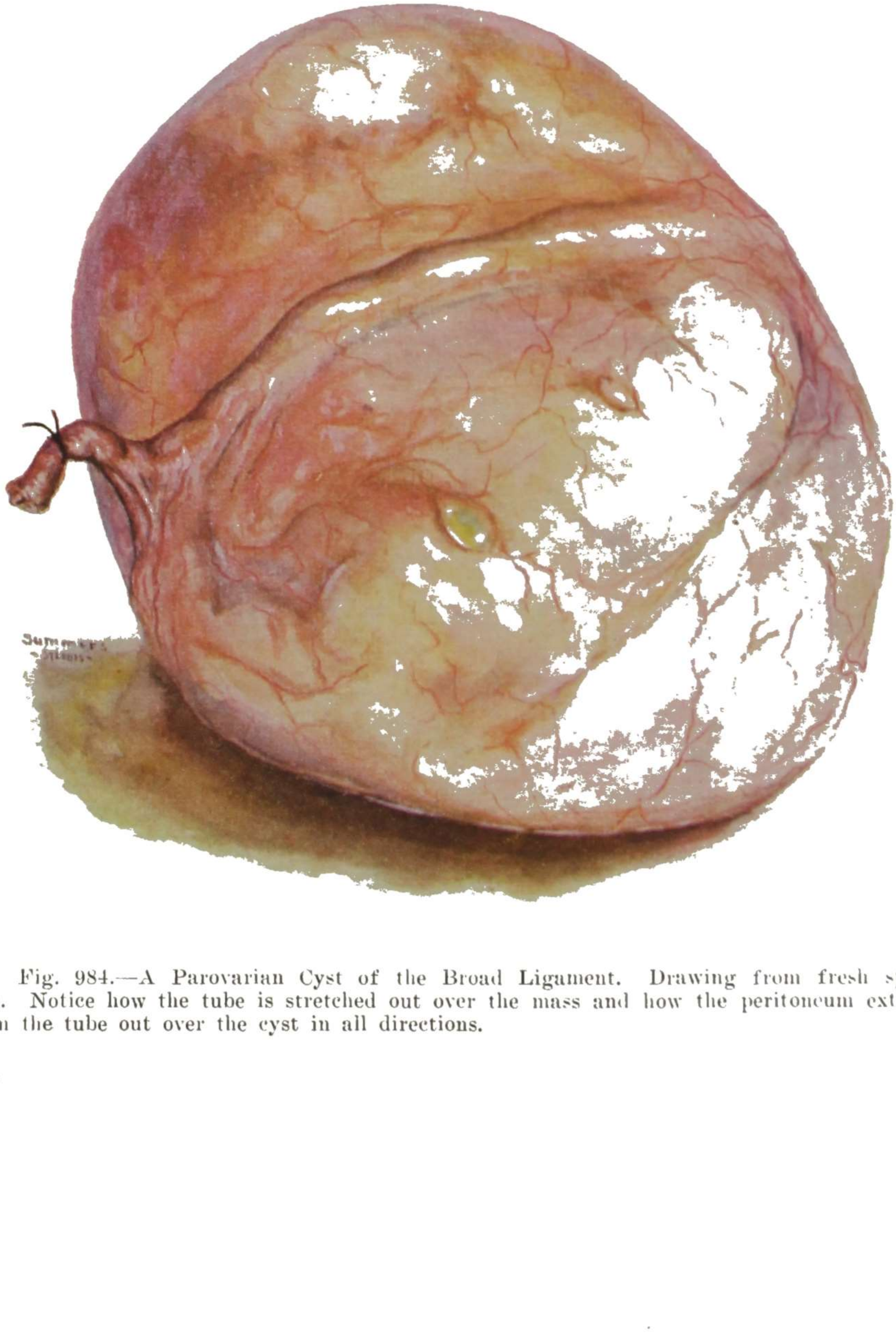


Fig. 984.—A Parovarian Cyst of the Broad Ligament. Drawing from fresh specimen. Notice how the tube is stretched out over the mass and how the peritoneum extends from the tube out over the cyst in all directions.

contained glands, was designated adenomyoma. Further study developed that the adenomyoma differs from the ordinary myoma, not only in containing glands but also in two other important characteristics. First, it shows a tendency to grow into the surrounding tissue instead of pushing it aside, that is, it is not well encapsulated like the regular uterine myoma but tends to infiltrate the surrounding uterine wall and become diffuse. Second, it is not confined to the uterus, but is found in many different situations in the pelvis and lower abdomen even as high as the umbilicus.

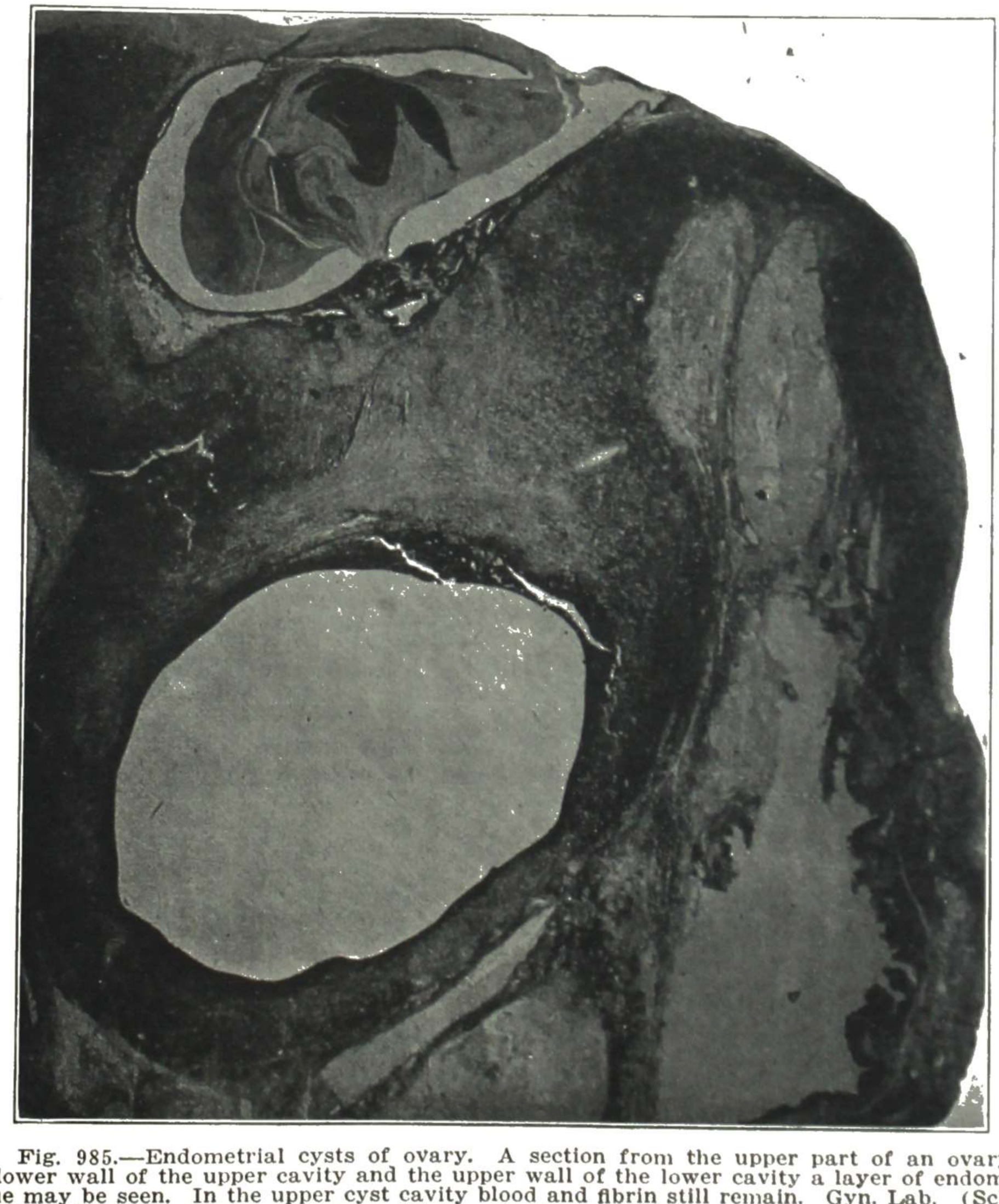
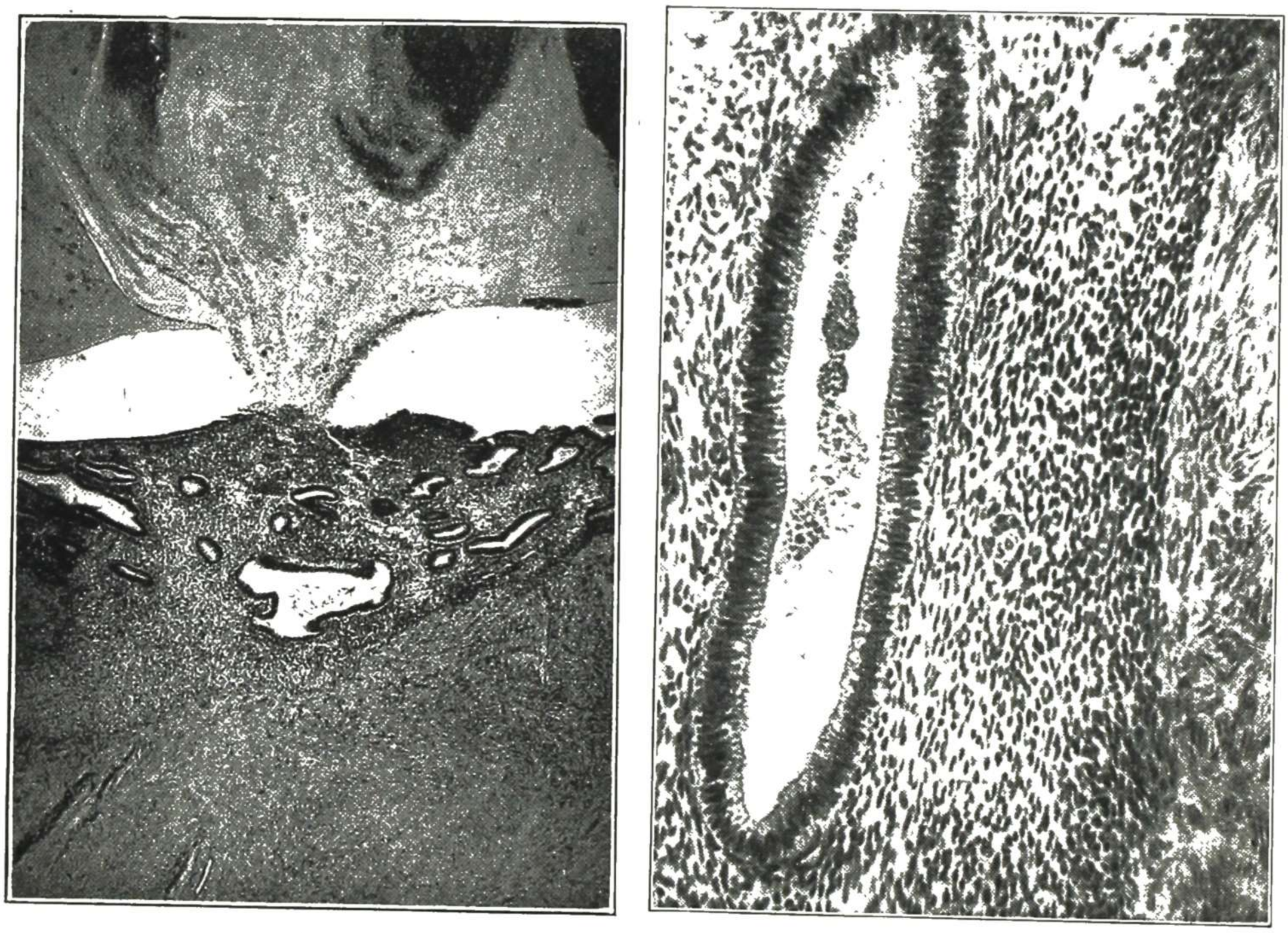


Fig. 985.—Endometrial cysts of ovary. A section from the upper part of an ovary. In the lower wall of the upper cavity and the upper wall of the lower cavity a layer of endometrial tissue may be seen. In the upper cyst cavity blood and fibrin still remain. Gyn. Lab. (Schwarz and R. J. Crossen—*Trans. Am. Assn. Obst., and Gynec.*)

Next arose the question as to how there came to be glands among the muscle bundles. Where did the glands come from? A careful study of the adenomyomas near the uterine cavity indicated that those glands came from outward growth of the glands of the adjacent endometrium. In some cases it was possible to establish a direct continuity of the glands in the endometrium with those in the tumor. But there were adenomyomas in the outer part of the uterine wall having no connection whatever with the endometrium. There were also similar tumors in distant situations, not even connected with the uterus. How did the glands, resembling uterine glands, get into those tumors distant from the endometrium? It was eventually discovered that there were certain cysts of the ovary con-

taining such glands, and that wherever they came in contact with the uterine wall there were ingrowths of these glands, forming an adenomyoma in the outer portion of the uterus. Again, leakage from these cysts carried gland cells which caused similar glandular ingrowths wherever they lodged.

The tracing of the connection between these cysts of the ovary and adenomyomas forms an interesting chapter in medical history. Cullen, in his illuminating writings on uterine adenomyoma and the distribution of the same in the pelvis and lower abdomen, called attention to the fact that they occasionally occur in the ovary. Finally Sampson, through his laborious and brilliant work, was able to establish the identity of the structure of a certain type of ovarian cyst with the uterine endometrium and with the glands in adenomyomas.



A. *B.*

Fig. 986.—Endometrial cyst of ovary. *A*, High power from the lower wall of the upper cyst in Fig. 985, showing typical uterine glands and stroma. *B*, Higher power, showing details of a gland and the surrounding stroma. The solid tissue about the two cysts is hyperplastic ovarian stroma. Gyn. Lab. (Schwarz and R. J. Crossen—*Trans. Am. Assn. Obst. and Gynec.*)

It had long been noted that old blood was frequently found in small cysts of the ovary. Aside from the normal blood-filled corpus luteum (which undoubtedly constitutes some of the "blood cysts" removed by inexperienced operators), blood from hemorrhage may be found in various types of cyst—the follicular cyst, the corpus luteum cyst, and the ordinary proliferating cysts (pseudomucinous and serous). These hemorrhages are all accidental. Sampson was able to show, however, that there is a particular type of cyst in which the extrusion of blood into the cavity is not accidental, but a part of the regular development.

This cyst is lined by a tissue made up of glands and stroma resembling the endometrium of the uterus. Not only does this tissue look like endometrium, but it also acts like endometrium—that is, it menstruates. Along with the uterine endometrium it passes through the regular phases of menstruation. Blood is extravasated into the tissue and passes into the cavity. In the closed cyst there is no outlet for this menstrual blood, so

it accumulates and distends the cyst. The retained blood undergoes more or less disorganization, and constitutes the dark chocolate-colored material which so often escapes from the cyst as the adhesions are broken in operative removal.

Definition.—In regard to terms used, "pelvic endometriosis" is the general term used to designate the appearance of endometrial tissue outside its usual location. If it appears in the ovary, it is likely to form a cyst, which is designated an "endometrial cyst" of the ovary. If the glands penetrate the uterine muscle, the process with the resulting condition is called "adenomyosis." If the adenomyosis causes a distinct tumor formation, that is called an "adenomyoma."

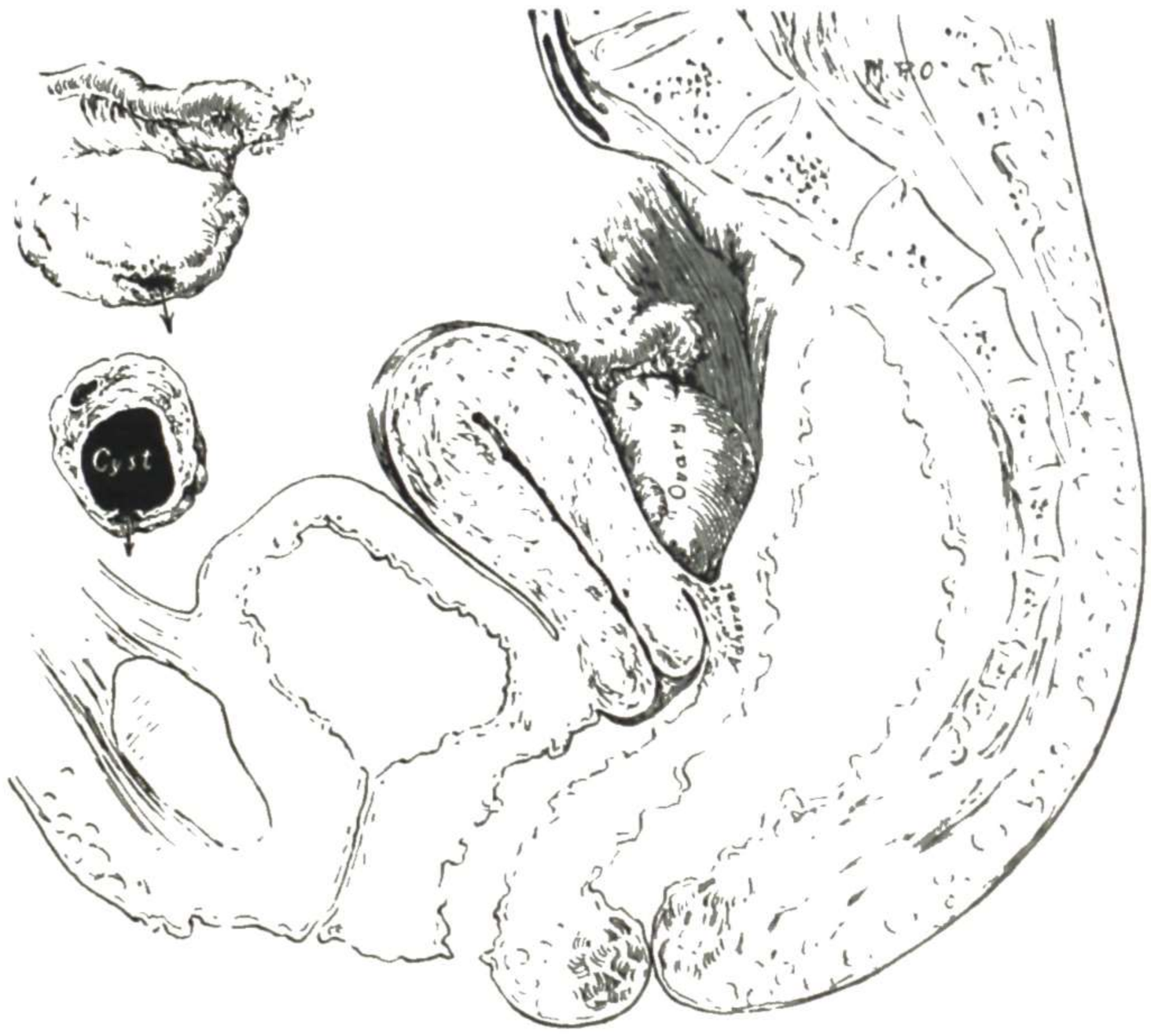


Fig. 987.—Endometrial cyst of ovary. The ovary is prolapsed and adherent. Perforation of the cyst wall has taken place, with gravitation of contents to the cul-de-sac and the formation of adhesions there. The insert shows the ovary sectioned and, also, the perforation through the cyst wall and ovarian surface. (Sampson—*Arch. Surg.*)

Etiology.—There are several theories as to the etiology of this condition.

1. Transtubal implantation (Sampson). This is the first theory offered. Sampson thought that in certain cases during menstruation some of the blood and endometrial tissue passed out through the tubes into the peritoneal cavity. This endometrial tissue became implanted and grew at the point where it happened to fall. Any condition causing obstruction to the free cervical exit of the menstrual blood was presumed to be a factor in this transtubal implantation. This tissue after becoming implanted continues to function as endometrium and, as a result, menstruates. After a number of menstrual periods the transplant becomes a blood-filled cyst.

Owing to the increasing pressure within and the endometrial growth penetrating the wall, there is some leakage of cyst contents into the peritoneal cavity. This endometrial leakage causes adhesions of the cyst to surrounding structures with endometrial penetration of the adherent area. Very frequently there is gravitation of material to the posterior peritoneal cul-de-sac with adhesions and penetration and infiltration there. This process of leakage and growth may continue, forming dense adhesions throughout the pelvis.

The arguments for the transplantation theory of the origin of endometrial ovarian cysts are: (a) in endometriosis the tubes are usually patent, (b) the islands of endometrial

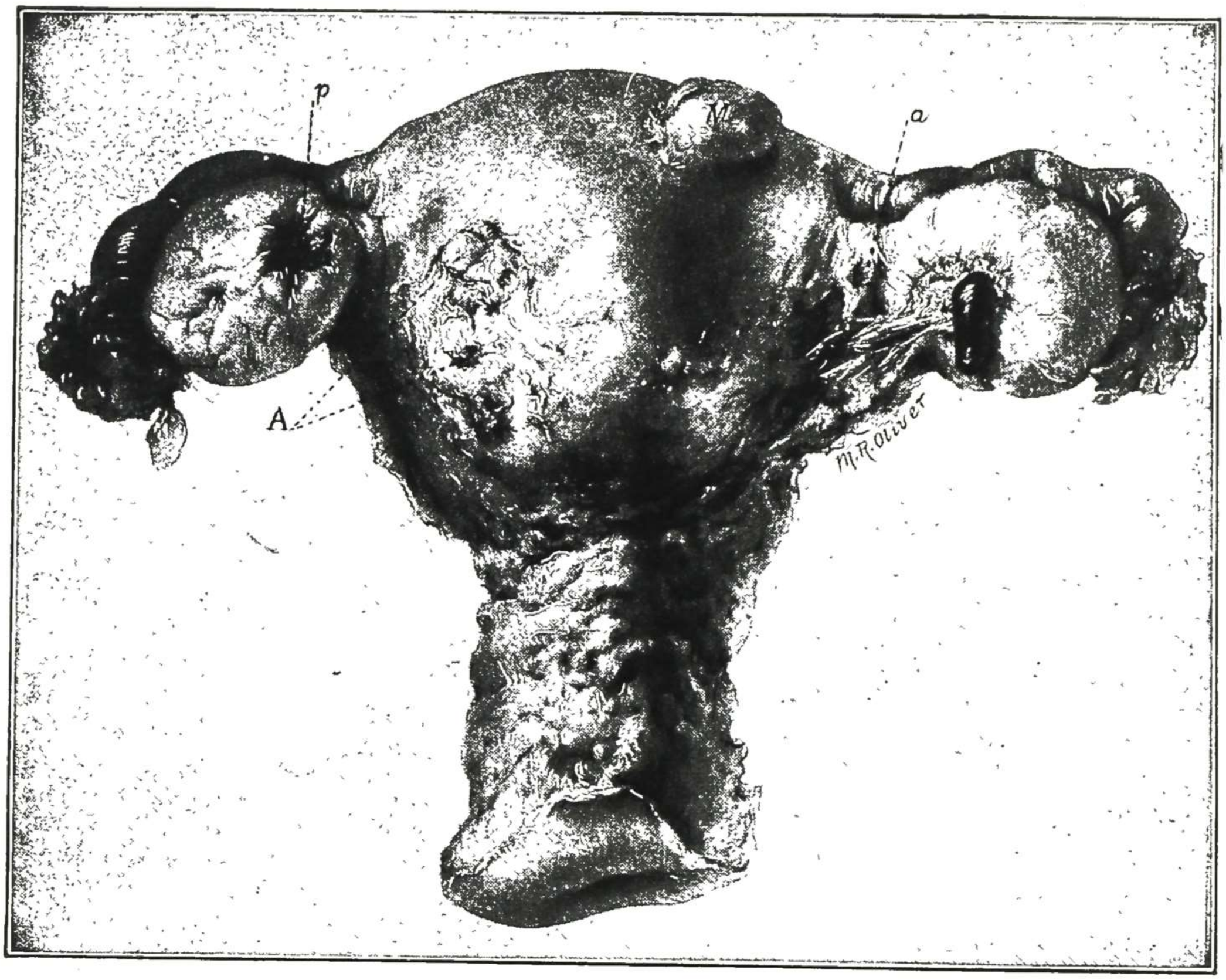


Fig. 988.—Endometrial cysts of ovary with peritoneal involvement (pelvic endometriosis). A cyst in each ovary has perforated, and from the cyst in the right ovary the contents are leaking out. At operation both ovaries were found adherent to the posterior surface of the uterus. Where the left ovary was adherent (*A*) a superficial adenomyosis is developing in the uterine wall. (Sampson—*Arch. Surg.*)

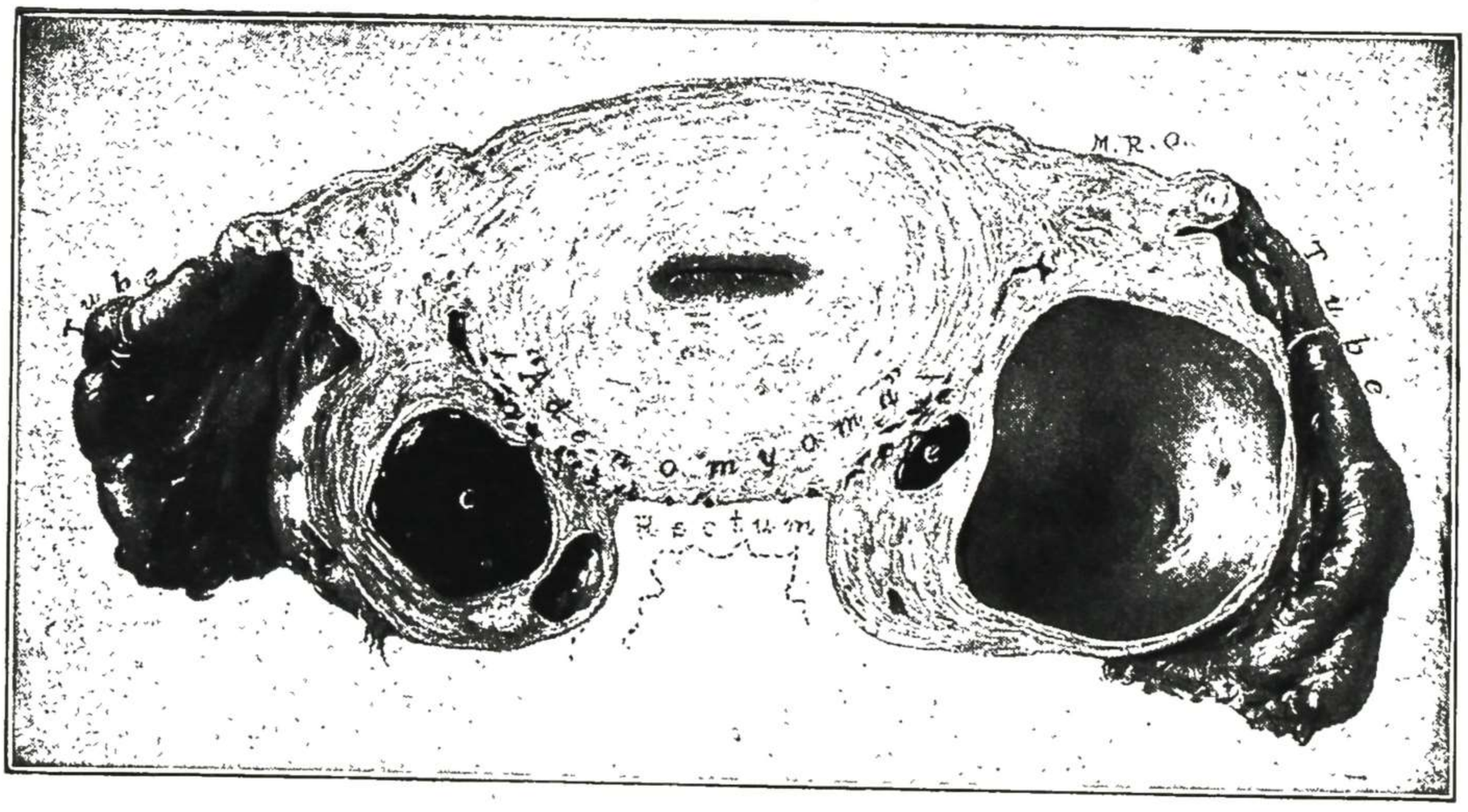


Fig. 989.—Pelvic endometriosis. Cross-section of the uterus and ovaries indicating the condition found at operation. Both ovaries were adherent to the posterior surface of the uterus and the implanted endometrial cells have grown into the uterine wall, forming superficial adenomyosis. Sections of the uterine wall showed no endometrial tissue between this area and the normal endometrium. The larger cavity in the right ovary is a simple follicular cyst. (Sampson—*Arch. Surg.*)

tissue are found where one would expect them if they were secondary to endometrial spill from the tubes, (c) endometrial tissue has been successfully transplanted in the peritoneal cavity of animals (Jacobson, and Crossen and O'Keefe), (d) blood has been observed coming from the fimbriated end of the tube at operation, and (e) the tissue seems to menstruate with each period similar to endometrial tissue, indicating that it is real endometrial tissue.

The arguments against this theory are: (a) tissue from the menstrual discharge in monkeys is desquamated dead tissue and will not grow in the peritoneal cavity of the monkey, even when a uterine fistula is made so that the menstrual flow empties directly into the peritoneal cavity (Heim), (b) this theory does not explain aberrant endometrial tissue occurring in distant structures, for instance, in the umbilicus or the inguinal canal, and (c) it does not explain such tissue found in the depth of the ovary without surface contamination.

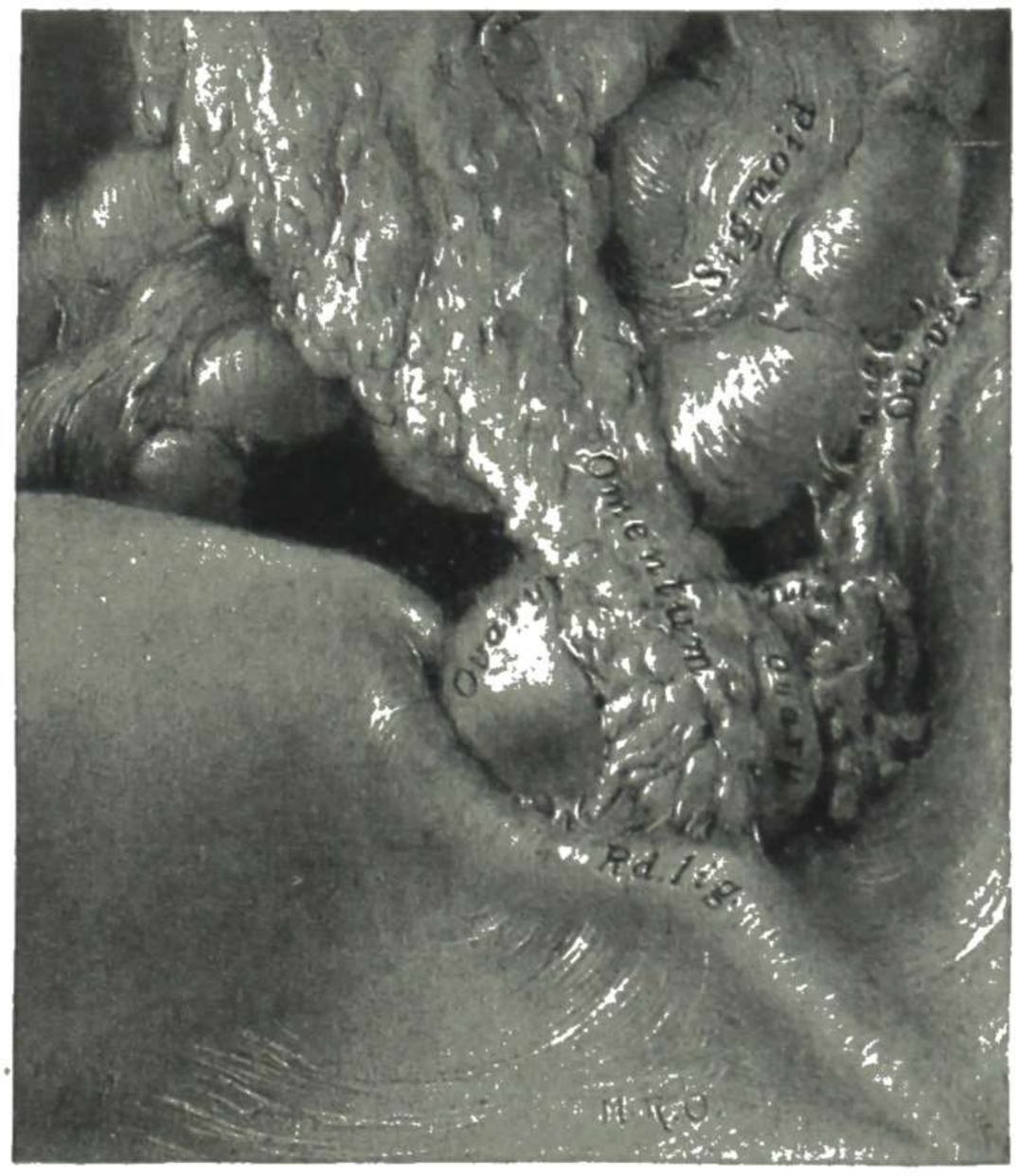


Fig. 990.

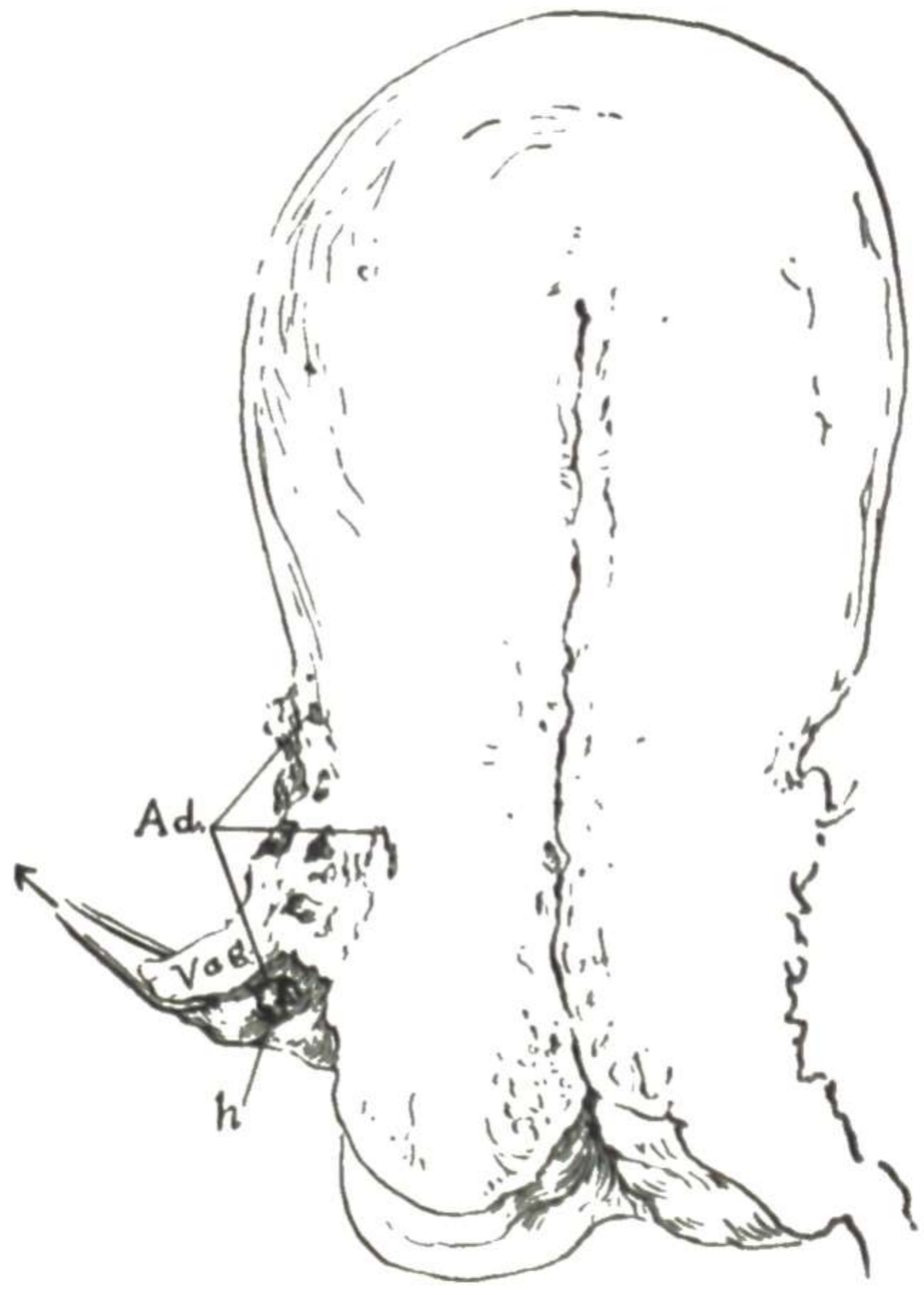


Fig. 991.

Figs. 990 and 991.—Endometrial cyst of ovary. Fig. 990, A small cyst of the left ovary has perforated and become adherent high up to the round ligament. The omentum also is adherent over it. On separating the adhesions, dark chocolate-like fluid escaped. Fig. 991. Section of the cul-de-sac area in the same case. Gravitations of leakage material have caused an implantation endometriosis at the bottom of the cul-de-sac. A small, blood-filled cyst of this endometriosis of the rectovaginal septum may be seen projecting into the vaginal cavity at the posterior vaginal vault. Compare with Fig. 992. (Sampson—*Arch. Surg.*)

2. Heteroplasia of the serosa or celomic epithelium (Iwanoff, Meyer, Fischel, Novak). This theory of the origin of endometrial cysts of the ovary is based on the embryologic fact that the lining mucous membrane of all parts of the müllerian canal (tubes, uterus, vagina), as well as the germinal epithelium covering the ovary, and the pelvic peritoneum, are all derived from the same parent tissue, namely, the celomic epithelium. The müllerian mucous membrane in all its varied forms is merely an invagination of the celomic epithelium, showing varying degrees of differentiation according to its location. Some of the less highly differentiated portions retain the power of further differentiation later in life, so that they may, under the influence of unknown stimuli, develop into differentiated tissue, such as tubal mucosa or endometrium. Whether this stimulus is of endocrine origin or whether it is due to some substance coming from the tubal ostium is still undecided. Also, there is the unsolved question as to whether all peritoneal cells or only certain ones, such as the "basal" cells (Meyer), have the power of differentiating.

In favor of this theory is the fact that it offers an explanation for all forms of endometriosis, for it is well known that remnants of peritoneal epithelium are frequently

present in the inguinal canal and in the umbilicus. Against this theory must be counted the fact that the adequate stimulation is still unknown. Also, the known tendency to wide vascular dissemination of bits of tissue from the uterus, particularly during pregnancy, might account for subsurface endometriosis in various situations.

Other theories have been suggested, namely, metaplasia of the lymphatics (Schiller) and metastases by way of the lymphatics or the blood stream (Halban, Mestitz). The distribution of the lesions practically excludes the lymphatic or blood stream metastases, and if the other method (metaplasia) does occur, it is very rare.

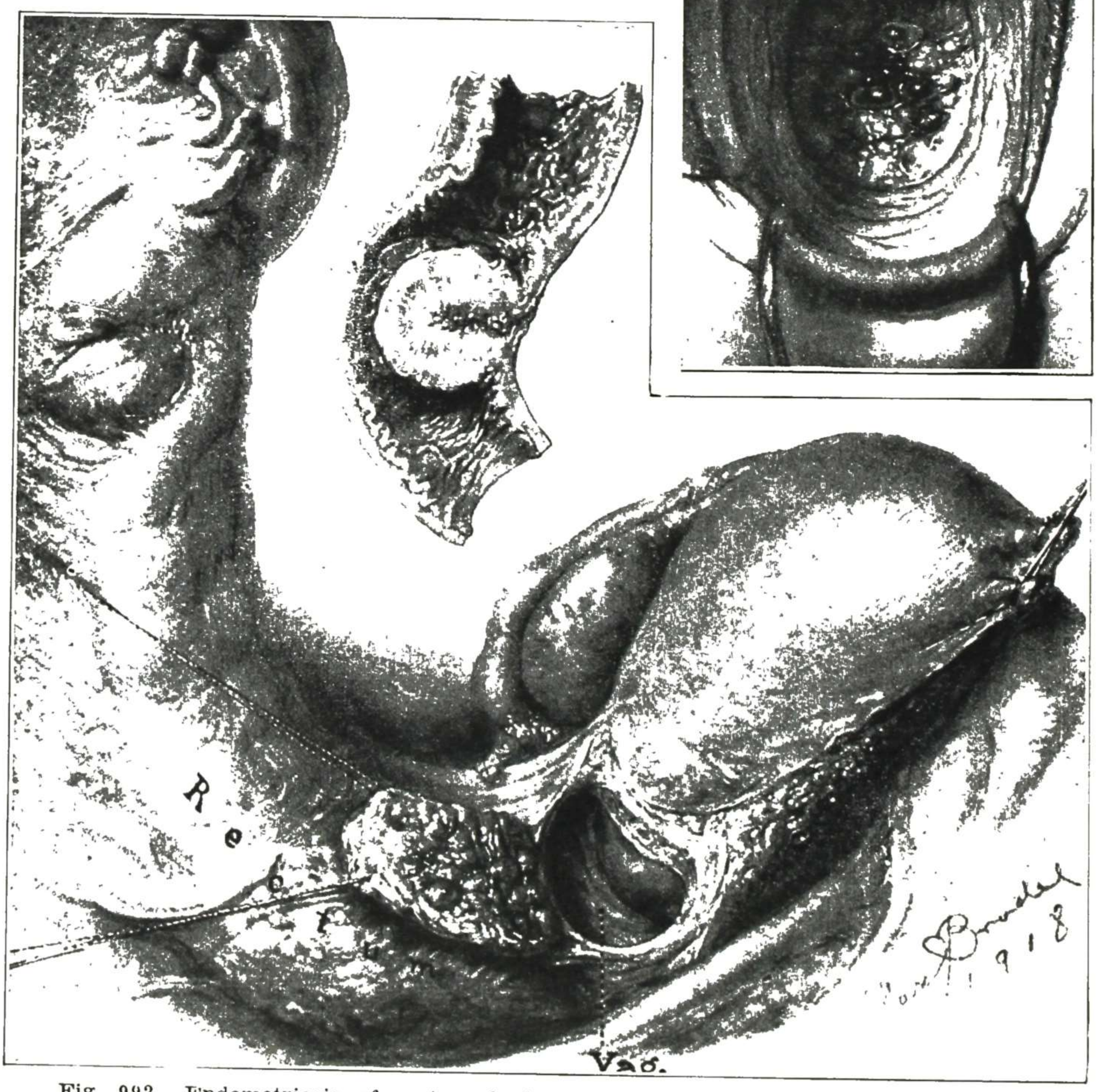


Fig. 992.—Endometriosis of rectovaginal septum, with coincident endometriosis of the sigmoid flexure which almost completely blocked the bowel. The insert at the upper right corner gives an excellent reproduction of the appearance through the vaginal speculum. (Cullen —*Arch. Surg.*)

Sampson does not hold that the transtubal transplantation is the only etiologic factor in endometriosis, but that it is the most important factor in causing the common clinical type. His indefatigable search for factual knowledge of this serious disease has resulted in one of the most comprehensive and helpful and beautifully illustrated studies in the history of medicine.

In a recent paper on the development of the implantation theory for the origin of peritoneal endometriosis he gives the following summary:

> In studying the pathogenesis of ovarian and other forms of peritoneal endometriosis, one must not lose sight of the important role evidently played by patency of the tubes.
>
> At times, during menstruation, blood, carrying bits of Müllerian mucosa, escapes through patent tubes into the peritoneal cavity. This blood may come either from the uterine or from the tubal mucosa. Circumstantial evidence indicates that Müllerian tissue

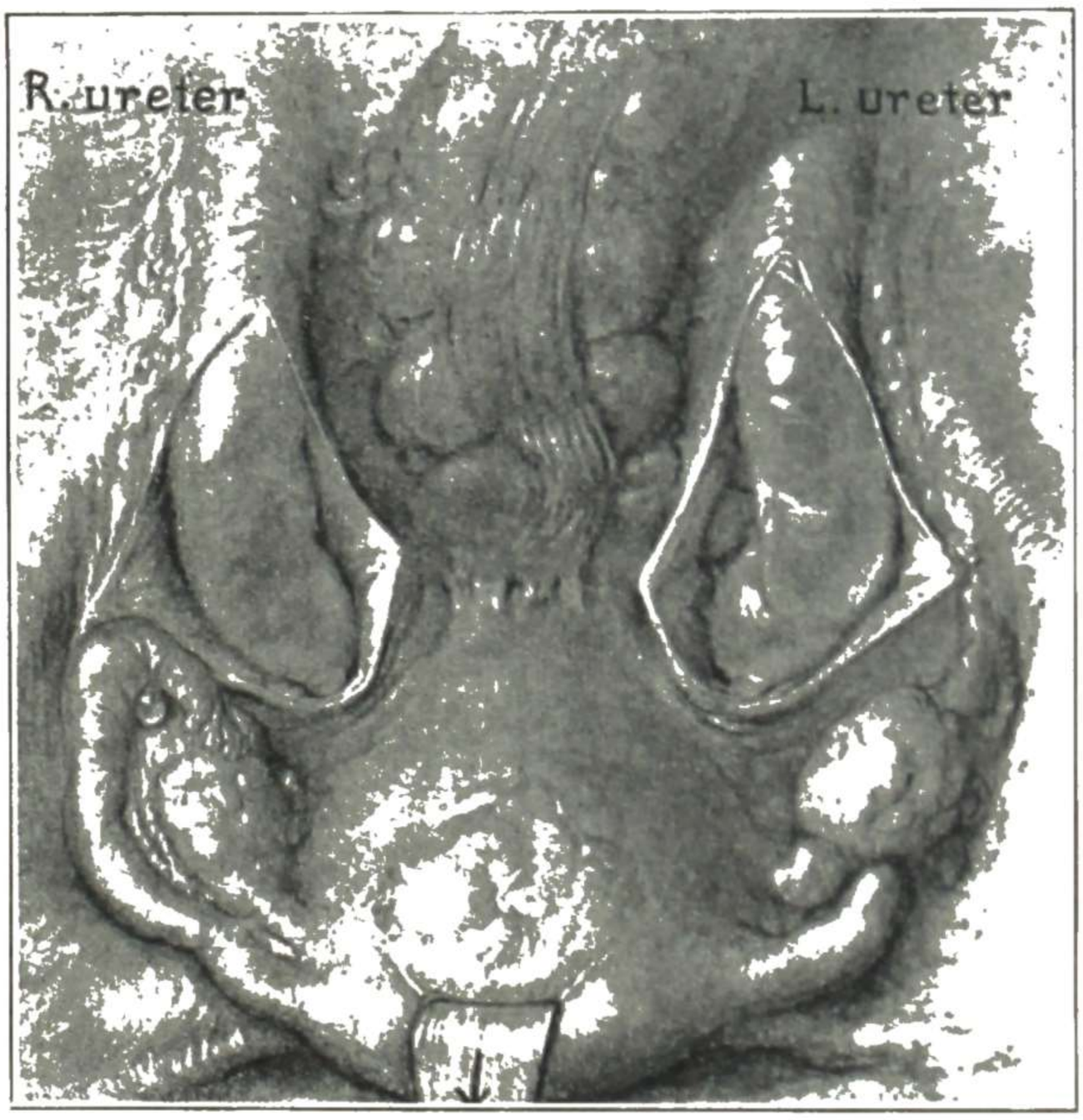


Fig. 993.—Remote results of an endometrial cyst of ovary. Patient aged twenty-five years, suffered at menstruation with pain in rectum and radiating down left thigh to knee. Trouble persisted. At operation, August, 1914, a cyst of the left ovary, size of an orange and filled with old blood, was removed. Some blood free in cavity. (Cyst had evidently perforated long ago with the formation of implantation endometriosis in cul-de-sac.) Some temporary relief from operation, but in February, 1916, polypi appeared at the vaginal vault, connected with an induration in the rectovaginal septum. Polypoid masses were removed but recurred, and microscopic examination showed them to be endometriosis. Operation in November, 1916, revealed the condition shown in the above drawing. The endometriosis of the rectovaginal septum had extended into the parametrium, constricting the ureters until they were both dilated as here shown. Uterus was removed but not all of the rectovaginal growth could be removed. Later, radium treatment. Improvement. July, 1917, patient was doing well, no pain in kidney regions. (Cullen—*Bull. Johns Hopkins Hosp.*)

in this blood, under favorable conditions, becomes implanted on any structure upon which it may lodge. These early primary implants occur most frequently in close proximity to the distal ends of the tubes, such as the lateral and under surfaces of the ovary, the lower portions of the posterior surfaces of the uterus and broad ligaments, and the bottom of the cul-de-sac. They may be present only on the ovary or ovaries, only on the peritoneum, or in both situations. Some of these implants remain small and superficial. The Müllerian mucosa in others invades its host much like implantation carcinoma. When it invades other organs or structures than the ovary, a type of endometriosis arises which both grossly and histologically often closely resembles a direct endometriosis of the uterine wall.

The invasion of the ovary by Müllerian mucosa implanted on its surface and the conditions resulting from it are in many ways similar to those arising from the invasion of the other organs and structures by this tissue except for one very striking difference. The ectopic endometrial cavities distended with menstrual blood in endometriosis, in other situations than the ovary, are usually small while those in the ovary frequently attain a large size, forming the well-known endometrial cysts of that organ. Whether small or large these ovarian cysts often rupture and some of their contents escapes into the peritoneal cavity frequently causing adhesions and additional implantations. In patients with peritoneal endometriosis associated with an endometrial cyst of the ovary, both primary implants from or through the tubes and secondary ones from the cyst may be present.

The study of peritoneal endometriosis also indicates that menstrual blood may not only escape from foci of endometriosis in other situations than the ovary, but adhesions and an additional spread of the endometriosis (secondary implants) may arise from this source. On account of the usual small size of the superficial foci of serosal endometriosis, the results of their participation in menstruation are not as striking as those which take place in the ovarian cysts.

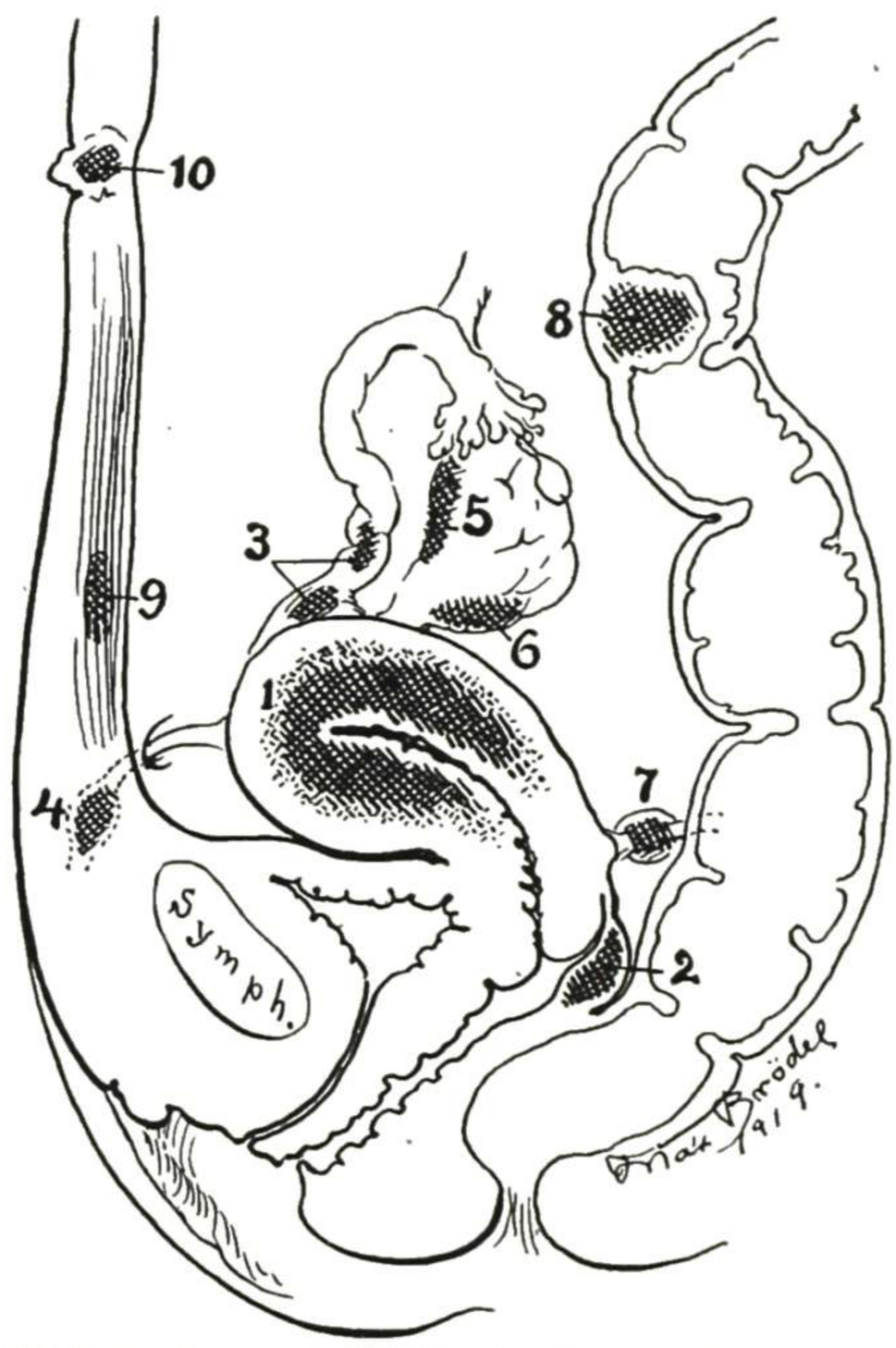


Fig. 994.—Sites at which endometriosis has been found. 1, Uterus; 2, rectovaginal septum; 3, tube; 4, round ligament; 5, ovary; 6, uteroovarian ligament; 7, uterosacral ligament; 8, sigmoid flexure; 9, rectus muscle; 10, umbilicus. As explained at the beginning of the chapter, when endometriosis occurs in a muscular structure, it is called adenomyosis, and if such growth develops in a way to form a distinct tumor it is called an adenomyoma. (Cullen—*Arch. Surg.*)

If bits of Müllerian mucosa carried by menstrual blood escaping into the peritoneal cavity are always dead, the implantation theory, as presented by me, also is dead and should be buried and forgotten. If some of these bits are even occasionally alive, the implantation theory also is alive.

The viability of this theory is of secondary importance to me as compared with the pleasure and the increased knowledge of this and kindred subjects which I have gained in these studies and the resulting more intelligent treatment of patients who have peritoneal endometriosis. There are many other interesting unsolved problems associated with the pathogenesis and life history of endometriosis of all types.

Since the attention of the profession has been drawn to the occurrence of this condition, it has been found to be fairly frequent. This process varies in extent from tiny "spots" on the surface of the ovary to tumors as large as a uterus at the sixth month of pregnancy. Usually these cysts are ruptured in removal, the reason being that the adherent structure comes in time to form a part of the wall of the cavity, and the cavity is necessarily opened when the separation is made. These cysts contain a thick chocolate-colored liquid, hence the term "chocolate cysts."

The epithelium lining these cysts varies a great deal. In some specimens the epithelium is strikingly similar to that of the endometrial glands. These glands are also surrounded by stroma similar to endometrial stroma. In other specimens the epithelium is not at all typical of endometrial glands, and indeed may resemble epithelial cells from any part of the body. Also, the stroma may be very scanty or missing entirely. There is usually evidence of old blood in the cavity and walls of these cysts. Figs. 985 and 986 show typical characteristics of the endometrial cyst. The leaking cyst contents may gravitate to the posterior peritoneal cul-de-sac, where they form strong adhesions and ingrowths, binding the rectum to the posterior surface of the uterus. The various resulting conditions are shown in Figs. 987 to 994.

The dense adhesions to the small intestinal coils and sigmoid and rectum and other structures seriously complicate the operation for removal. The early perforation with adhesions and the chocolate-like contents are the striking clinical features of these cysts, and Sampson designated them as "perforating hemorrhagic cysts" and also as "chocolate cysts." As the essential pathologic feature is the endometrial tissue in the wall, the term "endometrial cyst" has now been widely adopted. As previously mentioned, in many cases the aberrant growth of endometrial tissue is not confined to the ovarian cyst, but spreads to various other structures throughout the pelvis. This condition of widespread growth of aberrant endometrial tissue is appropriately designated "pelvic endometriosis."

Considered clinically pelvic endometriosis constitutes one of the very serious diseases of the childbearing period—serious on account of the recurring pain and disability, and serious because of the complications frequently increasing the danger of operative relief.

A type of endometriosis of particular interest to the surgeon is that due to operative implantation of endometrial cells or to operative creation of an avenue for implantation, as when a tubal stump is left uncovered. The fact that there have been a number of endometriosis lesions clearly due to this cause has a bearing also on the etiology of the other lesions.

Diagnosis.—In the first place, endometriosis is a disease of the age of ovarian activity, for its development and progress are dependent on the same ovarian hormones that cause the normal menstrual changes in the uterine endometrium. As the initial lesions are minute and their progress slow, it probably takes several years for the process to reach the stage of clinical symptoms. Consequently the lesions which have advanced sufficiently to cause pain and disability are found principally in individuals from thirty to forty-five years of age.

The frequency of this disease is rather startling. Sampson found it in 43 per cent of abdominal operations in patients between the ages of thirty and fifty. However, in some of these cases, operated on for other conditions, the endometrial involvement was very slight. In estimating the probable number of individuals with aberrant endometrial tissue in the pelvis, we must consider also the probable large number of persons in whom the involvement is so slight or so quiescent that it does not give rise to symptoms requiring them to consult a physician. Our present knowledge indicates that the smaller lesions are very erratic and uncertain in growth and may remain quiescent indefinitely.

Even with the progressive lesions there may be but few symptoms. It is surprising what extensive adhesions may form without symptomatic disturbance. For example, an ovarian cyst that has given the patient very little discomfort may at operation show extensive and dense adhesions. On the other hand, some patients suffer much pain and disability, the progressive pathologic process giving rise to marked symptoms and examination signs.

The bedside recognition of pelvic endometriosis is not as easy as might be inferred from the clear-cut pathologic changes. The difficulty in diagnosis comes from the fact that, though there may be definite symptoms and examination signs, these same symptoms and signs occur in other more common diseases. Consequently, the more common disease is usually decided on as the diagnosis, and endometriosis is encountered unexpectedly at the operation.

It may be said in a general way that endometriosis gives rise to the symptoms of chronic inflammation, without the infection and pus formation. There is the fixation of structures and induration and tenderness, and usually a definite mass as in inflammation. There is exacerbation of the pain and distress at the menstrual time with subsidence between, as often happens in chronic pelvic inflammation. So closely does the symptomatic picture resemble chronic inflammation, or a tumor with inflammation, that such diagnosis is usually made.

If, however, we forego the hazardous practice of jumping at a diagnosis from one or two prominent symptoms, and take the trouble to make a critical analysis of the features of the clinical picture, we are likely to notice some things about the case that do not fit in with a purely inflammatory condition. Such anomalous symptom or sign arouses suspicion that we are dealing with something more than inflammation or perhaps something entirely different.

The following are the items likely to arouse such suspicion:

1. *Absence of Definite Evidence of Infection.*—As the patient tells her story of pain and disability with fairly comfortable intervals, we naturally think of chronic pelvic inflammation. But when the attempt is made to determine the time of infection and its character, we are not successful. The history gives no definite indication of gonorrheal infection nor of puerperal infection. The objective findings also include nothing that might not be due to non-inflammatory irritation and infiltration. There is no telltale focus of chronic inflammation in the vulvovaginal glands or in Skene's glands or in the cervix. There is nothing in the temperature or leucocyte count definitely indicating infection. We are speaking of uncomplicated endometriosis. Of course, a patient may have infection along with endometriosis, in which case the symptoms of both diseases will be present.

2. *Fixation Without Evident Cause.*—As mentioned under Pathology, fixation of adjacent structures by ingrowths is a marked feature of endometriosis. This may take place so gradually and with so few symptoms that it is encountered as a surprise at the examination. When extensive fixation is found in the pelvis without a history of inflammation or preceding operation, endometriosis is to be suspected.

One very common form of this fixation is adherent retrodisplacement. There may be simply the fixation of the retrodisplaced uterus or there may be also the characteristic infiltration of the cul-de-sac area under the displaced uterus. This infiltration if at all extensive is likely to present a nodular "shotty" feel due to irregular islands of epithelial growth. When the areas of endometrial growth advance to the stage of menstruation, small collections of blood form in them. These feel hard at first but as they become larger or nearer the vaginal surface, their cystic character may be recognized.

Another form of fixation is adherent ovarian cyst. A small or medium ovarian cyst, which should be freely movable in the absence of inflammation, is found adherent, without any history of infection or other adequate cause for the fixation.

3. *Disproportion Between the Pain and the Palpable Lesion.*—This disproportion may be in either direction. As previously mentioned, there may be no pain or history of disability, in spite of the fact that examination shows a marked lesion with extensive fixation. This in itself indicates that the fixation is due to some process different from inflammation.

On the other hand, there may be marked pain and disability, much more than to be expected from chronic inflammation without abscess formation. In endometriosis marked pain is usually due to tension from extrusion of blood into a filled cavity or to peritoneal irritation from leakage. Consequently it presents certain characteristics, which are taken up later.

The important feature here emphasized is that the pain bears no definite relation to the size of the mass, often being very severe with only a small mass. In fact, severe pain has been reported in cases of endometriosis not yet advanced sufficiently to give any palpable mass. On this account, endometriosis is recognized as one of the causes of dysmenorrhea without palpable lesion—the diagnosis depending on the time and character of the pain.

4. *The Time and Character of the Pain.*—Keeping in mind the pathology of the disease, the characteristic feature being a closed sac with menstruating endometrium, the relation of the pain to menstruation becomes clear. It starts with the premenstrual swelling some days before menstruation and continues severe till practically the end of menstruation. The pain from tension of the sac will continue as long as additional blood is being extruded into the sac from the aberrant endometrial tissue lining.

With a chronic inflammatory mass or a tumor, the discomfort is likewise more marked at the menstrual time, but there is a difference in two particulars. First, the pain of ordinary menstrual swelling about an inflammatory mass or tumor usually becomes less as the flow is well established, while the pain of endometriosis is likely to continue severe all through the flow. Again, with ordinary menstrual swelling, the discomfort is only moderate and is diminished by rest and other measures that diminish general pelvic congestion, whereas the pain of endometriosis may be severe in character and persistent in duration in spite of palliative measures.

In cases of obstructive dysmenorrhea from cervical stenosis the pain may be very severe, but it comes only with the onset of the flow and disappears as soon as the flow is well established. Also, it is likely to be more intermittent and cramp-like than the persistent pain of increasing tension in a closed cavity. Again, dysmenorrhea from cervical obstruction usually dates from the first menstruation, whereas that from endometriosis is an acquired dysmenorrhea coming on later.

5. *Miscellaneous Points.*—In regard to the history, sterility, rectal pain, and dyspareunia are of rather frequent occurrence in endometriosis.

The *sterility* may have been absolute or there may have been children years before. Usually several years have elapsed since the last pregnancy. Evidently impregnation is interfered with in endometriosis a long time before the process reaches the stage of pain and disability that calls attention to it.

The incidence of *rectal pain* or pressure discomfort is due of course to the frequent involvement of the cul-de-sac area. When the cul-de-sac endometriosis extends to the connective tissue and the rectal wall, there is very likely to be deep rectal discomfort, off and on, especially at the menstrual time.

Occasionally *dyspareunia* appears, and gradually increases. This pain in coitus is more likely to be present when endometriosis involves the cul-de-sac area, though it may be absent

with extensive involvement of this region. Dyspareunia due to endometriosis appears without any apparent cause, such, for example, as infection. It is usually slight at first and increases gradually with the increasing infiltration and fixation of the tissues about the cervix. It is likely to vary considerably at different times, being most marked usually near menstruation.

In addition to the special points in the history there are also certain special examination findings that are frequently associated with endometriosis.

Cul-de-sac infiltration, causing palpable induration of the vaginal wall just back of the cervix, is a distinctive feature in certain cases of endometriosis. Involvement of the vaginal wall in this situation in the childbearing period is nearly always due to pelvic endometriosis or to inflammation. Consequently if infection can be excluded, endometriosis becomes probable. This probability is increased if there is evidence of endometrial involvement higher in the pelvis. In some cases the process in the posterior vaginal wall goes on to the formation of distinct "shotty" nodules. If these approach the surface so that the bluish color of the contained blood can be seen in the speculum examination (Figs. 991, 992), the diagnosis becomes positive.

Retrodisplacement of the uterus is found in a large proportion of cases of endometriosis. This may be because retrodisplacement favors the development of endometriosis or because endometriosis adhesions tend to pull the uterus into backward position. Perhaps both factors enter into the matter—the first in some cases and the second in other cases. At any rate, adherent retrodisplacement is found so frequently in endometriosis that that disease is to be suspected, especially if there is no history of infection to account for the fixation of the displaced uterus.

Fibroid tumor in the uterus is a common finding. Such a nodule may be an ordinary encapsulated myoma or it may be an adenomyoma. Endometriosis is to be suspected in any case of small uterine myoma with marked fixation without a history of infection.

An *associated endometrioma* of the umbilicus or of the inguinal region or in an abdominal-operation scar indicates the nature of the process going on deeper in the pelvis.

Occasionally *cystoscopic* examination will show the characteristic small blood cysts in the bladder wall. Such an examination is especially helpful in differentiating between endometrial infiltration and carcinomatous infiltration in patients approaching the menopause.

Proctoscopic examination is useful in patients with perirectal involvement. The induration from involvement of the culdesac and rectovaginal septum may bring up the question of carcinoma of rectal origin. In endometriosis proctoscopic examination will show normal rectal mucosa, except where the hemorrhagic cystic process has extended through the rectal wall.

In addition to differentiation from ordinary chronic inflammation, pelvic endometriosis must be differentiated from a tumor with complicating inflammation, from pelvic tuberculosis, and from ectopic gestation.

Treatment.—The treatment of pelvic endometriosis is based on the general principles of treatment of nonmalignant conditions—that is, conservative treatment when that gives sufficient relief, and radical treatment if serious symptoms persist. Minor degrees of endometriosis may pass unnoticed or give rise to only moderate dysmenorrhea relieved by sedatives. Hirst reports that large dosage of testosterone gave decided improvement, even to reduction in size of troublesome masses. The radical measures available are operation and irradiation.

Operation.—A mass in the pelvis causing persistent pain and disability in spite of conservative measures should ordinarily be removed, whether it is endometriosis or chronic inflammation or a new growth. Usually there is some question as to the exact nature of the mass until the abdomen is opened and the diseased area subjected to inspection and direct palpation.

The most important points to settle before deciding on operative treatment are: first, that there is a definite pathologic process not sufficiently relieved by palliative measures, and second, that the persisting pain and disability are serious enough to warrant the risk of an operation. In such a case if the patient is in good general condition, operative removal of the enlarging mass should be carried out promptly before some local or general complication increases the hazard.

Endometriosis is dependent on ovarian activity, and ablation of ovarian influence ordinarily stops the process. Then why not eliminate ovarian activity by irradiation (radium or x-ray), instead of subjecting the patient to operation? Operation is ordinarily better than irradiation for three reasons: first, to preserve ovarian activity if possible; second, to eliminate malignancy; and, third, to eliminate a mass causing pressure disturbance.

Preservation of Ovarian Influence.—In the childbearing period it is important to preserve ovarian activity. Though the condition appears to be endometriosis, it may be found at operation to be chronic inflammation or ectopic gestation or a new growth, any one of which could be removed and leave ovarian influence intact.

Even if the pathologic process proves to be endometriosis, it may be limited to structures that can be removed and still preserve ovarian tissue. An involved corpus uteri may be removed by supravaginal hysterectomy. Endometrial ovarian cysts can sometimes be removed with preservation of an uninvolved portion of an ovary. In a patient under thirty-five years of age it is worth some risk to preserve ovarian influence for the several years still remaining before the natural menopause. If the small areas of endometriosis left at such operation should show serious activity later, the ovarian influence may then be eliminated by irradiation.

Elimination of Malignancy.—This indication for operation assumes importance in patients approaching the age of forty. There is necessarily some uncertainty as to the nature of the process going on in the mass. The supposed endometriosis mass may be malignant, either primarily or as a later complication. In either case it is advisable that positive knowledge be acquired promptly, and also that the tumor be removed if practicable.

Elimination of Mass.—In well-marked endometriosis there is usually a mass causing pressure disturbance. It may be in the form of an ovarian cyst or it may be a uterus enlarged by adenomyoma. In either case the abnormal structure is likely to cause troublesome symptoms as long as it remains, hence the preferable plan of treatment is ordinarily that which removes the mass.

Irradiation Treatment.—Irradiation by radium or x-ray stops ovarian function and thus checks the recurring menstrual exacerbation and progress of the endometriosis. It does not remove the ovarian cyst or other mass, which in itself may keep up discomfort and disability. However, irradiation may be useful in the following two classes of cases.

Poor Operative Risk.—In a person seriously handicapped from the operative standpoint, irradiation may be used to check the increasing pain and disability from endometriosis. This applies especially of course to patients approaching the menopause, in whom the continuation of ovarian activity is not so important as in earlier life.

The preferable form of irradiation to employ depends on the particular conditions present. When the endometriosis is principally in the uterine wall (adenomyoma) a radium application within the uterus is the best plan, because concentrated irradiation is given at the seat of the process and without the extensive intestinal irradiation occasioned by x-ray. Also, radium application in the uterus works in well with diagnostic curettage which is needed to exclude malignancy and which may be carried out at the same time. On the other hand, if the endometriosis is scattered widely in the pelvis and unaccompanied by uterine bleeding indicating curettage, deep x-ray therapy is the preferable form of irradiation.

Irradiation treatment is employed on a tentative basis. It may give sufficient relief in a case of endometriosis, and it may not. Also, the possibility of an error in diagnosis is to be kept in mind, and if satisfactory result is not secured by irradiation in a reasonable time, operation is again to be considered.

Postoperative Activity.—When activity persists in an area of endometriosis after operation, irradiation treatment is to be employed. In some cases where it was thought best to leave an ovary, there may be new development of endometriosis or renewed activity in some small area left. Occasionally there is persistent activity even when both ovaries have been removed along with the endometrial cysts. In either case irradiation treatment is to be employed.

The following is a case in point. A patient, aged forty-six years, was sent to us by a general surgeon on account of uterine bleeding and an increasing pelvic mass which appeared some months after an abdominal operation which he had performed for her. Both the patient and the surgeon were considerably alarmed on account of the possibility of malignancy. The operation, four months before, was appendectomy and removal of an ovarian chocolate cyst with preservation of the other ovary. The patient recovered without disturbance and had two normal menstruations, and then the bleeding started.

Examination showed a firm, fixed mass the size of a small fist occupying the central pelvis. The mass seemed to be mostly enlarged uterus with surrounding adhesions. A diagnosis of endometriosis with adenomyoma of the uterus was made, and we decided on radium treatment for the adenomyoma with curettage to exclude malignancy. This treatment stopped all ovarian activity, and later the enlarged uterus diminished in size considerably.

In other cases of postoperative activity, with predominating peritoneal and connective tissue involvement instead of uterine, x-ray treatment was the form of irradiation used to stop the advancing endometriosis.

Special Dangers.—Experience has shown that operation for pelvic endometriosis carries certain special dangers. These dangers are due to the extensive dense adhesions caused by the unusual process. These adhesions are not simple agglutination of surfaces, as in inflammation, but real tissue ingrowths into the walls of adjacent structures, such as small intestine, sigmoid, and rectum. The two special dangers are, first, a tear into the bowel and, second, postoperative intestinal paralysis and peritonitis.

Injury to Bowel.—In endometriosis the adherent walls are fused by tissue growth and cannot be separated easily, as can inflammatory adhesions. Any attempt to separate them carries danger of a tear into the intestinal tract. This fact must be kept in mind in trying to enucleate the mass to be removed. Rough or hurried separation by palpation only is to be avoided, as the line of cleavage may extend into the bowel lumen. Dense adhesions should be carefully separated under sight as well as touch, and the line of separation should not be allowed to encroach on the intestinal wall.

It is important also to limit the separation as much as possible, breaking adhesions only where necessary to allow safe removal of the abnormal mass. The cyst wall should be removed as far as practicable, especially the endometrial lining. It is permissible to leave some of the outer layer of the cyst wall, if necessary for the safety of the intestine or other attached organ.

In cases requiring removal of the uterus, the adherent rectum can usually be separated down far enough to permit supravaginal hysterectomy. An attempt to separate dense adhesions in the cul-de-sac sufficiently low to allow complete hysterectomy may cause a tear into the rectum. It is safer as a rule to leave the cul-de-sac adhesions and the cervix. If there should be a complicating cervicitis that persists, the cervix may be coned later from below.

Postoperative Peritonitis.—Another serious problem presented by these cases of endometriosis is to get the patient through the postoperative stage without intestinal paralysis and peritonitis. Just what factor it is that makes these patients so prone to postoperative intestinal paralysis and peritonitis is not altogether clear, for there is no primary infection. A plausible theory is that the extensive damage to the intestinal walls first interferes with peristalsis, causing postoperative intestinal paralysis, and second, favors escape of colon bacilli into the damaged area, causing peritonitis. Whatever the cause, the tendency to fatal postoperative peritonitis is painfully evident to those engaged in treating these pa-

tients. Several trying experiences in the handling of these cases convinced us that this disease constitutes one of the most serious pelvic conditions for which operation is required in the childbearing period.

The first of these experiences is recalled vividly because of the many days of anxiety before the patient was past the acute danger, and also because of the difficulty encountered later in closing the intestinal opening which had been made for drainage during the intestinal paralysis. At the primary operation typical endometriosis was found, with dense adhesions and the "chocolate" contents leaking from the cyst. There was no pus and no evidence of infection, consequently no drainage was employed, the abdominal wound being closed entirely as in all noninfected cases. In the next few days the patient developed intestinal paralysis with persistent reverse peristalsis and fecal vomiting. This was finally overcome by opening the distended intestine and draining away the contents. This maneuver permitted use of the stomach and upper intestine for purposes of nourishment. The postoperative course constituted a long hard siege, but the patient survived the acute symptoms and the intestinal tract finally resumed its normal function. Then came the problem of closing the large artificial fistula remaining from the intestinal drainage. This proved difficult but was finally accomplished, and the patient eventually made a complete recovery.

In the second experience a young married woman, in good general health, had a painful pelvic mass requiring operation. The operation revealed bilateral ovarian cysts with extensive adhesions and "chocolate" contents. There was no pus and no evidence of infection. The cysts were enucleated, and the abdomen was closed as usual. After operation intestinal paralysis and a low-grade peritonitis developed. The peritonitis increased, an acute nephritis developed, the patient went from bad to worse, and finally died in spite of peritoneal drainage and intestinal drainage and everything else that was done.

In studying over these two experiences the decision was reached to drain all cases of extensive endometriosis or of extensive adhesions suspicious of endometriosis, and this plan has been followed since with satisfaction. The results have been so uniformly good that since adopting drainage these cases are not dreaded, as they formerly were.

Not long after adopting the drainage rule in these cases, the senior author was called hurriedly one night to a hospital to see in consultation a patient who was then dying of peritonitis. A young married woman of prominent family had been subjected to operation for a troublesome pelvic mass. No pus was found and after the intra-abdominal work was finished the abdomen was closed with expectation of prompt recovery. The development of fatal peritonitis was a great surprise and shock to all concerned. Inquiry revealed that extensive dense adhesions were encountered in the operation and also some cysts having typical "chocolate" contents.

In another instance, happening to meet a colleague in one of the hospitals, he inquired abruptly, "Do you drain in all cases of endometriosis?" On replying, "In all cases of any extent," he stated, "I wish I had," and then related the details of a case of endometriosis in which the patient had just died of postoperative peritonitis.

CHANGES DEPENDENT ON ENDOCRINE DISTURBANCE IN DISTANT ORGANS

Occasionally marked changes in the structure of the ovary are brought about by altered endocrine activity in a distant organ or by a growth in the distant organ causing an upset in the normal endocrine balance. There are two main types of such changes found in the ovary: the theca-lutein cysts and follicular atrophy.

Theca-Lutein Cysts

Etiology.—It is now well known that hydatidiform mole, chorioepithelioma, or adenoma of the pituitary can cause marked enlargement of the ovaries, due to the formation of multiple theca-lutein cysts. Excess of anterior pituitary hormone is the fundamental cause.

The immediate treatment, when the diagnosis is positive, is interruption of the abnormal pregnancy by emptying the uterus. The elimination of the pathologic process in the uterus may cause the ovarian cysts to subside and the ovaries to return to normal. If a chorioepithelioma is found, a complete hysterectomy and bilateral salpingo-oophorectomy followed by deep x-ray therapy is indicated as explained in Chapter IX.

Follicular Atrophy

This condition may be secondary to hyperplasia or adenoma of the adrenal cortex, basophilic adenoma of the hypophysis, or pineal tumor. The exact mechanism causing the serious ovarian changes is still under discussion. Cushing

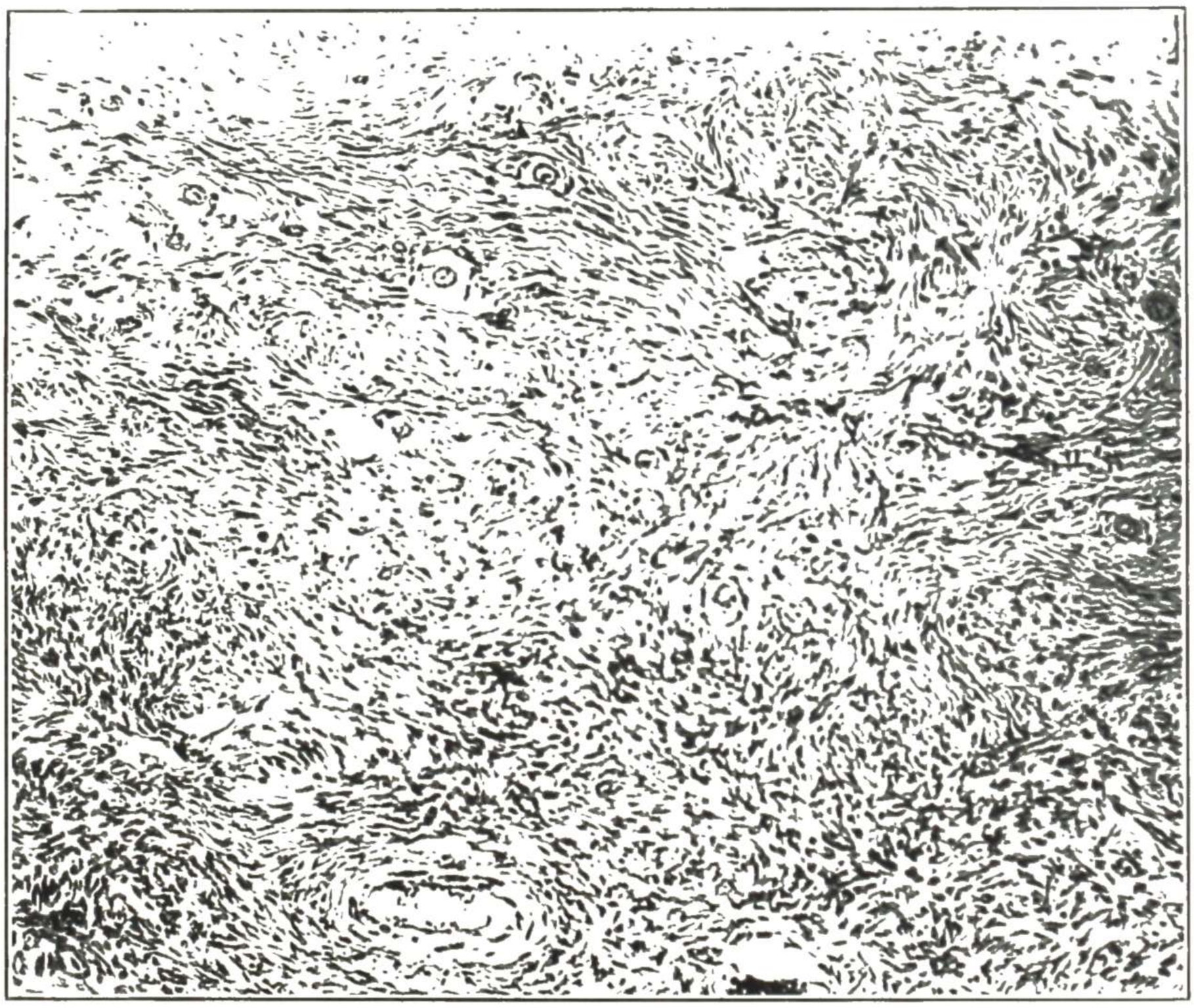


Fig. 996.—Atrophy of the follicular apparatus of the ovary due to hyperplasia of the adrenal cortex. Patient, aged nineteen years, had had amenorrhea for six months and was developing masculinity. Compare this atrophic follicular zone with the same area in a normal ovary (Fig. 10). The facial hirsutism in this case is shown in Fig. 997. Gyn. Lab.

felt that they are caused by the primary altered function of the pituitary due to the tumor composed of functioning basophile cells. Goldzieher and Koster, in discussing adrenal conditions, feel that in many of the cases the primary condition is one of adrenal hyperplasia or tumor. It is well known that basophilic adenomas are associated with marked hyperplasia of the adrenal as well as with hyperplasia of other endocrine organs, but whether the pituitary is the primary cause of the changes found has been questioned by many. An interesting discussion of various points is given under "Dyspituitarism" by Cushing, in the Harvey Lectures of 1932-1933, and under "Adrenals" by Goldzieher and Koster.

Novak reports extreme atrophy of the ovary with disappearance of the follicular apparatus in a case of adrenal cortex hypernephroma. In one of our cases of amenorrhea and developing masculinity, there was adrenal cortex hyperplasia. The ovaries were somewhat enlarged with atretic follicular cysts, but the microscopic picture (Fig. 996) indicated serious disturbance of the follicular apparatus tending toward destruction. Compare this dense ovarian

Fig. 997.—Hypertrichosis on the face in a patient of ours who had a hyperplasia of the adrenal cortex.

Fig. 998.—Extreme facial hirsutism in a case of female pseudohermaphroditism due to adrenal cortical hyperplasia, as was later demonstrated by autopsy. (Novak—*Am. J. Obst & Gynec.*)

cortex, showing only a few remnants of the follicular apparatus, with the normal ovarian cortex of childhood in Fig. 10, showing the usual abundance of functionating elements. The clinical symptoms corresponded with the follicular atrophy. The menstrual flow had gradually diminished, and had been entirely absent for the last six months. There were definite developments toward masculinity, consisting of appearance of hair generally, pubic hair extending upward toward umbilicus, hair on the face (Fig. 997), and hypertrophy of the clitoris toward the male type of glans. Fig. 998 shows very marked facial hirsutism in a case of adrenal hyperplasia.

OTHER BENIGN GROWTHS

Under this heading are grouped the proliferating cystadenomas (pseudomucinous and serous) and the simple solid tumors—fibroma and myoma.

PROLIFERATING CYSTS

Proliferating cysts are the ovarian tumors which attain such a large size. This is the form of growth ordinarily referred to when an "ovarian cyst" or "ovarian tumor" is spoken of.

The term "proliferating" is given to these growths because they have the faculty of generating new cysts within the original cyst or on the outside of it. They increase in size persistently, and there is no means of stopping their growth, except removal.

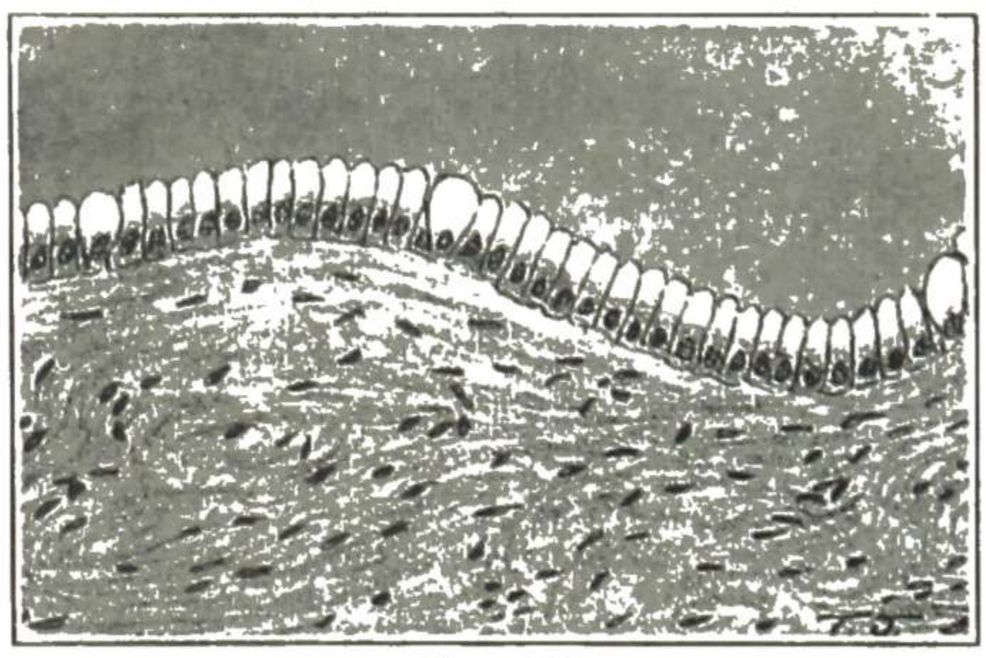


Fig. 999.

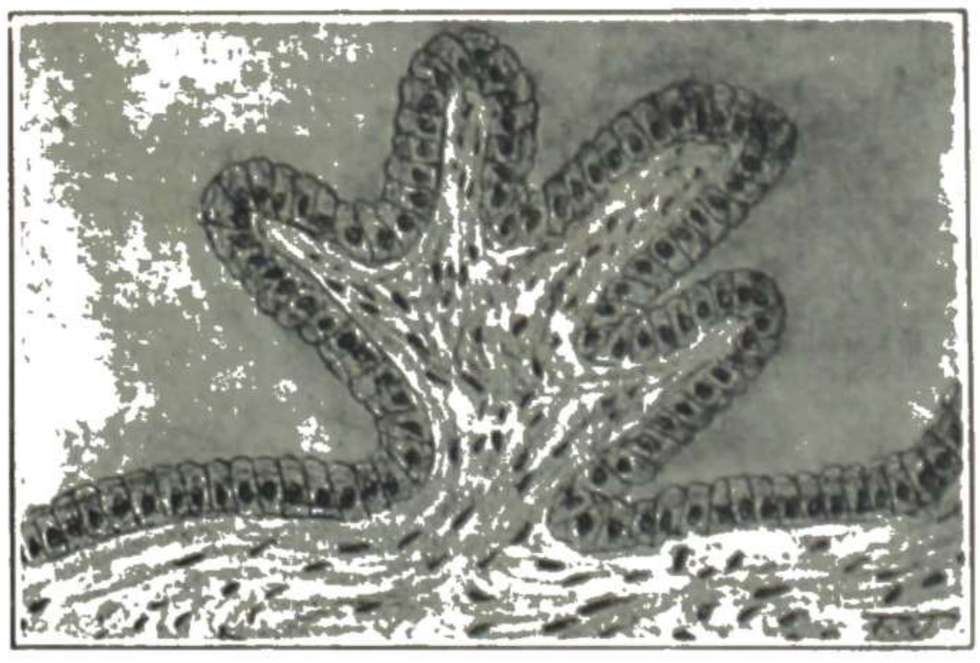


Fig. 1000.

Figs. 999 and 1000.—Indicating the difference between the cells lining a pseudomucinous cyst (Fig. 999) and those lining a serous cyst (Fig. 1000), as explained in the text. Columnar cells, nonciliated containing pseudomucin. Goblet cell present.

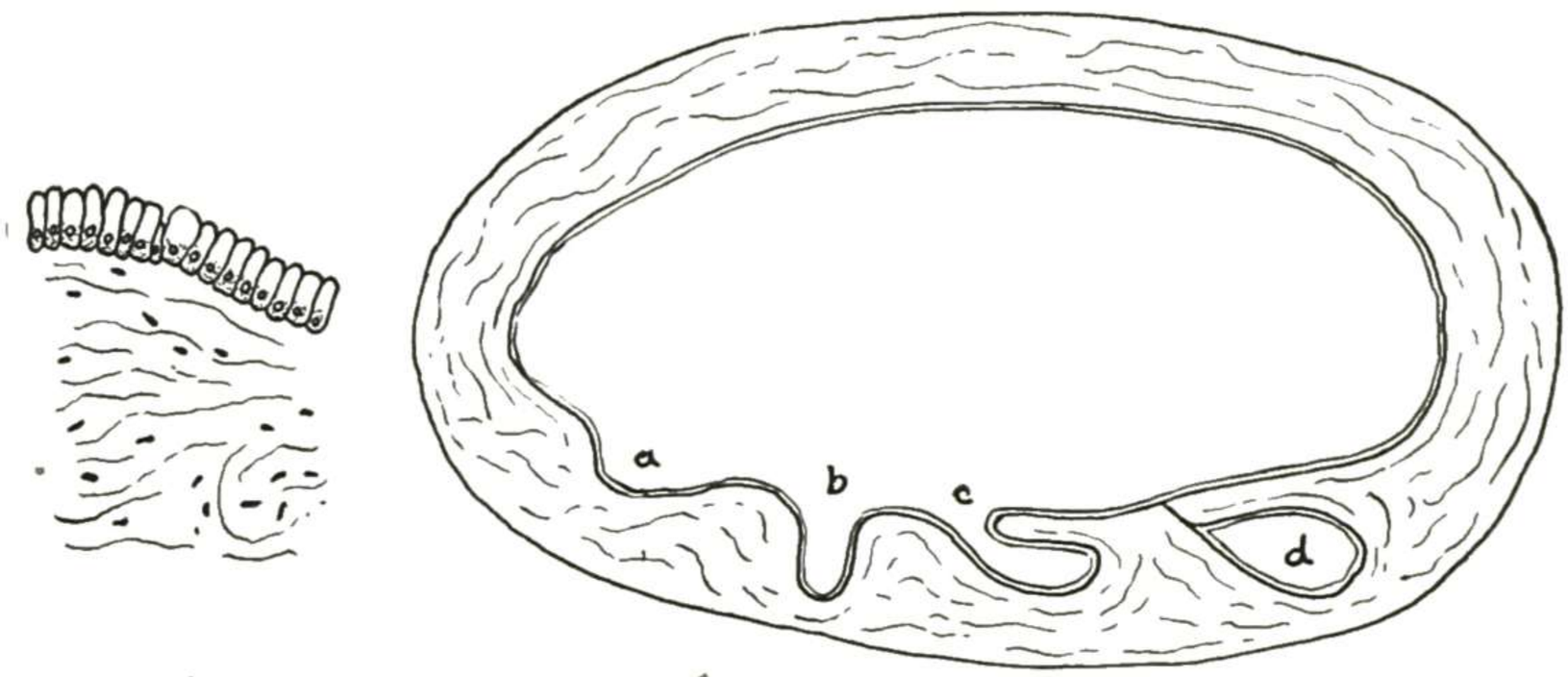
Pathology

The proliferating cysts, or cystadenomas, are of two kinds—the pseudomucinous and the serous.

Pseudomucinous Cystadenomas.—This form of tumor is known also as "paramucinous cystadenoma" and as "cystadenoma evertens." In these cysts the contents consist of a jellylike material which is secreted by the epithelial cells lining the cyst. This gelatinous material is the distinguishing characteristic of the pseudomucinous cystadenoma (Figs. 999 to 1003). On chemical examination it shows the reaction for paramucin or pseudomucin (not precipitated by acetic acid, but precipitated by alcohol as delicate threads, which

are insoluble in water; mucin is precipitated by acetic acid, and albumin is precipitated by heat). The color of this gelatinous material depends on the amount of blood coloring which has diffused through it from hemorrhage into the cyst, as explained later.

As the contents are formed by the secretion of the cells lining the cyst, there is a constant increase in the amount, and this causes constant internal pressure, which keeps the wall of the cyst tense. In this way the epithelial layer is kept spread out and does not usually pile up along the wall in the form of papillary projections. Rather the pressure tends to depress portions of the wall, and as the epithelial cells multiply they are pushed farther out in the wall in the form of glandlike depressions, hence the name "evertens." The depressions may become occluded at the neck and are thus cut off from the main cavity forming secondary cysts (Fig. 1001). These secondary cysts are found in great numbers about the primary cyst and occasionally one or more of the secondary cysts may become as large as the primary one.



A. *B.*

Fig. 1001.—*A*, High power microscopic field showing the type of cells lining a pseudomucinous cyst. *B*, Illustrates the process by which secondary cysts are formed. (Crossen and Crossen—*Synopsis of Gynecology.*)

The rule that pseudomucinous cysts are evertent is not absolute. In nearly all such cysts there are a few insignificant epithelial ingrowths, and in rare cases these growths may predominate, giving a distinct character to the growth (pseudomucinous cystadenoma invertens). Such atypical pseudomucinous cysts are nearly always small, indicating that there was not much internal pressure.

The tumor is usually multilocular, appearing as a collection of cysts, with a smooth, firm, glistening surface. If the wall is thick, the surface is white. If the wall is thin and translucent, the color of the fluid within can be seen shining through. The cut surface of the cyst wall shows numerous intramural cysts of varying sizes. Spurs and septa are frequently seen and represent the remains of adjacent cysts.

This is the most frequent ovarian neoplasm, comprising, according to the statistics of Pfannenstiel, 75 per cent of all ovarian tumors. It is unilateral in from 80 to 90 per cent of the cases.

These pseudomucinous cysts may grow to a very large size. Lynch gives an interesting compilation of "Mammoth Ovarian Tumors" in his monograph on *Pelvic Neoplasms.* In his review of the literature, he found 103 tumors weighing between 100 and 200 pounds, 9 between 200 and 300 and one, re-

ported by Spohn of Texas, weighing 328 pounds. No standard method of estimating the weight of these tumors has been followed. In the case reported by R. J. Crossen (Fig. 1004) the patient was weighed immediately before and after operation, which seems to be the most accurate of the reported methods of arriving at the weight of the tumor.

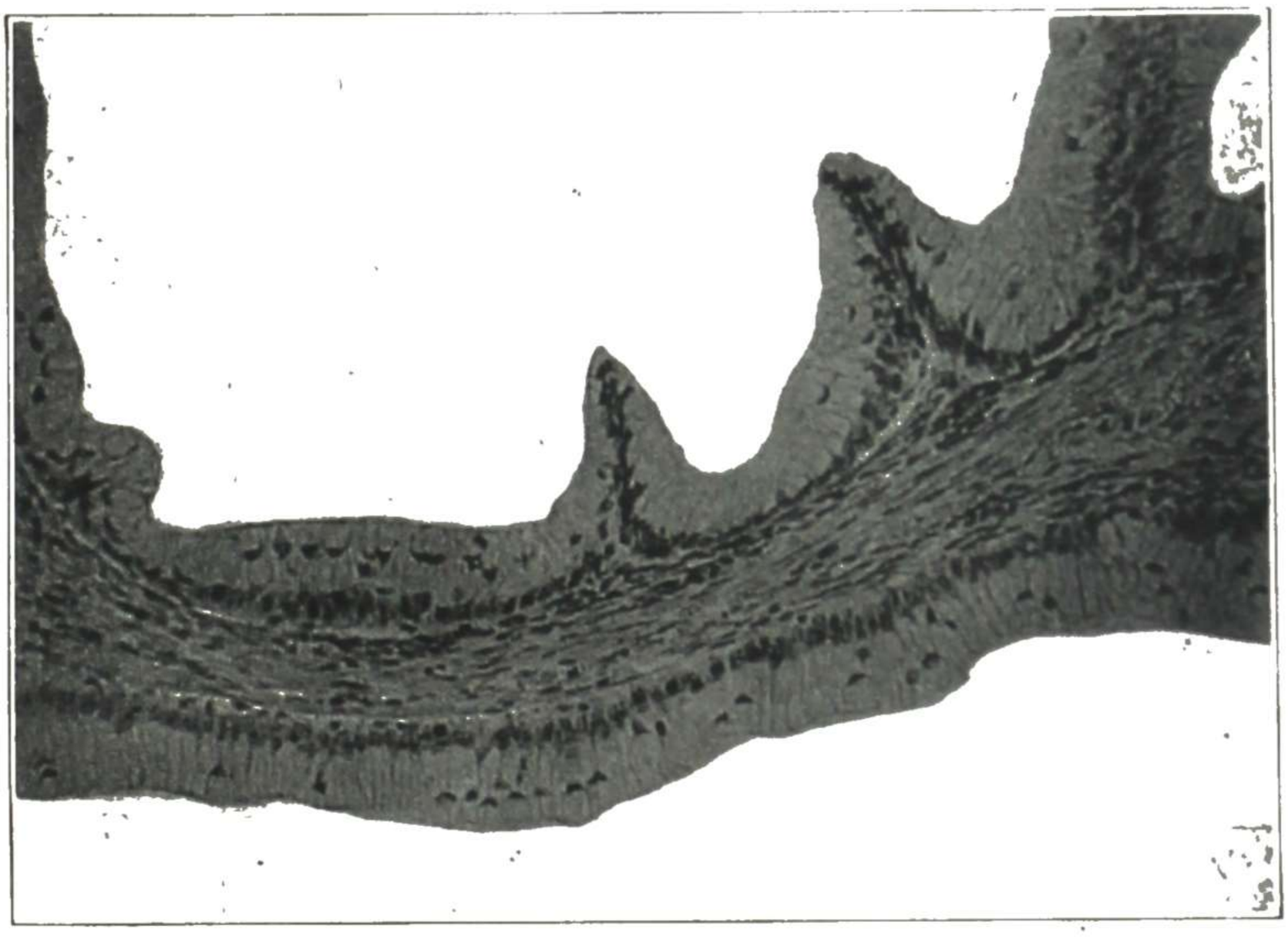


Fig. 1002.—Pseudomucinous cyst of ovary, high power, showing the typical cells lining a pseudomucinous cyst. Notice that the cells are very long, stain only lightly on account of the pseudomucin, and the nucleus is placed at the base. Gyn. Lab.

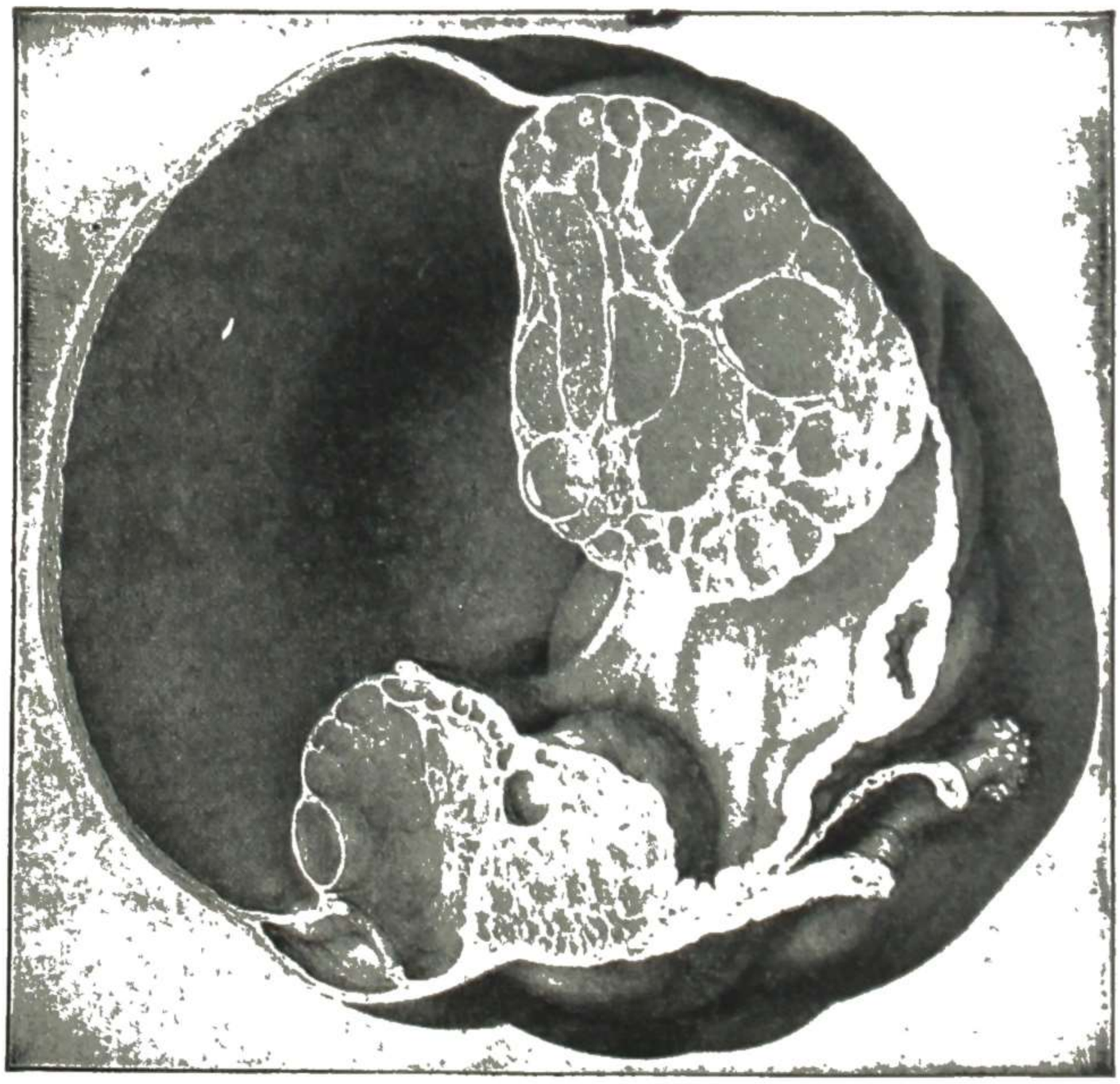
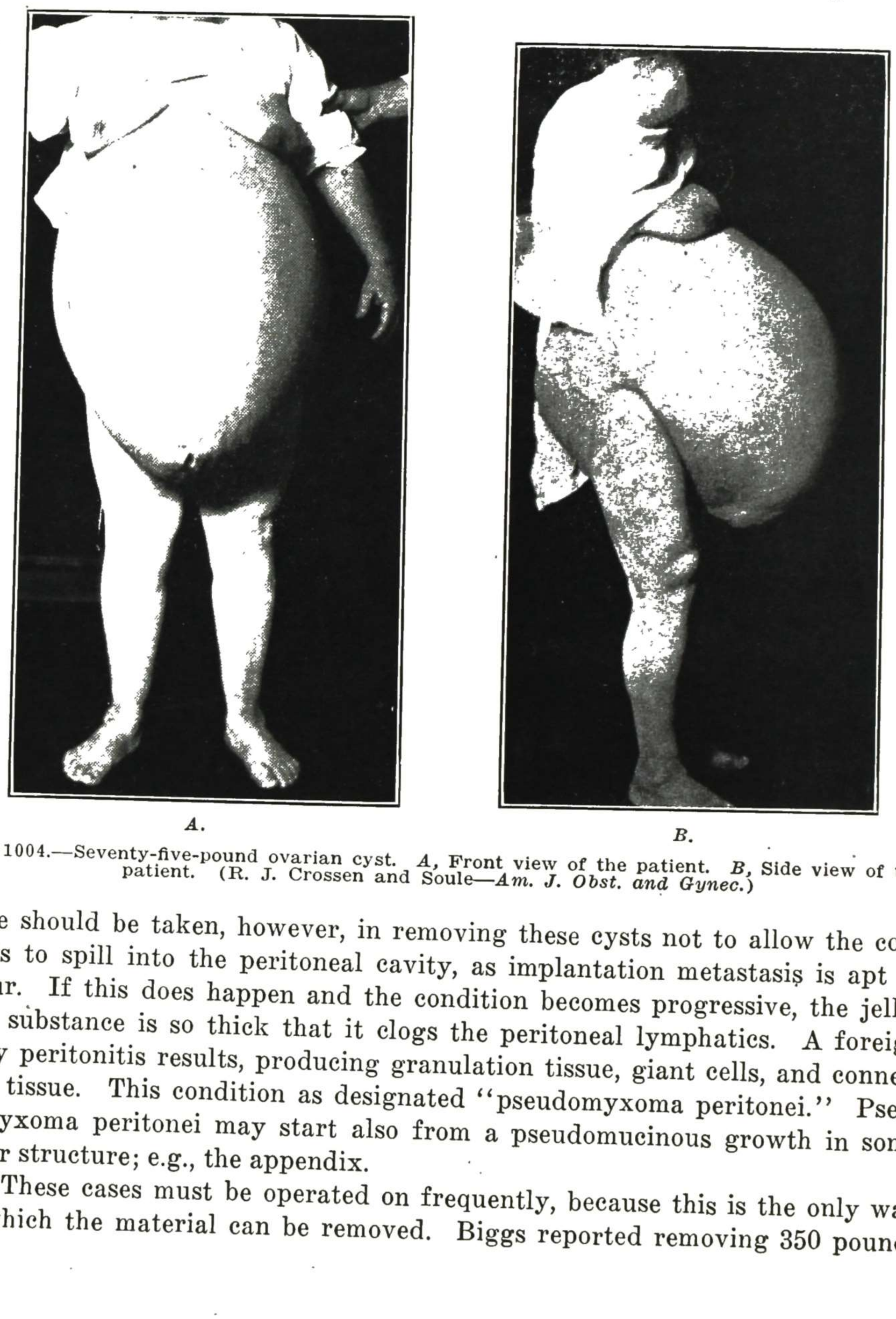


Fig. 1003.—A pseudomucinous cystadenoma of the ovary. Notice the development of secondary cysts in the wall of the large cyst. (Kelly—*Operative Gynecology.*)

Microscopic.—The walls of the cysts usually contain three layers—an outer fibrous layer, a middle layer of more cellular fibrous tissue, and an epithelial lining. The lining consists of high cylindrical cells containing a basal nucleus (Figs. 999 and 1002) similar to those lining the cervical canal but devoid of cilia. If there is marked intracystic pressure, these cells are flattened. The cells are in a single layer. Goblet cells are commonly found. Numerous small cysts are seen microscopically.

Implantation Recurrences.—These cysts are nonmalignant. Of course a complicating malignancy may develop in the cyst, but fortunately this is not common. Cures after complete removal of these cysts are close to 98 per cent.



A. *B.*

Fig. 1004.—Seventy-five-pound ovarian cyst. *A*, Front view of the patient. *B*, Side view of the patient. (R. J. Crossen and Soule—*Am. J. Obst. and Gynec.*)

Care should be taken, however, in removing these cysts not to allow the contents to spill into the peritoneal cavity, as implantation metastasis is apt to occur. If this does happen and the condition becomes progressive, the jelly-like substance is so thick that it clogs the peritoneal lymphatics. A foreign body peritonitis results, producing granulation tissue, giant cells, and connective tissue. This condition as designated "pseudomyxoma peritonei." Pseudomyxoma peritonei may start also from a pseudomucinous growth in some other structure; e.g., the appendix.

These cases must be operated on frequently, because this is the only way in which the material can be removed. Biggs reported removing 350 pounds

of this material in twelve operations over a period of nine years before death claimed the patient at seventy-five years of age. Death is usually due to mechanical interference in the abdominal cavity and adjacent tissues.

Etiology.—While the origin is not clear, it is possible that pseudomucinous cystadenomas arise from early cell-rests with intestinal-cell potentialities. Selma, in discussing ovarian tumors arising from embryonic rests states:

"Ribbert first advanced the theory that pseudomucinous cystadenomas are of teratomatous origin, with cells of intestinal anlage being the only ones to develop. This brings a very large group of tumors into the class of teratomas.

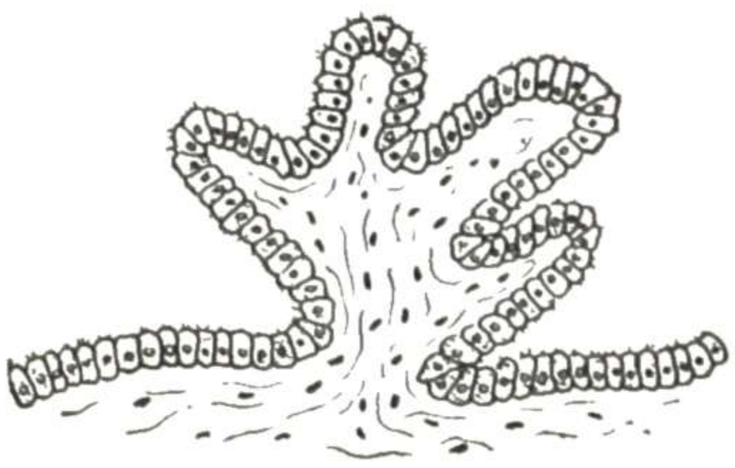


Fig. 1005.

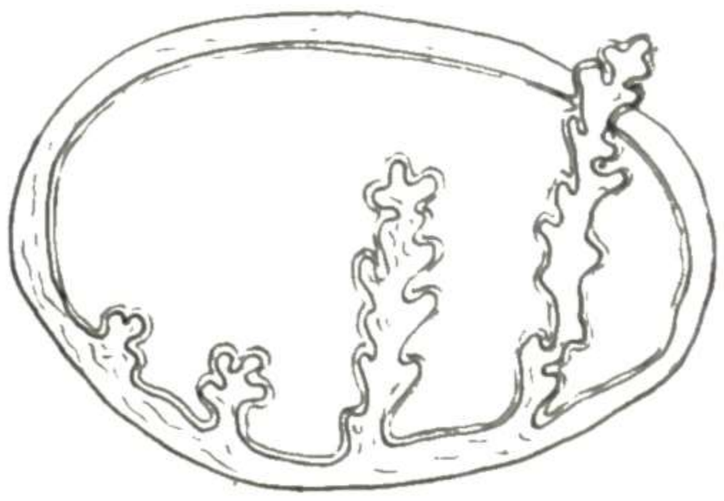


Fig. 1006.

Fig. 1005.—High power field of papillary projection showing ciliated, cuboidal cells.

Fig. 1006.—On right, papillary projections in cyst. (Crossen and Crossen—*Synopsis of Gynecology.*)

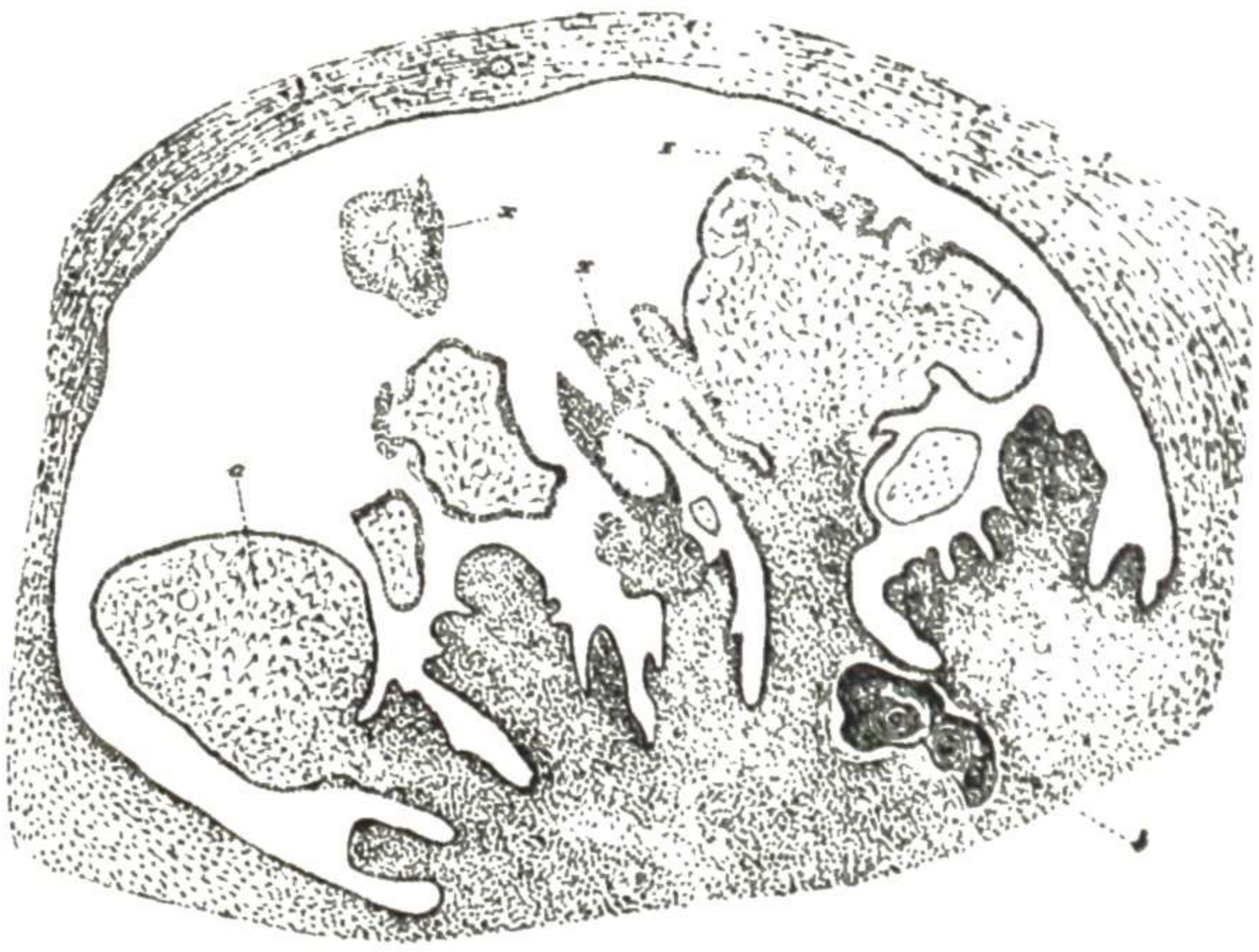


Fig. 1007.—A papillary cystadenoma of the ovary. The papillary projections within the cyst grow to the opposite wall and then penetrate it. (Pfannenstiel—*Veit's Handbuch.*)

In favor of his view is the fact that pseudomucinous cystadenomas have an epithelium strikingly similar to that of the intestine. Second, they occur frequently in association with the usual type of dermoid or teratoma. Third, the origin of pseudomucinous cystadenomas is not from the invaginations of the germinal epithelium, as has been shown for serous cystadenomas."

Additional items pointing in this direction are (a) that similar tumors occasionally originate from the intestine and (b) that similar cell growths are found at times in Brenner tumors. Proescher and Rosasco and also Novak discuss the relation of Walthard's cell islands to Brenner tumors and pseudomucinous cysts (see quotations under Brenner Tumors).

Serous Cystadenomas.—This form of tumor is known also as "papillary cyst" and as "cystadenoma invertens." The contents of the serous cyst par-

take of the nature of serum and do not present the gelatinous character of that of the pseudomucinous variety. On chemical examination, the contents show a large amount of albumin and no pseudomucin. The contents of the serous cysts, like those of the other variety, may vary much in color and consistency—this variation being due to the amount of hemorrhage into the cyst. The cells apparently have no secretion, and consequently there is no marked intracystic pressure as there is in the pseudomucinous cyst. On account of

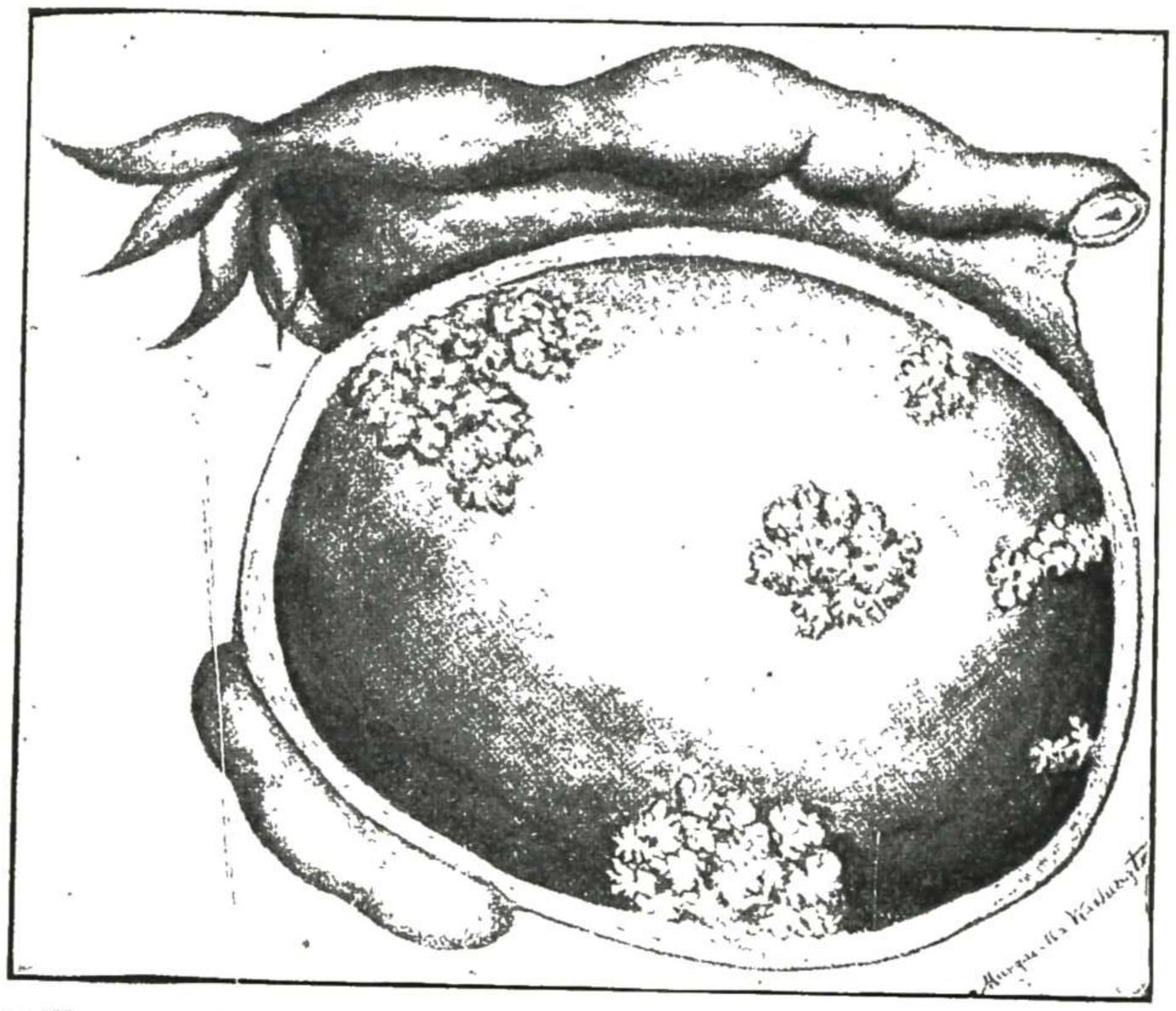


Fig. 1008.—A papillary cystadenoma, sectioned and showing the papillary projections into the cyst cavity. (Penrose—*Diseases of Women,* W. B. Saunders Company.)

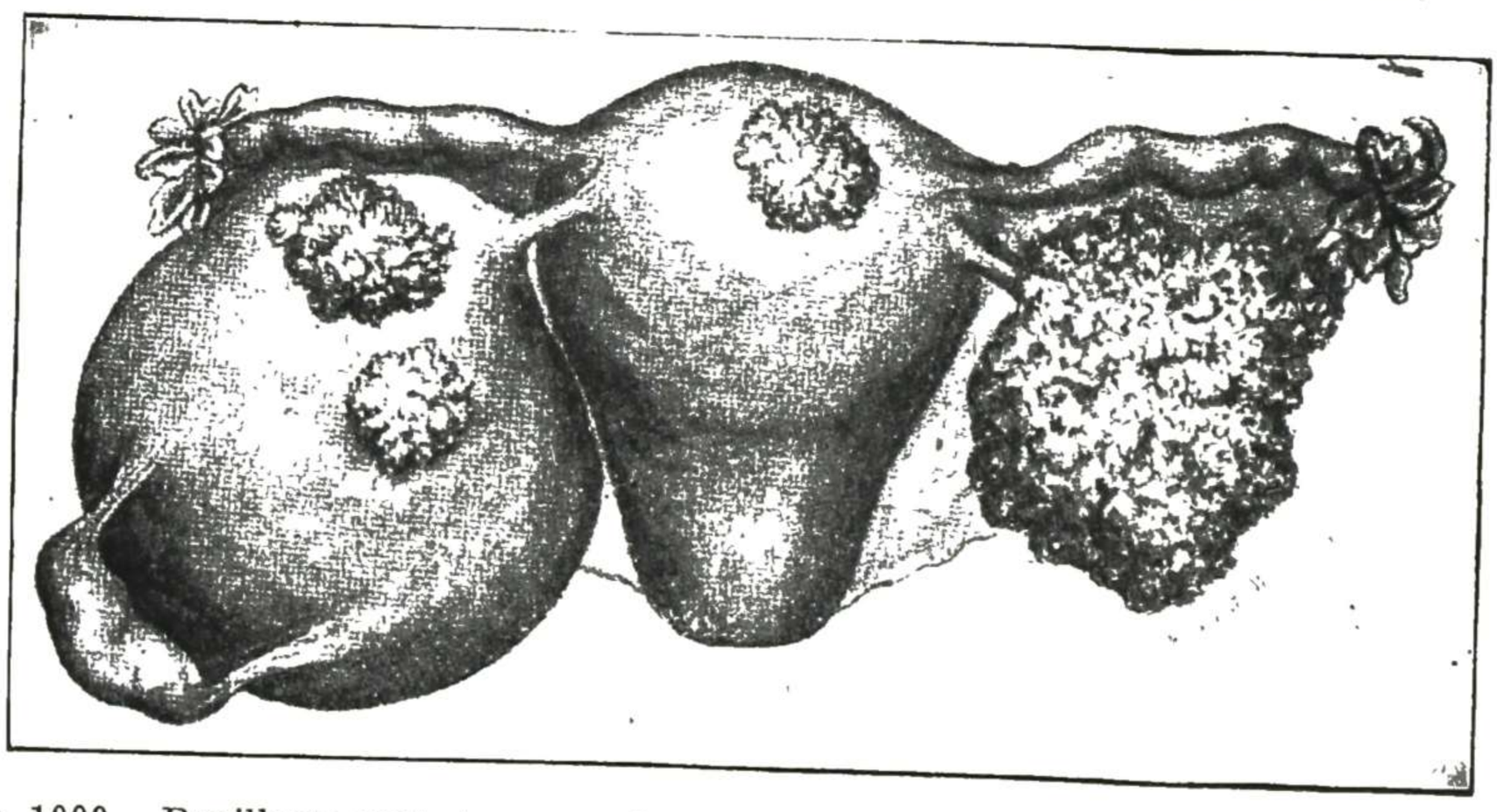


Fig. 1009.—Papillary cystadenoma of each ovary. On the left side the internal papillary projections have grown through the opposite wall and appear on the external surface. On the right side the papillary growths have obliterated all resemblance to a cyst, and appear simply as a cauliflower growth in the region of the ovary. Note the metastasis on the peritoneal surface of the uterus. (Penrose—*Diseases of Women.*)

this absence of internal pressure, the cells, as they proliferate, pile up, forming papillary projections into the interior of the cyst (Figs. 1005 to 1008); hence the name "invertens." These papillary masses (consisting of a layer of epithelial cells and some stroma), when they come in contact with the opposite wall of the cyst, penetrate the wall and appear outside as papillary growths on the external surface of the cyst (Fig. 1009).

Usually a few glandlike eversions may be found in the wall, but they are insignificant. Occasionally, however, a serous cystadenoma will present nearly altogether evertent growths (glandlike projections into the wall of the cyst) - serous cystadenoma evertens.

Etiology.—The serous cysts are usually bilateral. There are three theories as to their cause: (1) that they develop from the germinal or surface epithe-

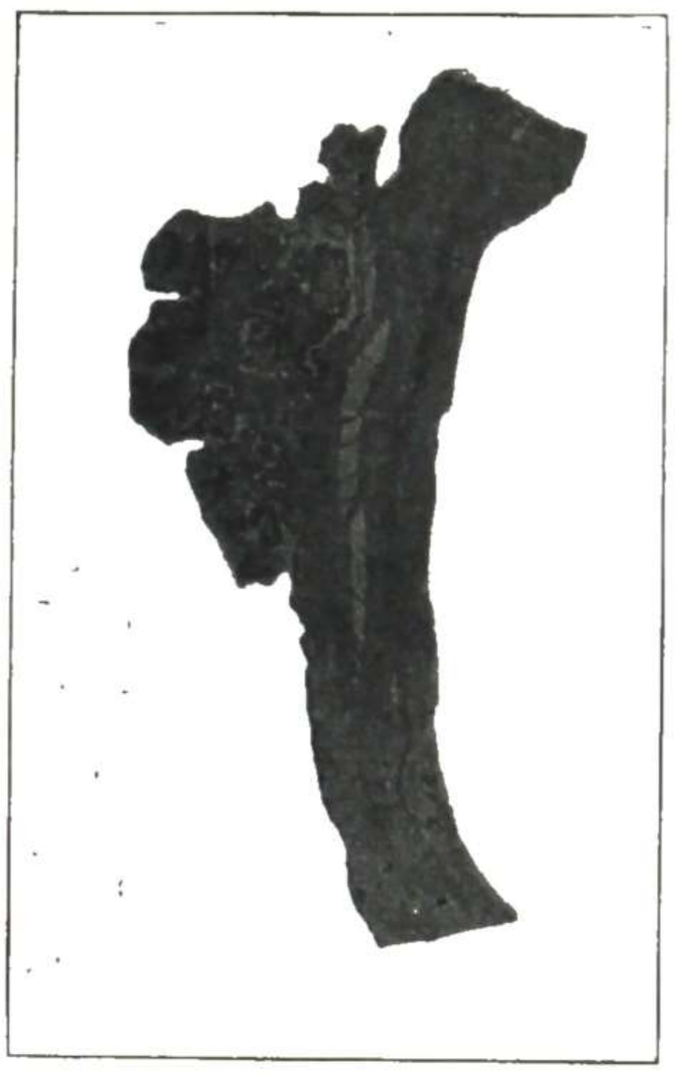


Fig. 1010.

Fig. 1010.—Wall of a benign serous papillary cyst. These projections are covered with epithelial cells that have no tendency to invade. Gyn. Lab.

Fig. 1011.—Papillary cyst. Low power of lining, showing its papillary character. Gyn. Lab.

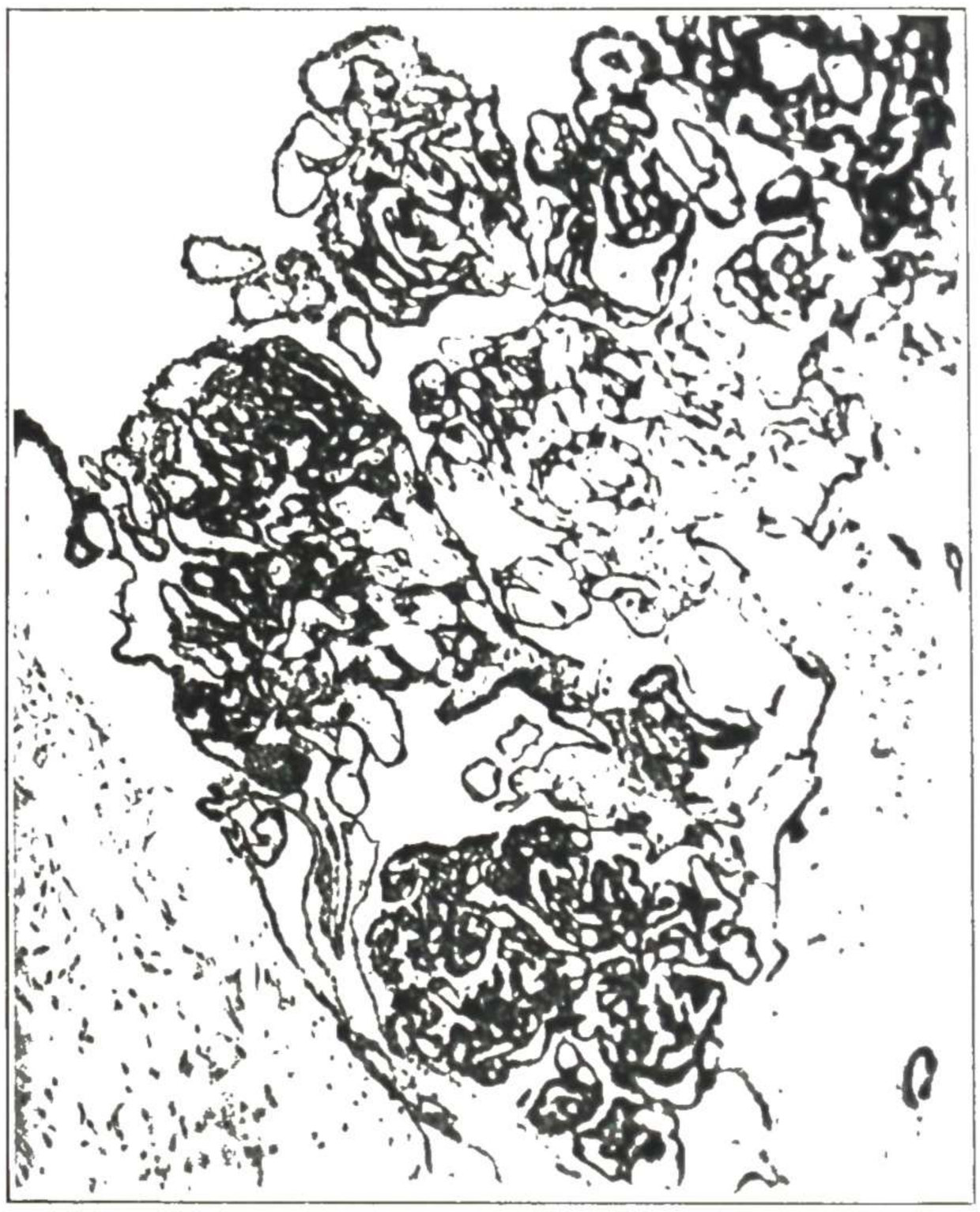


Fig. 1011.

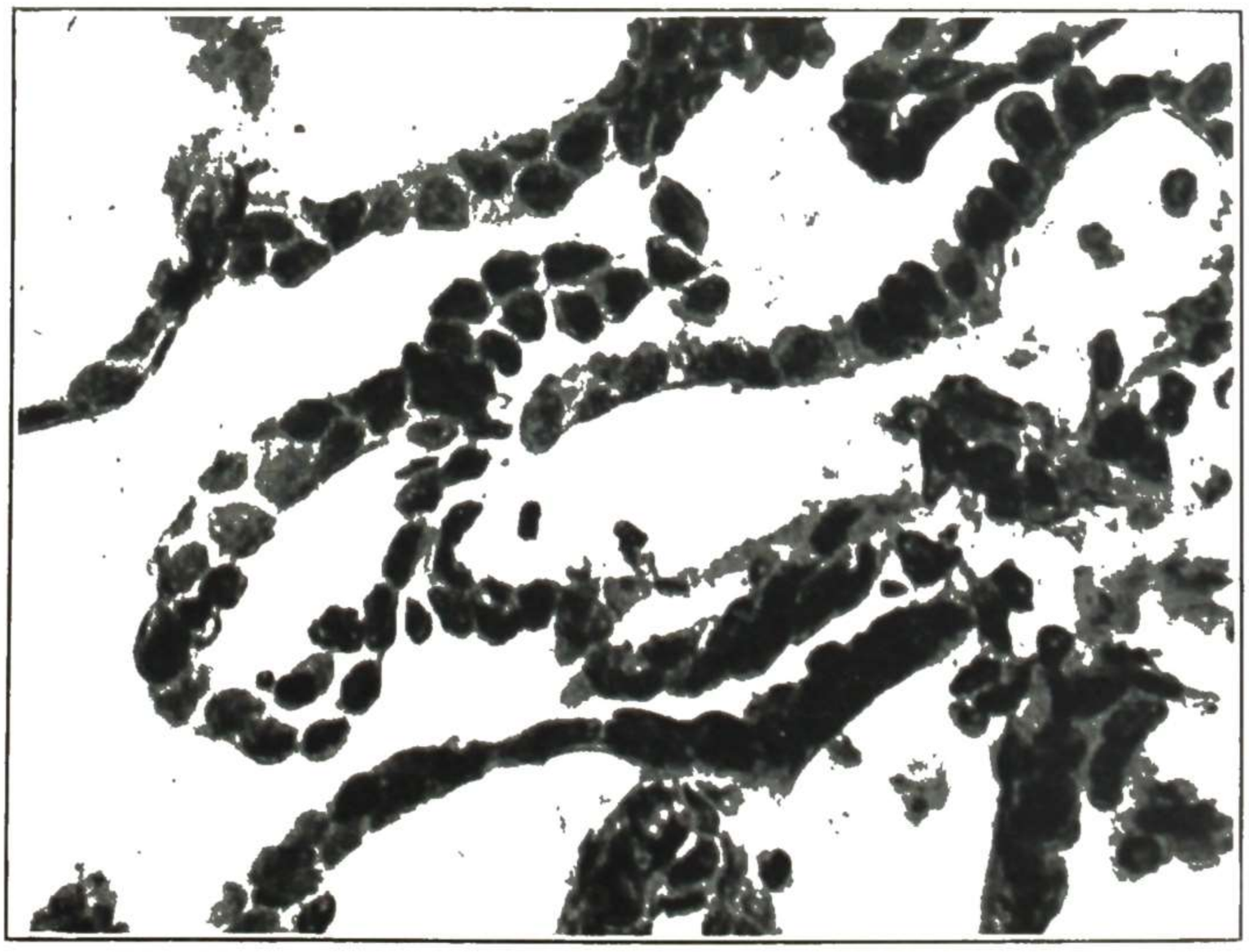


Fig. 1012.—Papillary cyst. High power showing the character of the cells covering the papillary projections. Gyn. Lab.

lium of the ovary (including invagination, tubules, and small cortical cysts), (2) that they develop from graafian follicles, and (3) that they develop from the wolffian tubules. McCarty made a careful study of cases of serous cystadenoma in which both ovaries were removed. In many of these cases one ovary contained the cyst and the other appeared grossly normal. He found that 100 per cent of these grossly normal ovaries (removed prophylactically because of a serous cyst of the other ovary) contained small cortical cystic structures, while only 60 per cent of a normal control group contained them. Two of the prophylactically removed ovaries showed beginning tumors arising from small epithelial cystic structures in the cortex, one an early carcinoma and the other a beginning papillary cyst. He concludes from his study (a) that most papillary ovarian cysts develop from the small germinal epithelial cystic structures found in the cortex of the normal ovary, and (b) that the grossly normal ovary associated with a papillary cyst of the other ovary is a potential danger and should be removed if the age of the patient permits.

Microscopic.—The cells lining the serous cyst are uniform in size and one layer thick. They are low cylindrical, with a centrally placed nucleus and a granular cytoplasm (Figs. 1000 and 1005), and the papillary masses present the pictures shown in Figs. 1010 to 1012.

Malignancy.—These serous cysts have a greater tendency to develop malignant complications than do the pseudomucinous variety, and because of their tendency to be bilateral both ovaries should be removed except in young patients. The percentage of cures is distinctly lower than with pseudomucinous cysts.

The characteristics of the pseudomucinous and serous cysts may be presented and contrasted concisely as follows:

Pseudomucinous Cyst	Serous Cyst
1. Contents gelatinous and secreted by the cells lining the cyst—may be any color.	1. Contents serumlike and not secreted by the cells lining the cyst—may be any color.
2. Secondary growths consist of glandlike projections outward (evertent) from the cavity into the wall, forming small cystic cavities in the wall.	2. Secondary growths consist of papillary projections inward (invertent) from the wall into the cavity, forming papillary masses which extend across the cavity and penetrate the opposite wall.
3. Lining cells contain pseudomucin, are columnar, with some goblet cells, and are not ciliated.	3. Lining cells contain no pseudomucin, are plain columnar, without goblet cells, and are ciliated.
4. Usually unilateral.	4. Usually bilateral.
5. Rarely ruptures spontaneously.	5. Usually ruptures at any early stage, because of perforation of the wall by the the papillary ingrowths.
6. Rarely causes peritoneal metastases.	6. Usually causes peritoneal metastases, consisting of widespread papillary growths.
7. Rarely undergoes malignant change.	7. Frequently undergoes malignant change.
8. Very common.	8. Not so common.
9. Cause unknown. See theory under Etiology.	9. Cause unknown. See theories under Etiology.

Clinical Manifestations

Taking up the clinical manifestations of the proliferating cysts (both pseudomucinous and serous), it is found that they may **occur** at any age, but are most frequent during the period of greatest ovarian activity, i.e., between the twentieth and fiftieth years.

In **shape,** a proliferating cyst may be spherical and regular in outline, indicating a single large cyst, or it may be irregular, presenting nodules indicating a multilocular cyst. In **size** these cysts vary from a small tumor the size of an egg to a large tumor filling the whole abdomen.

As to **appearance** when exposed by abdominal incisions, the wall of the cyst presents a white, glistening appearance. The thinner portions are straw-colored or green or black, according to their fluid contents. The surface of the cyst may be perfectly smooth, or may be covered by a papillary growth, or may be bound to adjacent structures by adhesions. The tumor usually has a distinct pedicle.

The **cyst wall** consists of three layers—an outer and inner firm fibrous layer, with a middle layer of looser tissue between them. In the middle layer of loose connective tissue the vascular supply is distributed.

The **contents** of cysts present marked contrast in consistency and in color. The contents may be thin like water (serous cysts), or thick and viscid and of gelatinous consistency (pseudomucinous cyst). The contents may be almost colorless or straw-colored or a dirty yellow, or green or black. The color depends on hemorrhage into the cyst. The coloring matter of the blood becomes the coloring matter of the cyst contents.

As these cysts enlarge they bear various **relations** to adjacent structures. If they rise out of the pelvis and enlarge in the abdomen, they may attain a very large size before producing serious symptoms. There they have plenty of room and expand freely, pushing aside the surrounding organs. If they become caught under the pelvic brim and develop in the pelvis, they soon begin to cause pain and other disturbances from pressure and distortion of the organs.

When the papillomatous growths within a cyst pierce the cyst wall (which happens most frequently in the serous cyst), peritoneal implantations may occur. In some cases these peritoneal implantations grow rapidly and fill the pelvis with papillary masses. In such a case the first impression, when the abdomen is opened, is that the pelvis is filled with a cancerous mass, which cannot be removed and which will soon cause death. Accordingly, in not a few cases, the operator, after scraping out some of the papillary bleeding growth, has closed the abdomen and told the patient or her friends that there was an inoperable cancer and that she could not long survive. Some such patients get entirely well after the operation. In other cases malignant change has already begun or begins later and the patient dies of carcinoma. In still other cases the growth itself becomes so extensive as to interfere with the functions of adjacent organs and thus causes death.

Symptoms and Diagnosis

An ovarian cyst usually develops slowly and may attain considerable size before it is discovered. Often it is noticed then only by accident.

The earliest symptoms are a feeling of weight and pressure in the pelvis, bladder irritability, slight menstrual disturbance, constipation, and perhaps some pain with bowel movement. The symptoms are not distinctive, but simply indicate some disturbing factor in the pelvis. As the tumor increases in size, distinct pressure symptoms appear and the general nutrition becomes affected.

There is enlargement of the abdomen, swelling of the feet from pressure on veins, pain from pressure on nerves, and dyspnea from pressure on the diaphragm. There appear, also, stomach disturbances, emaciation, and progressive weakness. In some cases there are attacks of local peritonitis, with severe abdominal pain and some fever, but these inflammatory symptoms are due to complications and do not belong to the natural history of the tumor.

Ovarian cysts grow slowly, usually taking several years to reach a large size. But they seldom stop growing. They persistently enlarge until the patient finally dies from exhaustion brought about by pressure effects on vital organs.

Fig. 1013.

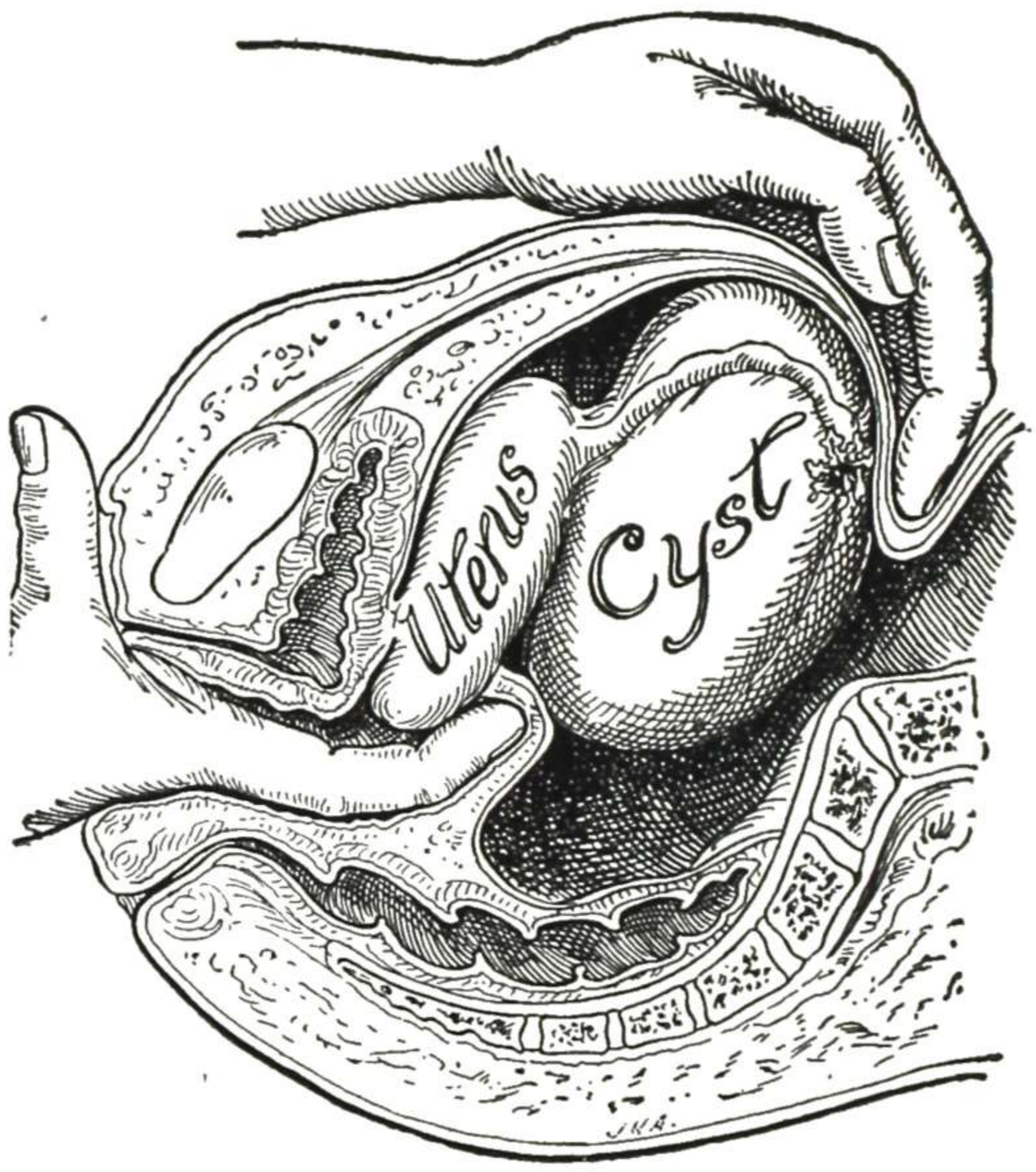


Fig. 1014.

Fig. 1013.—An ovarian cyst lying back of the uterus. (Ashton—*Practice of Gynecology,* W. B. Saunders Co.)

Fig. 1014.—Showing the method of testing the mobility of such a mass. (Ashton—*Practice of Gynecology.*)

The diagnosis in typical cases is easy, but in complicated cases it may be very difficult, and in exceptional cases a positive exact diagnosis is impossible before operation. Tapping the cyst through the abdominal wall as an exploratory measure is not advisable. An adherent coil of intestine may be punctured, or cyst contents may leak into the peritoneal cavity and cause fatal peritonitis. In a doubtful case, an exploratory abdominal section is safer and far more satisfactory in diagnostic results.

In taking up the differential diagnosis of ovarian cysts in general, it is at once apparent that the symptoms and diagnostic points are different in the different sized tumors.

Small Ovarian Cyst.—Considering the small ovarian cyst according to the seven principal diagnostic points in the palpation of pelvic masses (position, size, shape, consistency, tenderness, mobility, attachment—see Bimanual Examination of Corpus Uteri and Other Pelvic Masses, Chapter II, it is found that an ovarian cyst of this size presents the following characteristics:

1. Is situated in the lateral part of the pelvis, though in exceptional cases it may drop down directly behind the uterus or in front of it.

2. The small ovarian cyst is the size now under consideration—about as large as the fist or a little larger.

3. Is approximately spherical, though may be made uneven by secondary cysts.

4. Contains fluid (fluctuates).

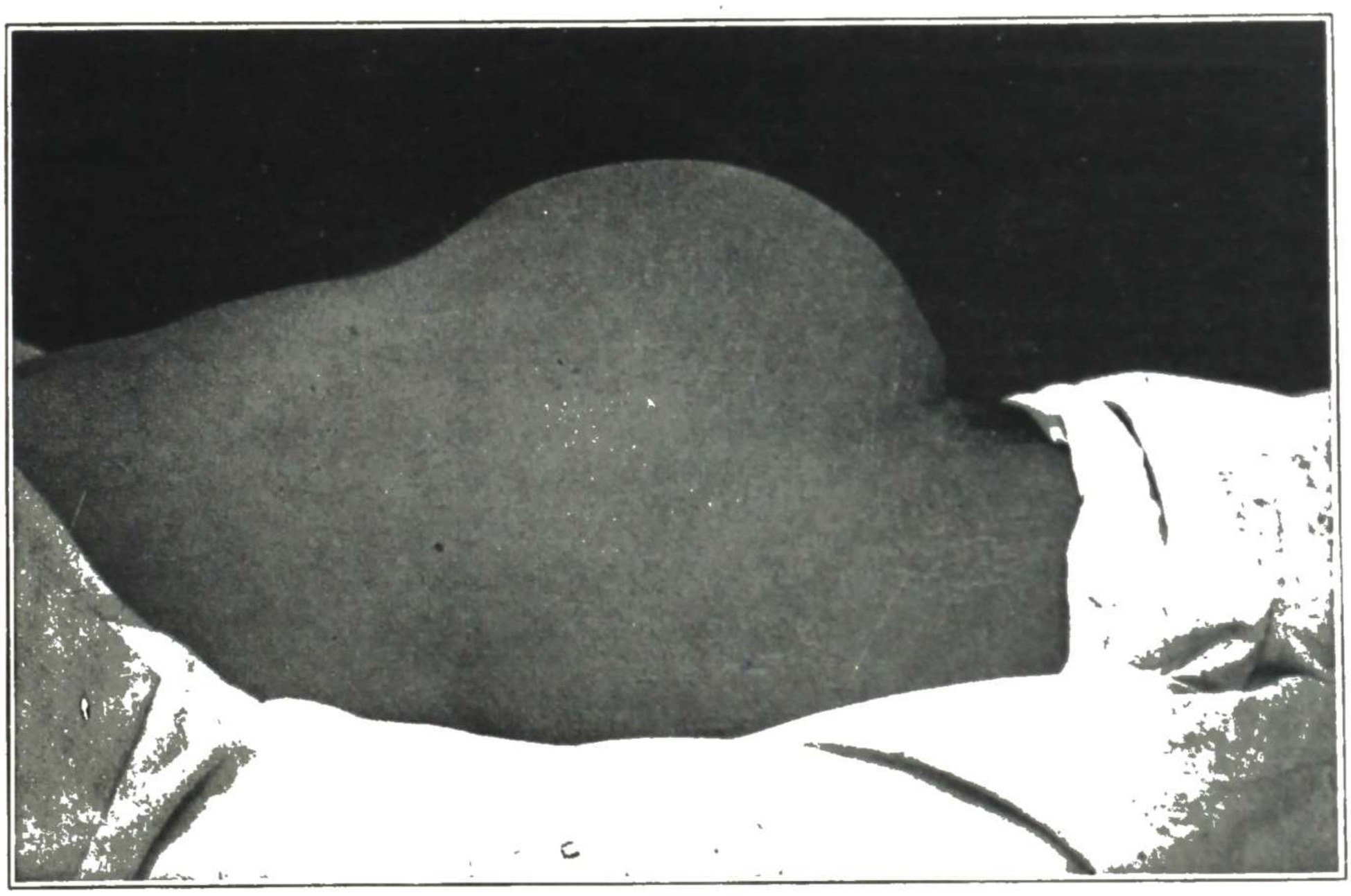


Fig. 1015.—Patient with a large ovarian tumor.

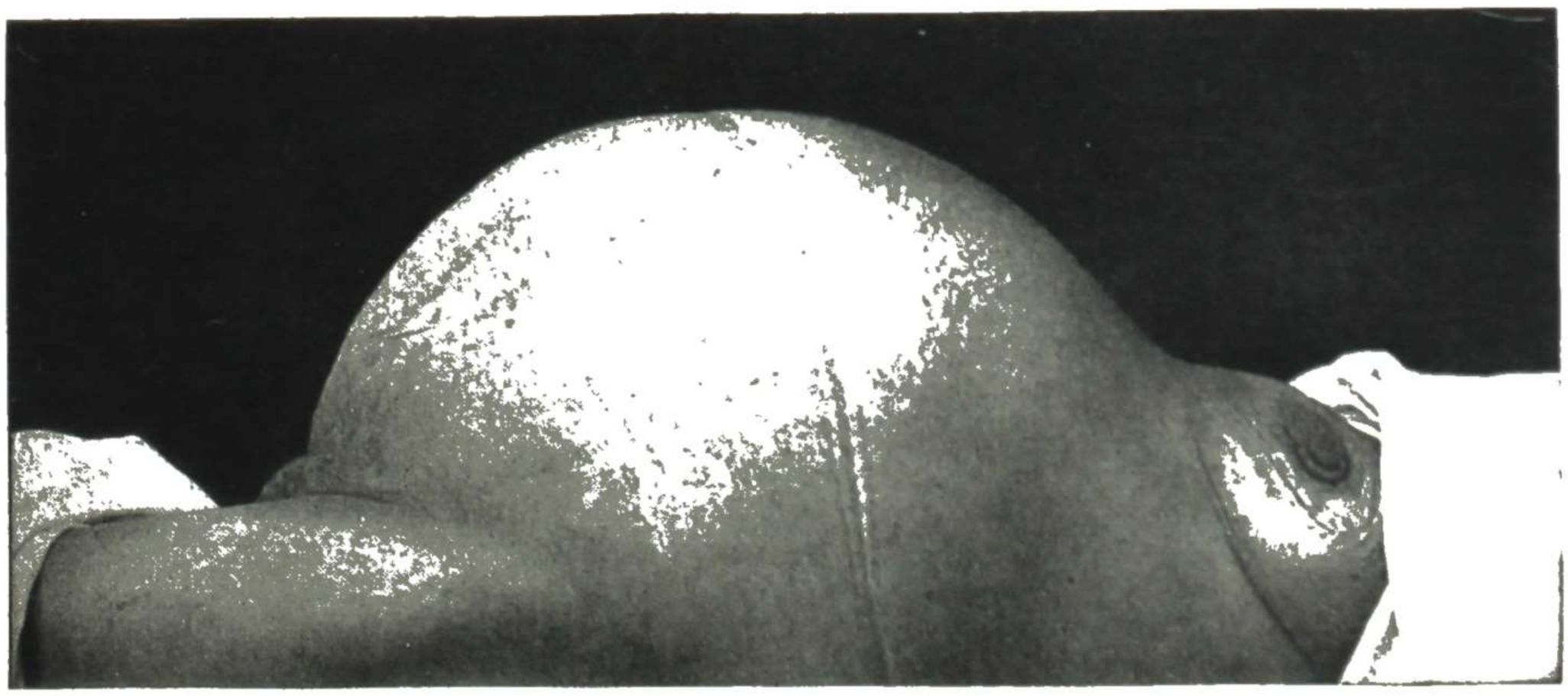


Fig. 1016.—Extreme ascites. In the patient of whom this photograph was taken, the abdomen was so distended with fluid that the wall was raised higher than the mesentery would permit the intestine to float, giving dullness about the umbilicus as well as elsewhere. The rise of the wall from below is rather abrupt. There is also edema of the wall, as shown by the persisting groove where the skirts were fastened about the waist.

5. Is not tender, unless complicated by inflammation or by torsion of pedicle.

6. Is freely movable (Figs. 1013, 1014), unless complicated by adhesions or caught under the sacral promontory.

7. Is attached in the lateral part of the pelvis. Apparently arises from the tubo-ovarian region. Lies beside the uterus, but is not attached to it and does not ordinarily modify it in any way, except to cause some displacement toward the opposite side.

If the cyst is uncomplicated, there is no history of pelvic inflammatory attacks—that is, the mass has progressed to its present size independent of inflammation or hemorrhage, which identifies it at once as a new growth.

The following conditions may be confounded with a small ovarian cyst and must therefore be taken into consideration in the **differential diagnosis:**

a. Salpingitis with exudate.
b. Pyosalpinx.
c. Hydrosalpinx.
d. Tubal Pregnancy.
e. Fibroid Tumor of the Uterus.
f. Retroverted Pregnant Uterus.
g. Broad Ligament Cyst.

Large Ovarian Cyst.—A growth large enough to cause the abdomen to be prominent (Fig. 1015) must be differentiated from the following conditions:

a. Tympanites and "Phantom Tumor."
b. Obesity.
c. General Ascites (Fig. 1016).
d. Pregnancy (normal, with hydramnios, extrauterine).
e. Cystic Fibroid of Uterus.
f. Distended Bladder.
g. Tumor of some Abdominal Organ.
h. Tuberculous Peritonitis.

Complications

Having determined that an ovarian cyst is present, we must then consider certain complications that may be present or that may appear later. These complications are as follows:

1. Local peritonitis, forming adhesions.
2. Hemorrhage into the cyst.
3. Rotation of the cyst, producing torsion of the pedicle.
4. Inflammation and suppuration of the cyst.
5. Rupture of the cyst.
6. Ascites accompanying the tumor.
7. Intestinal obstruction.
8. Pregnancy accompanying the cyst.

1. **Local Peritonitis** is accompanied by some pain and tenderness over a part of the tumor. There may be some fever, but usually this symptom is not marked; the process consists simply of irritation at some portion of the outer surface of the cyst and the formation there of plastic exudate, binding the cyst to some adjacent organ or to the abdominal wall. In a few days the pains disappear, but the exudate remains, becomes organized, and forms an adhesion, which may interfere more or less with the subsequent operation.

2. **Hemorrhage into the Cyst** is what gives the various colors to the cyst contents. This hemorrhage usually takes place slowly in small quantities and without clinical symptoms. Occasionally, however, a copious hemorrhage takes place, usually from some interference with the venous return, such as twisting of the pedicle or pressure of an enlarged uterus, or it may follow tapping of the cyst. The hemorrhage may be so severe as to cause collapse of the patient.

3. **Rotation of the Cyst** may take place where the pedicle is long (Figs. 1017, 1018). The amount of rotation varies from a half turn to several complete turns. Torsion of the pedicle is supposed to be favored by an injury, such as a fall or blow, and by active exercise, and also by the alternate filling and emptying of the bladder and the bowel, and during pregnancy by the enlargement of the uterus.

Fig. 1017.—Ovarian cyst with a long slender pedicle. (Montgomery—*Practical Gynecology.*)

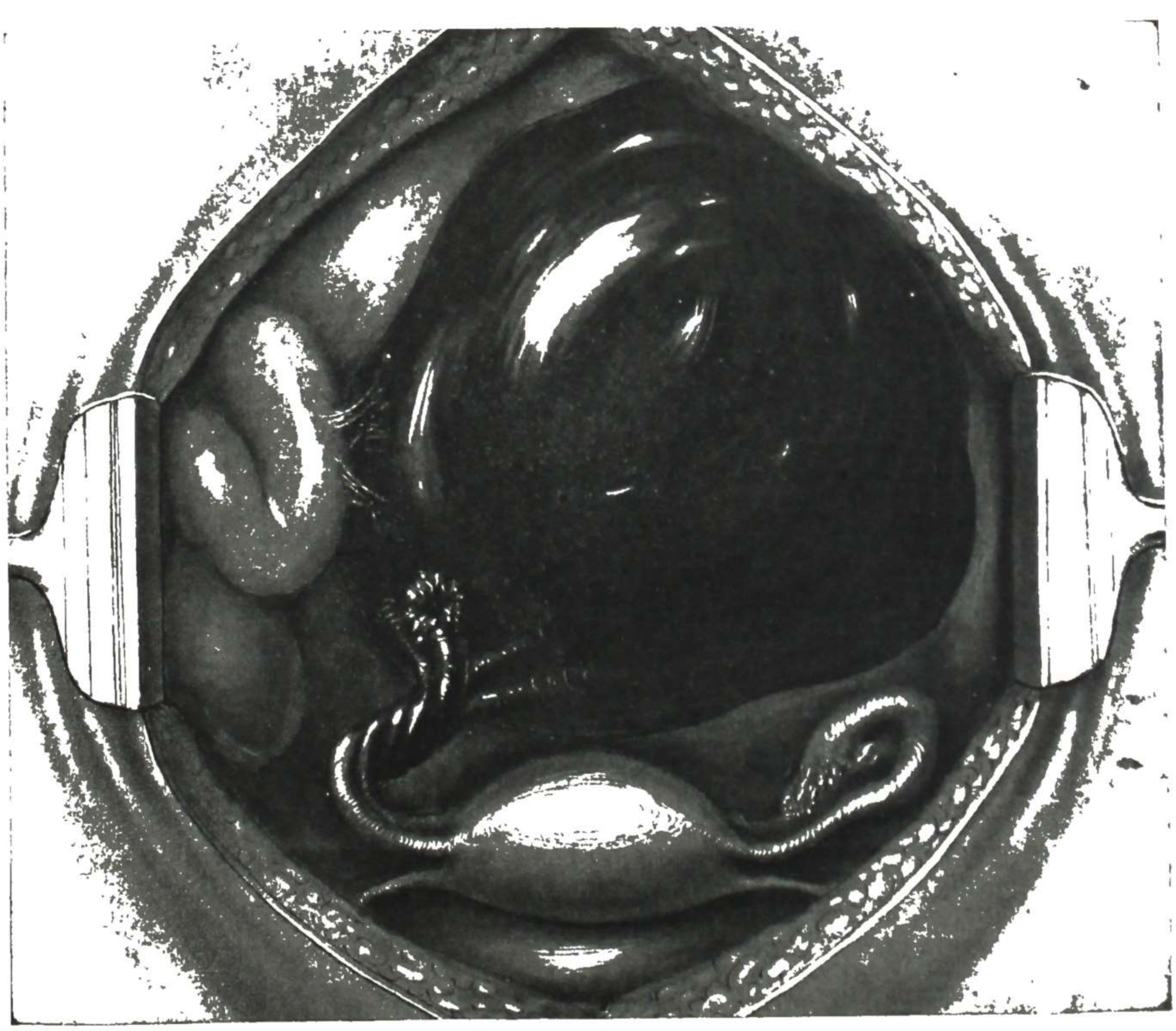


Fig. 1018.—Indicating an ovarian cyst with twisted pedicle. The turning of the tumor twists the pedicle, blocking the circulation and causing thrombosis in the pedicle and throughout the tumor. The extravasation of blood causes the affected tissues to become black.

The effect of torsion of the pedicle on the circulation of the tumor depends, of course, on the amount of rotation. The veins are the first to suffer. The flow of blood in them is impeded, causing the tumor to become engorged, and there is hemorrhage into the interior of the cyst, either in the form of extravasation or the rupture of a vein with severe hemorrhage. If the twisting increases, there is thrombosis of the vessels (Figs. 1019, 1020) and extravasation of bloody fluid into the peritoneal cavity, and later necrosis of the tumor, followed by fatal peritonitis. The symptoms of torsion of the pedicle are very marked. When a patient with an ovarian tumor complains of sudden pain in the abdomen and vomits, and there is a sudden increase in the size of the tumor, it is probable that torsion of the pedicle has taken place. In some cases there are repeated attacks of slight torsion.

4. **Inflammation and Suppuration of the Cyst** are, of course, due to infection. The infection may come from the intestinal canal or from the bladder or from a fallopian tube or from tapping the cyst. The most common source of infection is the fallopian tube. The patient contracts salpingitis, adhesions form between the inflamed tube and the cyst wall, and infection spreads along these adhesions, and invades the cyst. Adhesions with some portions of the intestinal tract, especially with the appendix, may likewise lead to infection of the cyst. Tapping, which was formerly a common procedure, often led to infection of the cyst. Dermoid cysts are especially prone to suppuration. Infections of cysts are not uncommonly seen in the course of the acute infectious fevers, especially typhoid.

The symptoms of suppuration of the cyst are pain, fever, tenderness over the tumor, rapid pulse, exhaustion, and emaciation. If the suppurating cyst does not speedily cause death by peritonitis, it may later rupture into the intestine or bladder or vagina. The teeth, hair and pieces of bone discharged in rare cases from the urethra or rectum are usually due to suppuration of a dermoid cyst.

5. **Rupture of the Cyst** may be sudden, as from a fall or blow or other injury, or it may be the result of a gradual thinning of the cyst wall. The result of rupture of the cyst depends on the quantity and quality of the cyst contents. In unilocular cysts with non-irritating fluid, rupture may produce no severe symptoms. There are some weakness and abdominal pain and marked diuresis, the patient sometimes passing several gallons of urine in twenty-four hours. The abdomen, which was prominent from the tumor, becomes flattened and lax. The physical signs change from those of encysted fluid to those of free fluid. The cyst may not refill, and if no inflammation takes place, the patient recovers. But this favorable termination takes place only in rare cases. In the great majority of cases of cysts, rupture causes peritonitis, which may be very severe and rapidly fatal.

Rupture of a cyst is indicated by the sudden disappearance of the tumor or marked diminution in its size, accompanied by evidences of free fluid in the peritoneal cavity and collapse of the patient, and later peritonitis and death.

6. **Ascites.**—A small amount of ascitic fluid may be present with many cysts, but a large quantity is rare so long as the tumor retains its normal condition. Consequently, the presence of considerable ascitic fluid with an ovarian cyst becomes of diagnostic importance. The ascites may, of course, be due to some heart trouble or kidney trouble or liver trouble, or may be due to peritoneal tuberculosis. Aside from such complications, ascitic fluid is indicative of some serious complications; e.g., a papillary cyst, especially after malignant change, or rupture of an ordinary cyst.

7. **Intestinal Obstruction.**—This may be caused by direct pressure of the tumor or by adhesions which contract and narrow the intestine. It is, of course, a very serious complication and is indicated by the ordinary symptoms of intestinal obstruction appearing in the presence of an ovarian tumor.

8. **Pregnancy** may accompany an ovarian cyst, adding much to the difficulties of diagnosis.

Treatment

The treatment of the **proliferating cysts** is removal by operation as soon as found, if the condition of the patient will permit.

These ovarian tumors are not at all influenced by palliative measures, they do not stop growing spontaneously, and they tend to cause death within

Fig. 1019.—Dermoid Cyst of Ovary with Torsion of Pedicle Causing Thrombosis. At operation the tumor was so large and adherent that extension of the incision above the umbilicus was necessary for its removal. The twist in the pedicle, which included also the fallopian tube, showed two complete turns. It was necessary to remove the corpus uteri along with the tumor, and the uterus is shown opened. Color drawing from fresh specimen. (Crossen and Crossen—*Operative Gynecology.*)

Fig. 1020.—Double Ovarian Cyst with Torsion of Pedicle Causing Thrombosis. At operation the left tumor appeared as a black mass, due to extensive hemorrhage into it. The tumor of the other ovary showed no torsion and no circulatory disturbance. It was necessary to remove the corpus uteri along with the tumors. The twisted area has been untwisted. Notice at the edge of the uterus the clear-cut margin of the thrombosed area. The rounded swelling between the uterus and the tumor is due to a hemorrhage into the tissues just beyond the twist. Color drawing from fresh specimen. (Crossen and Crossen—*Operative Gynecology.*)

a few years. Consequently they should be removed as soon as found or as soon as the patient can be put in condition for the operation. Sometimes the patient is in such a weakened condition that she must be given a course of treatment before operation. Some general disease, such as kidney, heart or lung trouble, may make it necessary to delay the operation until the patient can be put in better condition.

Then, again, the patient may be in such condition that a radical operation would be almost certainly fatal. In such a case it would, of course, be useless to operate. In some such inoperable cases the patient may be rendered temporarily more comfortable by tapping the cyst with a trocar and drawing off the fluid. In all cases of proliferating cysts, however, in which the patient is in suitable condition, the tumor should be removed by operation.

SIMPLE SOLID TUMORS

Simple solid tumors of the ovary are infrequent and usually small. Fibroma is the principal one, though myoma or adenomyoma may occur.

Fibroma of the Ovary

Ovarian fibromas are rare tumors comprising about 2.5 per cent of all ovarian tumors. Little is known about etiology of fibromas. They have been found at ages ranging from ten to eighty. They are bilateral in about 20 per cent of the cases, and ascites is almost always present if the tumor is at all large.

Fig. 1021.—A small ovarian fibroma. Cross-section, showing the typical fibromatous structure and a well-defined capsule. Gyn. Lab.

These may occur as small circumscribed tumors of white pearly appearance embedded in the stroma or on the surface of the ovary, or they may be diffuse, involving the entire ovary. Clemens reported a large one weighing 40 kg. On cutting into the tumor, it is usually found to be cartilaginous or of bony hardness, but it may be soft if edema or necrosis is present. Occasionally one finds areas of calcification and even ossification.

Four cases of ovarian fibroma with associated ascites and hydrothorax were reported by J. V. Meigs in 1937. Others later reported several cases of this "Meigs' syndrome," and a 1943 article by Meigs, Armstrong and Hamilton brought to 27 the reported cases of ovarian fibroma with this striking complication, which is remarkable because of the comparative rarity of ovarian fibroma.

The treatment is removal of the growth, and thorough microscopic investigation of it. Carcinoma of the ovary is so insidious and symptomless in the earlier stages that any ovarian mass must be held under suspicion, particularly if solid and in a patient of cancer age.

MISCELLANEOUS RARE TUMORS

A *lymphangioma* was reported by Siddall and Clinton, a *ganglioneuroma* by Schmeisser and Anderson and a *mesonephroma* by Jones and Seegar. The latter state:

> In reviewing over 350 true neoplasms of the ovary, a group of 6 has been separated on the basis of their pathologic characteristics. Schiller has recently described a similar group of cases and believes them to be derived from mesonephric tissue. It is the purpose of this paper to describe the clinical and pathologic characteristics of these tumors and to discuss their histogenesis. These tumors occurred after the age of forty and presented no characteristic clinical features. Four were found to be benign and two malignant.

The ovary is the source of so many different kinds of tumors that every specimen should be submitted to microscopic check-up, and every atypical specimen should be carefully studied as to exact type and probable origin. When we can substitute demonstrated facts for the present interesting but uncertain theories, we shall have attained the long-sought goal of a comprehensive satisfactory classification of ovarian tumors. To assist in this direction a responsible American Registry of Ovarian Tumors has been established, for special study of specimens and slides sent to it, as explained by Novak (see Additional References).

CANCER OF THE OVARY

In the ovary as elsewhere malignant disease appears in the two common forms—carcinoma and sarcoma. We have already considered various special ovarian tumors in which definite malignancy was manifested in some cases of certain types. Here the common forms of cancer are considered.

Pathology

Of the two forms, carcinoma and sarcoma, carcinoma is by far the more frequent.

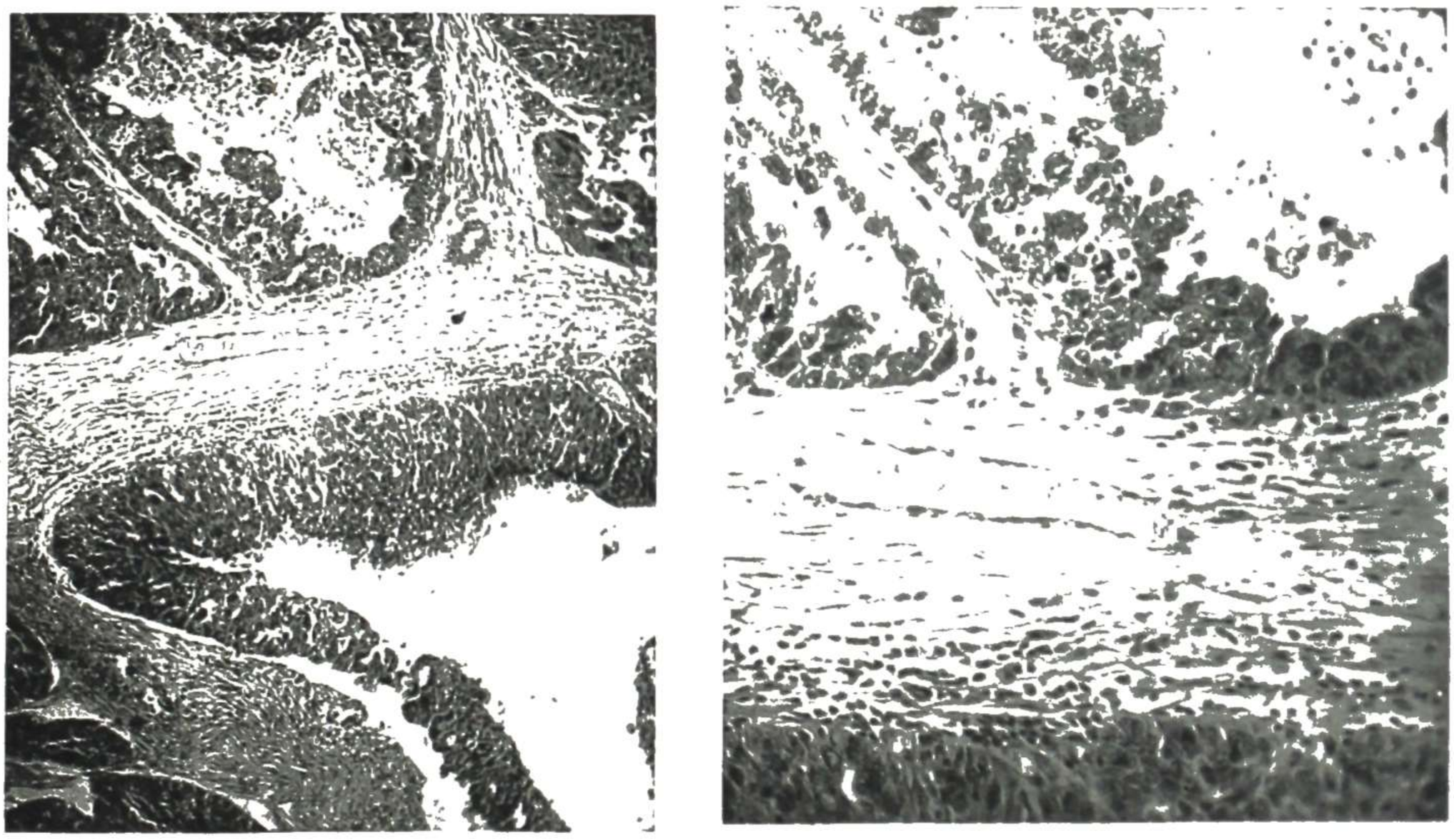
Carcinoma.—This form of malignant disease may be primary in the ovary or may be secondary to a growth in some other structure.

Primary.—Carcinoma developing with the ovary as the primary focus is found in from 10 to 12 per cent of ovarian neoplasms. Those arising in papillary cystadenoma form by far the largest group, with pseudomucinous cysts and dermoids accounting for from 3 to 5 per cent. In a series reported by Pfannenstiel, the carcinoma was bilateral in 90.9 per cent. The highest incidence occurred between the ages of forty-five and fifty-five, but they have been found in young children and elderly women. There is an accompanying ascites in 78 per cent of the cases.

The gross appearance varies with the type of carcinoma. In the slower growing type, secondary to a cyst, the surface of the cyst is usually studded with papillae. On opening the cyst the cavity is found to be filled with a granular cauliflower-like material. If proliferation is very rapid, the tumor

may be solid, but they are usually soft. On opening this type of tumor the inner pulp pouts out through the rent in the wall. In some specimens the solid areas resemble soft white brain tissue.

The microscopic examination of this tissue shows glandlike areas in the slower growing tumors (Fig. 1022), while in the more rapidly growing tumors there are solid interlacing cords of cells with no attempt at gland formation.



A. *B.*

Fig. 1022.—Malignant papillary cyst. *A*, High power, showing the piling up of the epithelial cells and other characteristics of malignancy. *B*, Still higher power of the left central area in *A*, showing the individual cell characteristics. (Erdmann and Spaulding *Surg., Gynec. and Obst.*)

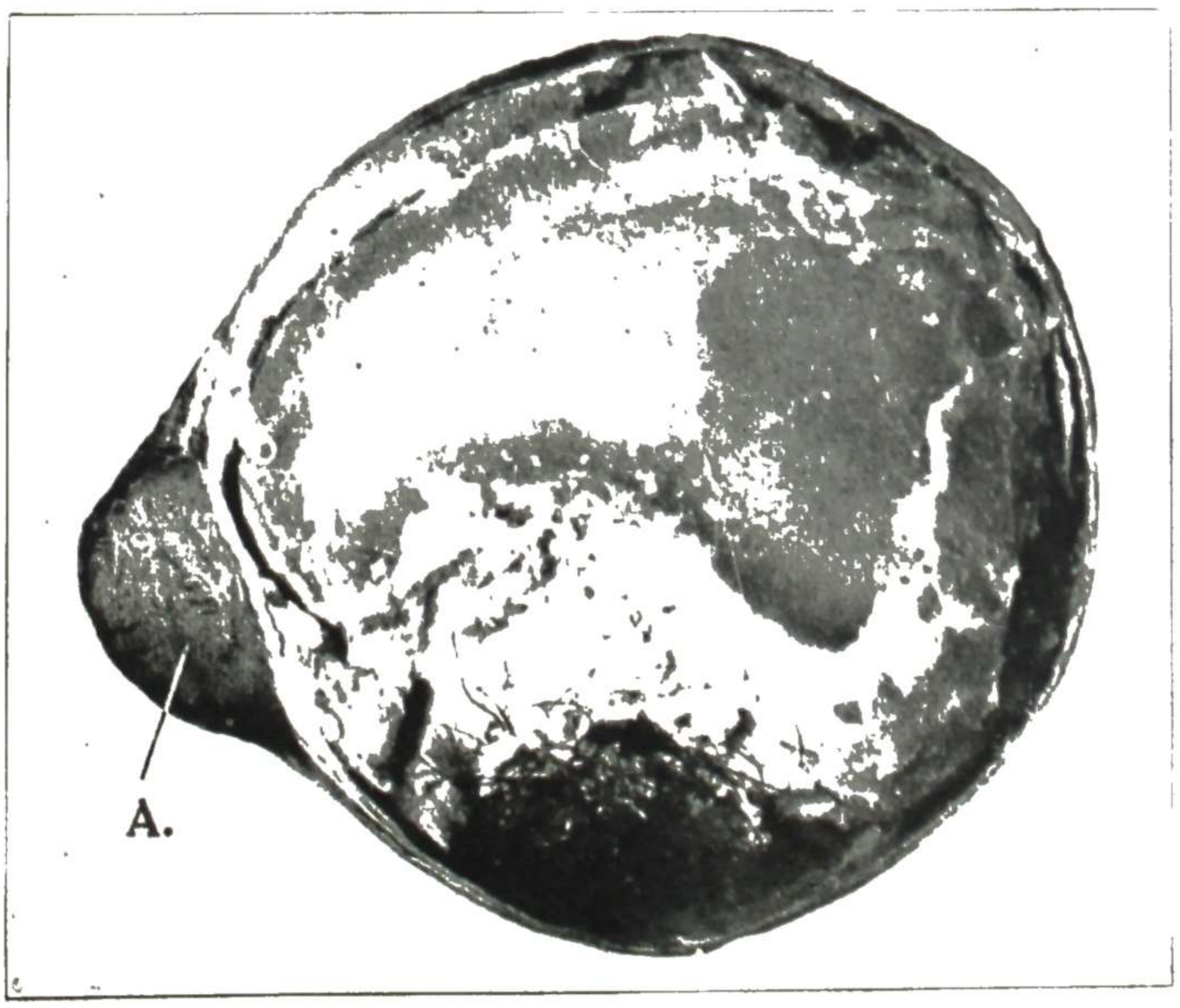


Fig. 1023.—A dermoid cyst of the ovary showing beginning carcinoma at *A*. (Spalding *Am. J. Obst.*)

Occasionally one can trace the epithelium in the glandlike structures from a single layered benign epithelium to a frankly malignant multilayered polymorphus atypical epithelium.

Occasionally a carcinoma develops in a dermoid, and is usually of the squamous-cell variety arising from the epidermis in the dermoid. Fig. 1023 shows such a growth. Solid primary carcinomas of the ovary are rare.

Some are of the medullary type. They are of soft consistency as the result of degenerative processes, which are clearly shown on cross-section.

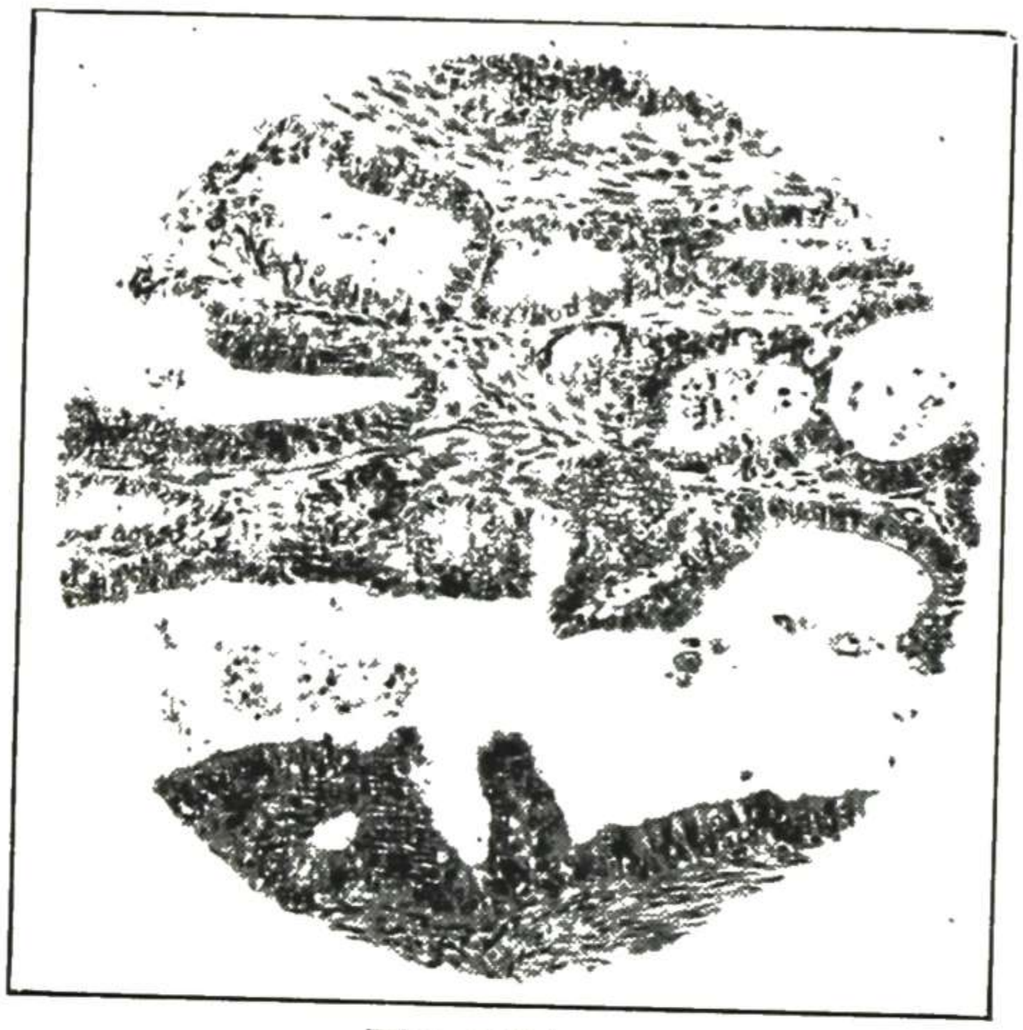


Fig. 1024.

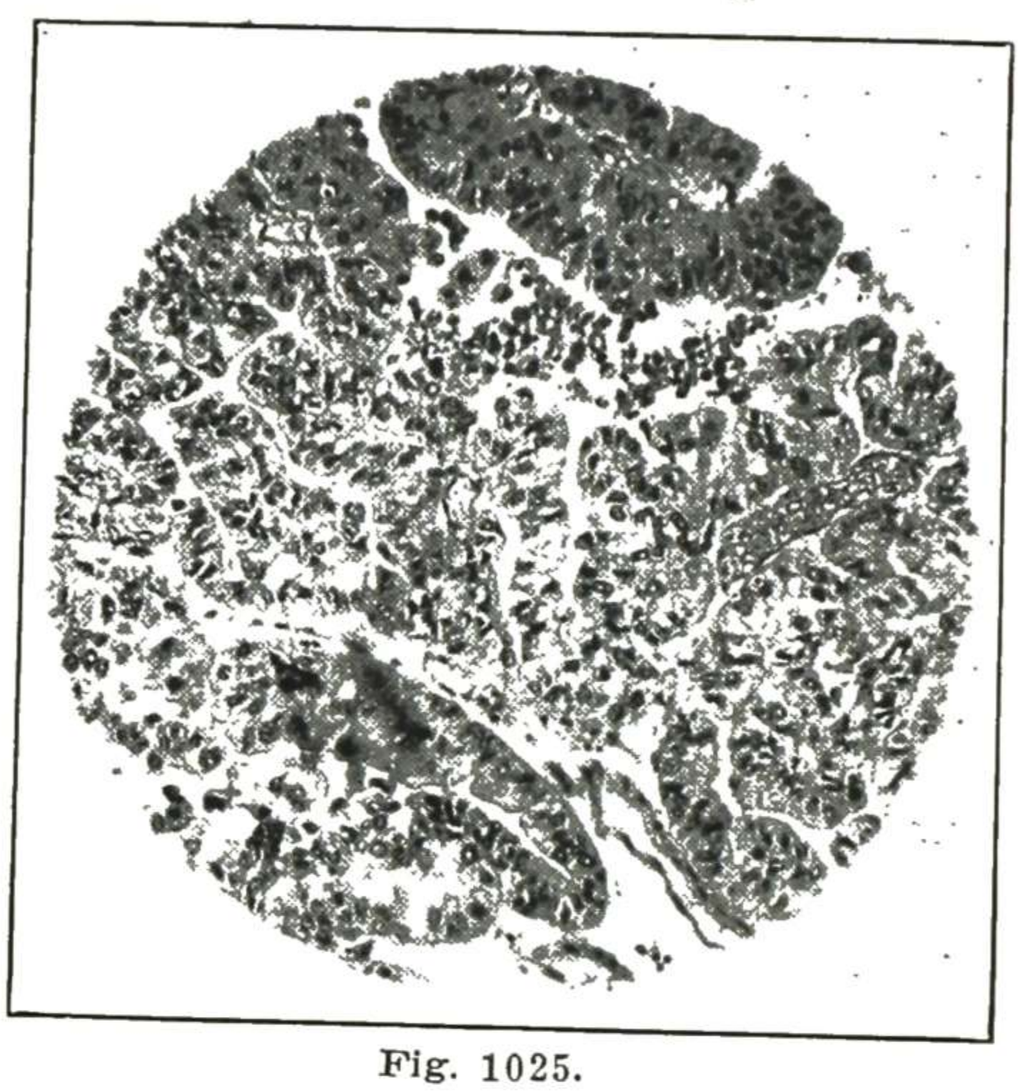


Fig. 1025.

Fig. 1024.—Ovarian carcinoma, Grade I. There is good glandular formation, with well-differentiated columnar epithelium. The mature type of structure is maintained throughout, except in occasional areas where early malignant changes are seen, such as the epithelial cells piling up in numerous layers in the glands or penetrating the stroma. This is the least malignant type. (Montgomery and Farrell—*Am. J. Obst. and Gynec.*)

Fig. 1025.—Ovarian carcinoma, Grade II. Glandular and papillary structures are still present, but they are poorly developed. The columnar epithelium is not so well differentiated. There are moderate variations in the size and shape of the cells, nuclear changes, and more extensive infiltration. In this type the malignancy has increased very decidedly. (Montgomery and Farrell—*Am. J. Obst. and Gynec.*)

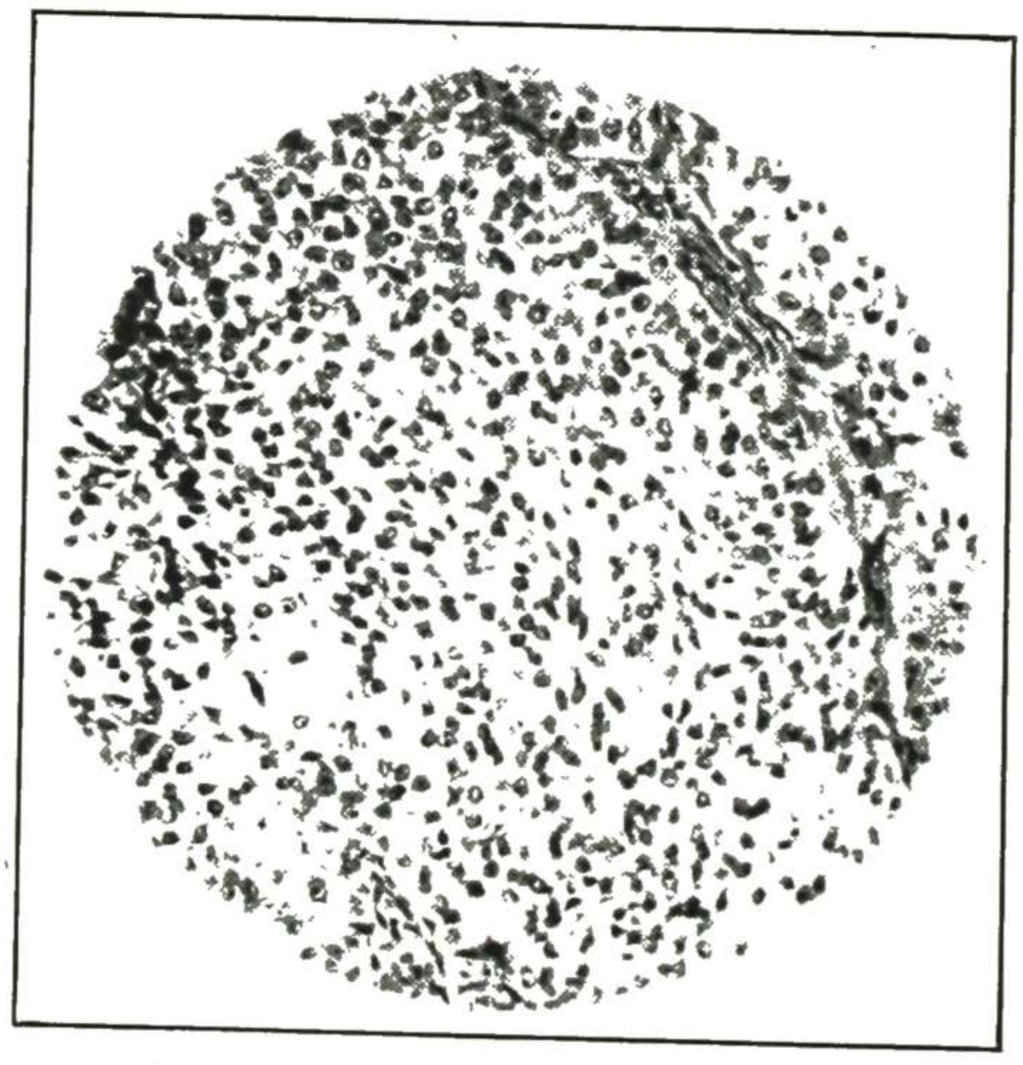


Fig. 1026.—Ovarian carcinoma, Grade III. There is little evidence of glandular or papillary structure, the fields showing practically solid carcinoma. There are marked nuclear changes and undifferentiated epithelial cells. This is the most malignant type. (Montgomery and Farrell—*Am. J. Obst. and Gynec.*)

Local metastases are the rule, especially to the surrounding organs and the peritoneum. The lymph glands commonly involved are the inguinal and lumbar and supraclavicular.

Pathologic Grading.—Various groupings have been proposed with a view to definite pathologic classification of ovarian carcinomas, to aid in accurate recording and reporting of cases so as to permit analysis and comparison, as to prognosis in the different classes and as to results of various kinds of treatment. The following classification, suggested by Taylor, seems a practical and

Fig. 1027.

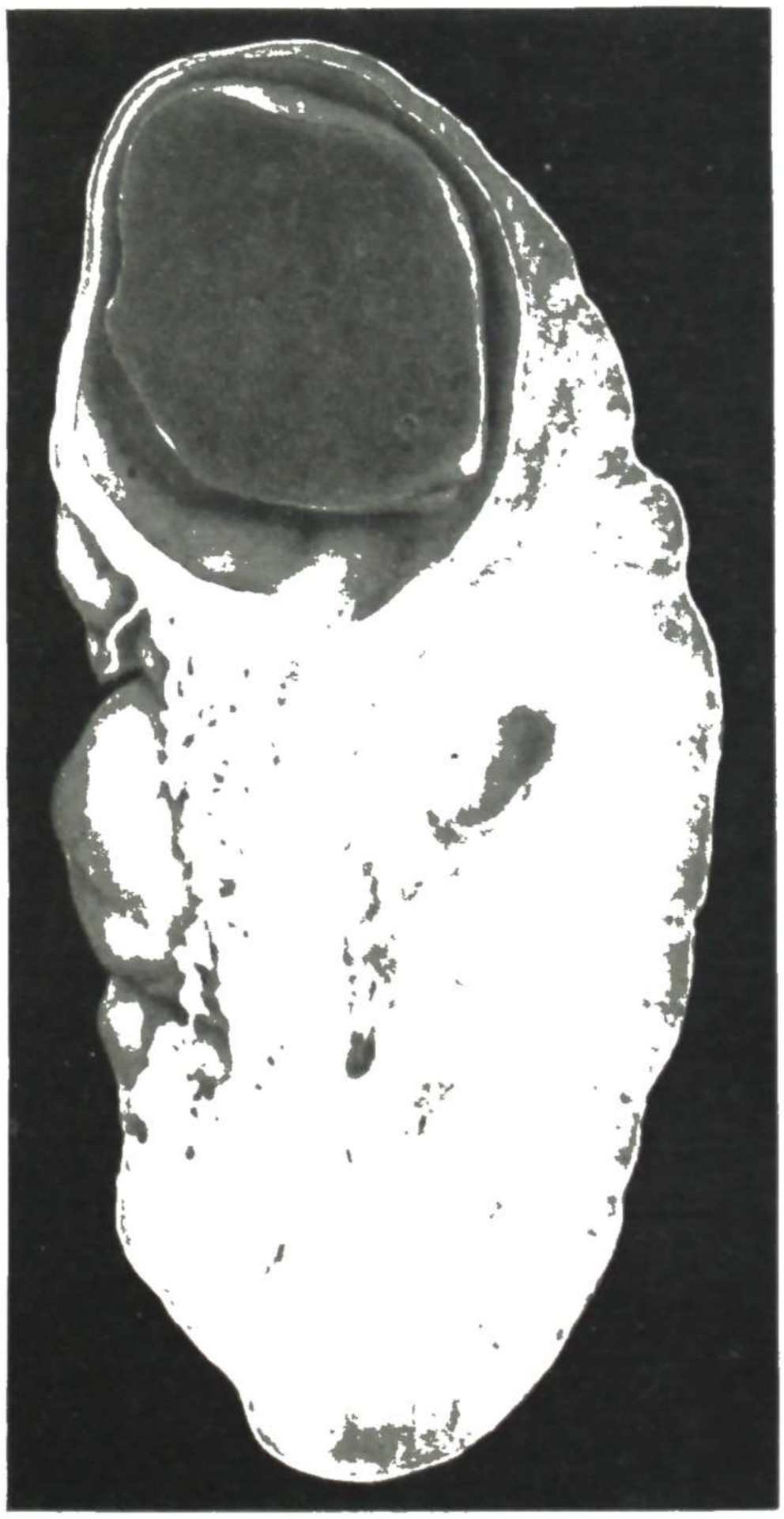


Fig. 1028.

Fig. 1027.—Krukenberg tumor of ovary.
Fig. 1028.—Same specimen shown in section. Gyn. Lab.

satisfactory one. It was used by Montgomery and Farrell in classifying their cases for clinical discussion, and the microphotographs showing a typical slide for each of the three grades are from their report.

Fig. 1024 shows Grade I, which has well-marked glandular character, and represents the lowest grade of malignancy. Fig. 1025 shows Grade II, which has only imperfect gland formation, and represents increased malignancy. Fig. 1026 shows Grade III, which has no gland formation, and represents the highest grade of malignancy.

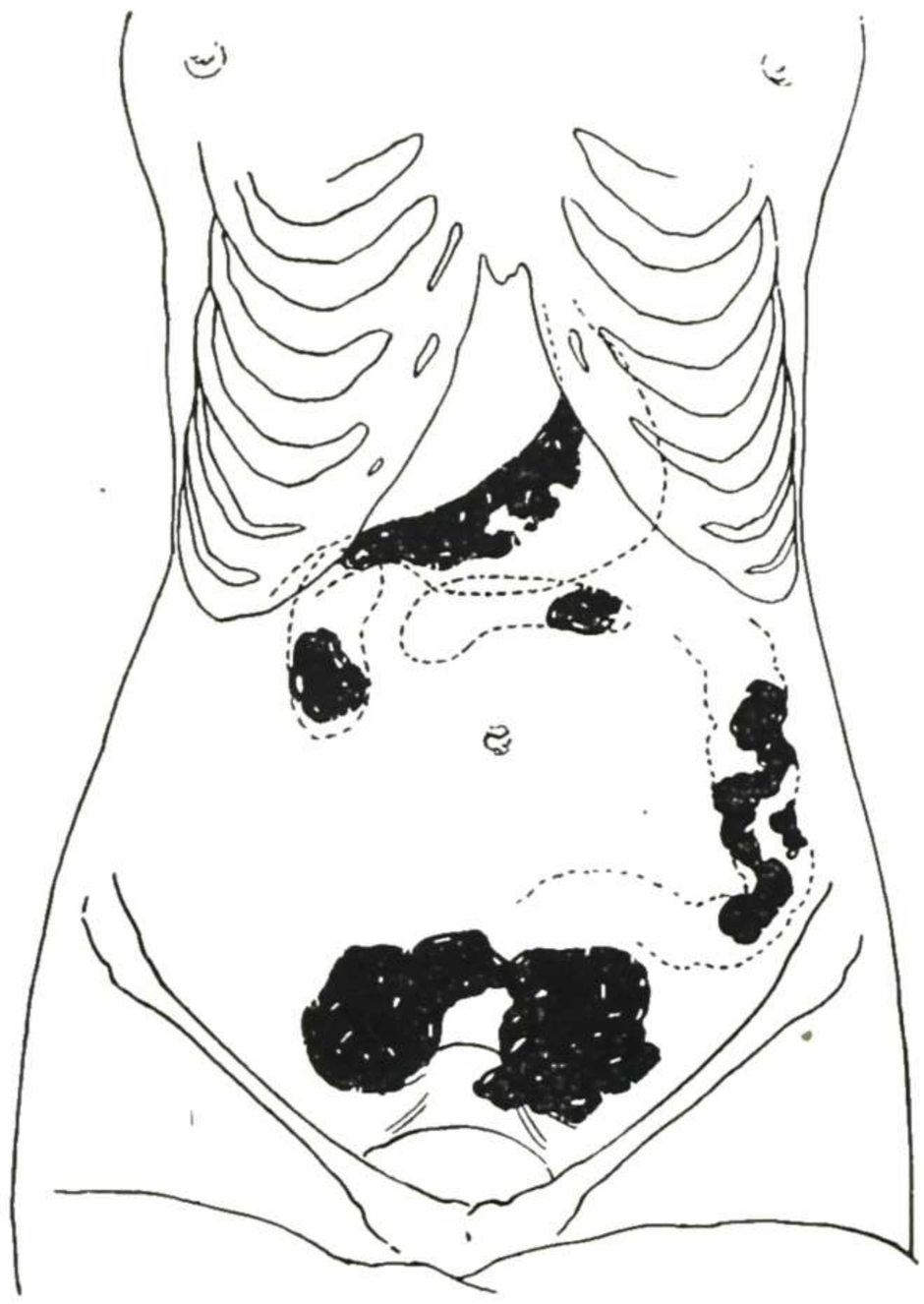


Fig. 1029.

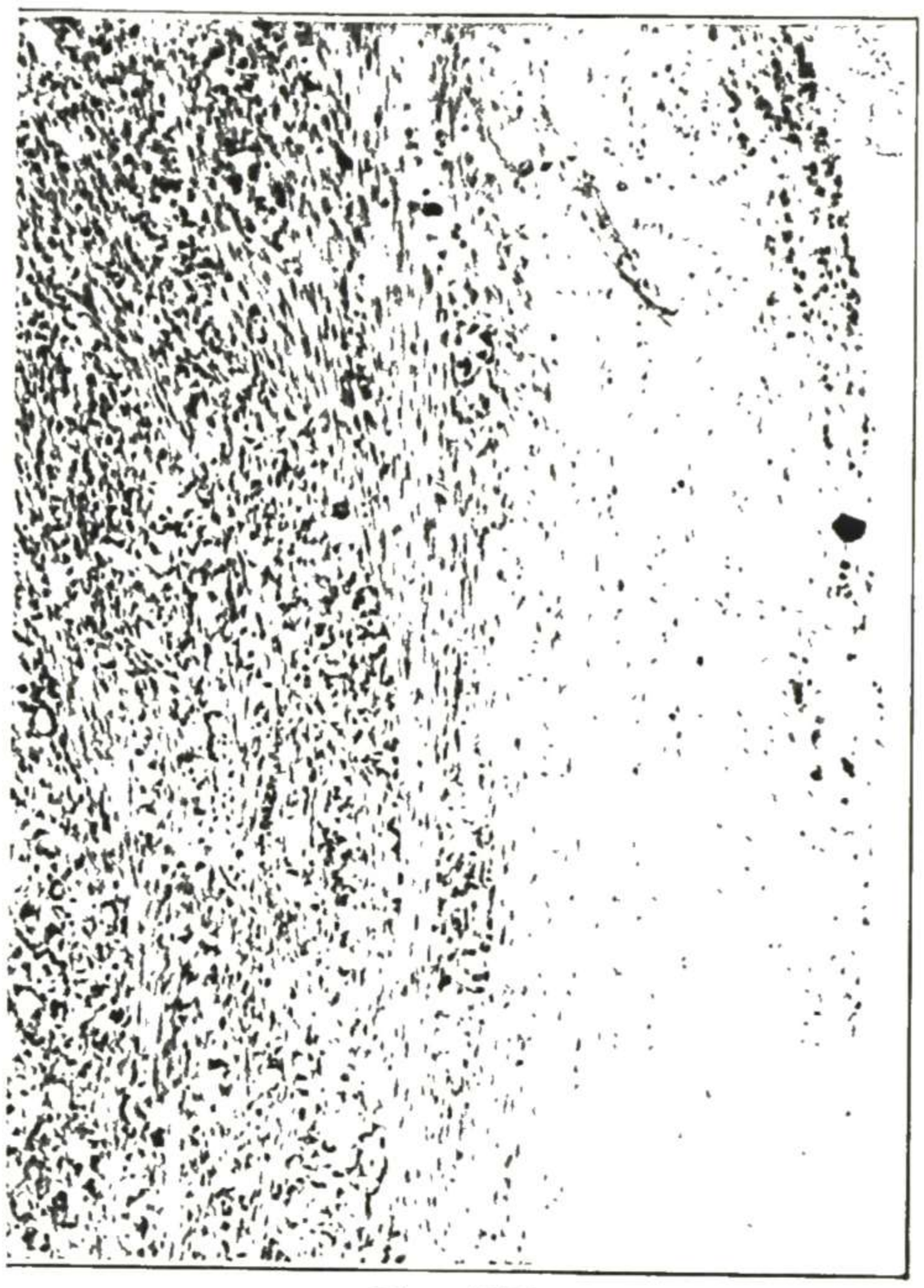


Fig. 1030.

Fig. 1029.—Krukenberg tumor, indicating the primary growth (in the stomach) and the distribution of the secondary growths in this case (both ovaries, right kidney, pancreas, and sigmoid flexure of the colon).

Fig. 1030.—Krukenberg tumor of ovary. Microscopic section, low power. Gyn. Lab.

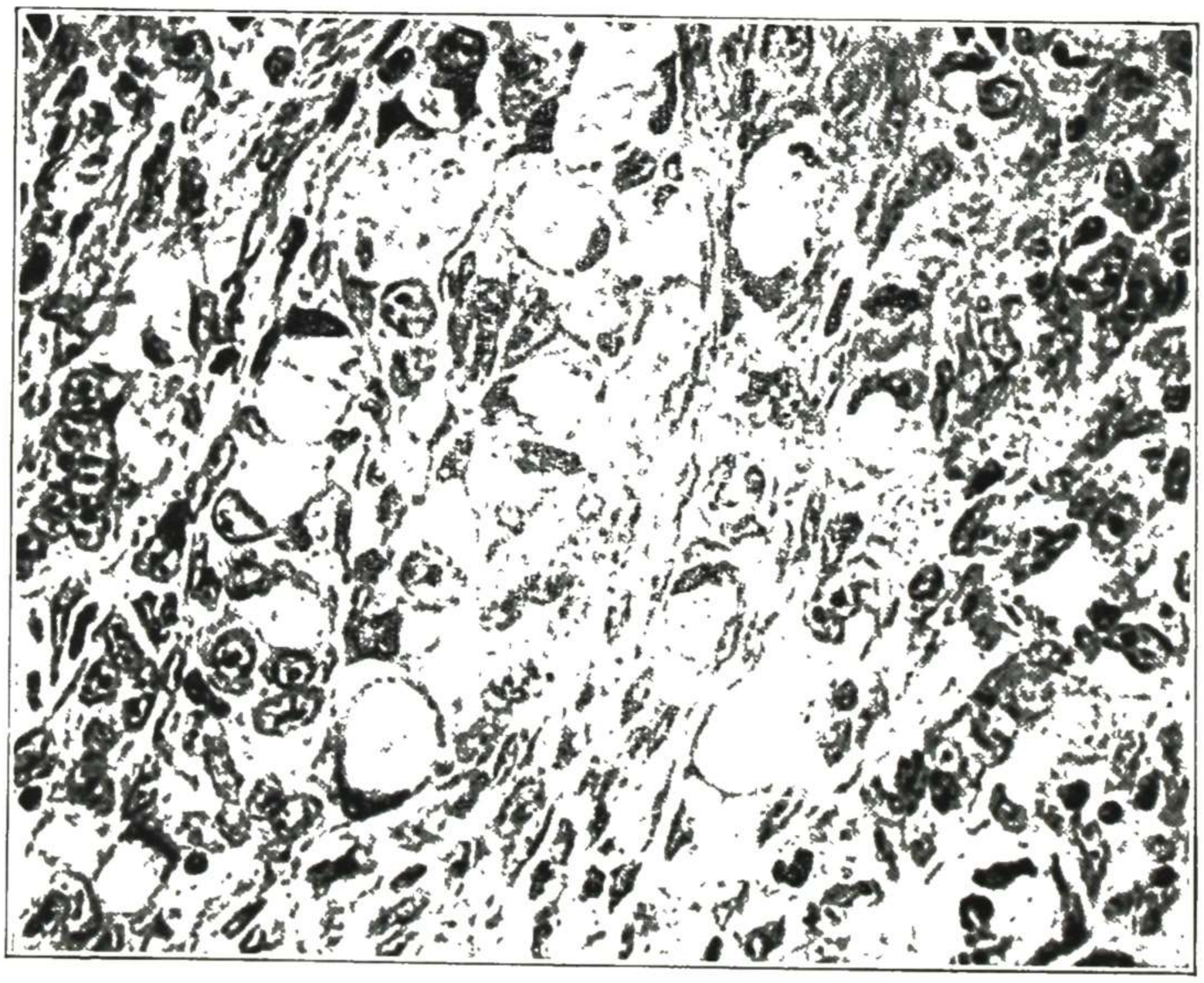


Fig. 1031.—Krukenberg tumor of ovary. High power of specimen shown in Fig. 1030. The characteristic "sickle" or "signet ring" cells are well shown. Gyn. Lab.

For the reasons above mentioned, every specimen of ovarian carcinoma sent to the laboratory should have this grading recorded, and the classification in this respect should be included in the report to the physician.

Secondary.—Metastatic carcinoma of the ovary is not uncommon. In a series of 79 ovarian carcinomas secondary to primary tumors in the abdominal cavity reported by Schlagenhaufer, 61 were of gastric origin, 10 intestinal, 7 gallbladder and 1 probably pancreatic. Handley in 442 autopsies on patients dying of mammary cancer found metastases to the ovaries in 13.4 per cent.

In the early stages the metastases appear as small circumscribed nodules on the surface or in the substance of the ovary. The lesions are usually bilateral and subsequent growth of these ovarian tumors is very rapid. Early death of the patient usually prevents the tumors from becoming very large, though some large ones have occurred.

The most typical of the metastatic ovarian growths is the Krukenberg tumor, which is secondary to a certain type of gastric and intestinal carcinoma. These tumors are fairly large, as a rule, are smooth, and have a glistening white surface. They are usually solid and are hence easily mistaken for sarcoma. The gross and microscopic characteristics of such a tumor are shown in Figs. 1027 to 1031.

The microscopic examination of the Krukenberg tumor shows an edematous connective tissue of spindle cells, of various sizes, shapes, and staining qualities, interspersed with areas of necrosis and myxomatous degeneration. The cells which are characteristic of this tumor, however, are the large mucus-producing epithelial cells. These cells may be scattered through the connective tissue stroma or they may form alveoli. In the cells that are filled with the mucin the nucleus is pressed against the cell wall forming a crescent (Fig. 1031). The names of "seal ring," "signet ring," or "sickle" cells have been applied to these cells, and their presence aids in the diagnosis of the Krukenberg type of tumor.

The other types of metastatic tumors reproduce cells similar to those of the primary carcinoma, as do also the growths reaching the ovary by direct extension.

It is probable that other secondary carcinomatous growths are started in the ovaries by particles which have become detached from the primary carcinoma and through peristalsis and gravity have been carried to the ovaries deep down in the pelvis. It is this fact which most plausibly explains the common bilaterality of the solid ovarian cancers, a point of great practical importance and well justifying the demand of certain writers always to remove both ovaries even if only one macroscopically seems affected by a malignant growth.

For this same reason it becomes imperative in all cases of diagnosed or suspected bilateral ovarian carcinoma to search most carefully for a possible primary carcinoma in the gastrointestinal tract or in another organ within the abdominal cavity. It is obvious that in these cases operative efforts of necessity must prove futile.

Sarcoma.—Sarcoma of the ovary may be of the spindle-cell or round-cell variety and may be primary or secondary.

Primary.—Between 2 and 5 per cent of ovarian growths are primary sarcomas. One has been reported by Doran in a seven months' fetus, and this is the one type of tumor which is more common in young people. Pfannenstiel states that 40 per cent of the patients are under twenty-five years of age and Hubert collected 200 cases in children. Frank states that in his series they were most frequent between the ages of eighteen and twenty-five years. Bloody ascites is almost always present.

These malignant tumors are usually secondary to a fibroma of the ovary.

The gross appearance and the consistency of these tumors depend upon the degree of maturity of the constituent cells and on the amount of fibrous tissue present. The soft friable tumors are the round-cell tumors while the spindle cell variety is firmer and whiter in color. These tumors are usually bilateral and are shaped like a large kidney, due to the fact that the hilus

Fig. 1032.

Fig. 1033.

Fig. 1032.—Sarcoma of the ovary secondary to a sarcoma, originating in a uterine myoma. The sarcomatous infiltration has involved old remnants of a corpus luteum. Gyn. Lab.

Fig. 1033.—Mitotic figure in sarcoma cell. (Caylor and Masson—*Am. J. Obst. and Gynec.*)

remains retracted while the rest of the ovary enlarges. Tumors of the round cell type are so friable that they frequently fall apart when being removed at operation. The surface is usually irregular but fairly smooth, and there are necrotic areas present. On cut surface, one sees cystic cavities from necrosis or hemorrhage.

Frank divides the microscopic types into those in which unripe cells predominate and those in which the ripe cells make up the larger part of the tumor. The unripe types approach most nearly the embryonal types, and these include the round cell, the polymorphous and giant cell, and the myxosarcomas. The spindle cell, myosarcoma, chondrosarcoma, and osteosarcoma are made up of well-differentiated cell types. There is usually a mixture of these various types of cells in different parts of the tumor. In 100 cases of ovarian sarcoma,

reported by Wolff, 44 per cent were spindle cell, 38 per cent round cell, 5 per cent mixed, and the remaining 13 per cent were osteo-, myxo-, and melano-sarcoma (secondary).

The spindle cell tumors microscopically show a less differentiated fibrillar structure than do the benign fibromas. The cells are more ovoid, and the nuclei stain irregularly. Mitotic figures are frequently seen. Multinucleated cells are not uncommonly found. Areas of necrosis are common.

The round cell type may occur as either small round cells or large round cells. Occasionally they assume an alveolar arrangement. Necrosis and hemorrhage are very common in these rapidly growing tumors. The small cells somewhat resemble lymph cells.

Durfee, Clark and Peers reported a primary lymphosarcoma of the ovary.

The polymorphous cell or mixed cell variety is characterized by the marked variation in the size and shape of the cells and by the frequent occurrence of giant cells. In the myxosarcomas the so-called star cells are present, containing flagella-like processes.

Secondary.—The melanosarcomas are usually secondary, though they may arise from a melanoma from skin in a dermoid cyst. These contain melanin and have the same characteristics as a melanosarcoma elsewhere. Other secondary sarcomas present the characteristics of the growths from which they come. Fig. 1032 shows a sarcoma of the ovary secondary to a sarcoma arising in a uterine myoma. A rapidly growing sarcoma furnishes good examples of mitosis (Fig. 1033).

The well-differentiated cell tumors rarely recur when removed early. The less differentiated tumors, especially the alveolar type, are most malignant and usually recur within two years. Operative cures in some series run as high as 33 per cent.

Diagnosis and Treatment

Owing to the rarity of solid tumors of the ovary and the absence of distinctive symptoms, the **diagnosis** is usually made only after the abdomen is open. In the case of a firm mass presenting the symptoms and signs already described for a small ovarian tumor (except fluctuation) a probable diagnosis of solid tumor of the ovary may be made.

If there is ascites, the fluid from tapping should be centrifuged and the residue fixed, cut and stained for microscopic examination. It may show cancer cells and even a special type of cancer cell, thus permitting a very definite diagnosis.

The great majority of ovarian carcinomas occur in the ages between forty and sixty. Lynch in his instructive paper reviewing 110 cases of ovarian cancer presents an *age-incidence* chart, a *duration of disease* chart covering 49 cases, and a *survival* chart covering 62 cases.

The **treatment** for every solid tumor of the ovary is prompt removal by operation. Prompt removal is important because of the frequency of malignant development. If the growth is already inoperable, then deep x-ray treatment is advisable and may give considerable relief.

In regard to ovarian malignancy brought to light at operation, several important questions arise, including the following: What types of operation

should be employed in the different conditions found? Is irradiation treatment afterward of definite value? What is the prognosis (patient's life expectancy) in the various classes of ovarian malignancy? Help on the problems in this connection has been given by several writers in reporting series of cases.

Montgomery and Farrell, in reporting 22 cases, reviewed the literature and found that of the nearly one thousand cases of ovarian carcinoma reported, very few were recorded in sufficient detail to be used in a critical analysis of results. Among the conclusions at the close of the analysis of their cases are the following:

A comparison of the results of treatment in various series of reported cases of ovarian carcinoma is difficult because of the lack of uniform data. If accurate statistics as to the efficacy of any treatment are to accumulate, it is important that the histologic type of tumor, its grade of malignancy, degree of operability, and the amount of irradiation administered be noted in case reports.

The histologic grading of malignancy is important in the prognosis of ovarian carcinoma. Only one patient in our series whose tumor was of high-grade malignancy has survived for more than five years. All others with tumors of intermediate and high grades of malignancy are dead. Those with tumors of the intermediate grades lived longer than those in whom the malignancy was of a high grade. The more completely operable the tumor the greater the life expectancy.

Postoperative roentgen irradiation is often of value in relieving pain and ascites and in reducing the size of the tumor. Comparison of this series of patients given postoperative irradiation with a group treated by operation alone, indicates that the duration of life is longer in the irradiated patients. Nearly all patients with ovarian carcinoma, regardless of the hopelessness of the prognosis, where the general condition permits, should have postoperative irradiation.

Pathologic Grading.—The details of pathologic grading of ovarian carcinomas, representing degrees of malignancy, are described and illustrated under Pathology.

Clinical Grouping.—The importance of the clinical grouping of ovarian carcinoma cases is emphasized by Montgomery and Farrell, and the grouping they suggest is a practical and helpful one. The essential features are as follows:

Clinical Group I. The tumor is completely removable, and without involvement of any other structure, as far as can be determined at operation.

Clinical Group II. The tumor is completely removable, but with some disturbance of other structures, such as adhesions or involvement of another structure which can be removed (e.g., the other ovary, bilateral tumors).

Clinical Group III. The tumor is only incompletely removable, on account of definite extension to structures left. This group includes all cases in which a partial operation is done, with the hope of taking care of the remaining part by irradiation.

Clinical Group IV. The tumor is irremovable, because of extensive involvement of adjacent parts or because of distant metastasis. Only a specimen of the growth can be removed at the operation.

Types of Treatment.—In an interesting paper on ovarian tumors, H. C. Taylor, Jr., presents the following helpful suggestions as to the handling of patients with carcinoma of the ovary:

At three stages in the treatment of a case of ovarian carcinoma, decisions must be reached as to the course to be followed. (1) When the patient is first seen, whether an operation is to be performed; (2) when the abdomen is open, how extensive an operation is to be undertaken; and (3) after the operation is complete, whether x-ray is to be given.

1. *Operability.*—In many cases of ovarian cancer a definite diagnosis is not arrived at till the abdomen has been opened, so that one must recognize laparotomy as usually the first procedure. This should not, however, be the invariable approach because the surgical exploration of advanced cases is accompanied by a high mortality rate.

Attempt should be made, therefore, to eliminate two categories from the group to be operated upon. (1) In all cases of apparently malignant ovarian tumor the possibility of the growth being secondary in the ovary must be thought of. X-rays of the gastro-intestinal tract should be made, and operation given up when any other lesion besides the ovarian is discovered. (2) Certain very advanced cases with ascites, cachexia, large pelvic tumors, and upper abdominal masses, are readily recognizable as inoperable, and these cases should have their treatment limited to external radiation.

2. *The Extent of the Operation.*—When at the time of operation the growth is found apparently confined to one or both ovaries, there is a general agreement that a complete hysterectomy should be performed, with the removal of both appendages. The preservation of an apparently uninvolved ovary is rarely to be considered, for as Norris has shown, in 17.5 per cent of such cases the grossly normal ovary is later found in the laboratory to contain foci of cancer cells.

The extension of the operation to the removal of single metastatic lesions from organs outside of the pelvis is a dubious procedure. Only in the case of an isolated metastasis in the omentum whose removal does not increase the severity of the operation to an appreciable degree, is such a procedure justifiable, and one patient so treated at the Roosevelt Hospital was in good health when last seen four years after her operation. Resection of part of the bladder or intestine was carried out in a few of the earlier cases but proved both futile and dangerous.

When cancer is found widely disseminated on the pelvic or general peritoneum, a question arises as to whether any surgical procedure should be carried out. Such a condition was found in approximately half of the Roosevelt primary cases. It has been our practice under such conditions to remove as much of the tumor tissue as possible, partly because of the temporary palliation, partly because of the improved psychologic effect on the patient resulting from the disappearance of visible evidence of tumor, partly because of the possibility that x-ray may be more efficient when directed at smaller masses of tissue.

3. *Postoperative Radiation.*—In view of the bad results obtained by the simple surgical treatment of ovarian cancer, postoperative radiation therapy should be given in practically all cases. This opinion is held as a result of favorable reports from outside sources although our own series shows no cures and no increase in the average duration of life attributable to x-ray or radium therapy. The relative failure in this series is very likely dependent upon inadequate dosage.

Kean's conclusions in reporting work of the New York Cancer Institute are as follows:

> All cases of ovarian carcinoma should be treated by surgery and irradiation.
> Many types of carcinoma of the ovary are radiosensitive.
> Life is definitely prolonged in many cases where surgical treatment has been combined with irradiation, as against those patients who had surgical treatment alone.
> Even in hopeless cases the patient may benefit a great deal by palliative x-ray therapy.

This corresponds with the experience here (Mallinckrodt Institute of Radiology, furnishing x-ray service to the Washington University Group of Hospitals), both as to our personal experience in having patients definitely benefited by the x-ray treatment and as to the general experience of the Institute.

When the diagnosis of malignancy is fairly certain and the patient is in or past the climacteric, it is advisable to give the radiation (deep x-ray therapy) before operation. This preliminary radiation checks the carcinoma activity temporarily and lessens the danger of spreading active malignant cells in the operative area. It is well to wait some weeks after the radiation before doing

the operation—long enough to obtain the desired cancer-cell devitalization from the x-ray and for the patient to make good recovery from the digestive disturbance of this deep therapy.

When the diagnosis is doubtful and there is a fair chance of nonmalignancy, and especially in younger patients, operation at once is advisable, the question of radiation treatment being postponed till the diagnosis is settled at operation or by subsequent microscopic examination.

Taylor gives in a recent article the changing conception of ovarian tumors, and tackles again the old and ever-new subject of classification.

The Question of Operation

Reviewing the subject of ovarian cancer, with its symptomless development and the possibility of malignancy in any uncertain ovarian mass, there stands out one question of special importance in regard to every mass felt in this region, namely, "Is operation needed or not needed?"

The advisability of operation in any case depends on the character of the mass and the symptoms resulting from it. A definite diagnosis identifies the character of the mass. In some cases the differential diagnosis can be made with reasonable certainty. In other cases the diagnosis remains doubtful despite the use of the various diagnostic measures.

The pathology, symptomatology, and diagnosis of the various types of ovarian tumors have been considered in detail and we shall now pass to certain points of special importance in deciding what should be done for the patient. We shall consider first the cases in which the diagnosis is clear, and afterward the cases in which the diagnosis is doubtful.

Diagnosis Clear.—In these cases in which the diagnosis is fairly clear as to the character of the mass, one may be guided by the following general statements:

Follicular cysts and *corpus luteum cysts* seldom require operation. These cysts are usually small and are not likely to increase to a serious extent. Occasionally an ovary thus enlarged will prolapse and give persistent symptoms requiring operation, or still more rarely, such a cyst will enlarge sufficiently to cause symptoms from pressure or from torsion of the pedicle. But usually these simple cysts do not cause symptoms nor necessitate operation. Most of those which are removed are so treated incidentally in the course of an operation for some more serious trouble.

Theca-lutein cysts (due to hydatidiform mole in the uterus) are enormously enlarged graafian follicles. This great enlargement of the ovarian follicles is due to the excessive formation of stimulating hormones by the cells of the new growth in the uterus. When this excess hormone formation is stopped by removal of the uterine growth, the giant follicles may return to near normal size. Hence, they should be given a chance to do so without abdominal operation, except in those cases where they are already causing serious pressure disturbance.

Even when the cystic enlargement of the ovaries is so great as to cause marked abdominal enlargement, the plan of treatment is to eliminate the hydatidiform mole by uterine curettage and give a chance for the ovarian enlargement to subside without operative disturbance of the ovaries. Thus, the ovarian endocrine function and the possibility of future childbearing are preserved.

When the abdomen has been opened under the tentative diagnosis of an ovarian cyst requiring removal, if both ovaries are found to be involved by many cysts with very thin walls and clear contents, care should be taken to eliminate hydatidiform mole of the uterus with resulting theca-lutein cysts of the ovaries before doing radical surgery on the ovaries.

Involvement of the ovaries by theca-lutein cysts is so extensive and deep-seated as to give the impression that all ovarian tissue and ovarian function are already destroyed and hence excision of the cysts and ovaries is needed. But in reality there is much ovarian tissue left, though it is so thinned out by the crowded cysts that it cannot be identified. A history of recent menstruations indicates functioning ovarian tissue despite the deceptive appearance. If menstruation has been missed for a month or two, this should arouse suspicion of early pregnancy with possible hydatidiform mole and resulting theca-lutein cyst enlargement of the ovaries. Irregular bloody discharge with undue cystic enlargement of the corpus uteri (beyond that expected from the duration of pregnancy) are further indications of possible hydatidiform mole formation.

In such circumstances radical operation on the ovaries is contraindicated. The larger cysts may be punctured to relieve pressure, the abdomen closed, and then the uterus curetted. The curettage may bring out the small grapelike cysts characteristic of hydatidiform mole, and thus at once confirm the diagnosis. At any rate, the curettage will give tissue for microscopic examination and elucidation of whatever pathological process is going on in the uterus.

The Aschheim-Zondek test is helpful not only in the early diagnosis of hydatidiform mole, but also in determining whether active chorionic tissue persists after curettage. If the microscopic investigation of curettings shows chorioepithelioma, appropriate radical measures are to be employed promptly.

A small *parovarian cyst* may cause no symptoms and show no tendency to increase in size, in which case operation is not necessary. Such a cyst, however, should be watched by check-up examinations, that any tendency to progressive increase may be noted.

Endometrial cysts are very erratic in growth and in the causation of symptoms. Incidental findings at operation and in postmortem work indicate that small areas of endometriosis may remain quiescent indefinitely. Hence small to medium endometrial lesions which consist principally of firm induration back of the uterus laterally and cause no serious symptoms do not require operation. Accompanying distinct cyst formation, however, indicates a stage of progress which usually requires operation.

All other growths of the ovary, such as the proliferating cyst, dermoid, teratoma, granulosa-cell tumor, arrhenoblastoma, dysgerminoma, Brenner tumor, carcinoma, and sarcoma, require operative removal because of the pathological character, which threatens the life of the patient. Such growths, even though not yet causing troublesome symptoms, should be removed promptly. The risk of operation in such a case is much less than the risk of waiting.

Of course any ovarian growth causing troublesome symptoms, even the simple growths previously mentioned, should be removed unless there is some overbalancing contraindication.

Diagnosis Doubtful.—When the exact character of the mass still remains doubtful after careful analysis of the history and examination findings, the diagnostic problem shifts to a group determination. Is this lesion one of a group requiring operation or one of a group in which operation is contraindicated?

In settling this point we must consider the various conditions which may be present. In doing so we must keep in mind not only primary conditions but also possible complications. For the purpose of such consideration the cases may be divided into two groups, one presenting a medium-sized mass as the principal feature, and the other presenting an enlarged abdomen.

Medium-sized Mass.—A mass of moderate size (from medium orange to large grapefruit) without acute symptoms may be due to ovarian tumor, full bladder, uterine pregnancy, tubal pregnancy, myoma, chronic adnexal inflammation, pelvic endometriosis, pelvic tuberculosis, or some extragenital conditions, such as diverticulitis, tumor of sigmoid, cecum, or rectum, or a mass from the urinary tract.

If acute symptoms are present, we must consider ovarian tumor with complications (torsion of pedicle, inflammation, endometriosis, intracystic hemorrhage or appendicitis), tubal pregnancy, uterine pregnancy with complicating inflammation, myoma with associated appendicitis or salpingitis, and extragenital conditions which might give rise to a painful mass in this area.

In the groups requiring operation may be placed ovarian tumor with troublesome symptoms (whether the symptoms are from the tumor or from some complications that can be taken care of at the operation), tubal pregnancy, and appendicitis. In the group in which operation is contraindicated may be placed at once uterine pregnancy (except when there is some special complication), acute salpingitis, and the extragenital conditions with the exception of appendicitis. In these cases of possible extragenital lesion, operation is contraindicated until the required extragenital investigation and decision.

It is clear then that before advising operation we must exclude uterine pregnancy (except when complicated by some definite operative indication), acute salpingitis, and extragenital lesions except appendicitis. In cases in which pregnancy cannot be otherwise definitely excluded, an Aschheim-Zondek test may settle that point. It may become positive by the time menstruation is first missed or it may continue negative for six weeks of pregnancy. A positive reaction, however, indicates only that there are active fetal elements somewhere in the patient. Whether they are in the uterus or in the tube must be determined by other examination findings.

A filled or partially filled bladder may give a very deceptive cystic mass in the pelvis and in some cases catheterization may be necessary to exclude it. In those cases in which extragenital lesions cannot be clearly excluded as the cause of the mass, it is ordinarily advisable to have a gastrointestinal x-ray series in the possible intestinal cases and a cystoscopic investigation in the possible urinary-tract cases.

Before advising against operation we must exclude ovarian tumor with troublesome symptoms, tubal pregnancy, and appendicitis (either as a primary condition with a large mass of exudate or as an active complication of some other mass). Until these menacing conditions are definitely excluded, the case must be considered possibly one for prompt operation.

In myoma, chronic adnexal inflammation, pelvic endometriosis, and pelvic tuberculosis, operation may or may not be required, depending on the particular conditions present in each case. The determining conditions for each type of lesion are considered in the appropriate chapter.

Enlarged Abdomen.—In a doubtful case where the principal feature is enlargement of the abdomen, presumably by an ovarian tumor, the other conditions to be considered are obesity, tympanites with relaxed wall, ascites, encysted fluid (peritoneal tuberculosis), uterine pregnancy, extrauterine pregnancy, large myoma, distended bladder, hydronephrosis, pancreatic cyst, and enlarged spleen or liver.

All of these conditions are of gradual development, and the absence of acute threatening symptoms permits taking sufficient time for deliberate investigation of all the possibilities. Such differential diagnostic investigation carried out systematically to the limits, usually clears up the case as far as important uncertainties are concerned. In this connection the following special points should be kept in mind. Extrauterine pregnancy may advance to term with a remarkable absence of acute symptoms. A large myoma may have a considerable portion cystic, thus adding to the difficulties of differential diagnosis. A chronic distention of the bladder may be obscured by the statement of the patient that she passes urine frequently (distention with overflow). Some cases of peritoneal tuberculosis advance to abdominal enlargement with very few subjective symptoms, and the same may be said of hydronephrosis and of pancreatic cyst, hence the necessity for considering these lesions in all doubtful cases.

In the group of lesions requiring operation may be placed large ovarian tumor, extrauterine pregnancy, and large myoma. The group not requiring operation includes obesity, tympanites with relaxed wall, pregnancy, and distended bladder. In ascites, encysted fluid (from tuberculosis or ordinary chronic inflammation), hydronephrosis, pancreatic cyst, and enlarged spleen or liver, the decision as to operation for the lesion depends on the particular conditions in each case.

In cases of very large ovarian or parovarian tumor, the patient may be in such bad condition generally or locally as to make doubtful the advisability of attempt at radical operation. The special difficulties resulting from the great size of the growth are largely due to pressure. Though the abdominal structures will accommodate themselves in a remarkable way to a gradually enlarging mass, a limit is finally reached beyond which serious disturbances result from the pressure. The upward pressure crowds the diaphragm

and heart and lungs, causing at first disturbance on exertion and later necessitating the upright position in bed. Pressure on the large vessels causes edema of the lower extremities. Pressure on the deep vessels causes enlargement of the collateral vessels in the abdominal wall. Finally, pressure on the abdominal wall causes an increasing edema there, sometimes interfering with the circulation so much that dermatitis and superficial ulceration result.

These cases present a serious problem in handling so as to do what is necessary to put the patient on the way to recovery without at the same time upsetting her precarious reserve of vitality. The complications may interfere with complete examination, leaving one doubtful whether the condition is really ovarian cyst or ascites or a combination of the two. When the regular systematic differentiation has narrowed the diagnosis to this extent, there is a *temptation to employ paracentesis,* with the idea that it will easily settle the matter. There are some points to consider, however, before resorting to paracentesis in such a doubtful case. If it is an ovarian cyst, there is some danger of intestinal puncture. Though usually the intestines are pushed up above the tumor, a coil may be adherent anywhere over the anterior surface, especially in cases preceded or accompanied with inflammation. Again, there may result infection of the trocar-tract in the poorly nourished abdominal wall, thus interfering with subsequent operation. Third, the information gained by paracentesis is very limited compared to that supplied by a small abdominal incision and intraabdominal palpation.

Consequently, in the cases in which ovarian tumor cannot be excluded, the preferable plan usually is to prepare the patient for abdominal operation and then under local anesthesia open the peritoneal cavity by a small median incision. This incision may be made with the patient propped up, if the pressure-dyspnea prevents lying down. If an ovarian cyst is found, it may be tapped in a safe way and emptied to relieve the diaphragm pressure, after which the patient may lie down for respiratory anesthesia if such is required for the removal of the tumor.

In these doubtful cases this open incision is safer than the blind puncture of para centesis, yields more important diagnostic information, and permits removal of the tumor if such is found. If the doubtful condition proves to be ascites, information obtained through the open incision will indicate whether the ascites is due to liver disease or to malignancy at some other location in the cavity. Also, if the ascites is due to liver disease, helpful collateral circulation may be established by attaching the omentum to the abdominal wall.

Later publications emphasize two important points in connection with ovarian malignancy. Palliative medication in inoperable cases has been made more effective by the employment of androgen therapy. Beecham reviews the subject and also reports a group of cases in which the administration of testosterone propionate gave rapid and marked relief from pain, in addition to improving general condition.

In regard to diagnosis, the early stages of ovarian carcinoma are so symptomless that the growth is nearly always overlooked by both patient and physician until it has advanced to a stage beyond cure. The serious menace of "silent" ovarian carcinoma is considered with illustrative cases in a 1942 article by Crossen, along with details of effective remedial action.

CHAPTER XIII

MALFORMATIONS

The growth of an organ may be simply arrested or it may grow in the wrong way. In either case there results a malformation. Most genital deformities are due to partial arrest of development. To understand these malformations, it is necessary to understand something about the development of the organs.

POINTS IN DEVELOPMENT

The first structures indicative of the genitourinary organs are the **wolffian ducts,** which appear in the embryo about the fifteenth day, and the **wolffian bodies,** which appear on the eighteenth day. These structures represent the future kidneys and genital apparatus. They lie on each side of the median line.

During the fourth week another duct appears near the wolffian body on each side. These are the **muellerian ducts.** The wolffian ducts go to form the excretory ducts of the genital apparatus in the male. The muellerian ducts go to form the excretory ducts of the genital apparatus in the female. A part of the wolffian body of each side finally forms the genital gland of that side, i.e., the ovary in the female and the testicle in the male.

At the end of the first month the middle part of each wolffian body shows thickening and proliferation, resulting in the formation of elevated bands called "genital ridges." These are the earliest traces of the genital glands. For a few days they remain indifferent. Very soon, however, a difference in the two sexes is noticed. The primitive female gland "possesses a large number of the primitive sexual cells and evidences a tendency of its elements to arrange themselves into groups, in which the large primitive ova become central figures." The primitive male gland, on the other hand, shows a tendency to the formation of a network of cell cords—the forerunners of the seminiferous tubules. "Microscopic examination of the sexual primitive glands even at the end of the fifth week is capable of distinguishing the future sex of the being." In a short time there is a difference in the gross appearance of the gland, with a difference in the arrangement of the ducts.

The parts played by the wolffian ducts and muellerian ducts differ in the two sexes. In the **female** the muellerian ducts are the most important. The lower portions of the ducts of Mueller become fused and form the vagina and uterus, and the upper portions remain separated and form the fallopian tubes (Figs. 1034 to 1036). The lower end of the canal (future vagina) formed by the fused muellerian tubes is closed at first. Later the lower part of the septum, which shuts off this canal from the urogenital sinus, breaks down, permitting the canal (vagina) to communicate with the urogenital sinus. If this septum fails to break down, imperforate hymen results. The very end of