

CHAPTER IX

CANCER OF THE UTERUS

Cancer of the uterus is very common, running about even with cancer of the stomach for the sinister distinction of being the most frequent form of malignant disease occurring in the body. Welch, in a series of 31,000 carcinoma cases, found that the primary growth was in the uterus in 29 per cent and in the stomach in 21 per cent. Other series show somewhat different proportions. Of cancer of the female genital tract 93 per cent were uterine, according to the statistics of Hecht. Kamperman found cancer of the uterus in 4 per cent of all gynecologic cases.

Cancer of the uterus includes malignant growths of the cervix and malignant growths of the corpus uteri. Cancer of these two parts of the uterus differs so much in structure and in the problems of diagnosis and treatment that it is advisable to consider them separately. The disease occurs as carcinoma or sarcoma.

The subject of this chapter then may be divided into three parts, as follows:

Carcinoma of the Cervix Uteri

Squamous-Celled Carcinoma (Epithelioma).

Cylindrical-Celled Carcinoma (Adenocarcinoma).

Carcinoma of the Corpus Uteri

Endometrial Carcinoma.

Chorionepithelioma.

Sarcoma of the Uterus (Cervix and Corpus)

CARCINOMA OF THE CERVIX UTERI

This term signifies malignant disease of epithelial origin, situated in the cervix. It may arise from the squamous epithelium covering the vaginal surface of the cervix, in which case it is a squamous-cell carcinoma or "epithelioma." It may arise from the glandular epithelium in the interior of the cervix, in which case it is a cylindrical-cell carcinoma and is ordinarily designated adenocarcinoma. The cervix is the most frequent site of cancer of the uterus. Frankl states that 89 per cent are located there. Cullen in a strict analysis of his 128 cases of carcinoma of the uterus found that 93 (73 per cent) were in the cervix.

Etiology

The underlying cause of carcinoma, as of other forms of new growth, is still a mystery. An enormous amount of experimental work the world over has been directed toward discovering exactly the nature of the cause. Though the primary object has not yet been attained, the work has resulted in the accumulation of a vast store of knowledge on the negative side, that is, show-

ing definitely what it is not. This is an important step toward the final solution of the problem of cause, and it is valuable also in that it enables separation of wheat and chaff in the accumulating great mass of cancer literature.

To mention only one point as an example, the available evidence indicates that cancer is not due to a specific infectious agent, of either the microscopic or ultramicroscopic (virus) type. This eliminates the probability of finding a specific vaccine or serum. In spite of this, the literature contains voluminous and circumstantial accounts of how the cancer germ was traced to its lair and given quietus by this or that vaccine or cancer serum.

In his recent interesting and instructive summary of the fundamentals of cancer therapy, as a basis of present treatment and future developments, Carl Voegtlin, Chief of the National Cancer Institute of the Public Health Service, touches on this etiological problem as follows:

Both clinical experience and extensive study of cancer in animals strongly suggest that cancer is caused by the transformation of the normal cells of the body into cancer cells through the operation of a great diversity of factors and agents operating from within or from without the organism. As far as known now the malignant transformation is irreversible and expresses itself in a varying degree of differentiation and increased rate of cellular proliferation. What one needs to know in order to discover a rational specific therapy is (1) why the biologic behavior of cancer cells differs from the original normal cell and (2) what kind of biochemical differences account for the differences in biologic behavior. Such fundamental questions can be answered only on the basis of a much better understanding of cell physiology and biochemistry, as well as the functional and chemical interrelation of the various tissues and body fluids. There is reason to hope that this approach will be fruitful, given sufficient time.

Though the underlying cause of cervix cancer has not yet been discovered, some contributing factors have been identified, including age, chronic irritation, certain types of endocrine imbalance, and certain vitamin deficiencies. In regard to age, cancer of the cervix occurs most frequently in the decade between forty and fifty.

Koblanck gives the following age distribution from the statistics of 6,071 cases of both types of cervical carcinoma collected from the literature: Ages ten to nineteen, 2 cases, 0.03 per cent; twenty to twenty-nine, 220 cases, 3.6 per cent; thirty to thirty-nine, 1,472 cases, 24 per cent; forty to forty-nine, 2,168 cases, 33.7 per cent; fifty to fifty-nine, 1,464 cases, 24 per cent; sixty to sixty-nine, 531 cases, 8.7 per cent; seventy to seventy-nine, 214 cases, 3.5 per cent. Of 1,583 cases of cervical cancer reported by Schreiner and Wehr in 1934, 4.9 per cent were in women aged thirty or younger. The decade forty to fifty is the age of greatest frequency, but cervical cancer may occur at any age. Findley has reported a case in a six-month-old infant.

In regard to chronic irritation, *pregnancy* with associated lacerations of the cervix at delivery and subsequent chronic cervicitis plays an important rôle. The incidence of carcinoma of the cervix does not rise with multiple pregnancies according to Deelman, who states that one childbirth is as effective a cause as repeated labors. The subsequent *chronic cervicitis* is apparently the important factor in causing carcinoma to appear so frequently in this location. In the previously mentioned series in young women, reported by Schreiner and Wehr, all but one had had children and all gave a history of leucorrhœa.

Bailey studied 850 infected cervixes in "an inquiry into the basic cause and nature of cervical cancer," and reached the conclusion that chronic cervicitis is a definite and important factor in the causation of squamous-cell carcinoma of the cervix. He states among his findings: "Cervicitis and erosion of the cervix are definitely related to cancer of the cervix. . . . This relationship is effected through the agency of a factor common to both—an associated inflammatory exudate in contact with the epithelium. This is the intermediate causal factor, and is constant." This sums up the findings of authorities on this point, and it is hardly necessary to go into the various details worked out in the many papers on it.

The relationship of *leucoplakia* of the cervix to carcinoma was discussed to some extent under Leucoplakia, and it would be well to refer back to that in taking up this subject. In articles by Hinselmann, Hofbaur, Schmitz and Benjamin, and others a direct relationship, at least in certain cases, is clearly demonstrated. Borst states that the importance of leucoplakia in the development of carcinoma merits further clinical and pathological investigation. Schmitz cites cases showing the origin of carcinoma from leucoplakia. Hinselmann cites six cases of traced leucoplakia of the cervix that eventuated in cancer.

The work of recent years in animal experimentation indicates that *excess estrin* in combination with chronic irritation increases the tendency to abnormal cell growth and cancer. The marked physiologic stimulation of the epithelium of the genital tract by estrin might well be a factor in abnormal growth if wrongly directed by disturbing conditions. This influence is further discussed under Carcinoma of the Corpus in this chapter and also under Delayed Menopause in Chapter XVI.

Pathology

Cancer of the uterus is, in the beginning, essentially a local process. The apparently independent growths appearing later in various organs are simply metastases from the primary tumor. This fact has been firmly established by the most thorough and painstaking investigation by many authorities. The supposition that it is simply the local manifestation of some constitutional dyscrasia has no foundation. The important bearing of this on treatment is apparent.

Carcinoma of the cervix occurs in two forms: squamous-cell carcinoma (epithelioma) arising from the vaginal surface of the cervix, and the cylindrical-cell carcinoma (adenocarcinoma) arising from the glandular epithelium of the cervical canal. The squamous-cell variety is by far the most frequent. In Cullen's reported series of 93 cervix cancers, 74 (79.6 per cent) were squamous-cell and 19 adenocarcinoma. In our Barnes Hospital series of 121 cervix cancer cases analyzed, 108 (89 per cent) were squamous-cell and 13 adenocarcinoma.

SQUAMOUS-CELL CARCINOMA

The squamous-cell cancer of the cervix originates from the squamous epithelial cells covering the vaginal portion. Arising from that part of the cervix known as the "portio vaginalis," it is sometimes spoken of as "cancer of the portio."

The disease begins as a spot of infiltration on the vaginal surface of the cervix, at a point of persistent irritation. If the patient happens to be examined at this stage, the irritated spot is seen. That is all. There is no pain, there may be no bleeding or discharge, though there may be some discharge from the preceding chronic irritation. So far as the naked-eye appearance is concerned, it does not differ materially from a small area of chronic inflammatory infiltration or erosion.

The essential pathologic change is in the character of the epithelial cells at that point, and later they penetrate into the underlying connective tissue, as shown in Fig. 761. This invasion is resisted by the leucocytes which collect in the adjacent tissue.

Gross Pathology.—As the process continues, the carcinomatous infiltration, with the opposing round-celled (leucocyte and lymphocyte) infiltration, penetrates deeper into the tissues and the small area of induration gradually increases in extent. A small abrasion or ulcer appears (Fig. 762), or there may be a raised papillary area (Fig. 763). This usually bleeds slightly when

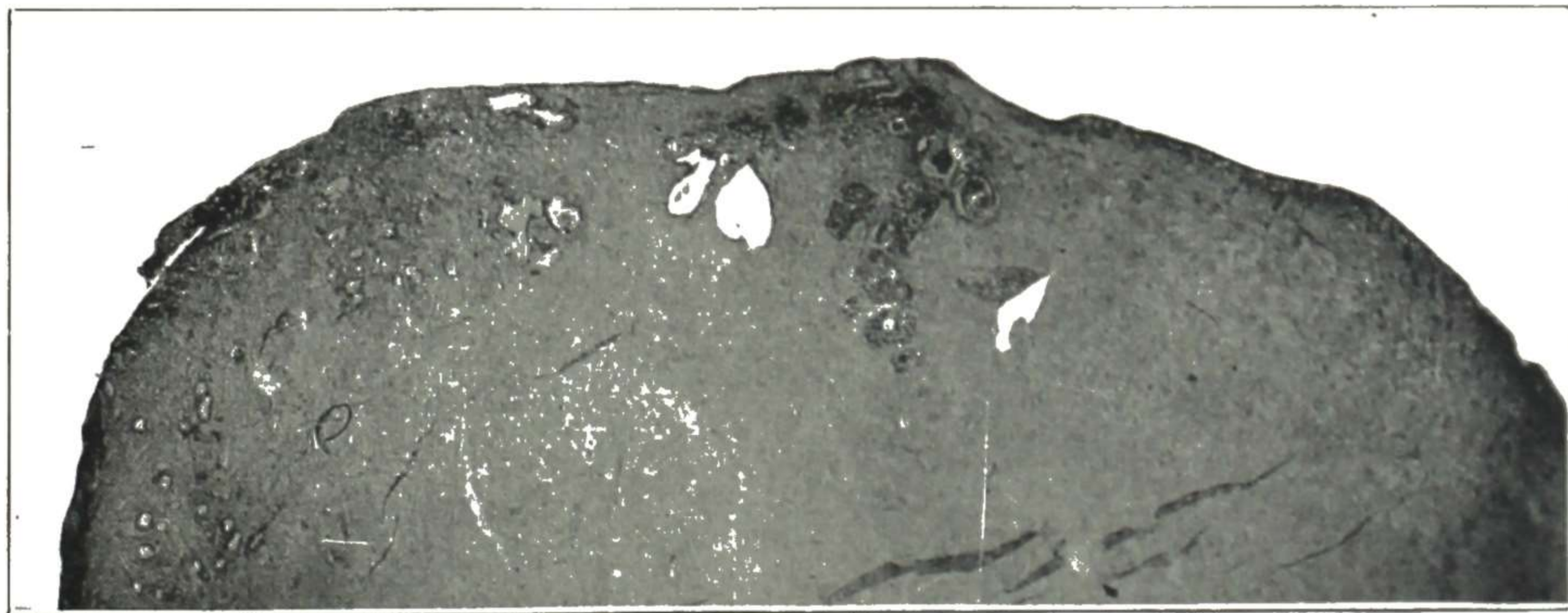


Fig. 761.—Section of a small squamous-cell carcinoma of the cervix. Section of the entire width of the cervix. At the left is seen the wall of the canal, with cervical mucosa and glands. At the upper left angle is the external os, and some distance out from the external os is the carcinoma. It is situated in an area of old erosion, remnants of the glandlike depressions being still present under the surface.

Surface inspection of this cervix would show only an area of irritation—nothing suggestive of the sinister activity going on underneath. Gyn. Lab.

touched. Frequently the first evidence of anything wrong noticed by the patient is this slight streak of blood or spot after coitus or after extra walking or other exertion. Already the disease has penetrated deeply into the cervix and out into the parametrium, as indicated in Fig. 764.

As the disease extends in the cervix, infiltration becomes appreciable on palpation and more ulceration (which may be mistaken for laceration or erosion) may be seen through the speculum. The disease is continuously progressive, the destructive cells penetrating more and more of the surrounding healthy tissues and to adjacent lymph vessels and glands, until there is a continuous mass of cancer tissue blocking the pelvis as in Fig. 765, with extensions to higher pelvic and abdominal glands (Fig. 766).

If there is much ulceration the cervix may be destroyed, its location at the vaginal vault being occupied by a granulating cavity as in Fig. 767. On the other hand, particularly in the aged with very slow-growing epitheliomas,

the formation of contracting scar tissue may so draw in the affected region that it cannot be seen. In such a case it can be appreciated only by palpation, which reveals induration at the vaginal vault (Fig. 768). All this time the growth is extending out into the parametrial tissues toward the adjacent organs and the pelvic wall.

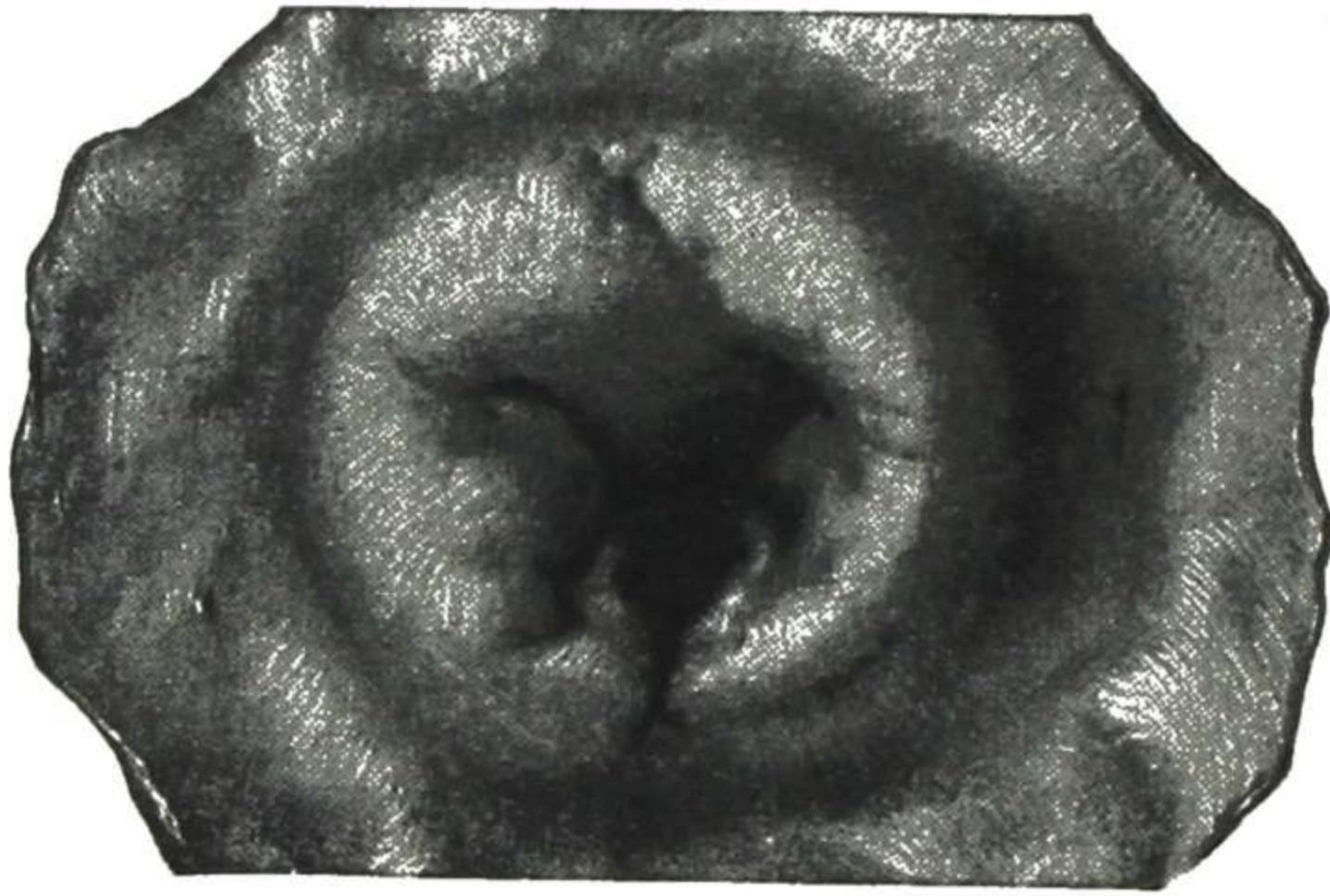


Fig. 762.

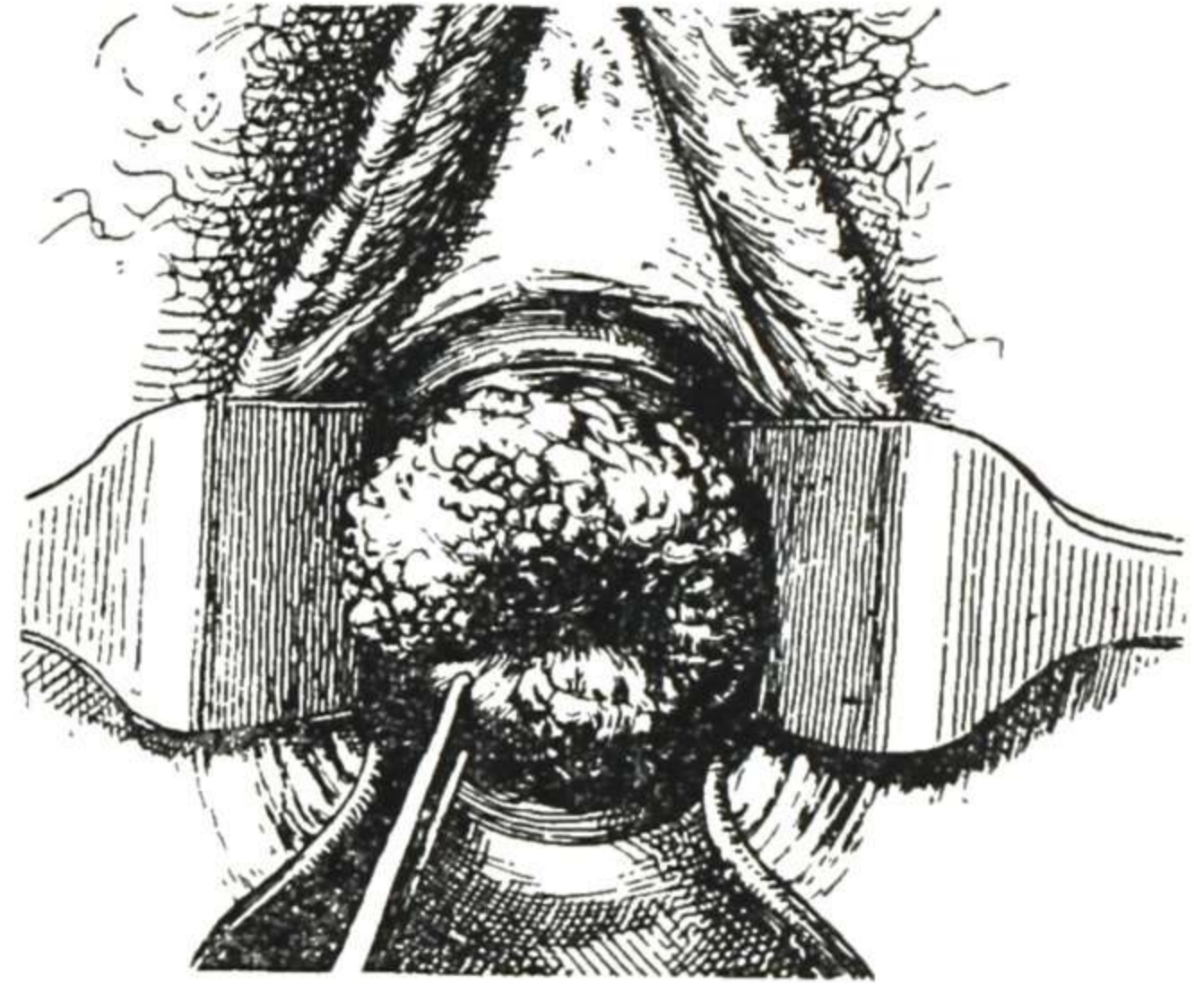


Fig. 763.

Fig. 762.—Drawing from a specimen of squamous carcinoma, or epithelioma, of the cervix. Notice that it has begun at one of the angles of the stellate tear. Gyn. Lab.

Fig. 763.—Epithelioma of the cervix, appearing as a papillary growth. (Kelly—*Operative Gynecology*.)

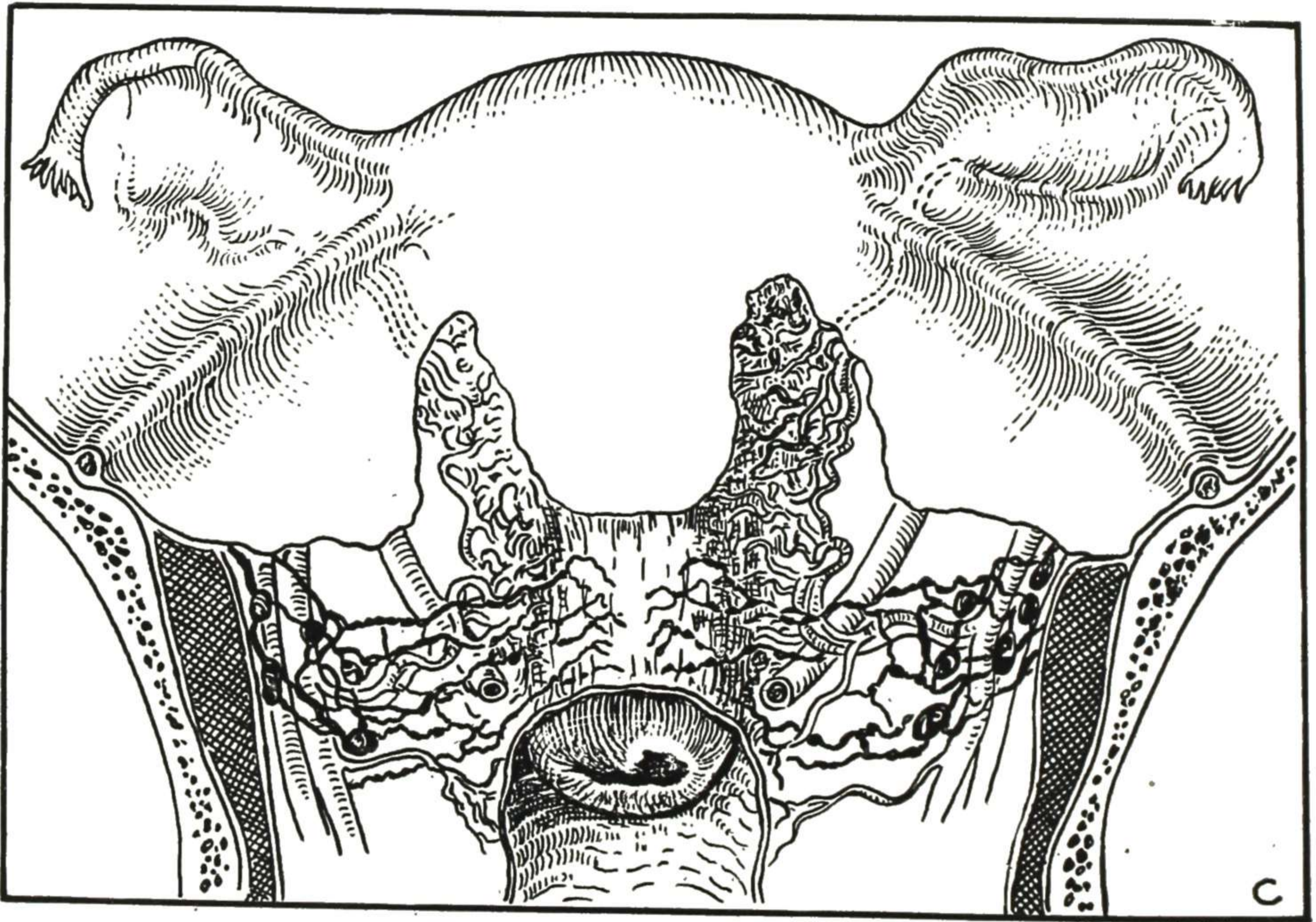


Fig. 764.—Early extension to deep-lying structures at the pelvic wall, as here indicated, before troublesome symptoms appear, is the cause of the high percentage of advanced cases found at first examination and the low percentage of cures.

In certain cases the carcinomatous ulceration extends into the bladder and into the rectum (Fig. 769), causing leakage of the contents of those organs into the vagina. In the later stages there may be compression of the pelvic

nerves and vessels, causing severe suffering and persistent edema of the lower extremities. Compression of the ureters with back-pressure destruction of the kidneys, as in Fig. 770, is a frequent terminal condition.

A **clinical classification into stages** is required for recording the extent of the disease in each case, along with the treatment measures employed and the

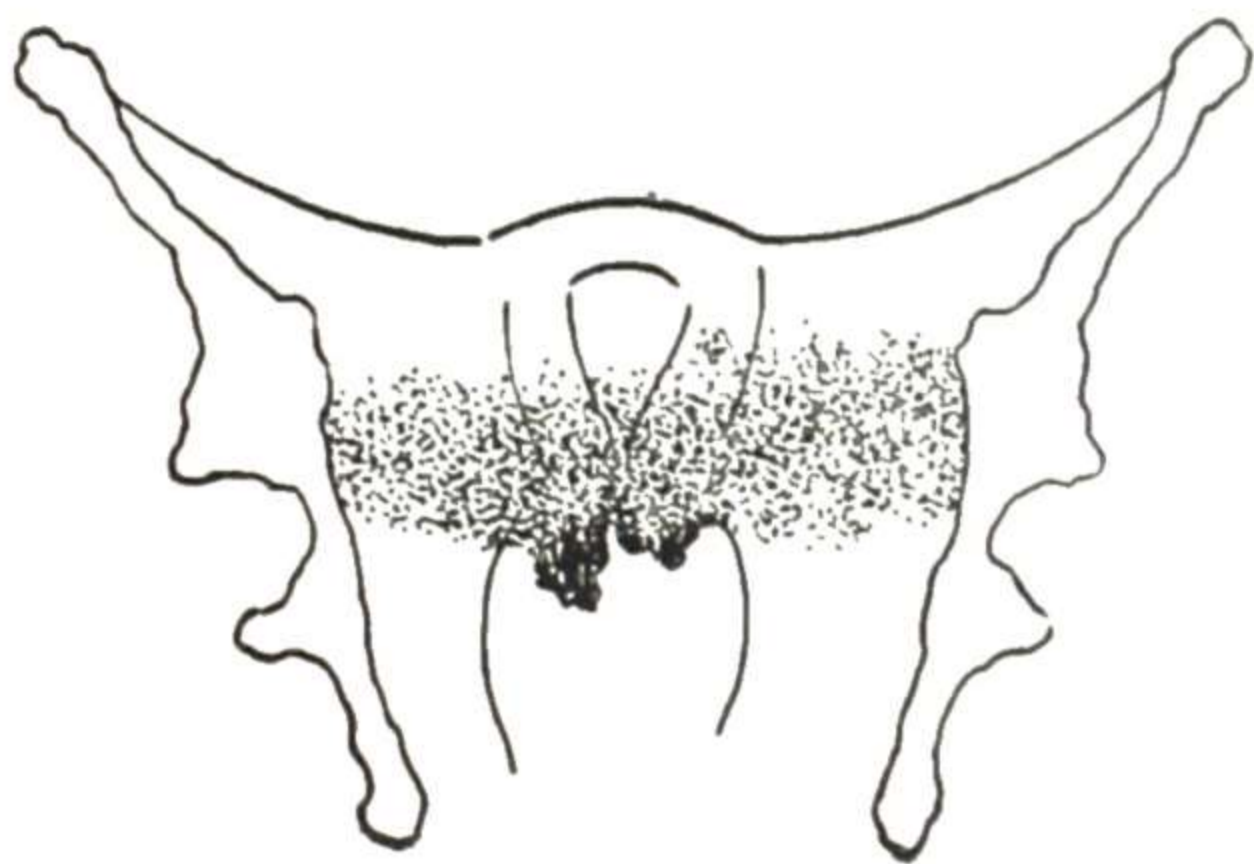


Fig. 765.

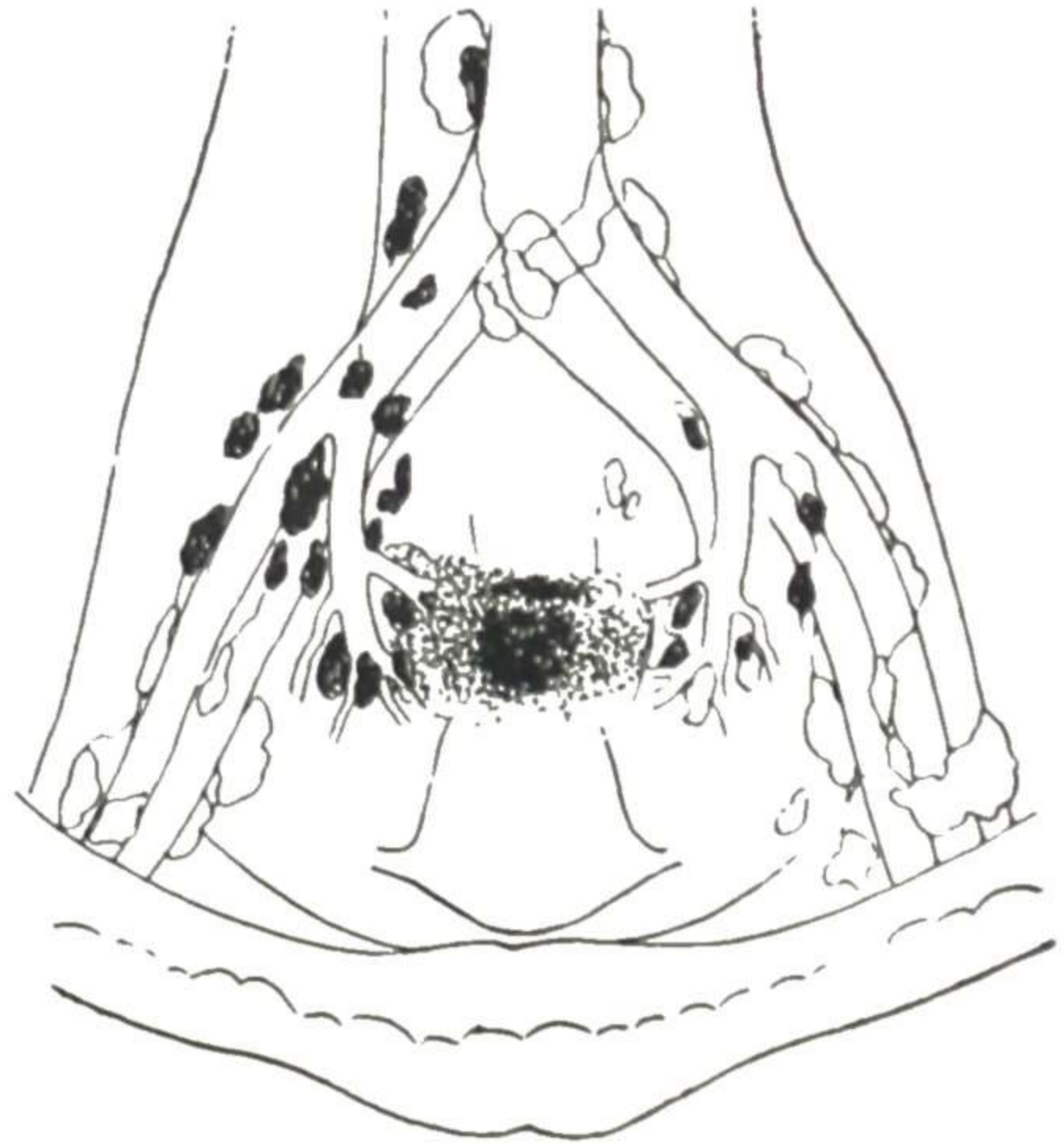


Fig. 766.

Figs. 765 and 766.—Diagrammatic representation of pelvic extension of carcinoma of cervix uteri. Fig. 765. Parametrial involvement extending out to the pelvic wall on each side. Fig. 766. Involvement of the pelvic lymph glands. The general location of the different groups of glands is indicated by the dim outlines, and the involved portions by the dark areas. The internal iliac (hypogastric) group are usually the first involved.



Fig. 767.

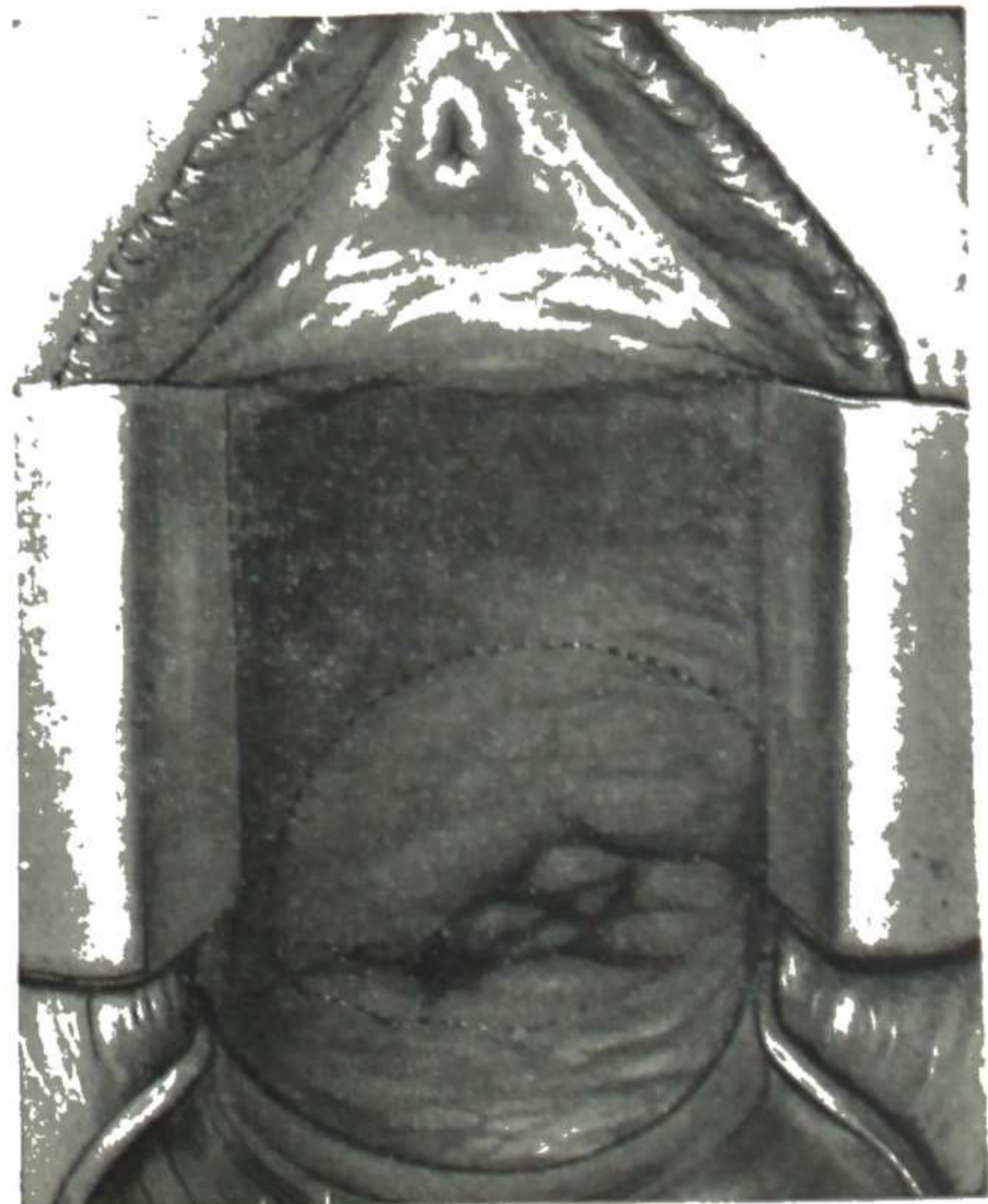


Fig. 768.

Fig. 767.—Epithelioma of the cervix. The cervix has been destroyed, leaving only an area of cancerous ulceration at the top of the vagina. (Kelly—*Operative Gynecology*.)

Fig. 768.—Epithelioma of the cervix. The cervix has been destroyed and the affected area has been drawn in by the gradual contraction of the infiltrated tissues, until no cancerous tissue can be seen. Palpation, however, shows that there is infiltration of the area enclosed within the dotted line. (Kelly—*Operative Gynecology*.)

results attained. The same classification should be used by all workers. A uniform classification in stages representing the extent of involvement is imperative for comparison of results of various methods of treatment. The classification of the Cancer Committee of the League of Nations is satisfactory; it is already in rather general use and is the only classification likely to come into universal use. It groups the cases of cancer of the cervix into the following four classes representing the different stages of the disease.

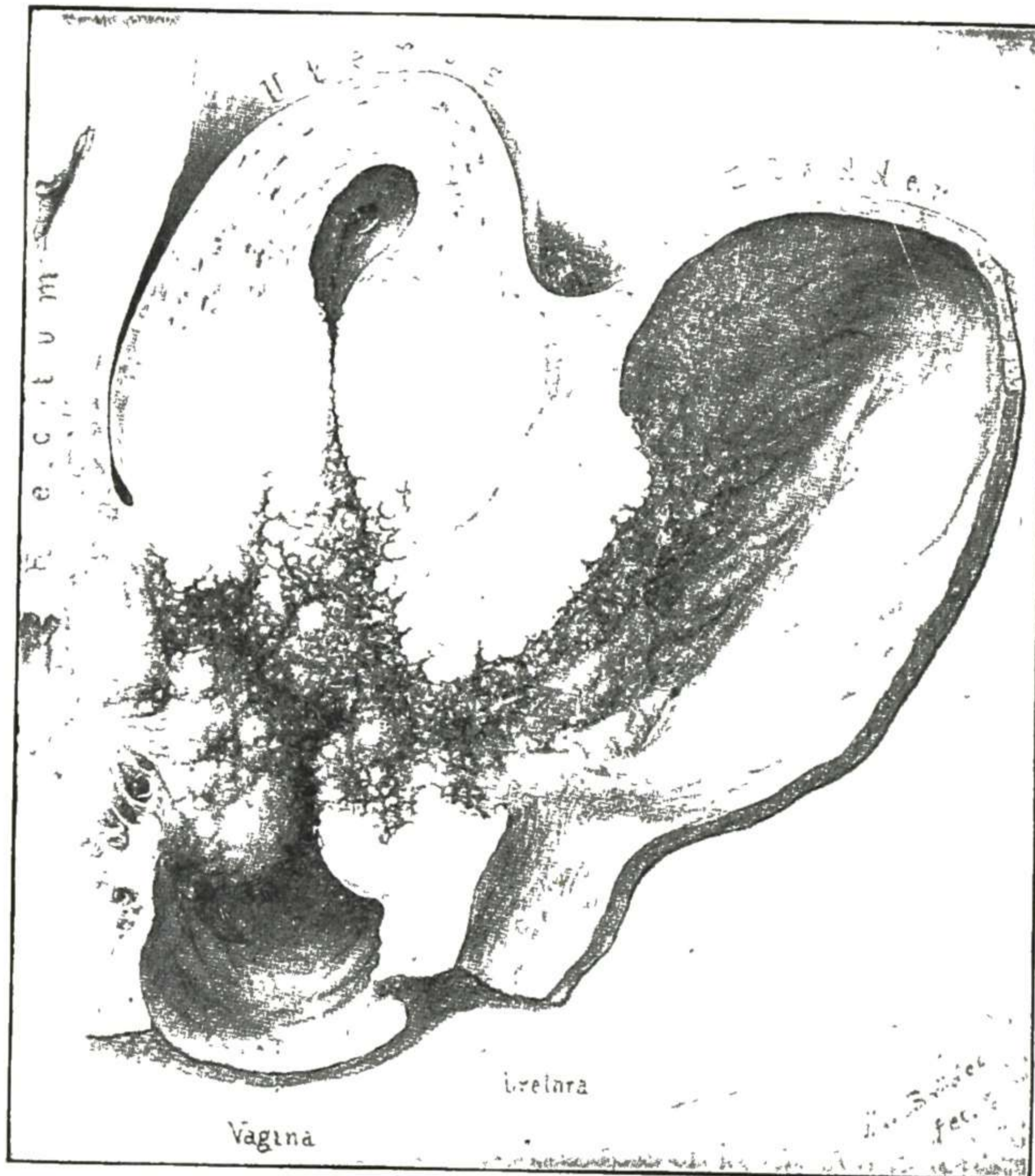


Fig. 769.—Case of carcinoma of cervix uteri (squamous type) which has extended into the bladder and the rectum, causing a fistula from each of those organs into the vagina. (Kelly—*Operative Gynecology*)

Stage I. The growth is limited entirely to the cervix. The uterus is freely movable, and no paracervical infiltration can be detected.

Stage II. The parametrium is involved. The infiltration can be palpated under the vaginal wall or beside the cervix. The palpable infiltration may extend outward nearly to the pelvic wall, but the uterus still retains mobility. This stage includes the old "borderline operable" group.

Stage III. The parametrium is involved to the pelvic wall on one or both sides, with partial or complete fixation of the uterus.

Stage IV. The cancer has invaded adjacent viscera or extensively involved the vagina or produced distant metastases.

In the case of each patient, the evidences of the extent of involvement should be worked out sufficiently to permit accurate assignment to class. Accuracy is enhanced by deciding definitely as to the class at the time of examination and then recording the decision. This obviates the difficulty encountered when trying later to classify a borderline case with some needed detail missing. This accurate classification is best made during examination under

the analgesia for the radium implantation. Deep rectal palpation of the broad ligament of each side is most helpful in determining the fact and the extent of parametrial involvement.

For emphasis, it is well to repeat that a universal international classification is imperative for accurate comparison of the results of the various methods of treatment. The continued use of personal or provincial classifications, instead of the international one, interferes seriously with this comparison of treatment results, which means so much in the endeavor to give each patient the best chance of cure. Personal predilections as to the details of various stage-divisions should yield to the necessity of one universal and clearly understood classification. The League of Nations' classification is already widely used,



Fig. 770.—Case of carcinoma of cervix uteri in which the parametrial involvement has obstructed the ureters, causing serious dilatation of them and of the kidney pelves. (Kelly—*Operative Gynecology*.)

and it should be adopted in all countries by all workers. If anyone wishes to divide further one or more of the stages in reporting his cases, there is no objection to that—provided the subgroups are clearly defined and do not extend beyond the stage divided. For example, if one wishes to use Schmitz's division of early cases into (a) lesions 1 cm. or less in diameter and (b) lesions larger but still confined to the cervix, these subdivisions may be conveniently designated Stage I-a and Stage I-b.

Associated Diseases also add to the pathological picture in some cases. The advanced ulcerating growths are nearly always infected and may present sloughs at the vaginal vault. If the cervical canal is blocked there may be

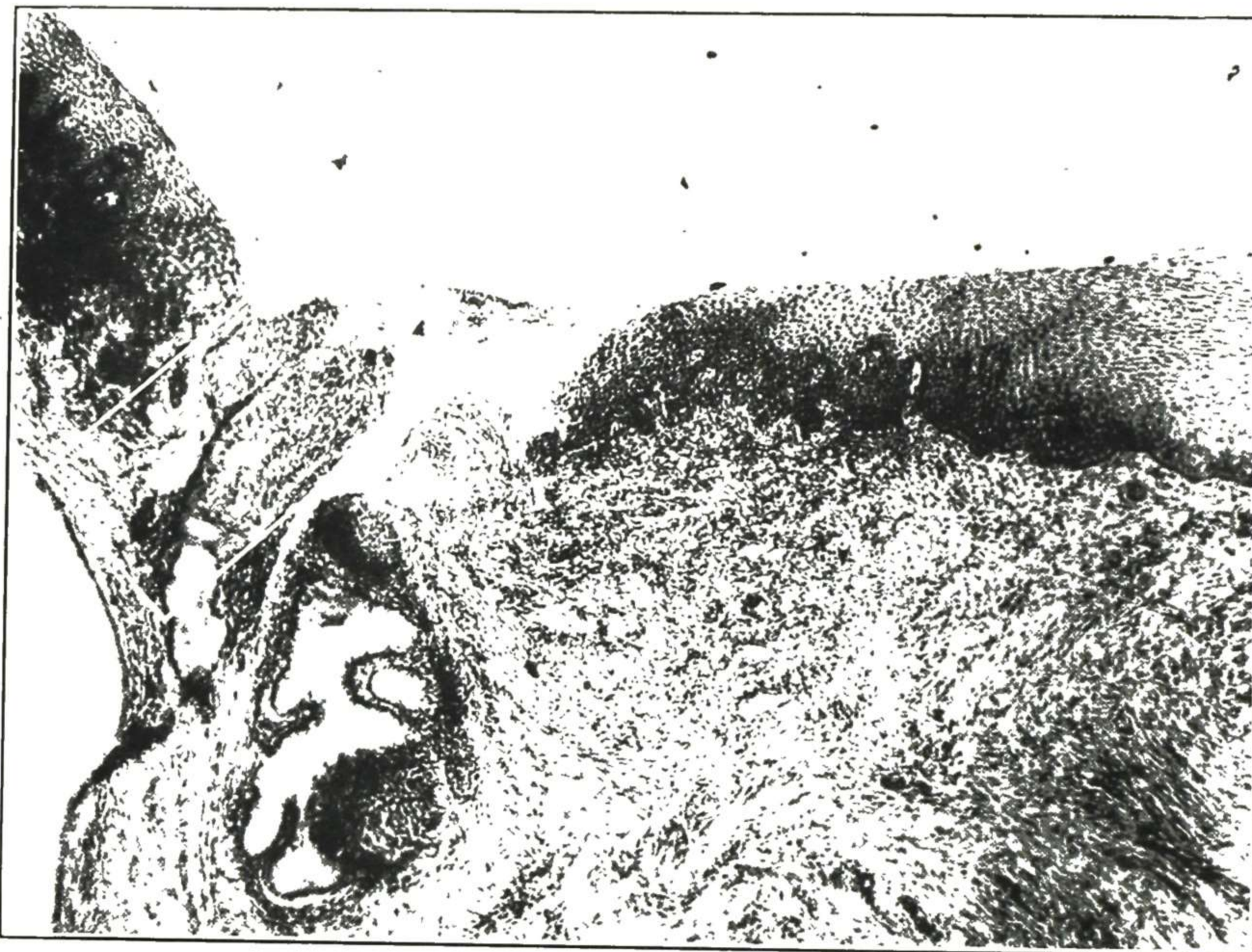


Fig. 771.—Early squamous carcinoma of cervix. Section through a diagnostic clipping from a suspicious area on the cervix. Gyn. Lab.



Fig. 772.—From the section shown in Fig. 771, illustrating the peculiar bud of abnormal cells, which has its own special blood supply. This is the reverse of the above photomicrograph. Gyn. Lab.

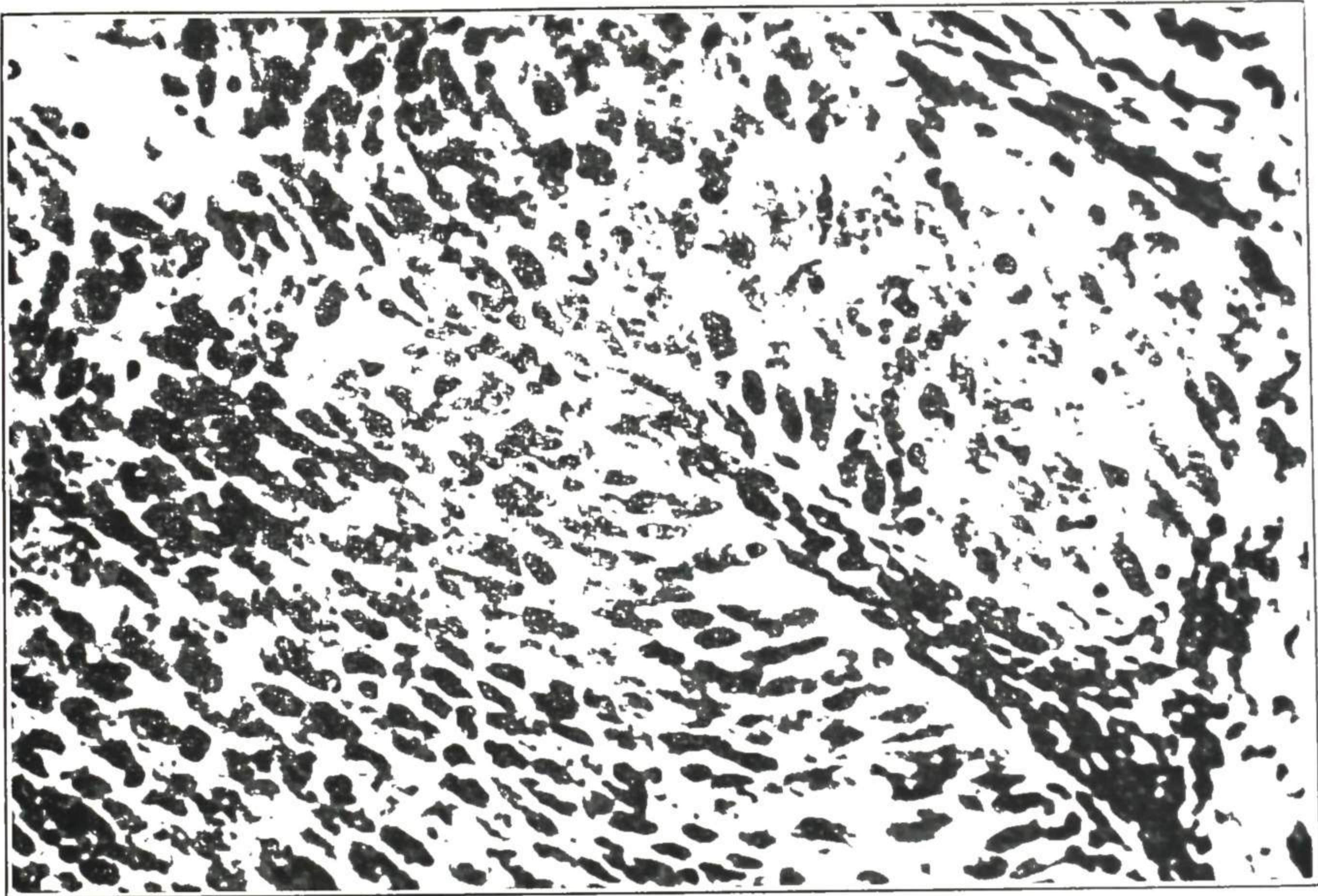


Fig. 773.—High power, showing characteristics of the cells and their distribution along the area of the blood supply. Gyn. Lab.

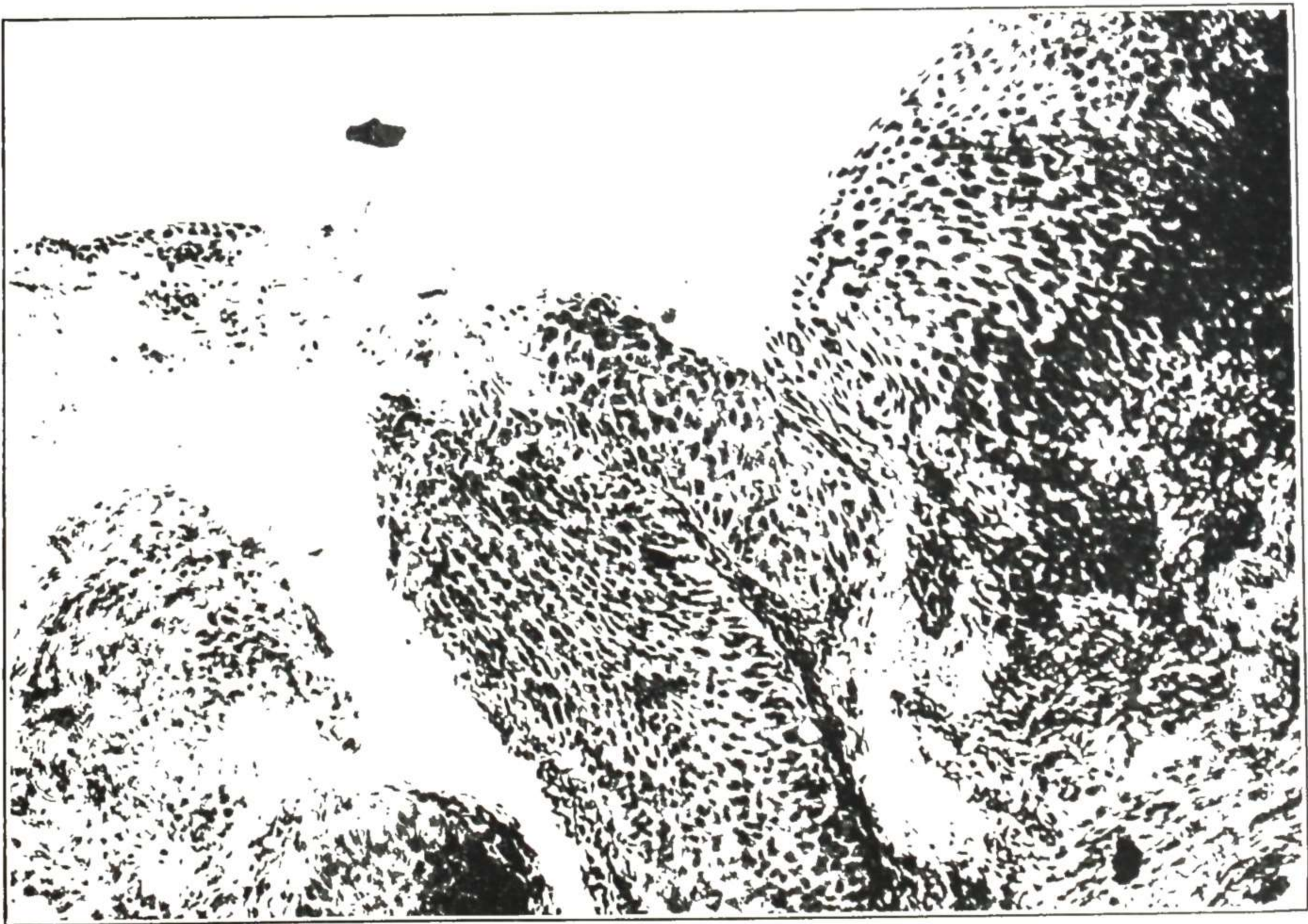


Fig. 774.—Another view of Fig. 771, showing the distinct junction line of the abnormal epithelium with the fairly normal, at the upper right portion of the field. Gyn. Lab.

pyometra above, with a thinned-out uterine wall. The inflammatory complications add much to the patient's distress and to the difficulties of palliative treatment.

Myoma may be a complication as shown in Fig. 733. *Pregnancy* is sometimes a complication. Carcinoma of the cervix may appear while the patient is pregnant, or occasionally pregnancy may take place in the early stage of carcinoma of the cervix. In either case the effect of pregnancy is to hasten the progress of the carcinoma. The softening of the tissues and the congestion associated with pregnancy seem to favor rapid extension of the malignant disease.

The duration of carcinoma of the cervix is variable, the limits ordinarily being from one to three years. The duration depends somewhat on the kind of tumor (the softer the tumor the more rapid the growth), upon the age of the patient (the younger the patient the more rapid the growth), and upon the proximity to childbirth—those carcinomas appearing within one year after parturition progressing very rapidly.

These are only general rules, to which there are, of course, exceptions.

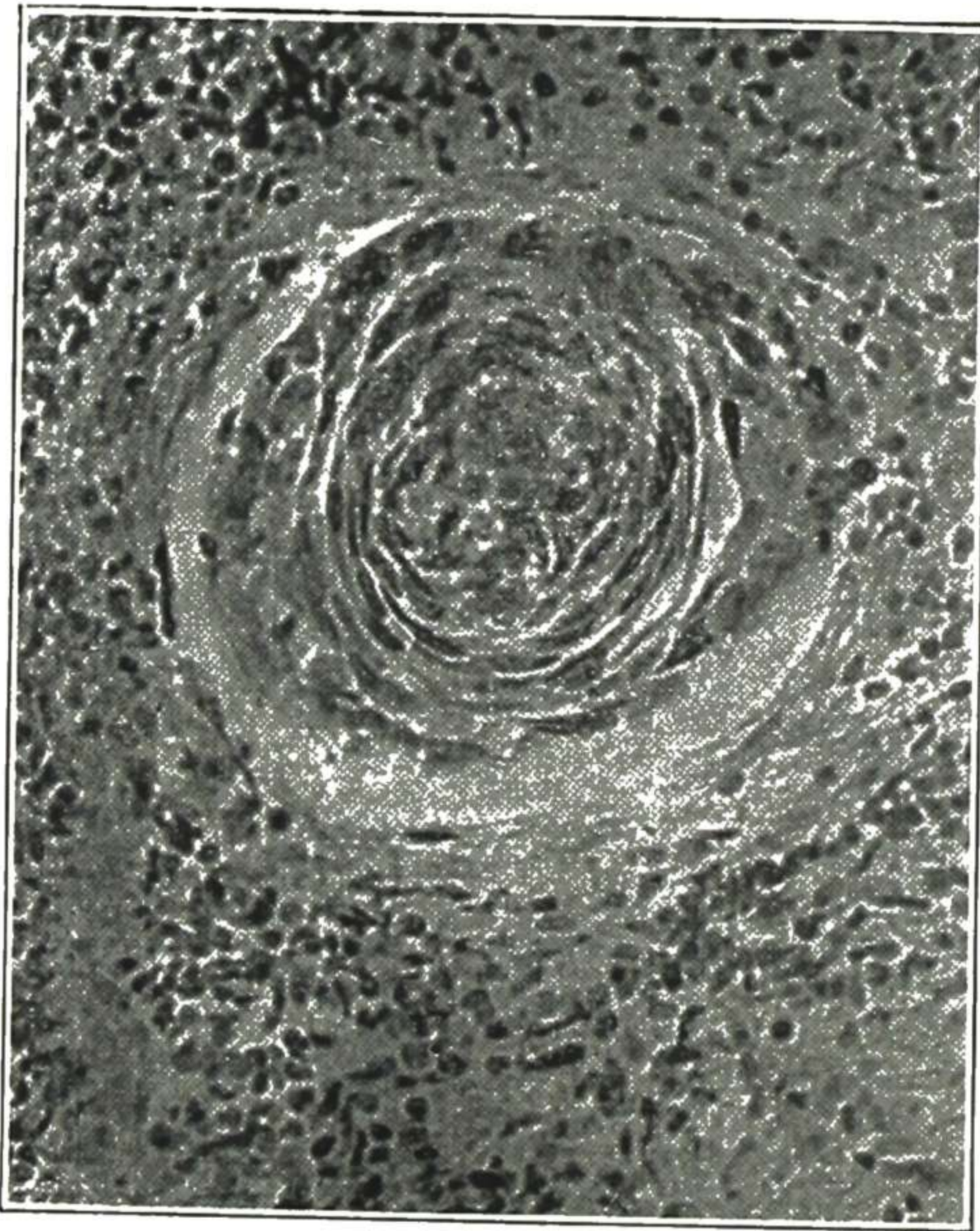


Fig. 775.



Fig. 776.

Fig. 775.—An epithelial pearl from a squamous carcinoma of the cervix uteri.

Fig. 776.—A carcinomatous plug growing within a cervical gland, the walls of which do not yet show carcinomatous change. From a squamous carcinoma of the cervix. Gyn. Lab.

Microscopic Pathology.—Various phases of the microscopic picture of squamous-cell carcinoma of the cervix are shown in Figs. 771 to 776. Fig. 771 shows an interesting young carcinoma in the form of a projecting bud. In Figs. 772 and 773 the higher magnifications bring out the characteristics of the cancer cells growing rapidly about a vascular core which nourishes them. Inspection of the right upper corner of the photomicrograph in Fig. 774 will show a line of demarcation between the cancer area and the comparatively normal epithelial covering of the cervix. The characteristic "pearl" formation is shown in Fig. 775, and carcinoma cells growing into a cervical gland in Fig. 776.

The **pathological classification** as to **cell type** of the squamous-cell carcinomas of the cervix gives three types or grades, arranged according to the average maturity-appearance of the cells.

Grade I. This is the spinal-cell type (Fig. 777). It is the most mature. The cells resemble those of the upper layer of the squamous epithelium. They are large with well-defined borders. The nuclei are large, but there is such an abundance of cytoplasm that they seem relatively small. The nuclei frequently contain a nucleolus, and they take a rather light blue stain. Pearl formation is common in this Type I class.

Grade II. This is the transitional-cell type (Fig. 778). The cells resemble the middle zone of the cervical epithelium. These cells are round or cuboidal in shape, with an ill-defined cell membrane. The nucleus is large in comparison to the cytoplasm, and it takes a deep hematoxylin stain.

Grade III. This is the fat spindle-cell type (Fig. 779). The cells are oval shaped, with a large nucleus and almost no cytoplasm. The cells are closely packed, and the nuclei stain darkly. These cells do not closely resemble any of the layers of the normal epithelium, but they are more like the basal layer than the other two.

These grades represent an ascending scale of malignancy, from the mature-cell slow-growing cancer to the immature-cell rapidly-growing type. Different cell-types may often be found in different parts of the same tumor, so the grading represents only the preponderating cell type. The immature cells are less resistant to radiation, and it was hoped that this pathologic grading could be used as an aid in selecting treatment, dosage, etc. This did not prove out, however, because of the uncertainty as to whether the diagnostic specimen represented the preponderating cell type in that case. The diagnostic-specimen grading may aid some in prognosis, for if grade III that shows at least part of the cancer has been growing rapidly with consequent greater chance of wide-spreading distribution.

There are certain **borderline conditions** which create much difficulty in the microscopic identification of beginning cancer. The questions as to when a chronic inflammation becomes precancerous, and at what particular stage it is definitely cancerous, have been debated for years among gynecologic pathologists.

These questions have been investigated by workers all over the world and many excellent articles have appeared in the American, German, and French medical literature. The need of a clear enunciation of the microscopic findings which warrant a diagnosis of early carcinoma has been emphasized in a paper by Schmitz, McJunkin, and Macaluso. These workers studied serial sections of chronic cervicitis. In some of the borderline cases they submitted sections to several eminent pathologists. The opinions for and against cancer were fairly evenly divided. When such a situation exists, it is obvious that serious mistakes may occur and that further investigation and standardization are urgently required.

It is in the **early microscopic picture** that the diagnostic difficulties lie—in the stage before the invasive break through the basement line, and long before there are any clinical symptoms that we associate with cancer. Most gynecologic pathologists now believe that definite cancer changes can be recognized in the epithelial cells before the break in the basal layer which marks invasion, though there are some who still feel that invasion is necessary before a diagnosis of cancer can be made. Martzloff holds this opinion, and he demonstrated in leucoplakia of the cervix the following points which commonly are used as criteria in the diagnosis of cancer: irregular size, shape, and staining reaction of the cells, loss of polarity, epithelial whorls, mitotic figures, and multinucleated cells. Leucoplakia presenting such cell changes, however, is itself under serious suspicion of beginning malignancy. In fact, Martzloff himself states that in some cases of leucoplakia the cells have all the characteristics of cancer except invasion. He makes the point, however, that invasive power is not proved until actually exhibited.

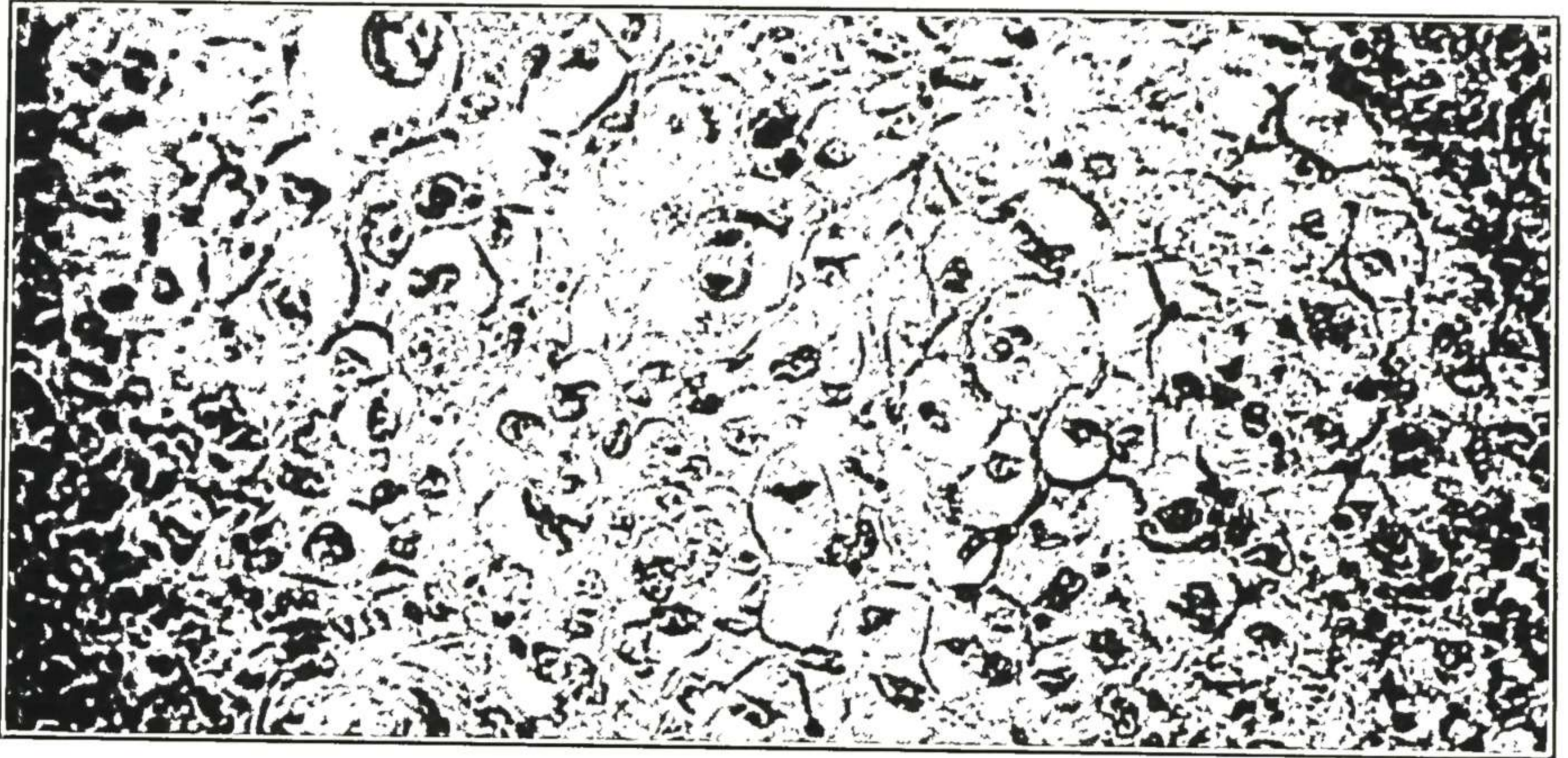


Fig. 777.—Squamous cell carcinoma of cervix. Grade I (spinal cell type). Gyn. Lab.

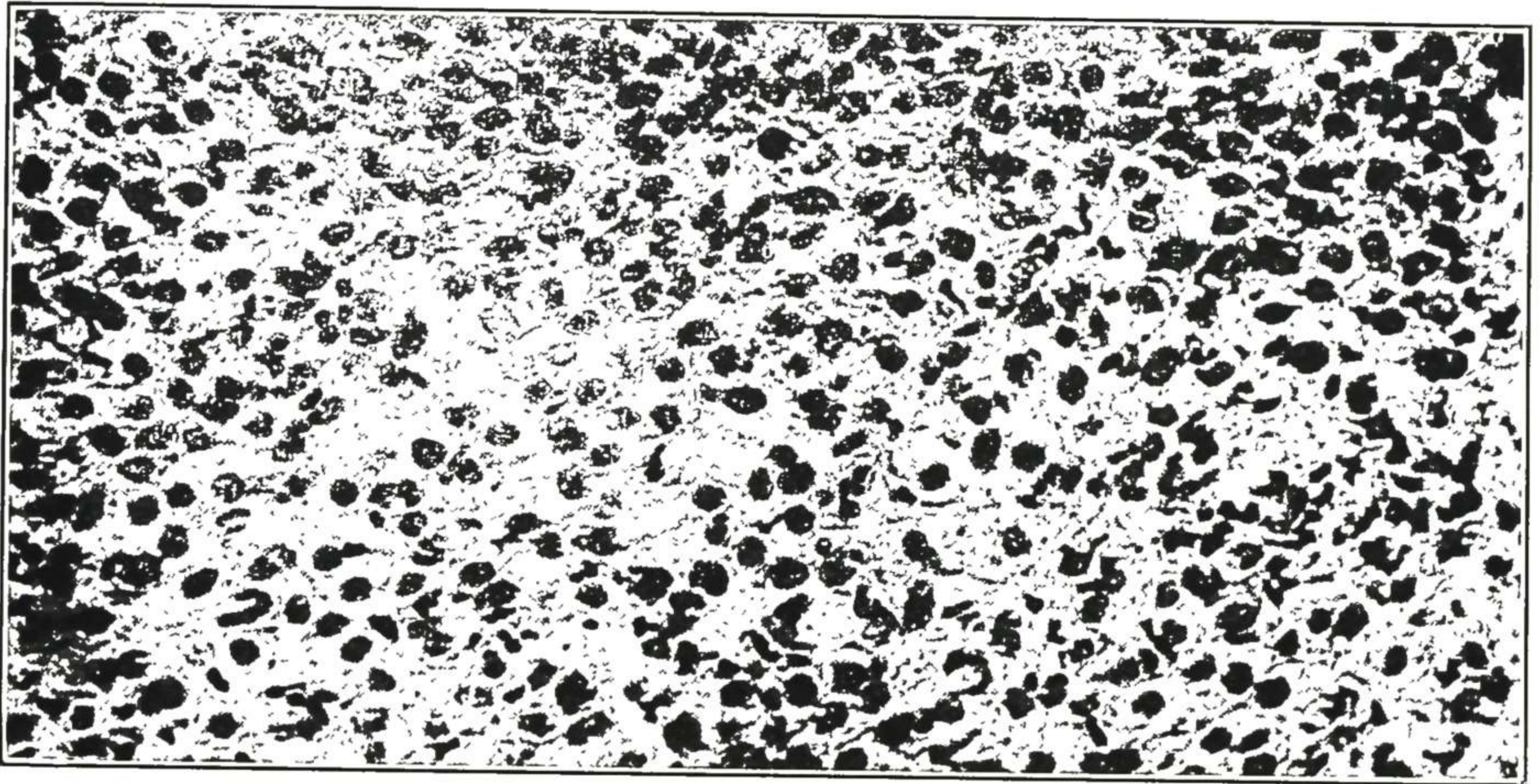


Fig. 778.—Squamous cell carcinoma of the cervix. Grade II (transitional cell type). Gyn. Lab.

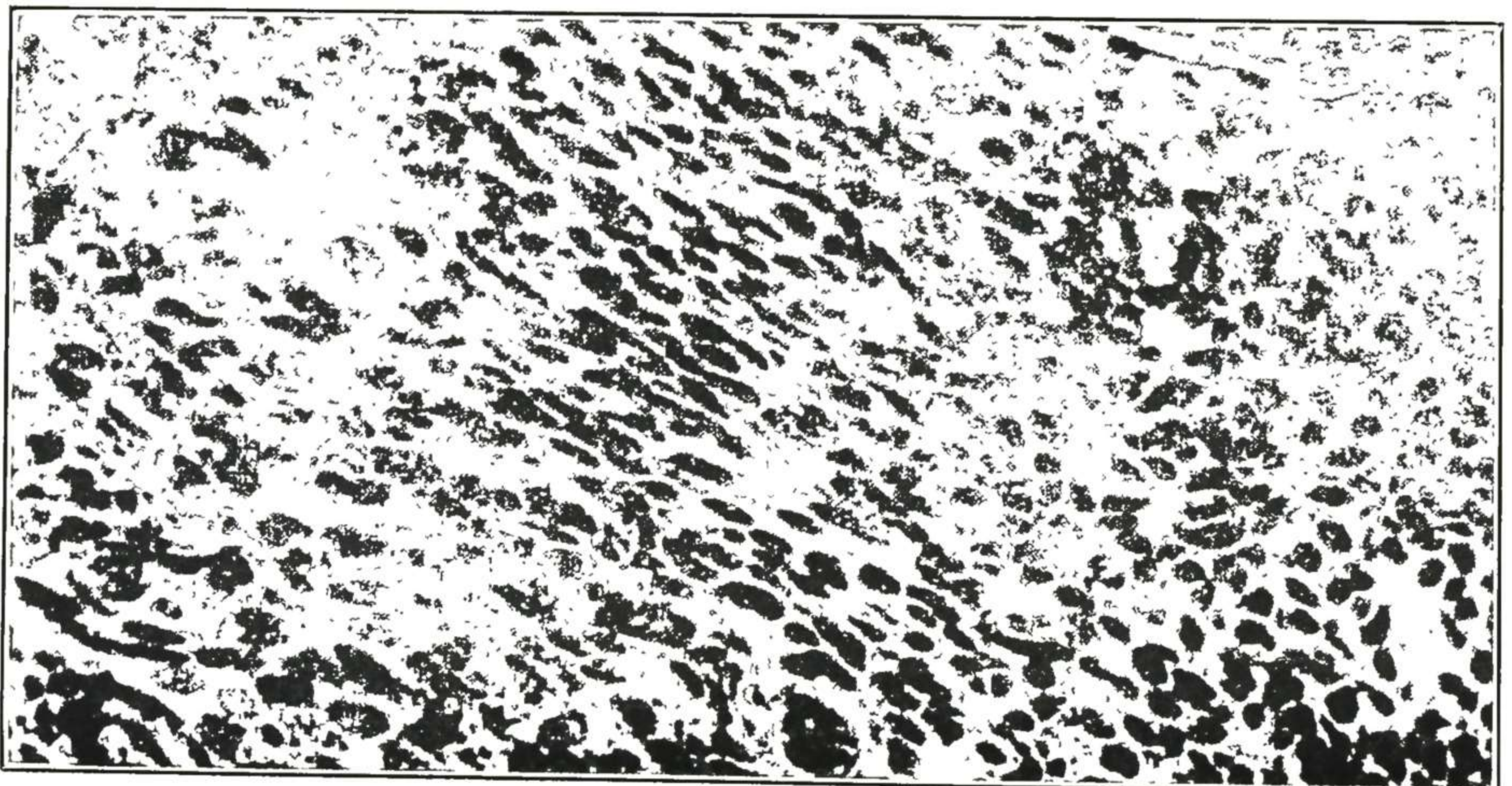


Fig. 779.—Squamous cell carcinoma of the cervix. Grade III (fat spindle cell type). Gyn. Lab.

Broders shows a striking example of epithelial cancer of the cervix still limited to the epithelial area (Fig. 780). Smith and Pemberton show the loss of the basal layer in Fig. 781-*A* and *B*.

In this connection, the line of junction of the cancer epithelium with the normal epithelium is an interesting area for study, as it shows the early cell changes in invasive cancer before the erratic activity has reached the basement line. Norris calls attention to this line

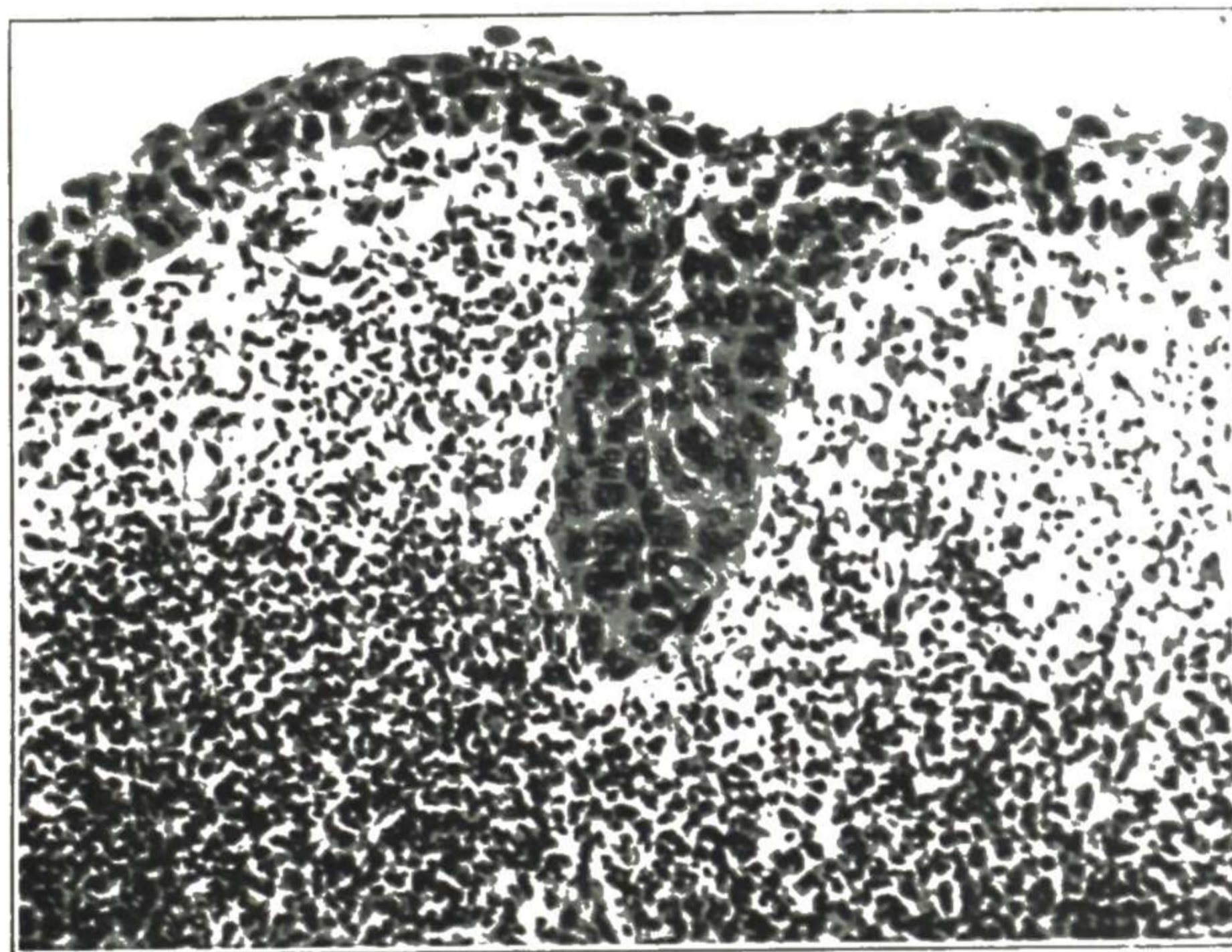
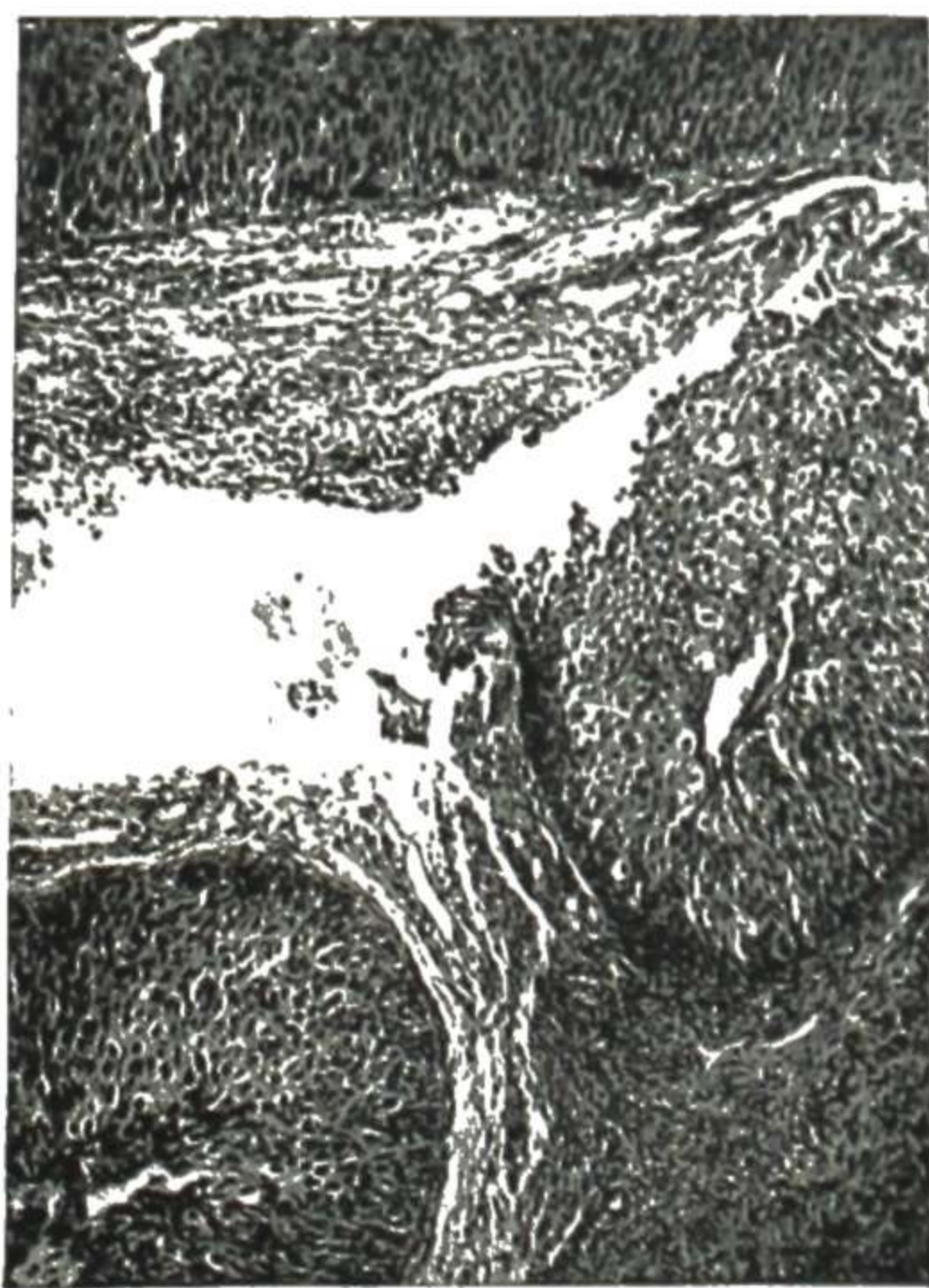


Fig. 780.—Squamous cell carcinoma in situ of the uterine cervix, in which the carcinomatous cells have replaced the normal cells and are appearing to function in a protective manner. There is no penetration of the so-called basement membrane; therefore, according to older teaching, the growth would be considered noncarcinomatous, or at most only precarcinomatous. (Broders—*J. A. M. A.*)



A.



B.

Fig. 781.—Carcinoma cells with the basement layer gone. *A*, The advancing cell columns. *B*, Higher power, showing the character of the cells. (Smith and Pemberton—*Surg., Gynec. and Obst.*)

of junction, as shown in Fig. 782. This section shows that the cancer changes in the cells may become quite advanced before they break through the basement line.

Incidentally, these slides show that the cell changes are more marked in the higher layers than in the basement area, which lends support to Montel's contention that the cancer originates in the upper layers of the epithelium. Montel holds that the basal layers being

intact in beginning cancer change indicates that squamous-cell carcinoma originates in the superficial layers, instead of in the basal layer, as held by Schiller.

In Fig. 783 is shown leucoplakia with erratic cell changes pronounced benign, which ten months later had advanced to invasive cancer (Fig. 784). Such experiences, along with the other facts cited, show the difficulties of the diagnosis of malignancy in borderline lesions of the cervix.

Stevenson and Scipiades reported eighteen cases of "noninvasive potential carcinoma" of the cervix, that is, presenting the cell changes usually considered indicative of cancer but without actual invasion. The potential invasive quality was shown by the fact that actual invasion later took place in two of the cases. In one of these two it was delayed for eight years, when the patient returned to the clinic with advanced cancer of the same cell type, which caused death in spite of active treatment.

Present information on this subject indicates that early cancers of the cervix may be divided into two groups, representing two stages in progress. First, there is the stage of epithelial change, which carries the epithelium from a group of normally functioning cells through the various erratic changes cited to the point where they are ready for

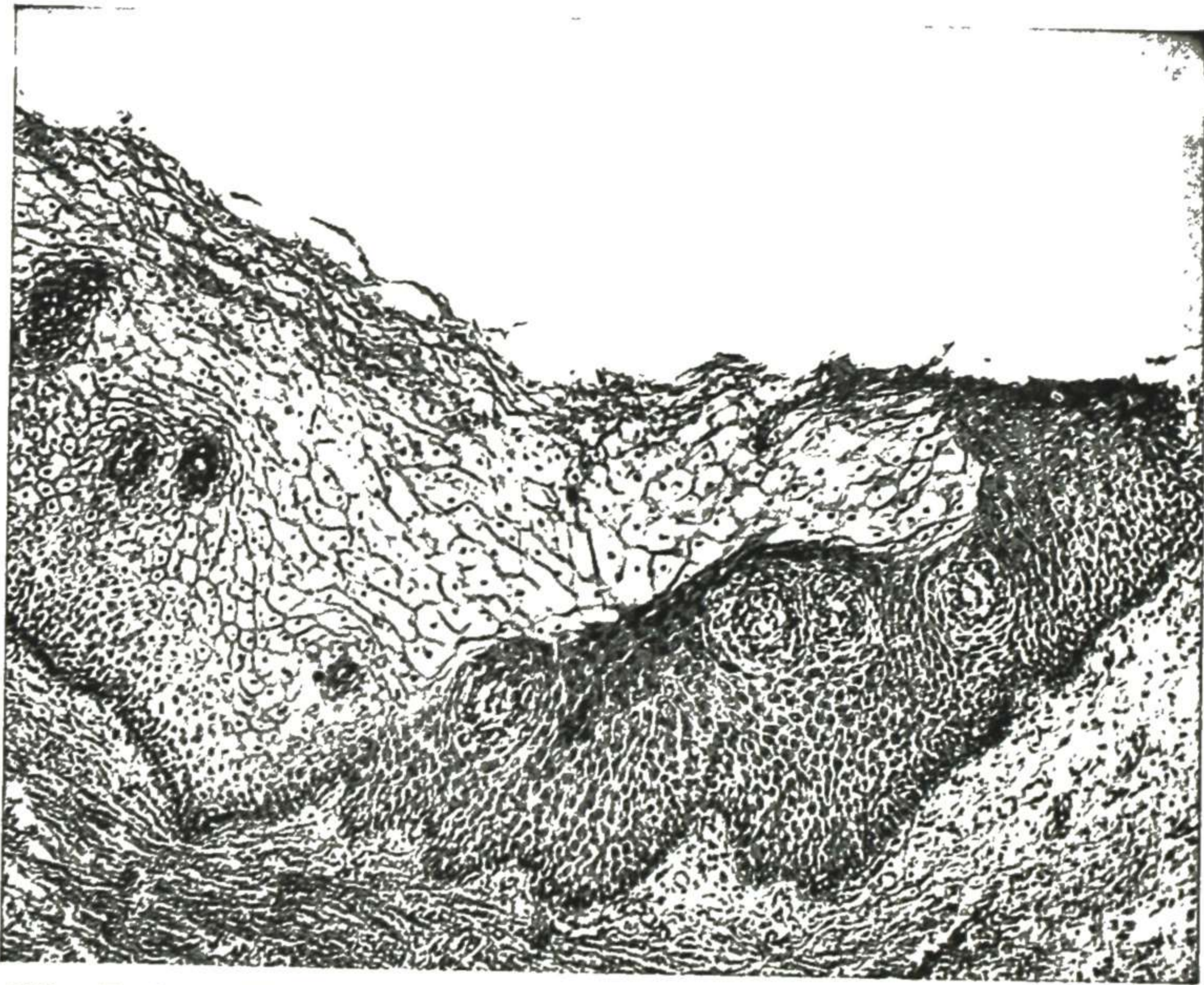


Fig. 782.—Early epidermoid carcinoma of the cervix, showing a clear-cut line of demarcation between the malignant and benign epithelium. This line is oblique due to the more rapid growth of deeper layers of the tumor. The cells of the latter exhibit the usual alterations in morphology characteristic of carcinoma. As is not unusual in some carcinomas, the basal layer is moderately well preserved. ($\times 80$.) (Norris—*Am. J. Cancer.*)

the invasion. Second, there is the stage of invasion, where the gradually developed abnormal cell activity and resulting products have so weakened the underlying tissue that invasion begins. Both of these stages are microscopic, and give no clinical disturbance which would arouse suspicion of malignancy, except evidence of some cervix irritation.

While it is clear that the real cancer cells (i.e., those which show their malignancy by invasion later or in another part of the same specimen) go through these two stages of progress, it seems clear also that not all cell groups showing the first stage pass to the increased erratic activity of the second stage (stage of invasion). The problem now is to distinguish between the erratic cells which are early cancer cells and the erratic cells which are essentially benign as far as future invasion is concerned.

Study of information available, including articles by Novak, Freedman, Smith and Pemberton, Broders, Norris, Henriksen, Schmitz and Benjamin, TeLinde, Hofbauer, Bailey,

Schiller, Stevenson and Scipiodes, and others, indicates that in the microscopic diagnosis of beginning cancer the following points should be taken into consideration:

1. Irregularity of cell arrangement—loss of "polarity." Loss of normal three layers.
2. Abnormal crowding of the cells.
3. Irregular staining of the cells with an increased avidity for basophilic stains.
4. Irregularity in the size of the cells and their nuclei. Occasionally giant cells are present.
5. Atypical or pathologic mitoses. The frequent appearance of mitotic figures in the field is significant, as indicating abnormally rapid cell multiplication. This point was emphasized by Cullen who, remarking that, of course, some mitosis must occur in normal growth and repair, stated that in his extensive histologic studies in the cervix, frequent mitoses were rarely encountered except where malignancy existed.

On the other hand, Henriksen found that in the normal cervix, "Mitoses and hyperchromatism are more frequently present than most observers have noted."

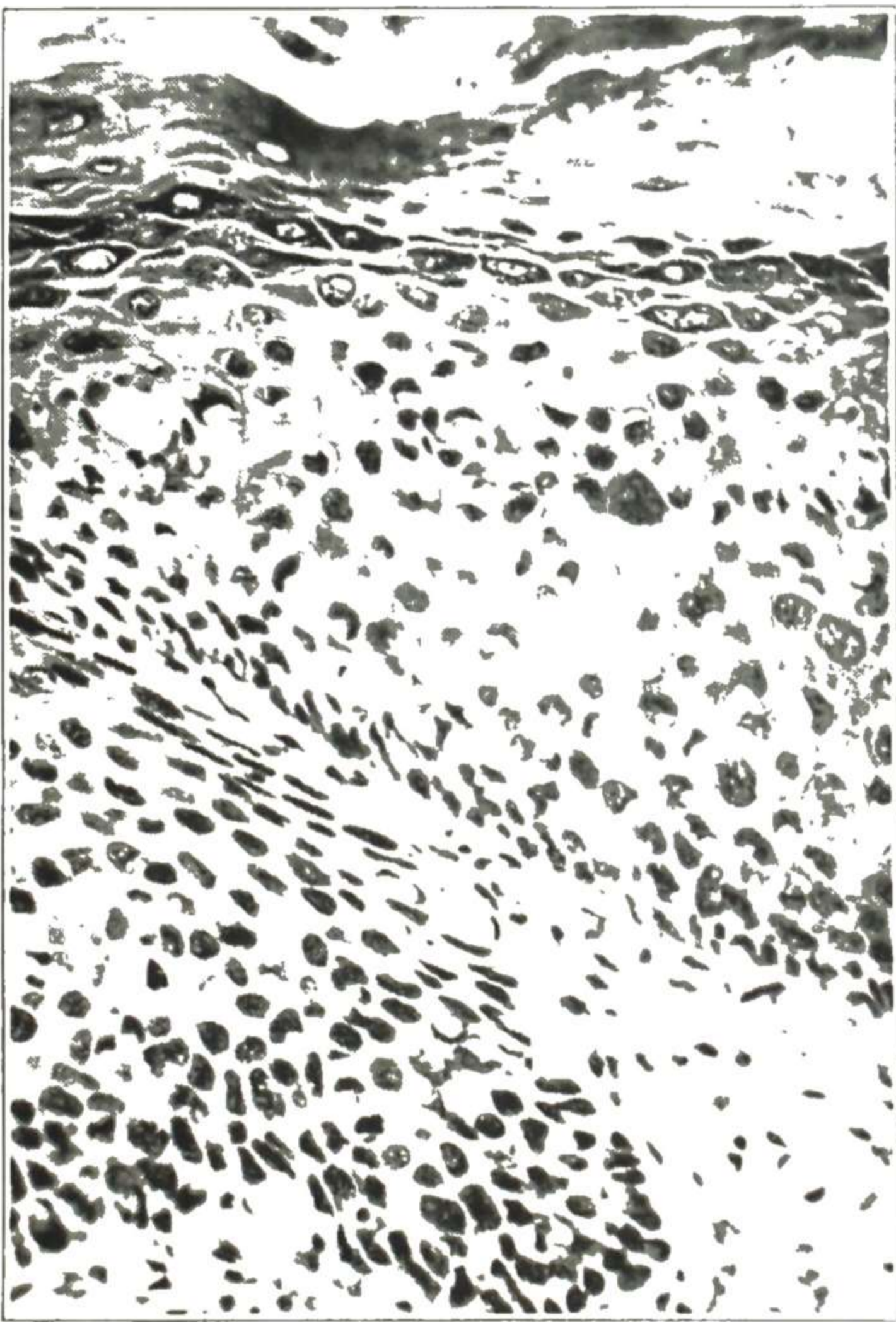


Fig. 783.

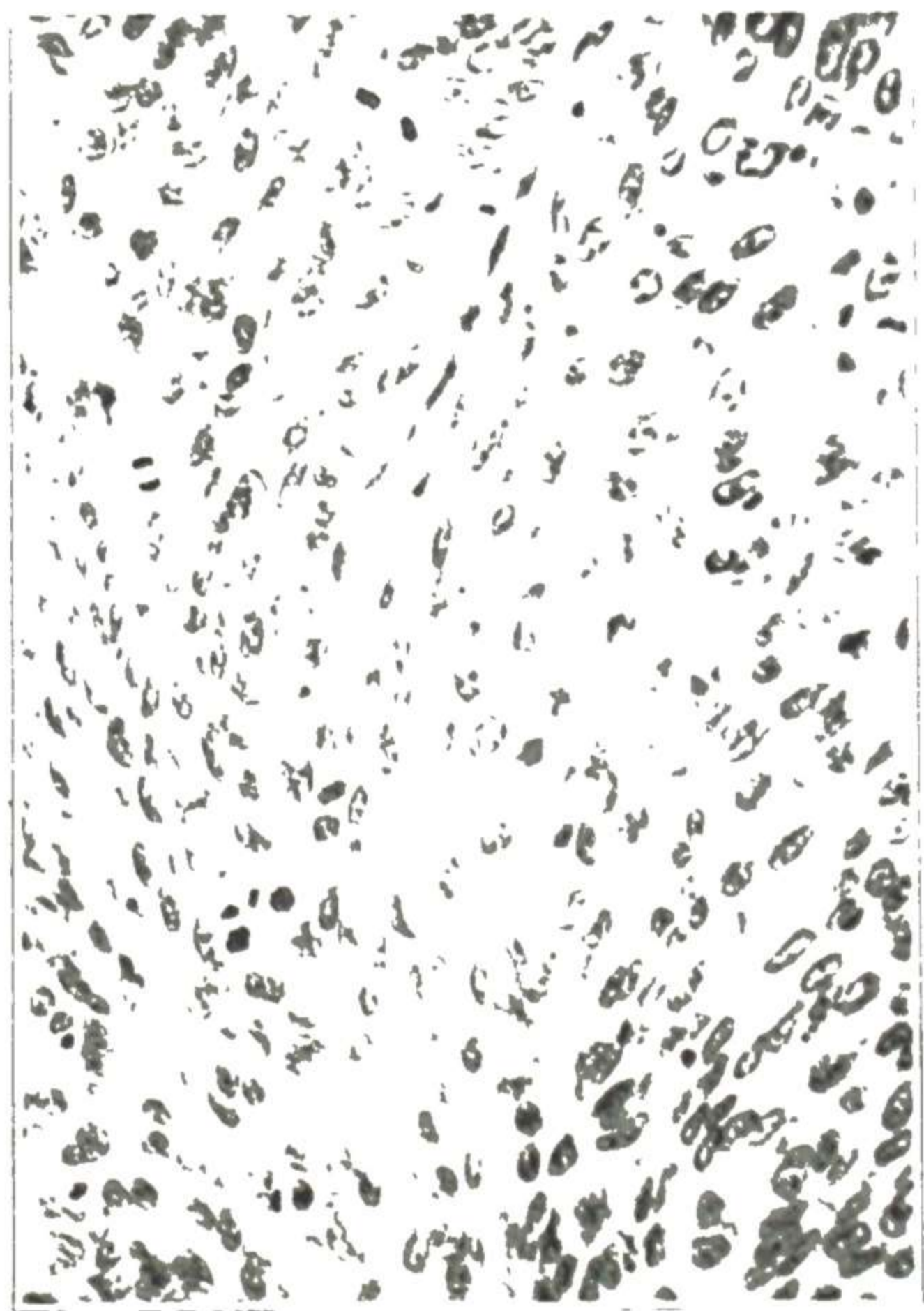


Fig. 784.

Fig. 783.—Leukoplakia of the nonkeratinizing epithelium of the portio vaginalis at the lip of the uterine cervix. Hyperkeratosis, parakeratosis and the formation of a well-defined stratum granulosum are shown. Intercellular, intranuclear, and perinuclear edema with variations in size and shape of the cells and hyperchromatism are present in the stratum spinosum and stratum germinativum. Reduced from a photomicrograph with a magnification of 475 diameters.

Fig. 784.—Primary epidermoid carcinoma of the uterine cervix from a biopsy specimen taken ten months after removal of tissue illustrated in Fig. 783. Neoplasia, anaplasia, and hyperchromatism with numerous mitotic figures are shown. Other fields show attempts at pearl formation. Reduced from a photomicrograph with a magnification of 500 diameters. (Schmitz and Benjamin—*J. A. M. A.*)

In addition to the unusual number of mitoses, there may be abnormalities in the mitotic configurations, indicating erratic distribution of the chromosomes. Figs. 785 to 791 show the normal mitotic figures for the various phases of normal cell division alongside an abnormal mitotic figure for each phase.

6. Marked round-cell infiltration. This is stressed by Smith and Pemberton, as are also dilated capillaries and indistinct basal layer.

7. Special blood supply developed by the suspicious group of cells. In one of our cases, a specimen from the cervix showed one suspicious slide, which was pronounced early carcinoma by Prof. O. H. Schwarz, largely on this account. Fig. 772 shows the bud of

abnormal cells still limited by the basement line. It may be studied further in Fig. 773. The central area of this growing bud shows that these cells in their erratic activity are developing a blood supply quite out of the ordinary in this region. In another part of the slide there was a disturbed area which might be invasion, but it might also be an artefact, so the diagnosis was decided largely by this interesting bud of abnormal cells creating an unusual blood supply.

On account of the borderline features with only questionable invasion, this slide was sent to several pathologists, and different opinions were received, a number of them against cancer. In the meantime, a conical excision of the cervix was made to obtain the whole region for microscopic study. This showed an area of carcinoma with frank invasion.

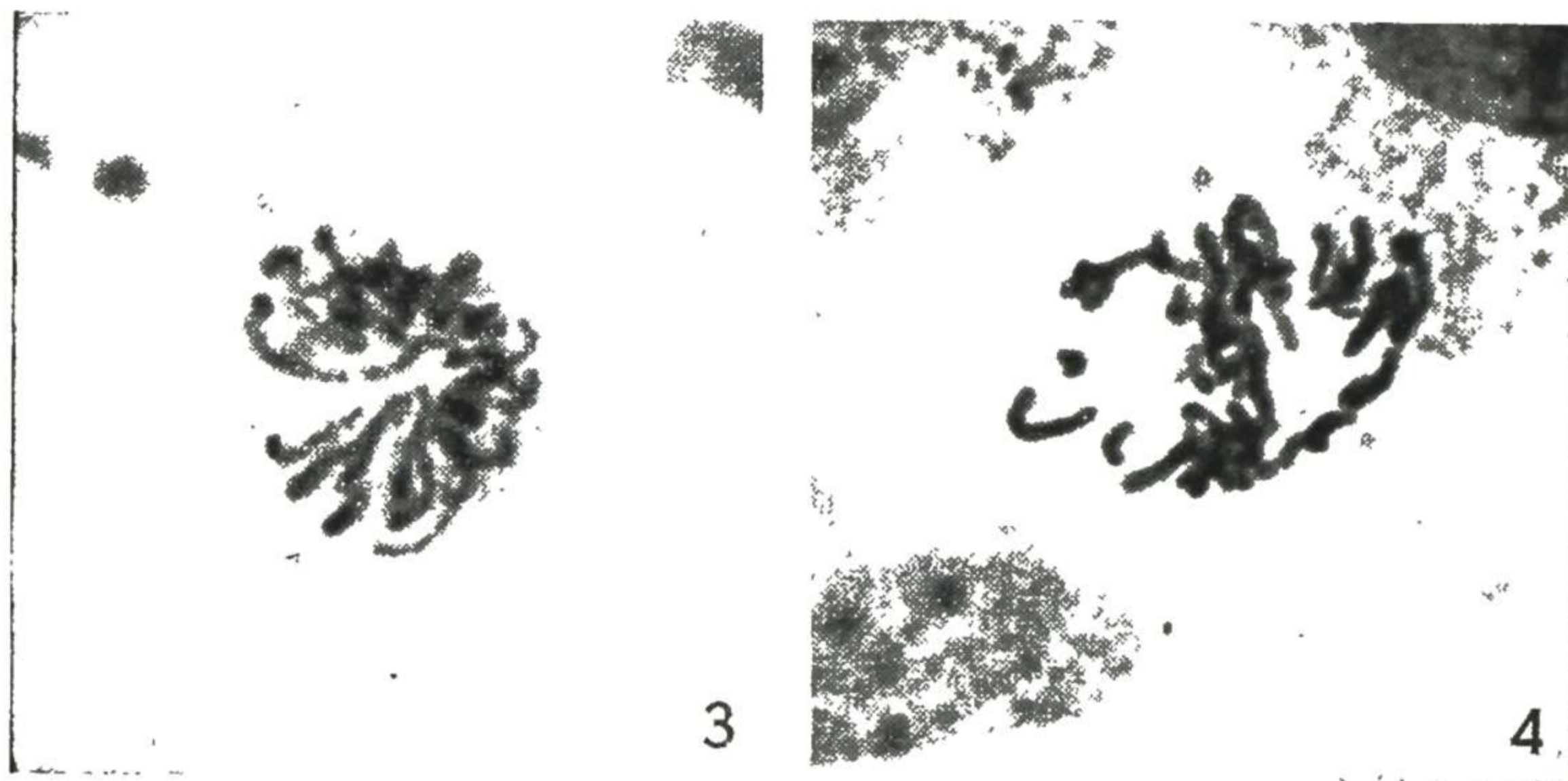


Fig. 785.—3, Early prophase of a normal cell division. 4, Early prophase, showing in this stage a delay in the regular formation which does not occur in normal cell division.—(Mendelsohn—*Am. J. Cancer.*)

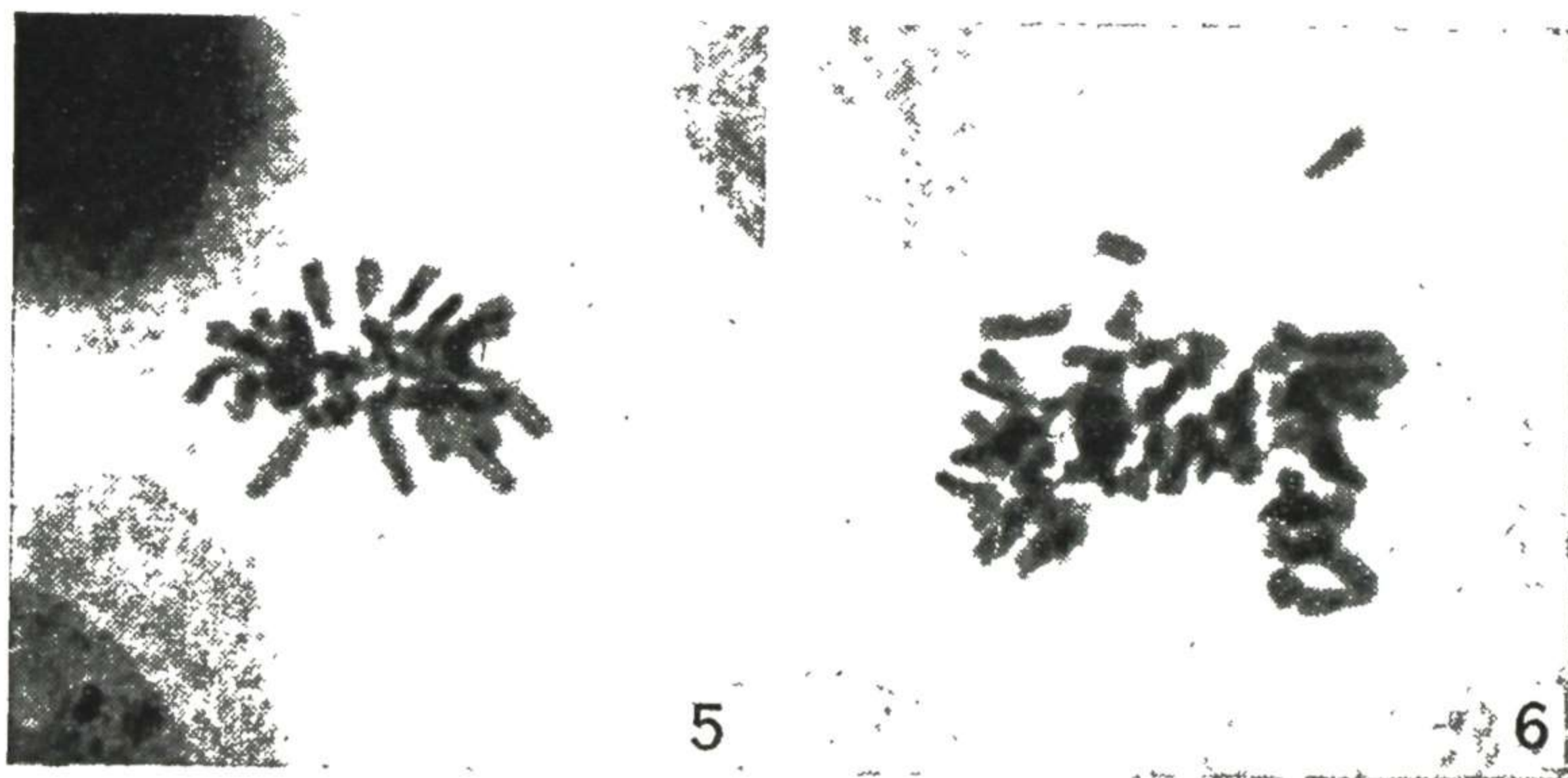


Fig. 786.—5, Early metaphase of a normal cell division, showing the splitting of the chromosomes in the regular way. 6, Early metaphase, showing a greater number of chromosomes than normal. Also, one chromosome is slow in reaching the metaphase plate and may not get into this mitosis. (Mendelsohn—*Am. J. Cancer.*)

8. Novak quoting Meyer emphasizes the point that in chronic cervicitis and erosion the invasion of the squamous epithelium follows the trellis furnished by the glandular framework, while in cancer the invasion does not necessarily bear any relation to the glands.

This calls attention to another factor in the difficulty of carcinoma diagnosis, namely, *epidermization*, which in this situation is usually of the extension type. The "creeping" of squamous epithelium under columnar epithelium and replacement of the latter is an important factor in the regular healing of cervical erosion. Epidermization deeper in the cervix seems to be an extension of this process to areas normally occupied by columnar epithelium. For an understanding of the process and the resulting microscopic characteristics, it would be well to review the text and illustrations under Erosion. Its extension to situations where it complicates the diagnosis of carcinoma is shown in Figs. 792 to 794.

In the differential diagnosis of epidermization, two points to keep in mind are: (1) that individual cell characteristics do not go beyond those of normal growing cells and (2) that the penetrating cells are distributed within the framework of the glands.

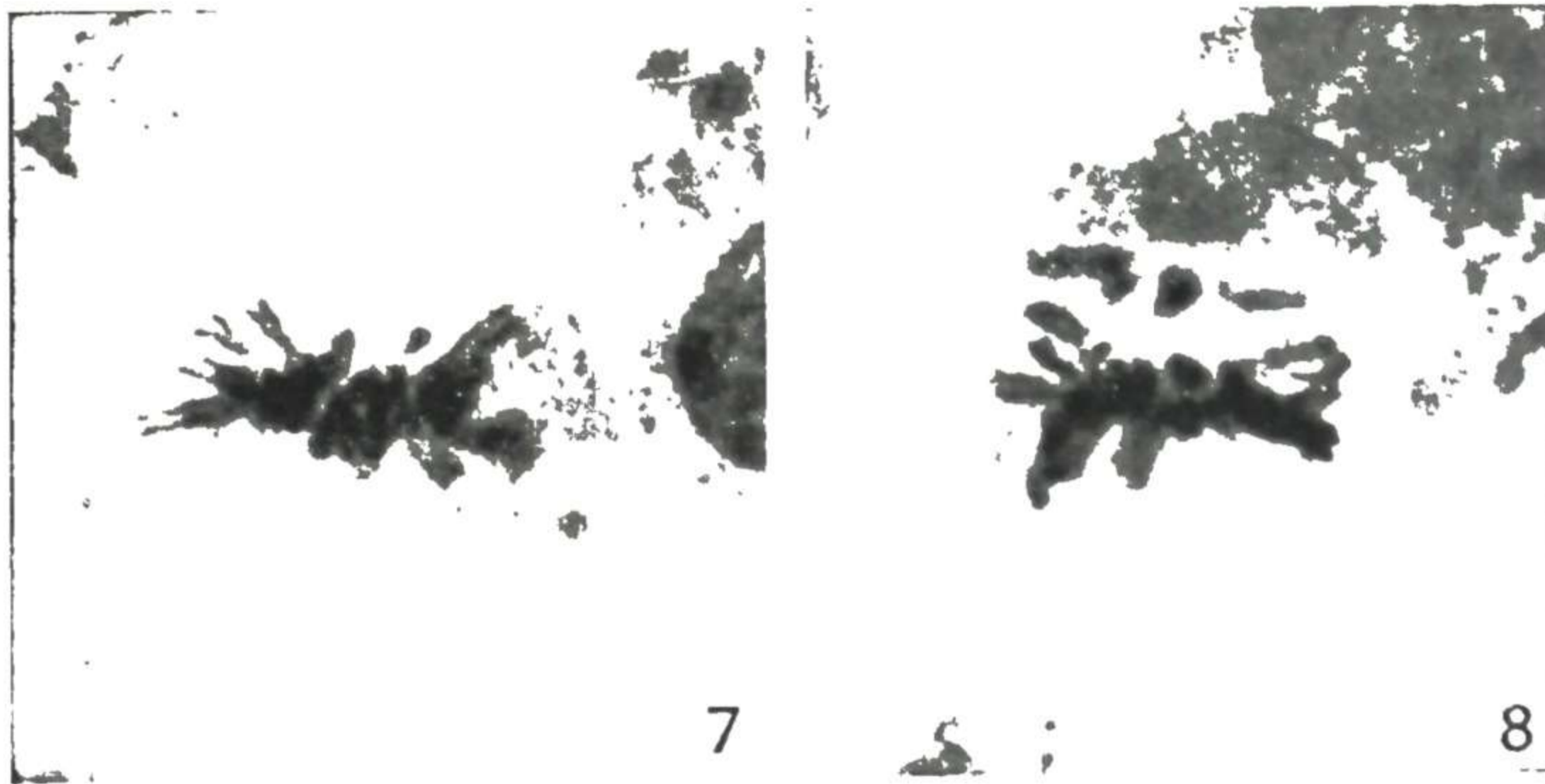


Fig. 787.—7, Metaphase of a normal cell division, showing the chromosomes more widely split in regular fashion. 8, Metaphase showing four chromosomes which have failed to assume their usual position on the metaphase plate. When this cell completes division, these four chromosomes will become aberrant. (Mendelsohn—*Am. J. Cancer.*)

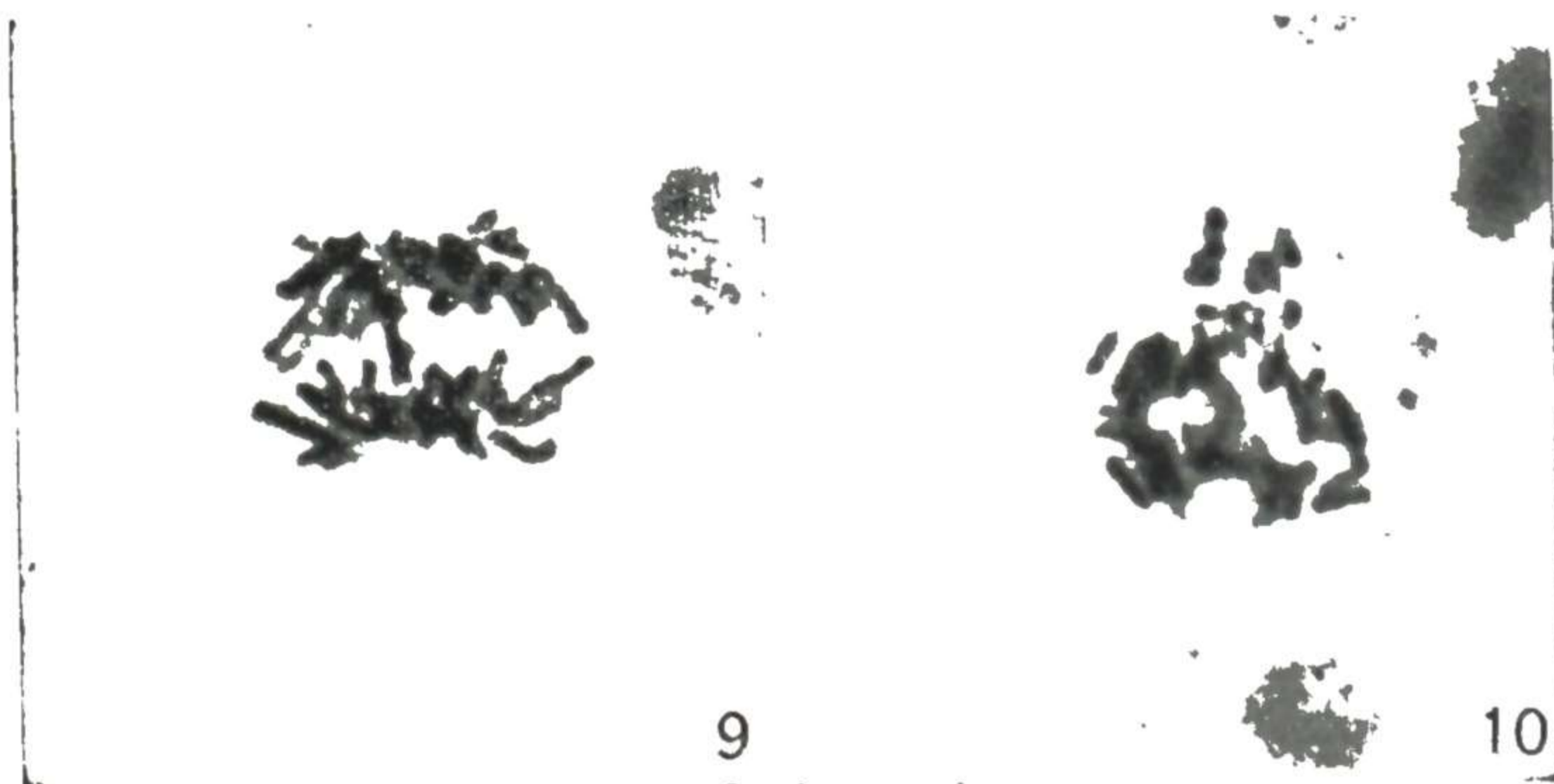


Fig. 788.—9, Anaphase of a normal cell division. 10, Anaphase showing a number of aberrant chromosomes which failed to enter the metaphase plate. These chromosomes will be taken up by one daughter cell and may either enter the new nucleus or else round up as a small chromosomal vesicle. This illustrates asymmetrical mitosis with unequal distribution of chromosomes. (Mendelsohn—*Am. J. Cancer.*)

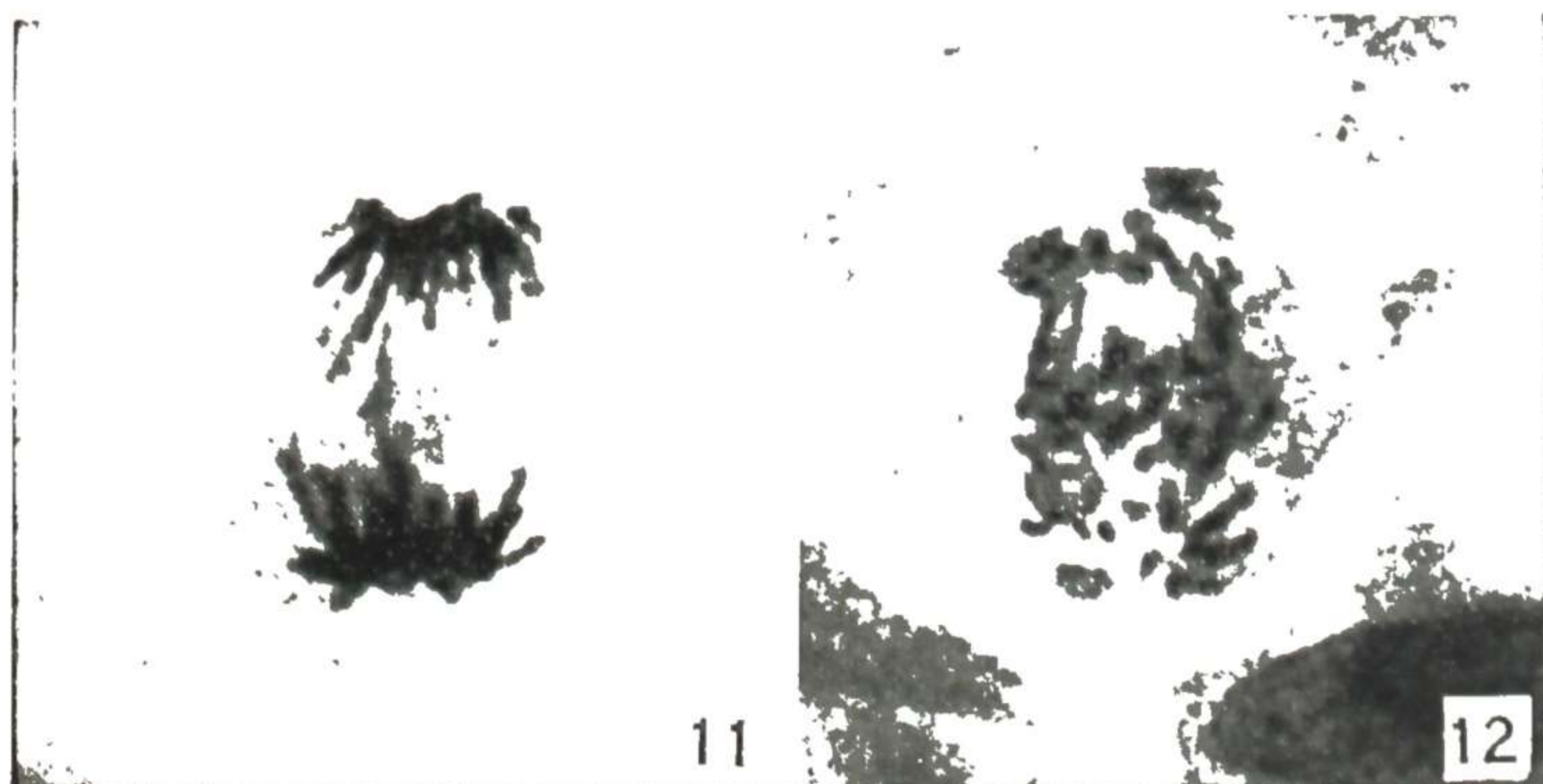


Fig. 789.—11, Telophase of a normal cell division. 12, Telophase showing a marked delay in the movement of the chromosomes. Although many chromosomes have reached the poles, there are many more still separating at the metaphase plate. It is quite possible that mitosis will not be completed and a cell will result with double the number of chromosomes. (Mendelsohn—*Am. J. Cancer.*)

In addition to the regular and essential elements of the diseased tissue, there are **secondary changes**. Areas of softening and degeneration occur in which the cells are broken down and become simply fluid and débris. Hemorrhage into certain parts of the growth may occur and, as a result of that



Fig. 790.—1, Early telephase of a cell which will divide into three daughter cells. It has three poles but only two spindles. The daughter cells will have an unequal distribution of the chromosomes. 2, Early telephase of a cell which will divide into three daughter cells. This one has three poles and three spindles. The spindle fibers do not show clearly. Each daughter cell will have more chromosomes than those in 1. (Mendelsohn—*Am. J. Cancer.*)

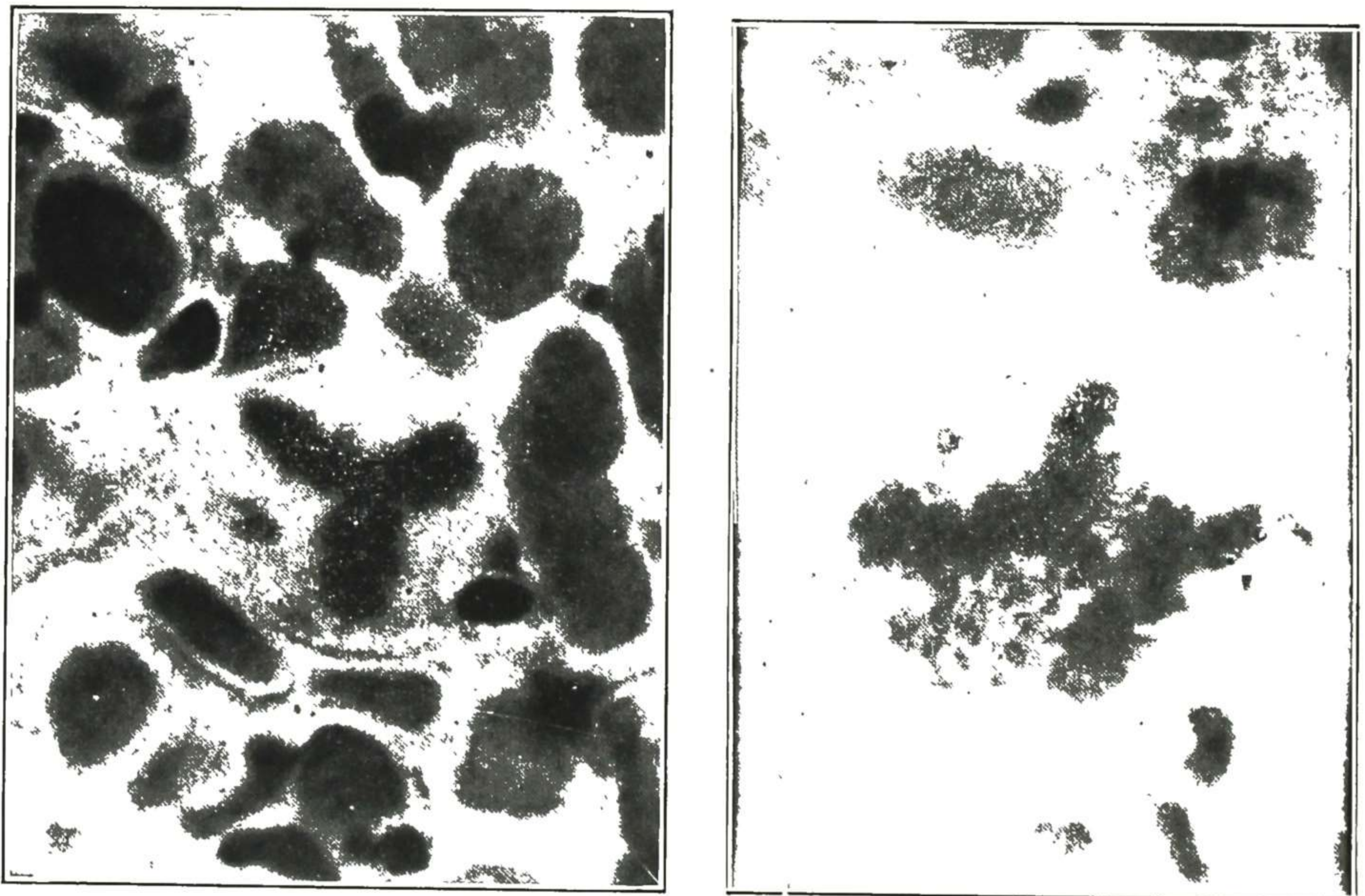


Fig. 791.—Abnormal mitoses. The photomicrograph to the left shows the so-called "Y" type of mitosis, and the one to the right shows the "H" type. In the case presenting these mitoses, the specimen consisted only of scrapings from the suspicious area of the cervix, and there was no piece of tissue large enough to show relations. The diagnosis had to be made from the cell characteristics, and these abnormal mitoses aided materially in the diagnosis of malignancy. The condition proved to be a squamous cell carcinoma. Gyn. Lab.

hemorrhage, there remain clots and discoloration and fluid. Infection may take place, leading to suppuration or sloughing. Occasionally lime salts are deposited in the cancer cells. This chalky deposit may be extensive and may even be found in the metastases.

Modes of Extension.—Carcinoma of the cervix extends in four ways—by continuity of tissue, by lymphatics, by the blood stream, and by implantation.

Extension by **continuity of tissue** is the principal method and, aside from exceptional cases, the only method in the earlier stages of the growth. In this method of extension, the carcinoma cells grow into the tissues against which they lie. This differs markedly from the way in which a nonmalignant tumor extends. A myoma as it grows pushes aside the adjacent tissues, but a malignant tumor as it grows *penetrates* the adjacent tissues and destroys them.

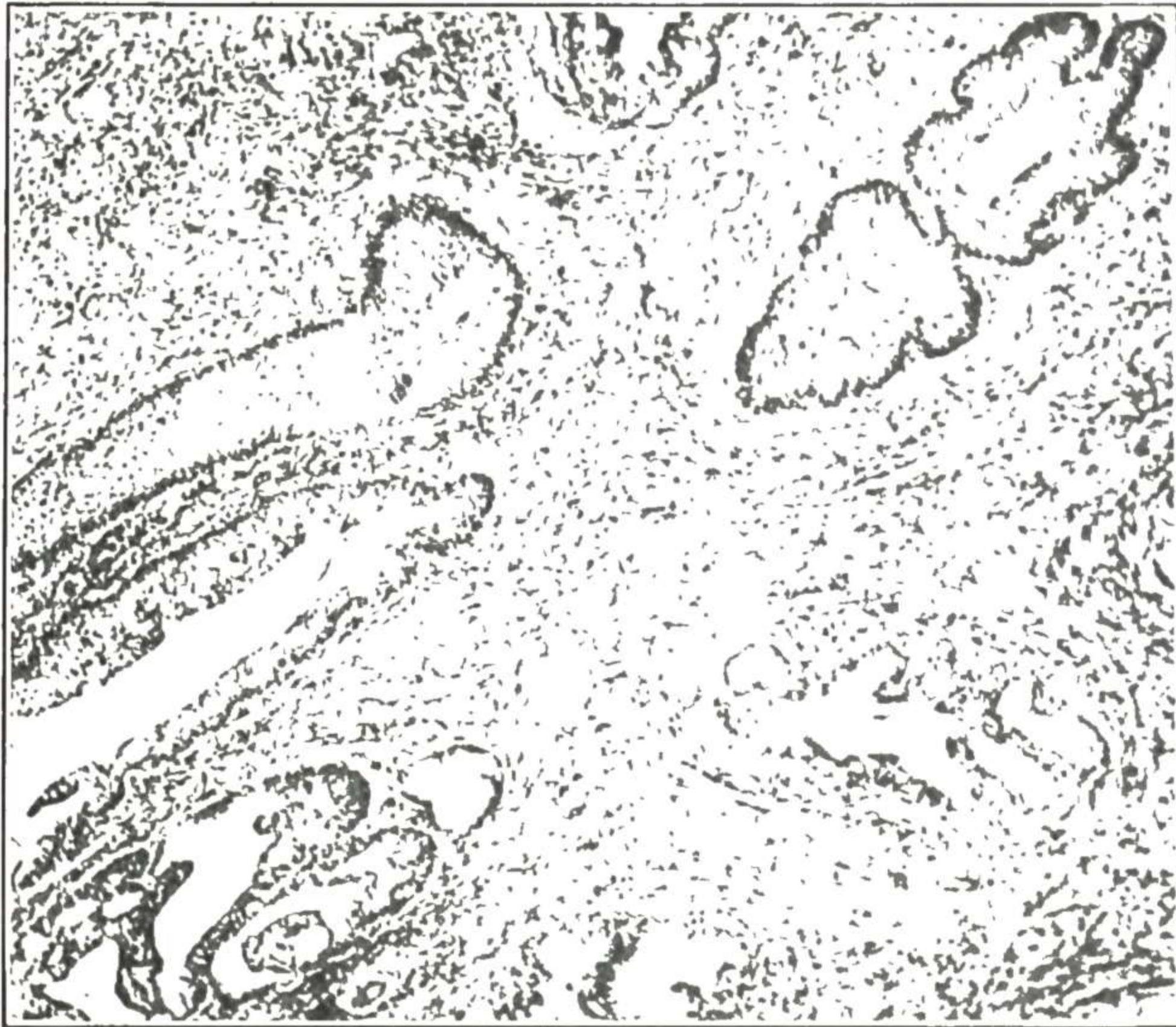


Fig. 792.—Showing, above and to left, a nest of epithelial cells resulting from an advance of epidermization process, the gland lumen being entirely filled, and the columnar epithelium being choked off. The gland below this, and also the one to the right, shows a less advanced stage of the same process, with some of the columnar cells still persisting. In lower left-hand corner is a fenestrated gland picture, produced by a combination of the same change with the adenomatous reduplication of the cylindric epithelium often seen in inflammatory lesions. No evidence of malignancy in any of these areas. (Novak—*Am. J. Obst. and Gynec.*)

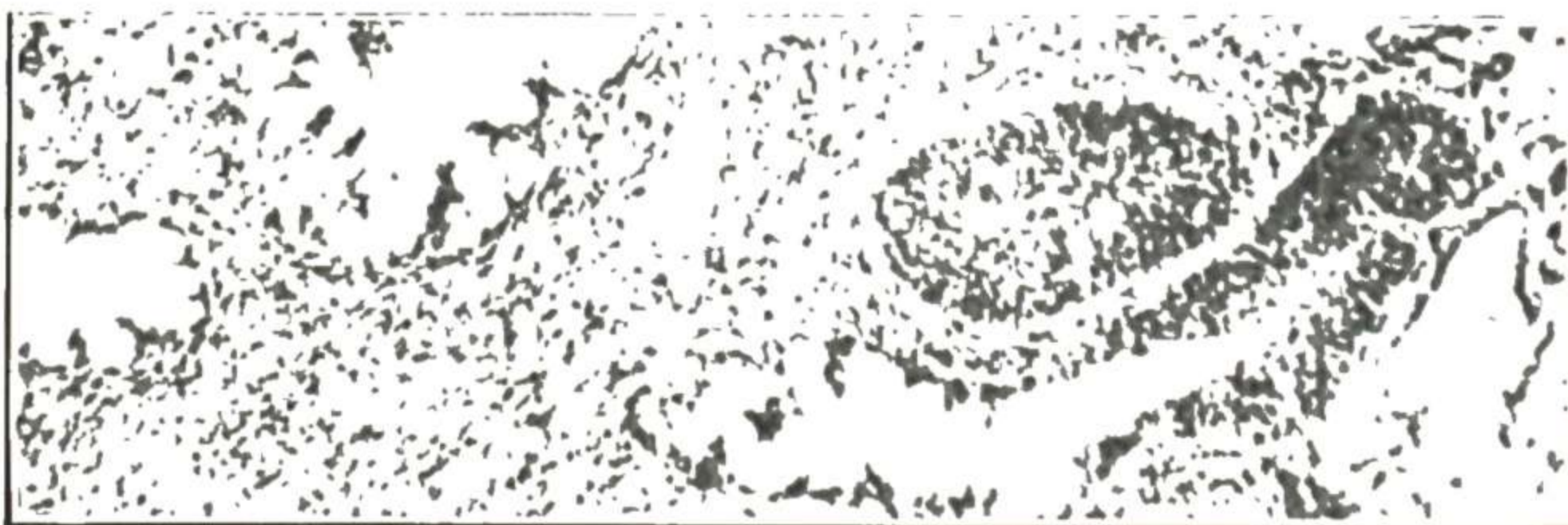


Fig. 793.—Early squamous cell cancer in a patient with only suspicious cervical lesion in which no biopsy was done. The diagnosis was made after and not before the operation, as might have been done. Note the difference between these cell nests and those shown in Fig. 792. Under the high power the cells are seen to be closely packed, placed chiefly like palisades perpendicularly to the basement membrane, and showing the usual cancer characters, mitoses, hyperchromatism, etc.). The cell nests here are independent of the glands, although of course glands are often invaded in cancer also. (Novak—*Am. J. Obst. and Gynec.*)

It is this insidious involvement of the contiguous tissues that makes most cervical carcinomas inoperable when first seen. It is this same gradual extension outward by continuity of tissue that later causes the patient most of her suffering and that in most cases causes her death by compressing the ureters, as shown in Fig. 770, and destroying kidney function.

In extension **through the lymphatics**, some carcinoma cells are caught in the lymph current and carried to lymphatic glands, where they lodge and grow and destroy tissue the same as the parent growth.

Winter found cancerous glands in only 2 cases in 44 autopsies on patients where the disease was confined to the uterus. Wertheim, in 60 operated cases, found involvement of removed glands in 15 per cent of early cases and in 31.7 per cent of all cases. Schauta made a most thorough autopsy study of 60 cases, in 40 of which the patients died from the natural effects of the cancer and in 9 from intercurrent affections. In 43.3 per cent of the whole series, the glands were entirely free of carcinomatous metastases. The lower (removable) glands alone were involved in 13.3 per cent, the upper (not removable) glands alone in 8.3 per cent and both lower and upper glands in 35 per cent.

Kundrat, in a study of 76 patients operated on by Wertheim, in which the parametrium was involved on one or both sides, found the glands entirely free of metastases in 71 per cent. The glands on one side were involved in 22 per cent, and the glands on both sides were involved in 7 per cent.

The glands are rarely involved until the cancer has advanced into the parametrium. Kundrat, in his analysis of 80 cases, found only 4 in which the glands were involved with the parametrium free.

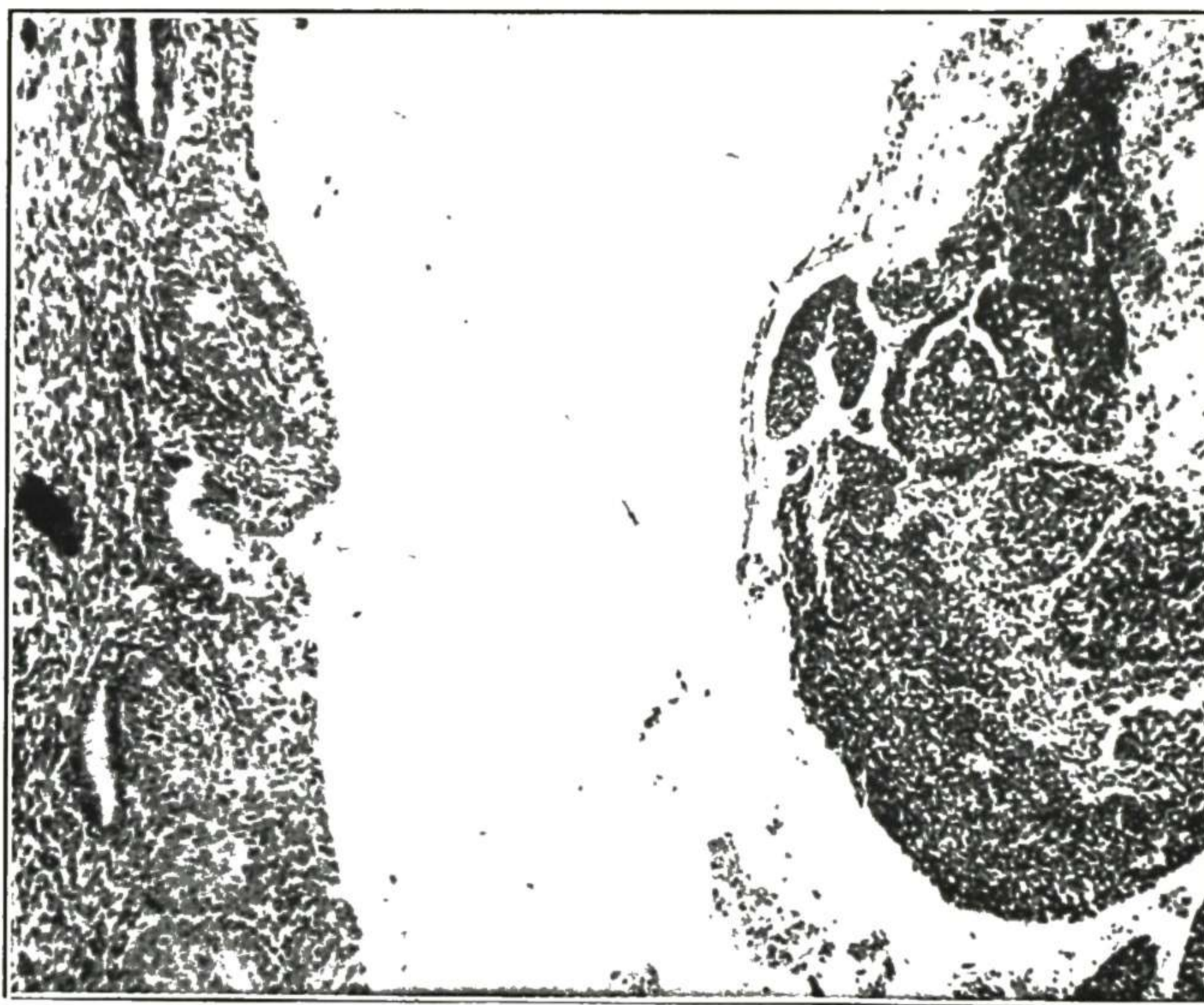


Fig. 794.—Section from the uterine cervix, showing inflammatory metaplasia or epidermization on one lip (left) and definite cancer on the other lip (right). (Novak—*Am. J. Obst. and Gynec.*)

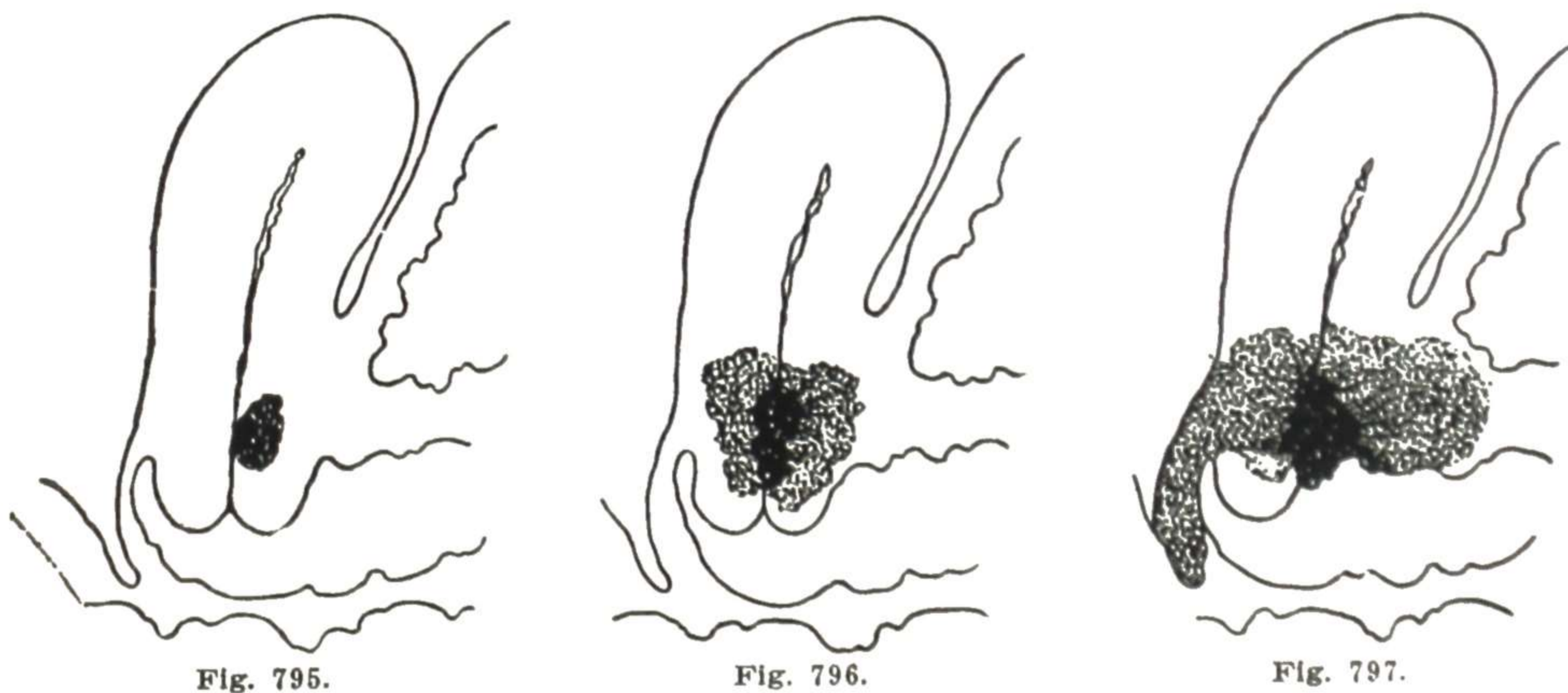
Enlargement of the regional glands is very common in the early stage of carcinoma but this enlargement is, as a rule, not due to carcinoma cells but to the inflammatory hypertrophy that nearly always takes place in the glands draining a region that is subject to severe chronic irritation. In exceptional cases, however, the glands may become infected with carcinoma cells at an early stage of the disease.

This matter of glandular involvement has a very important bearing on the question of operative treatment.

In extension **by the blood stream**, some carcinoma cells penetrate into a blood vessel, are caught in the current, and are carried to distant organs, where they lodge and grow and form metastatic tumors. In whatever kind of tissue

these metastatic growths are situated, they reproduce the structure of the parent growth. The lungs are most frequently affected, though there are many other organs that are affected occasionally. The possibility of metastases must be kept in mind in deciding whether or not a case is operable. If metastasis to distant organs has occurred, hysterectomy would, of course, be useless, except as a palliative measure. Such metastases, however, hardly ever occur except in the last stage, and then not very frequently. Winter, in 202 cases, found metastases in distant organs in only 2.5 per cent.

Direct Implantation of cancer cells into the healthy tissues of a raw surface takes place principally in operations for cancer—the cells being carried on the knife or scissors or other instrument, or on the fingers or sponges, from the infiltrated area to the healthy tissue which has been laid open in the operative work. Many undoubted instances of this occurrence are on record. It furnishes a strong reason for devitalizing cancer cells by radiation before operation and keeping the line of excision outside involved tissue during operation as far as conditions will permit.



Figs. 795 to 797.—Progressive development of an adenocarcinoma of the cervix. Fig. 795 originates from a gland within the cervix, in contradistinction to squamous carcinoma which originates from the squamous epithelium on the vaginal portion. Fig. 796. Extension throughout the greater part of the cervix. Fig. 797. Extensive involvement of pericervical tissues.

PATHOLOGY OF ADENOCARCINOMA

This type of cancer of the cervix arises from the columnar epithelium lining of the cervical canal and its glands. It comprises about 3 to 10 per cent of the cervical carcinomas. Healy found only 2.7 per cent in 1,574 cervical cancers. Cullen found 12.9 per cent in his early series. In our early series of 121 cases of cervical carcinoma 4 (about 3 per cent) were adenocarcinoma.

As adenocarcinoma is inside the cervix (Figs. 795 to 797), its presence is not appreciated until it has advanced sufficiently to cause bleeding or discharge which leads to investigation inside the cervix. The disease runs much the same general course as described for squamous-cell carcinoma, the cancer cells penetrating deeper and deeper into the cervix and out into the parametrium. After a time the cancer may extend to the external os, as a small swelling or as a papillary projection. The induration gradually extends and in time the pelvis becomes occupied by a firm fixed mass of infiltrated tissues, involving



Fig. 798.

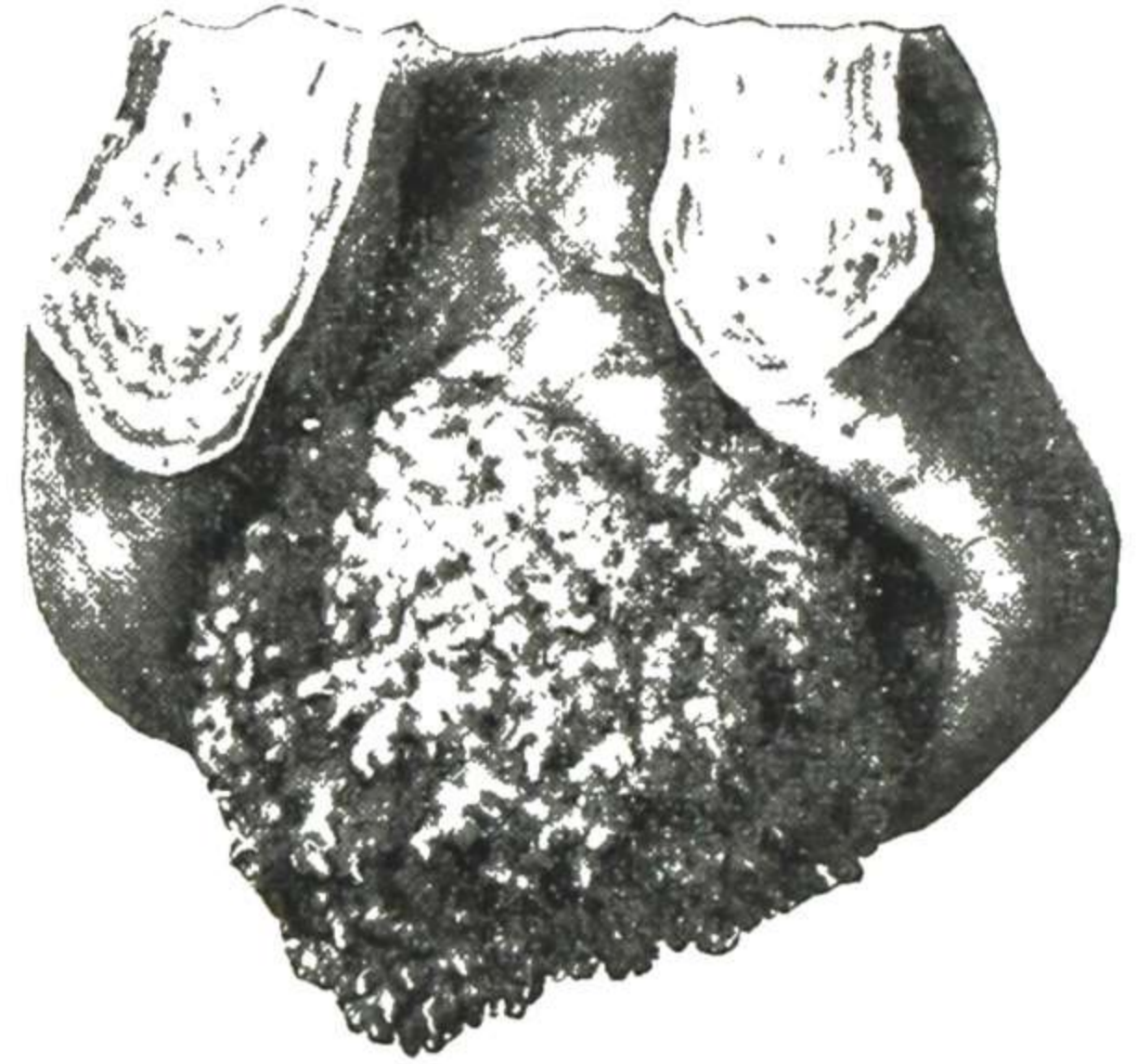


Fig. 799.

Fig. 798.—Adenocarcinoma of the interior of the cervix. A small swelling at the widened external os. (Sampson—*Bull. Johns Hopkins Hosp.*)

Fig. 799.—Drawing from an adenocarcinoma of the cervix forming a small projecting papillary mass. Part of the cervix has been removed to show the connection of the papillary mass with the cervical wall. Gyn. Lab.

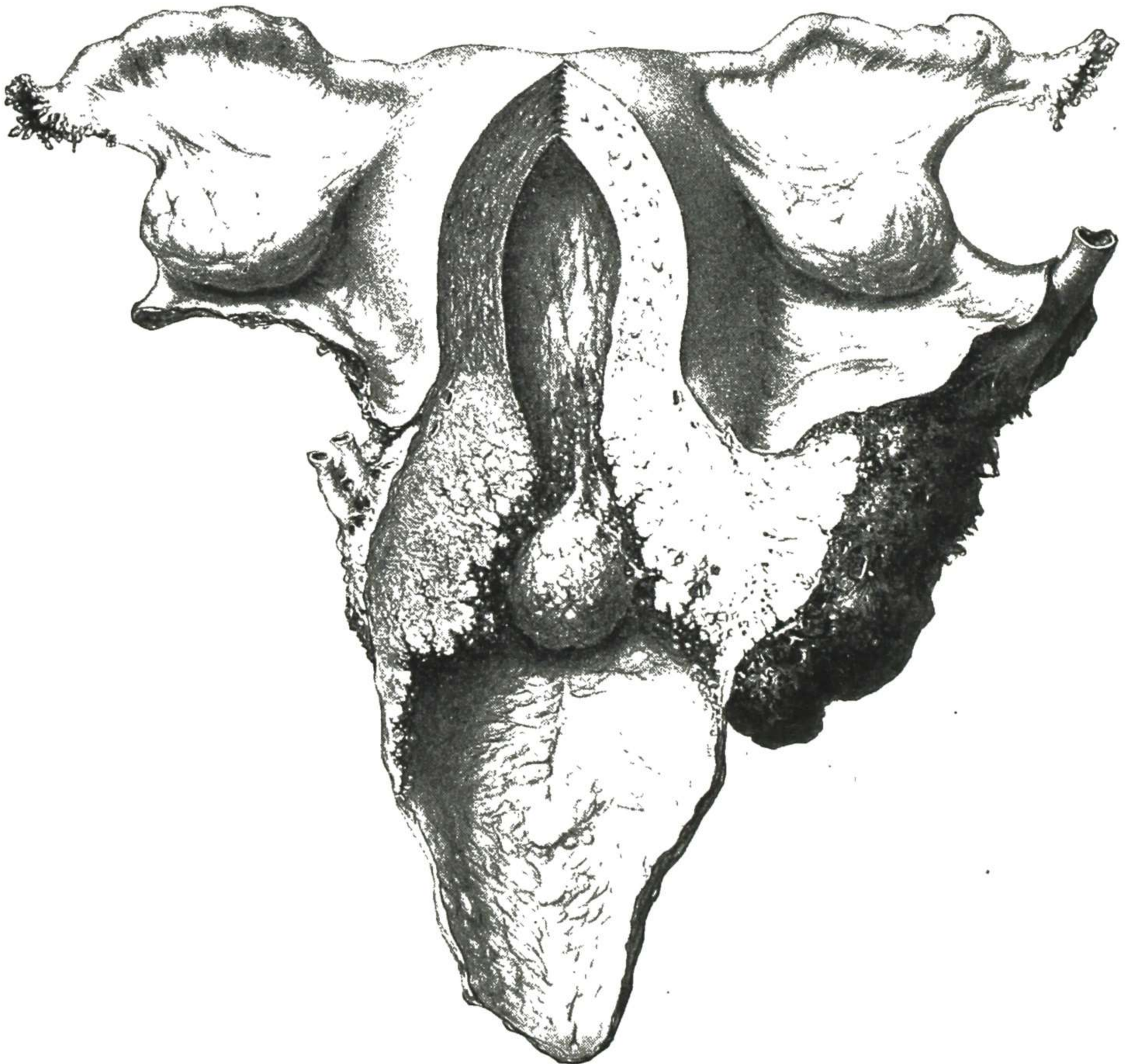


Fig. 800.—Still more advanced carcinoma of cervix (adenocarcinoma), ureters involved. (Kelly—*Operative Gynecology.*)

the parametrium to the pelvic wall and the rectum and the bladder. In some cases the ureters are gripped and constricted. Various stages in adenocarcinoma are shown in Figs. 795 to 800. Occasionally the cervical canal becomes completely blocked, with pyometra above from the accompanying infection.

Microscopic Pathology.—Adenocarcinoma of the cervix arises from the cylindrical cells lining the interior of the cervix and forming the cervical glands. It may then in the beginning be located near the external os in the cervical canal or in any part of a gland extending deeply into the cervical wall. As the cell columns penetrate the underlying tissues, the cells assume somewhat a gland formation owing to this derivation from gland-forming epithelium. This gland formation, however, is very irregular and atypical, being represented to a large extent only by solid columns of cells.



Fig. 801.—Adenocarcinoma of the cervix uteri. This photomicrograph is from the growing edge. Notice the normal glands and the carcinomatous glands in the same field. Gyn. Lab.

Microscopically, three groups are noted. In the first the glands are well differentiated and the only signs of malignancy are in the atypical cells lining the glands. The basement membrane is not broken, and the cells may be only a single layer thick. The glands are usually very irregular. In the second group are those cases in which there is definite invasion of the underlying muscle by irregular distorted glands. The lining cells are piled up in many layers and are themselves atypical cells. Mitoses are frequent. There is, however, a definite tendency toward gland formation. In the third group, the cellular growth is solid, with no attempt at gland formation. These are sometimes very difficult to distinguish from squamous-cell cancer, particularly if there is much associated epidermization.

Fig. 801 shows an adenocarcinoma of the cervix with glandular patterns.

Metastases.—These cancers metastasize early, because they are endophytic (ingrowing) rather than exophytic (outgrowing on the surface).

Symptoms

Study of the information given under pathology, gross and microscopic, will enable one to appreciate that *beginning carcinoma* of the cervix is *symptomless*. It is only after the carcinoma has advanced to tissue destruction that the telltale occasional spot of blood is added to the slight leucorrhoea of the chronic cervicitis.

This slight streak of blood is seen usually after extra exertion (extra work, long walk, lifting) or after a douche or after coitus. It is especially liable to appear within twenty-four hours after coitus. A history of such "spotting" calls for a most careful examination, that the presence or absence of carcinoma of the vaginal surface of the cervix or of the interior of the cervix may be certainly determined.

In addition to the absence of any marked disturbing symptoms in the early stage of cancer, there is another factor leading to its escaping notice till too late and that is the tendency of some physicians to overlook the significance of minor cervix irritation, either as indication of possible beginning cancer or favoring late development of it. Though the splendid cooperation and continuous efforts of many organizations have brought marked improvement in both the above-mentioned directions, there is still necessity for greater exertions. This is emphasized by the information obtained through McDowell's careful survey and analysis of cancer diagnosis in one of our large metropolitan areas. Utilizing death certificates and case records he found 59 per cent of the fatal cases had been diagnosed as malignant less than six months before death, and 80 per cent less than a year. The significance of this is apparent when we remember that cancer is a slow disease, requiring two or three years to run its course. It means that many of these individuals *with advancing cancer* were treating themselves with home measures or receiving minor office treatment by a physician.

Diagnosis

An early squamous-cell carcinoma of the cervix is shown in Fig. 761. On the surface there is only a small spot of irritation, with no indication of the sinister growth spreading to the interior of the cervix and branching in various directions. Only the physician who is alert to the possibilities beneath a spot of irritation would find this young carcinoma. Others would treat the cervix for simple inflammation, with the hidden cancer racing to the parametrium and to the deep structures along the pelvic wall. There, in brief, is stated and illustrated the physician's problem in the diagnosis of cancer of the cervix.

As we have seen, the pathologist has his problems in deciding whether or not a borderline microscopic picture is cancer, and as we shall see later, the public health official has the difficult problem of persuading people to consult the family physician for minor irritations and for examination to see if there is irritation not yet producing discharge, but we are concerned just now with what the examining physician must do to discharge the cancer responsibility he assumes when consulted by a patient complaining of some vaginal discharge or who comes for a general examination simply to know "if everything is all right."

In the first place, the physician must visualize to himself the possibilities in the situation on which he is giving responsible advice—advice on which the patient can place full reliance of future safety as far as present conditions are concerned. As an aid in this direction, I would advise the physician to think of the subject in such a way that, when consulted by a patient for examination, a picture similar to Fig. 761 automatically comes into the mind's eye. If it were not for the worry such graphic exhibit of facts might cause the patient, I would advise that an enlargement of this photomicrograph or some similar one be kept by the physician above his desk as he talks with the patient and assumes responsibility for her health.

There are two parts to the physician's task. The first part is to cause the patient to see the necessity of local examination, without causing her undue anxiety. This may usually be accomplished by explaining that there may be local irritation which has not advanced to the point of noticeable discharge but which nevertheless is a source of danger until eliminated. Hence the sensible thing is to determine whether there is any irritation and if so, eliminate it—then there is no remaining uncertainty nor occasion for worry. If the patient is one of those exceptional individuals who thinks the physician cannot have knowledge of possible conditions which she does not appreciate or see evidence of, the safest plan for the physician is to refuse to assume health responsibility for her. He has enough serious responsibilities to fulfill with the patients who cooperate, and it is better, on the whole, to lose a prospective patient occasionally than to assume responsibility blindly.

The second part of the task is to deal with conditions found on examination in a way definitely to exclude cancer, without causing the patient unnecessary trouble or expense. If the vaginal portion of the cervix is normal on inspection and there is no indication of trouble higher, that ordinarily suffices for the present. The patient is directed to return promptly if there should be any local disturbance any time. It is also explained to her that a general and local check-up at certain intervals, as a health assurance measure to catch any beginning disturbance in an early stage, is well worth the expense. The interval of probable safety varies, being usually put at six months or one year, depending on the condition of the complicated machinery and the local protecting surfaces in that individual.

This information as to the advisability of future examinations is an important part of the advice to the patient, and should be put in a way that she will appreciate the safety and reassuring satisfaction it gives her (rather than being anxious and frightened) and also in a way to make it clear that your responsibility cannot extend beyond the limits stated.

If the cervix presents irritation from cervicitis in any of its various forms, it must be dealt with adequately, which means (a) removal of the irritation and (b) definite determination whether or not there is any associated cancer. If conditions are such that these necessary requirements can apparently be met by a lactic acid douche and the simple office treatment measures already mentioned under Cervicitis, they are to be employed.

If the irritation does not clear promptly under this treatment, or if on first examination the irritation appears of chronic type not likely to clear

promptly, then conization should be carried out in a way to remove the whole affected area—that is, by the electric cutting-wire or the knife, as explained in detail under Cervicitis in Chapter VII. Endometrial curettage also is usually advisable in these cases, and if needed, vaginal plastic work may be carried out at the same time. The expense of conization and curettage with its few days' hospitalization, is a small price to pay for the elimination of irritation that may lead to cancer and the determination as to whether or not that disease has already begun. It is to their honor, and a justification of the implicit confidence of their patients, that physicians seek to spare the patient trouble and expense. But this kindly feeling can be carried to a point where it may do the patient irreparable harm. It is no kindness to a patient to give her the comfortable feeling that a small lesion carries no danger, and then have her return to you or to some other physician after a few months with an advanced cancer of the uterus or of the breast, as the case may be. The danger of such result from your consultation lies in the patient's interpretation of what you say and how you say it. Consequently, it is important to overcome the natural tendency to give desired assurance sufficiently to leave no loophole by which the patient may reason that there is no danger or that she can safely postpone the next visit or the additional examination and treatment measures you mentioned.

The evidences of advanced cancer have been sufficiently mentioned under Pathology and Symptomatology. They hardly belong under Diagnosis—the time for diagnosis is long before that.

Adenocarcinoma creates a special diagnostic problem in that it occurs inside the canal, which area is not visible on speculum examination. If there is a history of occasional show of blood or a discharge, with nothing about the vagina or vaginal surface of cervix to account for it, the solution of the problem is clearly indicated, namely, to carry out regular curettage and conization. This provides effective treatment for the bleeding or discharge, whether it comes from the endometrium or the cervical mucosa, and at the same time gives adequate specimens for determining with certainty whether or not there is beginning cancer in either location.

The other phase of this diagnostic problem is furnished by the patient who comes simply for a safety check-over and has no bleeding nor discharge nor other evidence of trouble in vagina or uterus. Of course we have been inclined hitherto to feel that, with the vagina and vaginal portion of the cervix free of irritation on inspection and no indication of trouble higher, we could safely assure the patient of normal conditions. But developments have raised a serious doubt.

The early diagnosis of endocervical cancer has the same requirements as the early diagnosis of cervical surface cancer, namely, that it be discovered *before* it has advanced to the stage of bleeding or discharge. These two so-called "early" signs mean a break in the surface (ulceration) and we know that in many cases the carcinoma penetrates deeply, by lymphatic or blood-vessel penetration or even by adjacent tissue involvement, while still protected by surface epithelium. Detection of cervix cancer in a really early stage requires removal of every spot of persisting irritation, and microscopic check-up

of it. We can see the spot of chronic irritation on the vaginal surface of the cervix but not the spot of chronic irritation inside the canal—hence the added problem.

The peculiarity of the endometrium, with its vascular phenomena resulting in normal bleeding and cast-off every few weeks, makes it particularly responsive to irritation whether on the surface or underneath, and consequently endometrial cancer is signalized early by increased flow or intermenstrual spotting, which the examiner can appreciate. An endometrial cancer patient who comes late, does so because the patient or the physician did not appreciate the possible sinister significance of irritation signs. But the endocervical cancer may give no early irritation sign, and yet we are required to decide whether or not a spot of irritation is present.

We desire to avoid causing the patient unnecessary trouble. On the other hand, this serious decision cannot be passed over lightly with wishful thinking and a reassuring guess. Some meet this problem by advising conization as part of the regular pelvic examination in patients past a certain age. At first thought this may seem unduly radical, but on second thought we must realize that a reasonably certain elimination of cancer or its early detection if present is well worth the expense and trouble of conization or of more extensive procedure if necessary.

We must not be lulled into false security by the fact that adenocarcinoma furnishes only about 5 per cent of cervix cancers, for squamous-cell cancers also occur in the canal, where the squamous epithelium extends up inside to meet the glandular epithelium. Wollner cites such a case in his instructive report on a series of cases on which he carried out routine conization for the purpose of systematic histological investigation. In fifty-nine patients, without symptoms or clinical findings indicating malignancy, in which he did conization he discovered carcinoma in two. In one of these the beginning carcinoma was inside the cervical canal but of the squamous-cell type, starting from the squamous epithelium in the lower part of the canal. He concludes that: (1) Conization should accompany curettage as a diagnostic measure, holding that curettage does not remove sufficient tissue from the cervical mucosa for conclusive microscopic investigation. (2) Every woman past the age of thirty should be considered as possibly harboring a beginning cancer of the cervix, and a conization tissue-examination is advisable to detect or eliminate the condition. In addition to the benefit to the individual patients this would result in the accumulation of histological studies contributing greatly to a better understanding of the physiology and pathology at a common site of carcinoma.

In adenocarcinoma, childbearing is not the important factor that it is in the squamous-cell type. Consequently the safety examination of the canal is advisable in the nullipara and in the unmarried of cancer age. Lash found an unsuspected adenocarcinoma of the cervix in a virgin of forty. It was discovered by removal of the uterus for myoma. There had been some bleeding, which was attributed to the obvious myoma. This carries the additional warning that a bleeding tendency with a myoma may be due to an associated cancer instead of the myoma.

There are **two encouraging features** that should be remembered along with the difficulties of early cancer diagnosis. When this really early diagnosis is made, cure is almost certain, running 95 per cent and higher where indicated radical measures are employed promptly. Again, recent investigations indicate that the period during which this early microscopic diagnosis may be made is a comparatively long one. The erratic cell changes cited and illustrated may continue many months and in exceptional cases some years before the break through the basement membrane and invasion of underlying tissues. **Knowing of this long period for genuine early diagnosis by the methods men-**

tioned, before symptoms or even subepithelial invasion, and viewing the steady stream of deaths from cervix cancer in the past, one can say, in looking back "What opportunities we lost!" and looking forward "What splendid promise for the future!"

Treatment

The principles of present-day treatment of this disease were summarized as follows by the senior author in an invited editorial, for the *American Journal of Surgery*, entitled "Treatment of Cancer of the Cervix Uteri:"

The most important advance in the treatment of cancer of the cervix is the shift from operation to irradiation. This change has been going on gradually for some years, and is now almost complete among the leaders in gynecologic work. Even those few who still employ radical operation, do not depend on the operation but use irradiation also in some form to reach the outlying cancer cells.

Despite the variety of classifications used and the consequent difficulties of critical comparison of results from operation and from irradiation, there is already apparent a definite statistical balance of cure-rate in favor of irradiation. And that is only part of the story. The radical operation has been developed practically to its limit, while irradiation is young and still developing rapidly. Again, irradiation can rescue many patients who have passed far beyond the reach of operation. Again, when depending on radical operation it is necessary in even the earliest case of cancer of the cervix to subject the patient to very grave risk, whereas with irradiation the patient is given a better chance of cure with much less risk in all stages.

My conclusions in this important matter were not reached hastily, but through critical study and a long experience of practical participation in radical operative treatment and in radical irradiation treatment for this disease. I deal with the subject from the standpoint of the practicing surgeon, anxious to give his patient every possible chance for life. There should be no antagonism of the surgeon to radium. It is simply another helpful instrument added to his armamentarium.

Effective irradiation treatment of cancer of the cervix is serious and hazardous surgical work. The shift of instruments from the knife to the more deeply penetrating radium does not lessen the surgical responsibility. If the dosage employed is too large for the particular conditions present in the pelvis, serious injury to important organs may result. If the dosage is too small, the patient is not given the chance for life to which she is entitled. The maximum dosage possible in a given case depends on a number of factors, including the location and size of the cancerous mass, the amount of involvement of each of the organs in the immediate vicinity, the extent and direction of ulceration, and the amount of fixation of the bladder and rectum by the carcinomatous infiltration. The accurate determination of these conditions and the utilization of that knowledge in effective radium treatment, require a large amount of experience and skill in pelvic work. While in some situations the radiologist without special local knowledge may give effective radium treatments, in carcinoma of the cervix conditions are such that the most effective treatment can be given only by one with special gynecologic training as well as radium training. His special knowledge of pelvic anatomy and pathology and his training in accurate pelvic palpation and diagnosis must all be utilized in the supreme effort to reach the marginal cancer cells with effective radiation.

There is a tendency among the inexperienced to regard the use of radium lightly. This tendency is encouraged by some of the radium-rental instructions given by commercial companies, which presume to fit the recipient for the safe and effective use of this dangerous instrument. It would be as reasonable to suppose that instructions issued with a scalpel would fit the recipient to use it safely and effectively in the eradication of cancer. Radium is as potent as the knife, and in inexperienced hands may produce as disastrous results, either in the form of injury to adjacent organs or as failure to save a life which might have been saved by effective use.

Of course, irradiation treatment does not exclude any work with the knife which may be helpful. In special conditions some vaginal operation or abdominal operation may permit more advantageous placing of the radium in its various forms. The important point in regard to any operative work employed, is that it should supplement irradiation and not displace it. Another important point is that any experimental work, not established by a record of five-year cures, should be presented as experimental only. Otherwise it may be accepted and used by the uninitiated as an established method of cure.

The most pressing problem just now is to bring the benefits of radical irradiation treatment to patients generally. The spread into general practice of this most effective treatment for this disease is very slow. There are reasons for this. In the first place, cancer of the cervix is very deceptive as to the extent of the lesion and the depth of penetration. What appears to be an early cancer of the uterus is really already a cancer of the outlying pelvic structures, for whose elimination hysterectomy as ordinarily performed is but a futile gesture.

A second stumblingblock to the general adoption of the most effective treatment is that many physicians find it difficult to understand how any other treatment could be more effective than operative removal. Now, while operative removal is effective as far as it goes, in most cases of cancer of the cervix it cannot go far enough to remove the outlying cancer cells. When only one patient in four can be saved by the most radical operation by the most experienced pelvic surgeons, what chance of cure has the patient with this widespread disease when subjected to operation by an operator inexperienced in this deep work in this difficult situation? The result as a rule is removal of little more than the uterus, leaving the deeper portions of the growth to progress and eventually cause death. Dependence on such incomplete operation deprives the patient of the chance for life which modern treatment would give her.

The treatment given patients with cancer of the cervix in any community is determined largely by the surgeons of that community. In every case the decision as to the type of treatment is a serious matter, for it may mean the difference between life and death for that patient. Hence the importance of the clear presentation, by the educational agencies of the profession, of the superiority of expert radical irradiation for this disease.

It seems to me that the clearness of such educational presentation and its effect in securing such treatment for these patients, are both diminished by coincident attractive delineation of the radical operation, with its wealth of pictorial detail which appeals so strongly to the uninitiated. Actions speak louder than words, and my feeling as to the importance of this matter is shown by my declining, as per the following letter, an invitation to present the radical operation for the symposium in this issue.

St. Louis, Mo., Nov. 27, 1934.

Dear Doctor Livingston:

I appreciate the compliment of your kind invitation to present the technical features of the radical operation for cancer of the cervix uteri for the *American Journal of Surgery*.

When this operation was our most effective means of combating this form of cancer, I gave much thought and work to the practical application of it to the cure of patients and to the helpful presentation of its technical details for the use of others. However, an advance has been made in the treatment of cancer of the cervix, which gives the patient a definitely better chance of cure than the most radical operation by the most experienced operators, and a far greater chance than operation as carried out by operators in general. Irradiation presents so much better chance of cure for these patients that it lays a serious responsibility on the leaders in this work (individuals and journals) to use their energy and talents to spread this information throughout the profession.

Feeling as I do, naturally I do not wish to further confuse the situation and push the radical operation by making a special presentation of it, with all the attractive illustrations and alluring details to which this operation so readily lends itself. In my *Operative Gynecology* I expect to retain a description of its principles and their application, because of its historical importance in the development of effective treatment for this disease. But as a method of choice in the handling of cancer of the cervix today, radical operation as opposed to irradiation is a back number—an obsolete method. However, it will probably take ten years yet for this knowledge to permeate the profession and bring to the patients generally the benefits of the most effective treatment, especially if journals and books push the operation.

Of course I appreciate that as an editor you wish to present all sides of the subject. This rather lengthy letter is simply a response to the courtesy of your kind invitation, giving the reasons for not being able to accept the same.

With best wishes in your difficult task,

H. S. Crossen.

I thought the letter would settle the matter as far as I was concerned, and that some one else would be commissioned to present the radical operation. But Dr. Livingston surprised me by patiently reading all the literature sent with the letter, and then countering with a statement that he had decided not to present the Wertheim operation and with a request that I submit an orienting editorial.

For detailed consideration of the various points reference must be made to published articles. Briefly, as elsewhere stated, present efficiency and future progress in the cure of cancer of the cervix are predicated on the following facts:

1. The successful care of a patient with cancer of the cervix is based upon an organized combination of expert services.
2. The crucial point of attack is not the uterus but the cancer cells along the pelvic wall. It is these outlying cells that must be reached and destroyed, or recurrence is certain.
3. Irradiation is the most important factor in attaining success in this concerted attack on the outlying cancer cells. There are exceptional conditions in which operative work with the knife also may be advisable, but whenever used operation should supplement irradiation and not displace it.
4. Too many of these patients are still being treated with halfway measures—with operations that never reach the outlying cancer cells, and with inefficient radium and x-ray treatments that carry no devitalization into the distant crucial zone.

That was a bold stand to take in those days, when controversy concerning this radical shift from operation to radiation was still raging, but time and experience have fully justified that stand, and it now constitutes the general rule of treatment in carcinoma of the cervix.

Radiation treatment is carried out by radium implanted in the uterus and deep x-ray therapy from the outside. Effective radium treatment, i.e., putting effective dosage into the area of outlying cancer cells, is based on the principle of extending the differential killing effect of radium (the cancer cells, being young, are more susceptible to radiation than the older normal tissue cells) by screening out the soft "burning" rays to permit heavy dosage of the deeply-penetrating hard gamma rays, as indicated in Fig. 802.

This is accomplished by means of metal screening and tissue screening and distance screening. The metal-covered radium is placed in the center of the cancerous cervix. The rectum and bladder are packed away by a firm vaginal packing of vaseline gauze, as shown in Figs. 803 to 805.

Deep x-ray radiation supplementing the heaviest safe dosage of radium, assists in reaching the outlying cancer cells with lethal dosage. Deep dosage is secured without damage to intervening tissues by employment of the principle of cross-fire, illustrated in Figs. 806 and 807. It is now usually applied through four to six fields—two in front lateral to the median line, two over the sacrum, and one over each hip when six fields are used. Fig. 808 shows the depth percentage distribution of radiation from a six-field application.

Occasionally the perineal field is used, principally in cases where the pelvic carcinoma has extended to the vaginal entrance. In addition to these external portals, intravaginal apparatus has been developed for giving deep x-ray therapy through the vaginal vault.

In the earlier days radium was almost our sole reliance in effective radiation of cervix cancer, but with advancing effectiveness of x-ray therapy it has become a decided help in this difficult task of devitalizing the outlying cancer

cells along the pelvic wall. Radium, however, is still our main reliance, though much is expected of future developments in deep x-ray therapy.

Of course continuous efforts to improve treatment results are being made in many directions, including implantation of radium directly into the outlying parametrium by long needles from the vaginal vault (Pitts and Waterman), direct x-ray treatment of the parametrium through the opened abdomen (Schumann), and operative removal of the lymphatic glands of the area (Taussig).

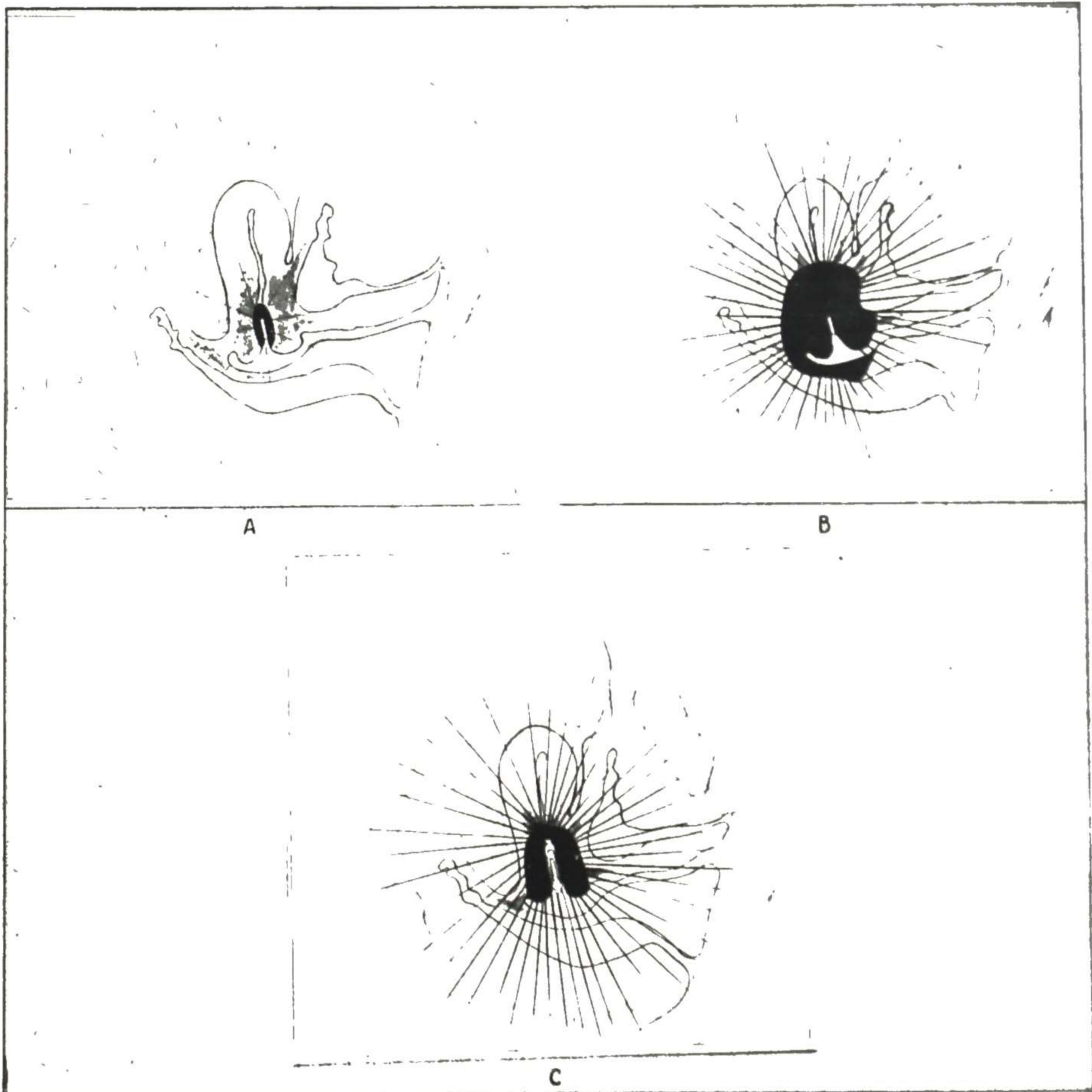


Fig. 802.—Metal and rubber screening. *A*. Indicating the effect of a small dose of un-screened radium, simply in the glass capsule. The dark area represents the sloughing and the few radiating lines the small dose of deeply penetrating rays. *B*. Indicating the effect when the dose of un-screened radium is increased sufficiently to give an effective dose of the penetrating rays. The slough is extended into the bladder and rectum. *C*. Indicating the effect of the metal and rubber screening. The sloughing area is limited, so that a large dose of the penetrating rays may be given without sloughing into the bladder or rectum.

Those interested in these special measures will find articles in the Reference List. These and other special measures are used as supplementary to regular radiation treatment, which is the main reliance in cancer elimination.

The effective treatment of cancer of the cervix, whether accomplished with the knife or with radium, is a major surgical effort with the patient's life

hanging on successful execution of it. Hence it should be undertaken only by those with the required training and experience. The technical details are considered in the operative volume. The preparations and immediate after-care are about the same as for radium treatment of myoma, where are given also the details of removal of the radium. Later the treatment is symptomatic with the patient returning at regular intervals for pelvic check-up to see if there is any evidence of recurrent cancer activity and to direct further radiation treatment if needed.

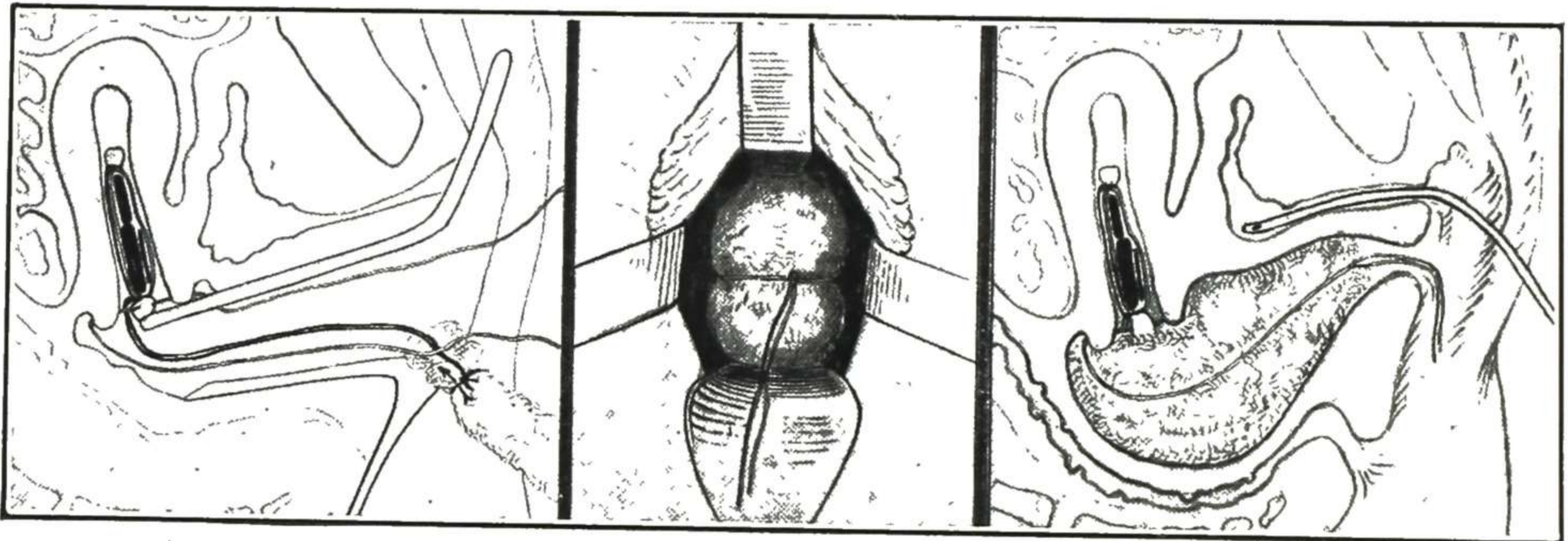


Fig. 803.

Fig. 804.

Fig. 805.

Fig. 803.—Anterior and posterior retractors in place ready to begin the firm vaginal packing with vaseline gauze, to push away the rectum and bladder as far as possible from the radium. This drawing shows also the long light-colored catgut suture passing through the cervix and rubber tubing (details of which are clearer in Fig. 753). It is well to tie the end of the packing to the radium string, as here shown.

Fig. 804.—The process of packing the vagina very firmly is facilitated by adding a ribbon retractor on each side, as here shown. The packing is in place, and the catgut tied over it.

Fig. 805.—Showing the firm packing in place, pushing away the rectum and bladder from the radium. Notice that the suture holding the radium package in position is tied over the gauze packing near the vaginal outlet, where it is easily reached for cutting and removal as explained in the text. The details of such removal have already been illustrated under radium treatment for myoma (Fig. 755). (Crossen and Crossen—*Operative Gynecology*.)

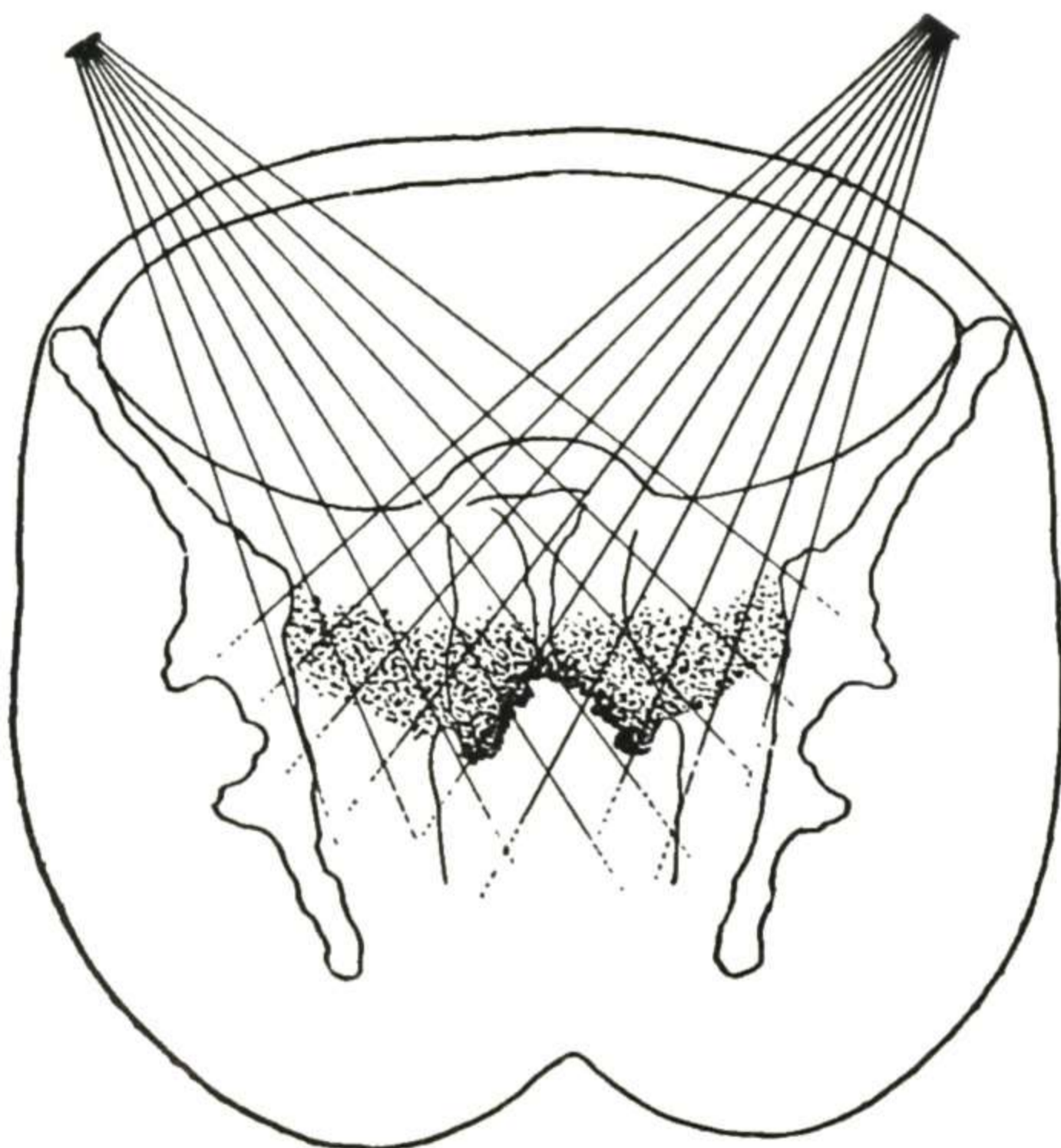


Fig. 806.

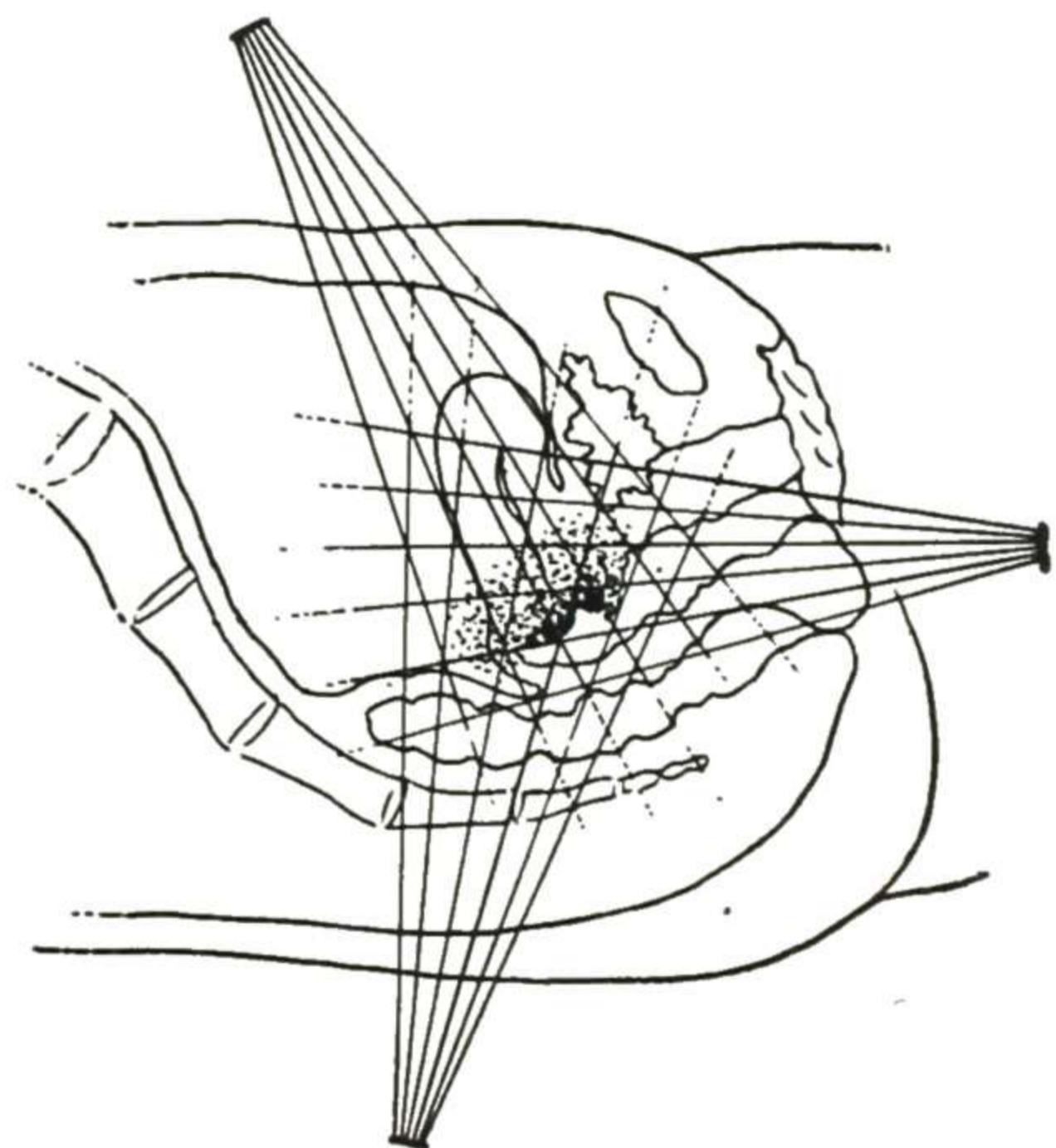


Fig. 807.

Figs. 806 and 807.—X-ray treatment of carcinoma of cervix uteri. In order to place sufficient dosage in the cancer area without injury to the overlying skin, extensive cross firing is necessary, and the use of many ports of entry, one after another. Fig. 806 indicates successive steps in firing through lateral portions of the abdomen. Fig. 807 indicates other ports of entry—the central abdomen, the sacral region, and the pelvic outlet. Improvements in technique have now made practical x-ray treatment through a vaginal speculum.

In the advanced cases the relief of pain is the important problem. Radiation is the most effective treatment. After it no longer helps and the milder sedatives fail, surgical measures including spinal injection and cordotomy are to be considered, for they may give much relief. Much was claimed for refrigeration treatment but the hopes have not been sustained. Vaughn, after a trial with several patients, concludes: "In my opinion this procedure is hazardous and is not justifiable in hopeless metastatic carcinoma."

When the advancing cancer causes a vesicovaginal or rectovaginal fistula, the problem of keeping the patient comfortable is greatly complicated. Much study has been given to meeting this problem, and help for the individual patient may be obtained by adaptation to her special needs of some one of the different types of apparatus devised, such, for example, as that shown in Figs. 537-539.

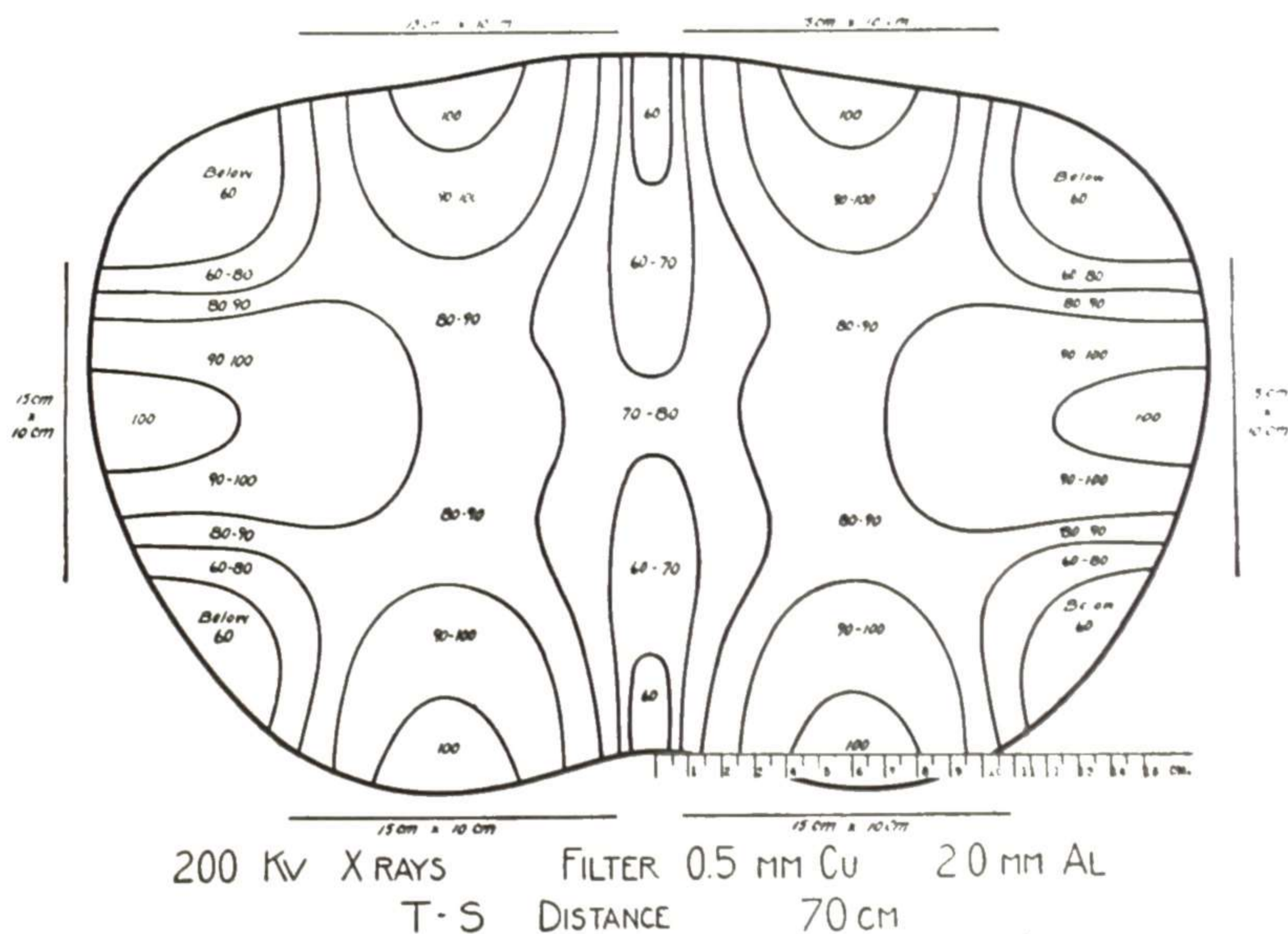


Fig. 808.—Distribution of roentgen radiation within the average female pelvis for the addition of lateral beams to two portals on both the anterior and posterior pelvic surfaces. (Arneson and Quimby—*Radiology*.)

PREGNANCY
WITH CERVIX CANCER

The guiding principle in the treatment of this condition is to treat the carcinoma. There are, of course, not only varying ages of pregnancy to be considered, but also varying stages of carcinomatous extension. Any combination of these two may be present in any given case, so a consideration of both factors guides one in determining the best treatment for the particular case.

Cases in early pregnancy with an early or late lesion should have adequate radiation immediately. This would of course kill the embryo and in most cases cause an abortion. If the uterus does not empty after six to eight weeks, it is emptied operatively by curettage.

When the pregnancy is between four and seven months the treatment depends upon the mother's desire for a living child and the stage of the preg-

nancy. With an early lesion in a pregnancy just short of viability in a mother very desirous of offspring, 3,000 mg.hr. of properly screened radium should be given. There should be a distance of at least five centimeters between the radium and the head of the fetus. External version and Trendelenburg position during radiation are advisable for protection of the child. This plan does not harm the fetus at this stage and may hold the carcinoma in check long enough to permit the delivery of a viable fetus. As soon as the child's chance of surviving is fairly good, a Porro cesarean section is done to rescue the fetus. Following this, radiation should be given as for any like case of carcinoma.

When the mother has children and the urgent indication is to save her to take care of them, adequate radium and x-ray radiation should be given at the outset. This causes the death of the fetus, and delivery is completed later, either from below or by cesarean section or Porro section as seems best in the particular case.

In pregnancy between seven months and full term in which there is an early lesion of the cervix, the treatment of choice is a cesarean section (Porro) followed by adequate radiation. When the lesion is more advanced moderate radiation is given first, followed by Porro section and then adequate radiation. This plan helps to reduce the operative risk by reducing the accompanying infection and by causing some regression of the carcinoma.

In the last group of cases, those at term, the management depends upon the condition of the cervix, presentation of the fetus, and extent of the carcinomatous process. As a general rule, delivery through a carcinomatous-riddled cervix is contraindicated. The dangers are hemorrhage from deep tears, sepsis, and spread of the carcinoma cells. In very early lesions, with the head low and a dilated cervix, delivery from below may be indicated. Unless conditions are favorable for delivery from below, or if the carcinoma is beyond the early stage, a Porro section followed by adequate radiation gives the patient the best chance to survive.

Baer's article is helpful, particularly in its classification of cases and treatment advice for various classes. Emge reviews extensively the effects of pregnancy on tumor growth, concerning which there is considerable difference of opinion among investigators. Chalfant and Mering give the details of the handling of a case with instructive comments.

Prevention

The subject of prevention of cervix cancer was discussed in detail by the senior author ("Prevention of Cancer of the Cervix Uteri," *Am. J. Obst. & Gynec.*) and the following summary is from that article.

The growing appreciation of the importance of the fact that we are not getting these cancers early in spite of all efforts to do so, has resulted in a careful and anxious re-examination of the whole situation as it relates to cancer of the cervix. There is much discussion of what constitutes the earliest cancer changes, and how they may be recognized in the microscopic examination of excised tissue. New methods of clinical recognition, such as ocular magnification in the vagina with the colposcope and chemical reaction with Schiller's iodine painting, are being tested for discerning beginning cancer changes in the epithelium of the cervix. All these steps for detecting the earliest cancer changes are

important and are to be encouraged. But far more radical measures than these are necessary to produce any marked advance in the prevention of deaths from this disease. It is necessary to attack this serious problem in some other way than by explaining cancer signs and symptoms to physicians and patients. *We must go back of the whole cancer picture, and remove the conditions which precede the cancer and cause it.*

It is well established that cancer development in this location is favored by long continued irritation in the form of chronic cervicitis, usually accompanied with laceration, eversion, infiltration, and cystic change. As we have said many times, these lesions are very obvious and their rôle in cancer origin is generally known, and yet they are allowed to go on and on well into the cancer age. Great pains are taken in cases of chronic cervicitis to detect the first signs of cancer so that treatment for cancer may be promptly instituted, whereas a far safer plan is to remove the chronic cervicitis promptly before it becomes cancer.

Chronic cervicitis may be cured by simple excision of the affected area of the cervix, and thus cancer prevented. But when cancer has once begun in the irritated area, cure is uncertain even by the most radical measures.

It is clear then that an important step in preventing deaths from cancer of the cervix is the systematic and early removal of those chronic irritative lesions of the cervix which precede cancer. Not only is this an important step, but it seems the only step by which to secure further marked reduction in deaths from this disease.

The importance of removing chronic irritative lesions in the cervix has long been recognized and emphasized by leaders in gynecology. Our hope is to supplement these sporadic warnings with a systematized plan of action which will deal effectively with this serious situation.

GENERAL PLAN OF ACTION

In formulating a systematized plan of action, the following three facts must be taken into consideration:

1. Thousands of patients are receiving palliative treatment for chronic irritative lesions in the cervix, such as cervicitis, "ulceration" of cervix, laceration, eversion, erosion, and polyps. The palliative measures keep the patients fairly comfortable, but they do not remove the deep chronic irritation which favors the development of cancer.

2. Other thousands of women are treating themselves for "a little leucorrhœa" in ways that may keep them comfortable but do not stop the process of cancer development in the irritated cervix.

3. There are other women in whom the chronic irritation in the cervix does not give rise to any symptoms that would cause them to suspect local trouble.

In the attempt to eliminate these chronic irritative lesions, which eventuate in a large number of deaths from cancer of the cervix, means must be found for reaching the above-mentioned three classes of persons. Effective work in this direction requires energetic action along two important lines as follows:

- A. Work by individual physicians with their patients, to the end that chronic irritation in the cervix be removed before it eventuates in cancer.

- B. Extension of present excellent educational work to include measures for making clear to the public the fact that cancer of the cervix develops without any warning signal, hence the importance of local examination, that any existing irritation of the cervix may be eliminated before cancer develops.

The above twofold plan takes care of the problem theoretically, but we cannot be satisfied with theory and principles only. This is such a serious matter that details must be carefully worked out and tested and every possible means devised and activity employed to secure results. The issue of life or death is being decided daily for many—even members of our own family may be crossing the line between inflammation and cancer. The working out of the principles of a plan is only a part, and the smaller part, of the solution of this great problem. Each of the two large divisions in the twofold plan mentioned has subdivisions which require careful and extended consideration in order to secure practical action and the attainment of definite results. We are concerned here principally with the work of the individual physician with his patients.

WORK OF PHYSICIAN WITH HIS PATIENTS

The physician is the leader and mainstay in this serious campaign. Each physician has it in his power to aid materially in the general reduction of deaths from cancer of the cervix and in saving his individual patients from this fatal disease. This is a wonderful opportunity for important constructive work by every physician. Cancer is such an extensive subject, with such deep and abstruse problems baffling the talent and facilities of great institutions, that we are inclined to think that important work in connection with it must be entirely the privilege of those with special training and special facilities. But here is an opportunity for every physician to give definite aid in the great fight which is going on all over the world to lessen the number of deaths from cancer of the uterus. No matter where the physician is located nor how limited his facilities, he has it in his power to take an important part in this great work. The details of effective work by the physician in this direction include the following:

1. In the handling of patients with inflammation or irritation of the cervix, chronic irritation must not be allowed to persist. This applies especially to patients past thirty-five, though cancer occurs also before that age. Having eliminated acute irritation by douches and local treatment, any remaining chronic irritation should be removed by conization or other radical measure. I do not care at this time to take up the pros and cons regarding the different methods of treating these minor lesions of the cervix; suffice it to say that the treatment should eliminate the chronic irritative lesion. Temporizing palliative treatments do not remove the danger.

It is important to remember that a certain proportion of cancers of the cervix (in some series as high as 10 per cent) occur before the age of thirty-five. This means that the old idea of postponing repair of the cervix to the end of the childbearing period is not safe. We know that chronic irritation in the cervix may result in cancer in younger women. Several cases in patients under the age of thirty have been reported. Consequently it is dangerous to allow irritation in the cervix to persist even in the childbearing period.

The only safe plan is to eliminate the area of chronic irritation. Carried out circum-spectly with care to avoid undue sacrifice of normal tissue and unnecessary scar formation, it should aid rather than interfere with subsequent childbearing. Even though there should be some laceration with a subsequent labor, repair of this is a minor matter compared to risking cancer development.

2. Patients in whom cervical irritation has cleared under treatment, should be watched by occasional check-up examination to see if the irritation returns.

3. Patients who come for other conditions, should be asked about leucorrhœa and other evidence of pelvic disturbance, that the required examination and treatment may be carried out.

4. Patients who come for other conditions and have no pelvic symptoms, present one of the difficult problems in this cancer prevention. We know that even without subjective symptoms there may be sufficient chronic irritation in the cervix to favor aberrant cell activity resulting in cancer. On the other hand, a practicable rule of action must take into consideration the patient's natural reluctance to examination not indicated by symptoms.

Here is where the leadership of the physician comes in. By tactful instruction, that causes no undue apprehension, the patient may be made to realize the advisability of a local examination as part of the general examination on which his responsible advice to her is to be based. The age at which such local examination is required in patients without pelvic symptoms will vary somewhat with the history and circumstances, but in general it is advisable by age thirty-five or earlier.

From the physician's standpoint, this local investigation as part of the general examination is imperative. His responsibility as the patient's medical adviser makes it necessary for him to know definitely whether or not there is beginning cancer of the cervix or chronic irritation there that may lead to cancer. The internist, the general practitioner—every physician who assumes the responsibility of advising a patient in regard to her general health—must keep in mind the possibility of symptomless chronic irritation in the cervix that may eventuate in cancer.

5. How often should the local examination be repeated? The patient will sometimes ask this question. And the physician should have decided it for himself in preparation for advising the patient, whether or not she asks it.

It is important to work out a practicable plan. The local examination should be made often enough reasonably to exclude irritation that would favor cancer development. At the same time the interval should be as long as is safe, in order to avoid unnecessary trouble and expense to the patient. Also, the choice of interval should be such as to appear reasonable to most patients when the matter is explained to them. The choice of a rather long interval which appears to the patient so reasonable that she returns regularly, will go much farther toward preventing cancer than the choice of an interval so short that the patient neglects it and finally gives up regular examinations. Considering the various angles of the matter, it seems to me that a reexamination once a year from age thirty-five to fifty-five, is a reasonable rule to incorporate in our advice to these patients.

The probability of the patient's cooperation in the idea of a regular yearly examination may be enhanced by pointing out that this twenty-year period is one of change in body structure and function, and that many authorities are recommending yearly general examination as a safety measure to determine how the various vital organs are standing the wear and tear of life's activities. This reenforces and emphasizes the idea of regular general examinations, of which the local examination is a part.

In the years before thirty-five and after fifty-five, occasional examinations are desirable, but for the present it seems best to concentrate on the twenty years mentioned, and to use our energy and educational facilities to drive home the importance of regular yearly examinations during that crucial period.

PUBLIC DISSEMINATION OF INFORMATION

It is necessary to give the public reliable information on this subject for two reasons: first, to supply to those persons who do not consult a physician the information they would not otherwise obtain and, second, to emphasize to patients the importance of following the advice on this subject given by their physicians.

An important part of the instruction of the public in this matter will come indirectly from the individual physician, through the general contacts and conversation of his patients to whom he has given advice.

The other important means of public instruction include the local and state and national medical societies and those special organizations of mixed professional and lay membership which have been so helpful in disseminating reliable information on health matters. The American Society for the Control of Cancer has done splendid work in educating the public to an appreciation of cancer symptoms and the importance of seeking prompt relief. To it naturally falls the leadership in this additional step for preventing deaths from cancer, namely, instruction of the public as to the necessity of regular periodic examinations for the discovery and removal of chronic irritative lesions which precede cancer. Considerable work has already been done along this line, but much more remains to be done in regard to cancer of the cervix.

In this campaign of cancer prevention and early detection the nullipara and the virgin must not be overlooked as victims of insidious cancer development. Cancer of the corpus uteri in considerable proportion of the cases is found in nulliparae, particularly in those with uterine fibroids. Even cervix cancer occurs in the nullipara and the virgin. Lash calls attention to the fact that Mattmuller found 9.7 per cent of nulliparae among 442 patients with cancer of the cervix and several of these were virgins. He reports a case of his own. In this patient, aged forty years, with uterine myoma, the intact hymen was so tight that examination had to be made by rectoabdominal palpation. The cervix was closed and smooth, corpus enlarged to size of a twelve weeks' pregnancy and hard and free, and adnexa presented no palpable lesion. The

myomatous uterus was removed and there was found, in addition, a carcinoma of the cervical canal (adenocarcinoma). Macfarlane, Fetterman and Sturgis conducted an experiment in cancer control and presented an instructive report on the periodic pelvic examinations in one thousand well women.

As previously mentioned under Chronic Cervicitis, the cancer-preventing results already definitely attained by effective treatment of chronic cervicitis are encouraging. Craig found that in 2,895 cases of cervicitis treated adequately and then followed for a period of ten years or more not one patient developed cervix cancer. Camperman estimated that cancer of the uterus is found in 4 per cent of gynecologic patients, and Frankl found that 89 per cent of uterine cancers are in the cervix. Accordingly, in this one series of 2,895 patients, cancer of the cervix was prevented in 112 women.

CARCINOMA OF CORPUS UTERI

Carcinoma of the corpus uteri constitutes a distinct class, having better prognosis than carcinoma of the cervix. It begins in the endometrium; consequently the tumor tissue is accessible to the curette at a very early stage. The growth is for a long time confined to the tissues immediately about the uterine cavity, the extension to the periuterine tissue being slow—hence the chance of cure is much better. Carcinoma of the corpus comprises 10 to 15 per cent of all uterine cancers.

Etiology

In regard to age, the decade for most frequent occurrence of corpus cancer is from fifty to sixty years, thus differing from cervix cancer which occurs most frequently in the decade forty to fifty years. Koblanck found 50 per cent of corpus carcinoma in the decade fifty to sixty years. In our series of 56 cases with five-year results, the age incidence by decades was: ages thirty to forty, 4 cases; forty to fifty, 15 cases; fifty to sixty, 21 cases; sixty to seventy, 13 cases; seventy to eighty, 2 cases, and eighty to ninety, 1 case.

In regard to pregnancy, Wilson concludes it has no etiologic importance, as an equal percentage occurred in the parous and in the nulliparous. In our series only 38 per cent were nulliparous.

As an etiologic factor in corpus carcinoma prolonged endometrial activity seems to be of definite importance. The relationship of undue endometrial activity at the critical age of declining function to the onset of endometrial carcinoma is an important subject, and one not yet clarified. Most gynecologists have a general feeling that late continuation of menstruation, into the period when the endometrium should be inactive, indicates a tendency to erratic epithelial activity and hence to cancer. However, the various points need to be investigated and the facts, pro and con, established by conclusive evidence. One of us (R. J. C.) has been working on this problem for some time, and in a preliminary report of an analysis of our own cases (J. Missouri M. A.) reached the following conclusions:

The occurrence of hyperplasia of the endometrium is an indication of excess estrogenic influence. Whether or not this excess estrin tends to induce

malignant development is a point still to be determined, though there is some evidence that it so operates at times in the breast and also in the uterus. It seems hardly probable that the normal stimulus to activity, on which the healthy functioning of the organ depends, would induce cancer which is an unhealthy functioning. The real cause is probably some abnormal condition of cell nutrition or environment (irritation), and the excess estrin may be only an index of nature's attempt to overcome the systemic or local abnormality.

While endometrial hyperplasia with its associated excess estrin may not be of importance in the childbearing period, when great activity of the endometrium is normal, our study and experience previously mentioned indicate that endometrial hyperplasia found in late menopause is of sinister significance, and should lead to radiation or other treatment for stopping such activity.

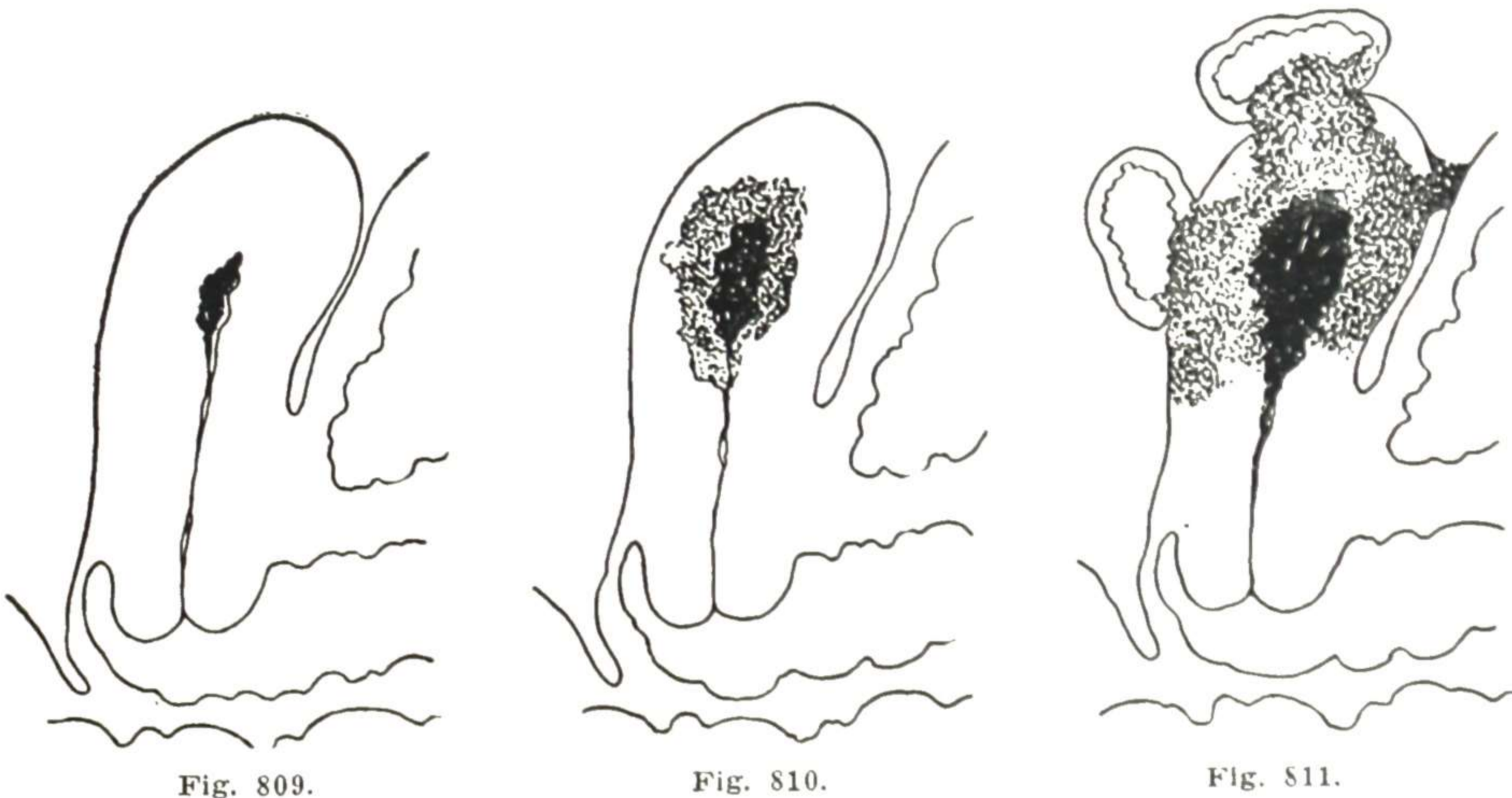


Fig. 809.

Fig. 810.

Fig. 811.

Figs. 809 to 811.—Progressive development of carcinoma of the corpus uteri. Fig. 809, Carcinoma of the corpus begins in the endometrium. Fig. 810, Extensive involvement of the uterine wall. Fig. 811, Extension through the uterine wall and involvement of adjacent structures.

Pathology

Gross.—In carcinoma of the corpus (endometrial carcinoma), the uterus may or may not be larger than normal. As this cancer occurs most frequently between the ages of fifty and sixty years, the uterus, in the early stage of the carcinoma, may be senile and considerably smaller than a normal adult uterus. As the disease advances the uterus enlarges progressively and as the process penetrates the wall, adjacent structures become involved. This progressive involvement is indicated in Figs. 809 to 811. Gross specimens of the disease in different steps of development are shown in Figs. 812 to 814.

Microscopic.—The microscopic characteristics of carcinoma of the endometrium are shown in Figs. 815 to 819. Endometrial carcinomas are graded into four classes, representing gradations in structure from the mature glandular form of mild malignancy to the immature solid form of great malignancy. This grading was suggested by Mahle, on the basis of MacCarty's standard of cell differentiation. Healy has done much helpful work in clinical

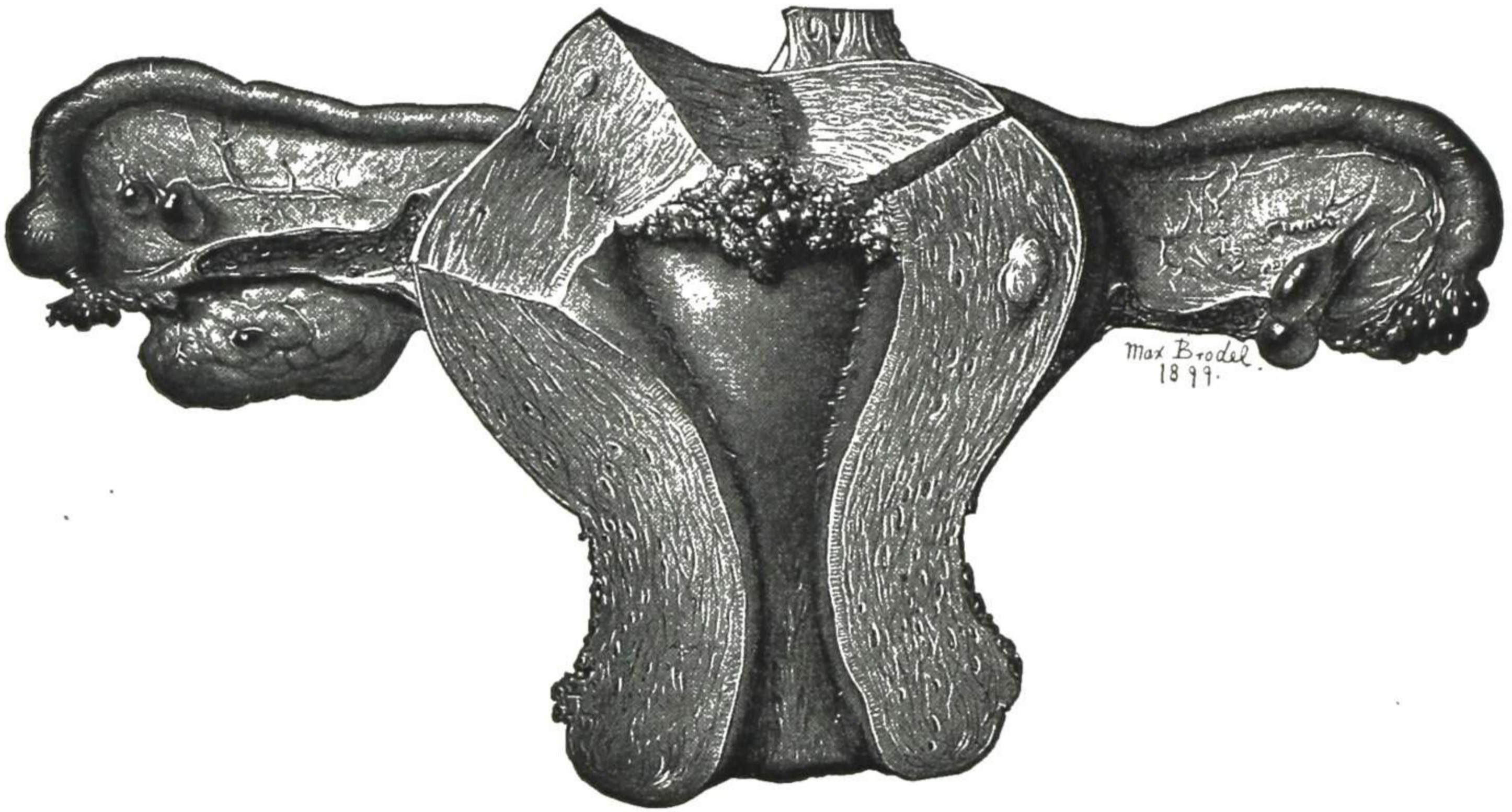


Fig. 812.—Beginning carcinoma of the corpus uteri. There is no external sign of the growth at this stage, except an occasional streak of blood in the leucorrhœal discharge. The diagnosis must be made by curettage. (Cullen—*Cancer of the Uterus*.)



Fig. 813.

Fig. 813.—Drawing from a specimen of a comparatively early carcinoma of the corpus uteri. Gyn. Lab.



Fig. 814.

Fig. 814.—Drawing from a specimen of a more advanced carcinoma of the corpus. The growth has invaded the muscular wall extensively, but the peritoneal covering of the uterus is not yet involved. Gyn. Lab.

application of the grading and in developing its general use, and his name is frequently attached to this grading system, though in his writings he gives full credit to Mahle.

In connection with the fact that this grading is based on the extent of departure from normal gland forms, it may be noted that endometrial hyperplasia represents a type of endometrial structure lying between normal endometrium and carcinoma of Grade I. In fact, the diagnosis in a doubtful case



Fig. 815.



Fig. 816.

Figs. 815 and 816.—Diagnostic curettings, under low power and high power. Gyn. Lab.



Fig. 817.—Adenocarcinoma of the corpus uteri. This is a section of the entire thickness of the wall of the removed uterus. The endometrium (left end) had been largely removed by a diagnostic curettage a few days before the hysterectomy. The diagnostic curetting is shown in Fig. 816. Gyn. Lab.

consists usually in determining whether the condition is hyperplasia or beginning cancer. Consequently the characteristics of hyperplasia are shown (Figs. 820 and 821) along with those of carcinoma, Grade I.

An interesting fact in connection with the slides showing hyperplasia and those showing carcinoma of Grade I is that they are from the same patient. One year after she was curetted and the hyperplasia found, symptoms returned requiring another curettage and the carcinoma of Grade I was found.

The points cited in the following differentiation into grades are largely from Healy's clear description (Healy and Cutter, *Am. J. Obst. and Gynec.*).

Grade I (Figs. 822 and 823). Papillary Adenoma Malignum. This is a characteristic form in which the growth is superficial and entirely papillary. The papillae are low, the cells are not very atypical, and there is no infiltration. As the cells are not multiplying rapidly, the glands are well formed. Some cases are extremely difficult to distinguish from adenomatoid endometritis. It is in this histologic type that cures following curettage have been observed.

Grade II (Figs. 824 and 825). Adenoma Malignum. This group comprises those cases in which the uterine glands are markedly enlarged and elongated. They are often thrown into folds and convolutions to form inside papillae. The cells are cuboidal or cylindrical and are arranged in compact layers about the gland lumen. The nuclei are very hyperchromatic, giving to the stained section a dark appearance. Mitoses are often abundant. The entire tumor appears to be composed of giant glands encroaching upon the interglandu-

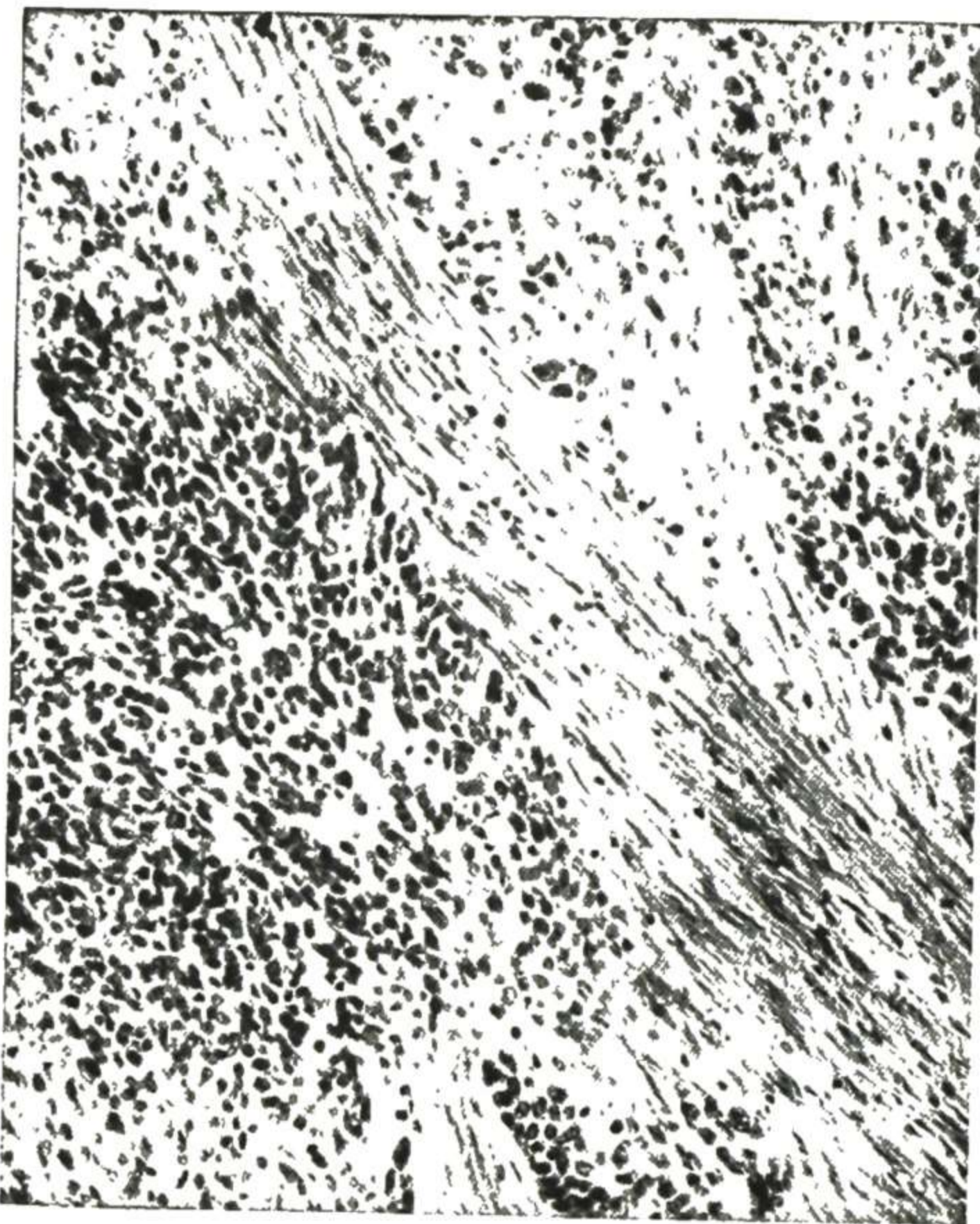


Fig. 818.

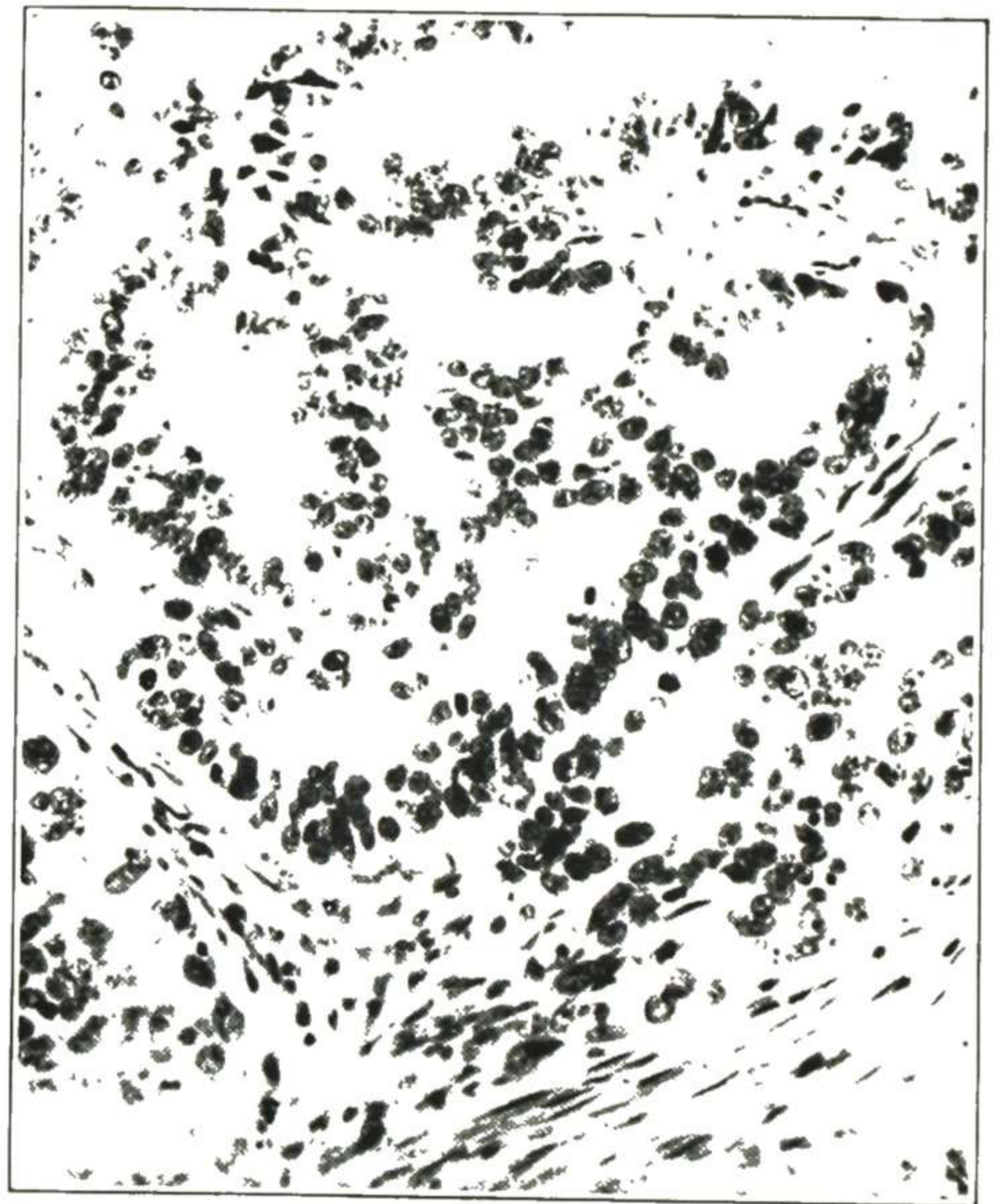


Fig. 819.

Fig. 818.—Same growth as in Fig. 817. This is at the spreading edge of the growth and shows the carcinoma cells penetrating the muscle tissue. Gyn. Lab.

Fig. 819.—Same growth as in Fig. 817, higher power. This is in a portion of the growth where the adenomatous arrangement of the cancer cells is well marked. Gyn. Lab.

lar connective tissue. The stroma is thus scant and adjacent glands come in direct contact. The polarity of the tissues is everywhere maintained. As Lindsay has emphasized, if at any point the cells show a tendency to form solid masses and infiltrate the stroma, the tumor should be classed as adenocarcinoma.

Grade III (Figs. 826 and 827). Adenocarcinoma. Adenocarcinoma includes all cases in which the tumor forms solid masses of cells which grow in cords and columns. There is definite loss of polarity with infiltration of the stroma. Signs of anaplasia are more marked than in adenoma malignum. The cells are more atypical. Not infrequently portions of the tumor show adenoma malignum and other parts adenocarcinoma. These tumors are classed as adenocarcinoma. Although the growth is more atypical than in adenoma malignum, the glandular arrangement is still maintained.

Grade IV (Figs. 828 and 829). Diffuse (Embryonal Anaplastic) Carcinoma. This group is characterized by a complete loss of polarity. The glandular arrangement is entirely lost. The growth is diffuse and is composed of small round and polyhedral cells,



Fig. 820.—Endometrial hyperplasia, for comparison with endometrial carcinoma, Grade I. Gyn. Lab.

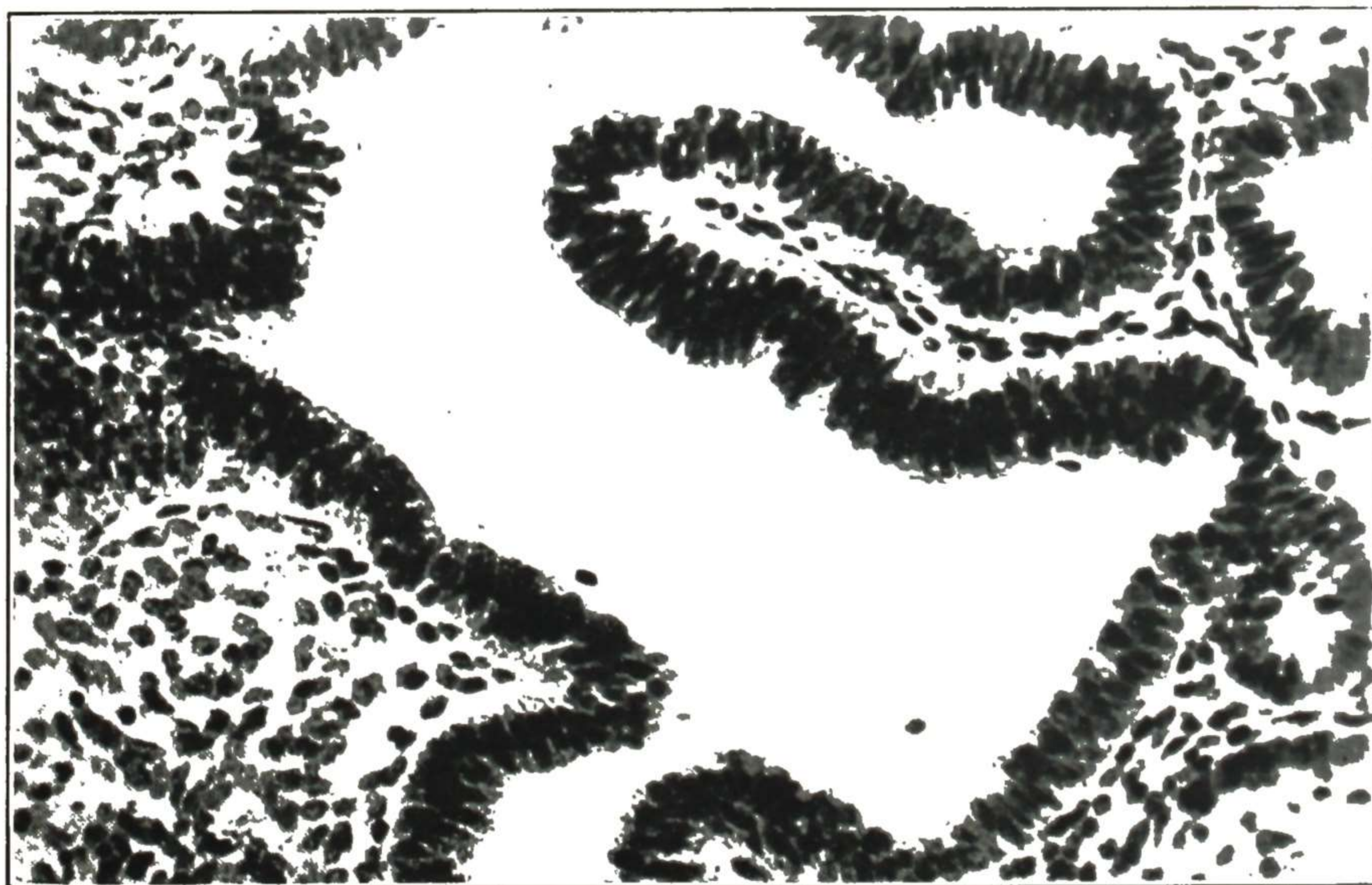


Fig. 821.—Higher power of the endometrial hyperplasia shown in Fig. 820. Gyn. Lab.



Fig. 822.—Endometrial carcinoma, Grade I. Note the well-developed glandular character and resemblance to hyperplasia, except for the abnormal piling-up of the epithelium and the character of the cells. Gyn. Lab.

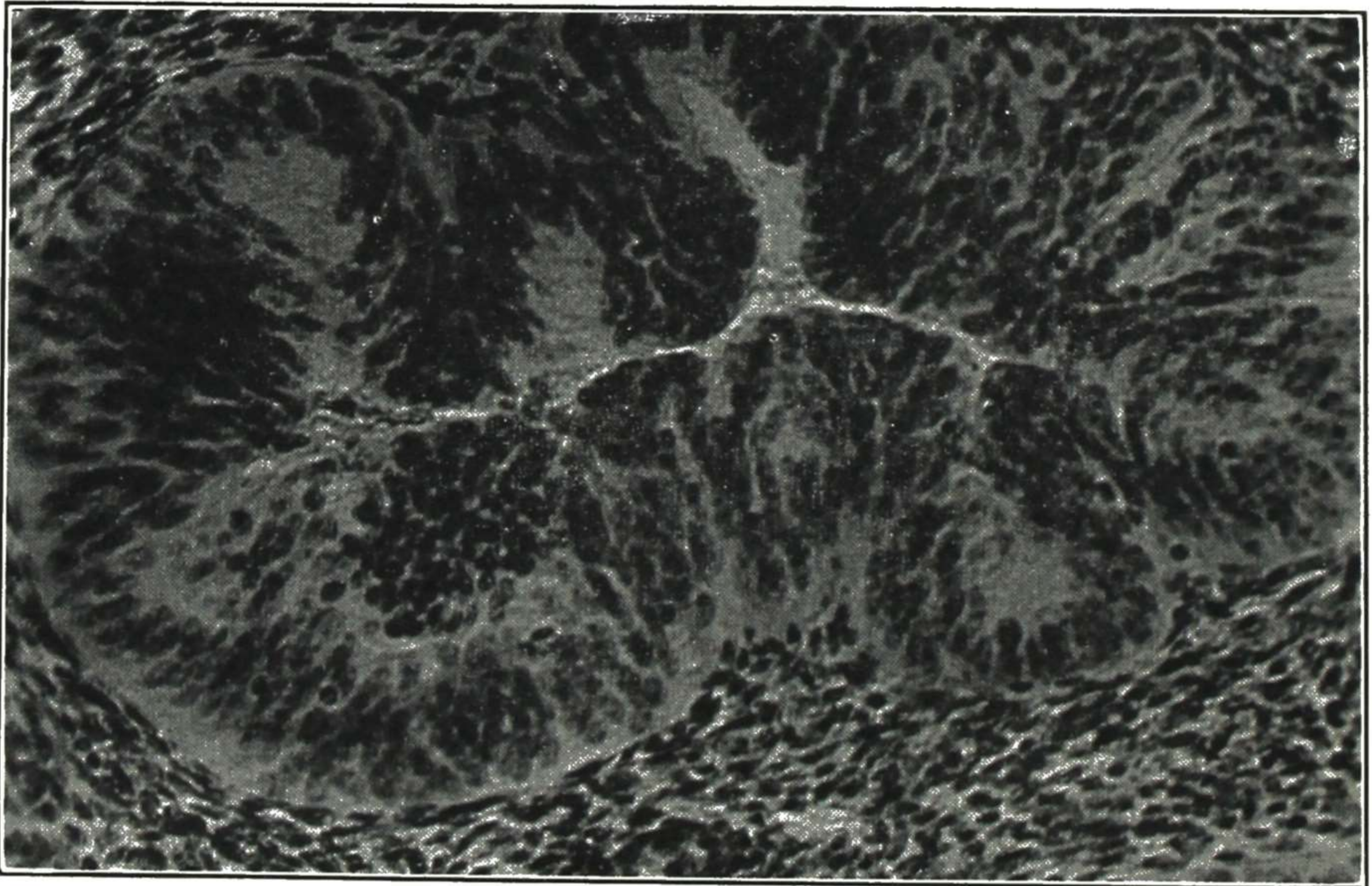


Fig. 823.—Higher power of Fig. 822, showing details of the cells and their arrangement. Gyn. Lab.

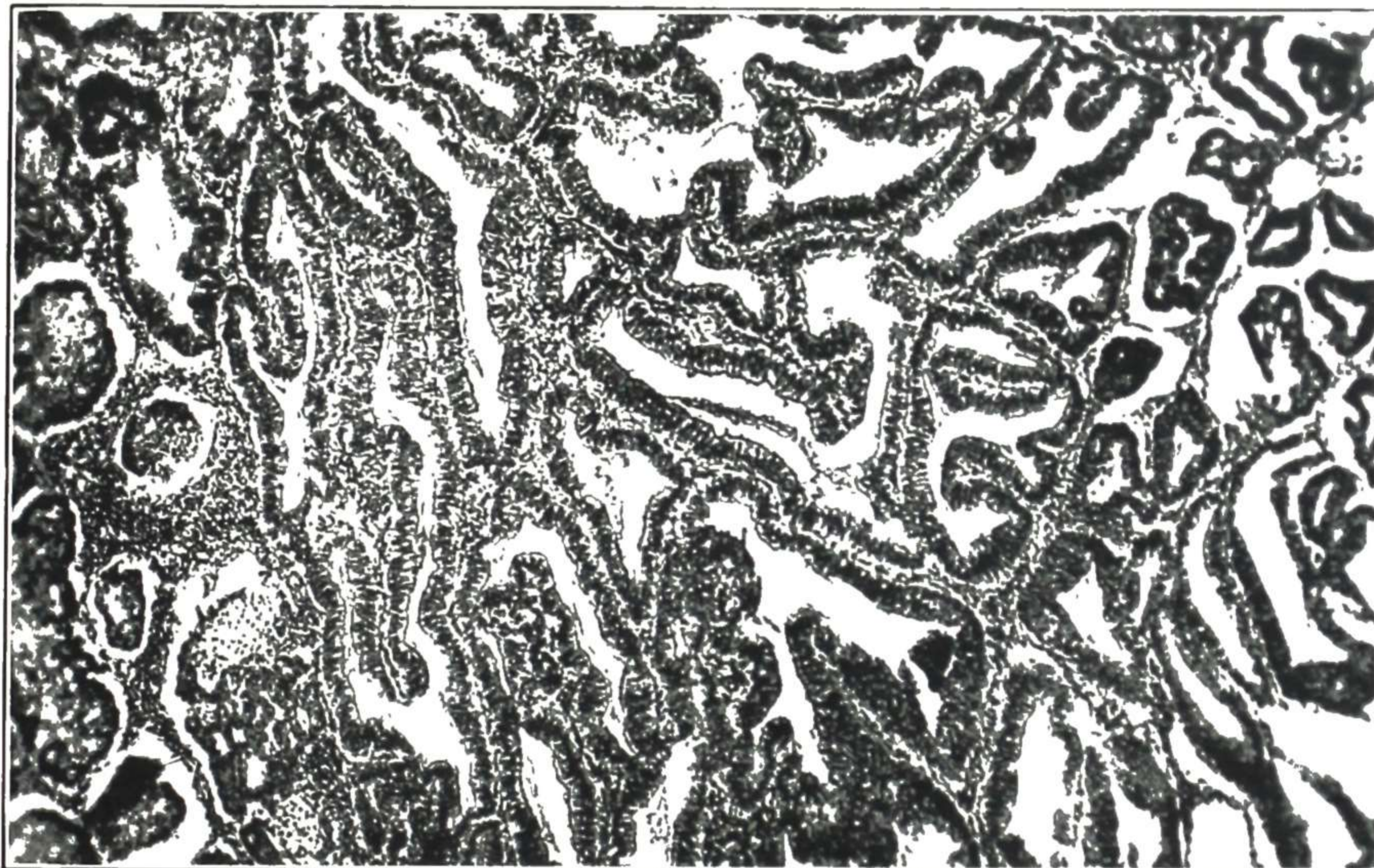


Fig. 824.—Endometrial carcinoma, Grade II. Notice the increasing departure from normal gland characteristics, as explained in the text. Gyn. Lab



Fig. 825.—Higher power of Fig. 824, showing details of the erratic cell activity. Gyn. Lab

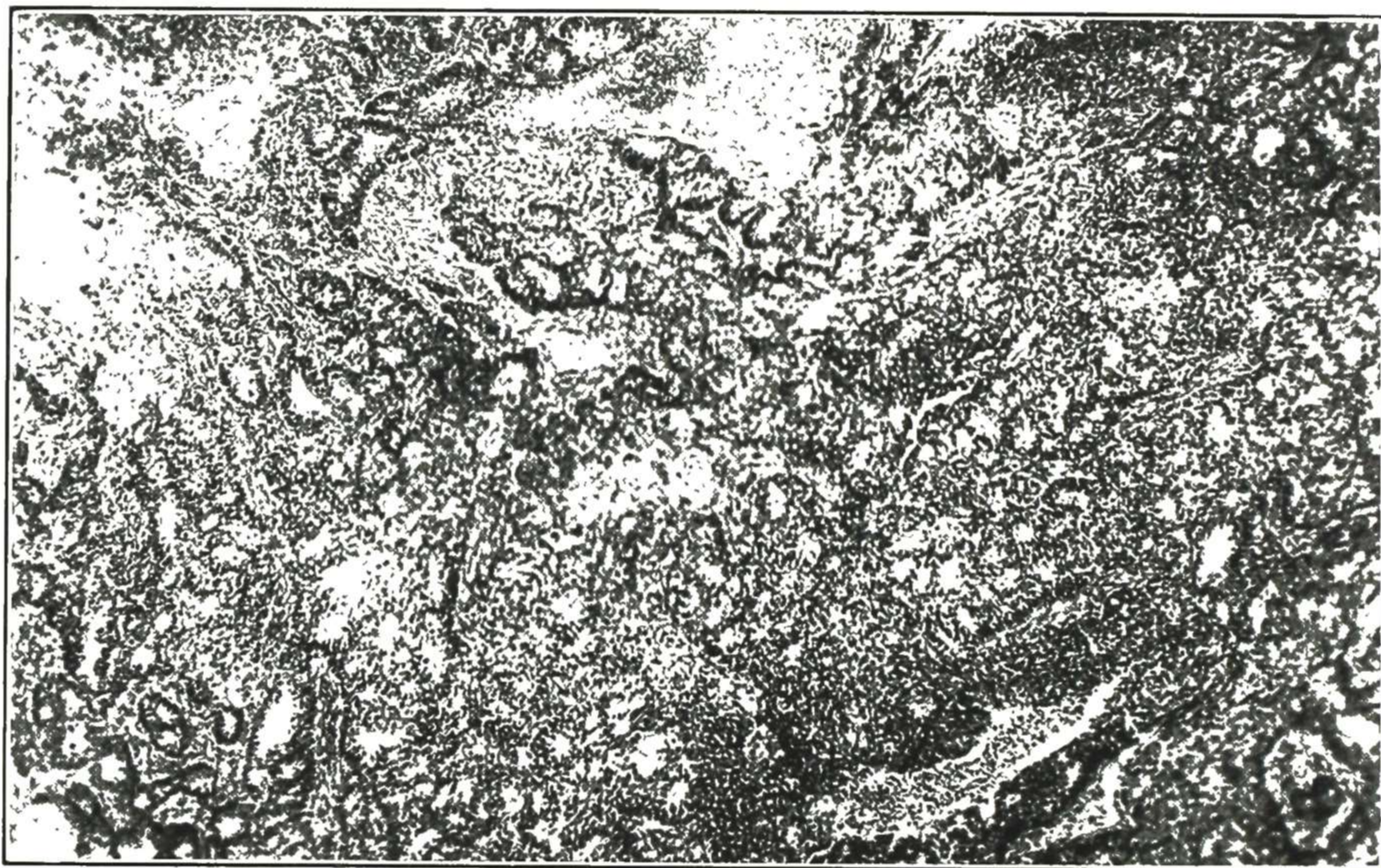


Fig. 826.—Endometrial carcinoma, Grade III. Shows the increasing tendency to solid invasion, but there are still irregular gland patterns. Gyn. Lab.

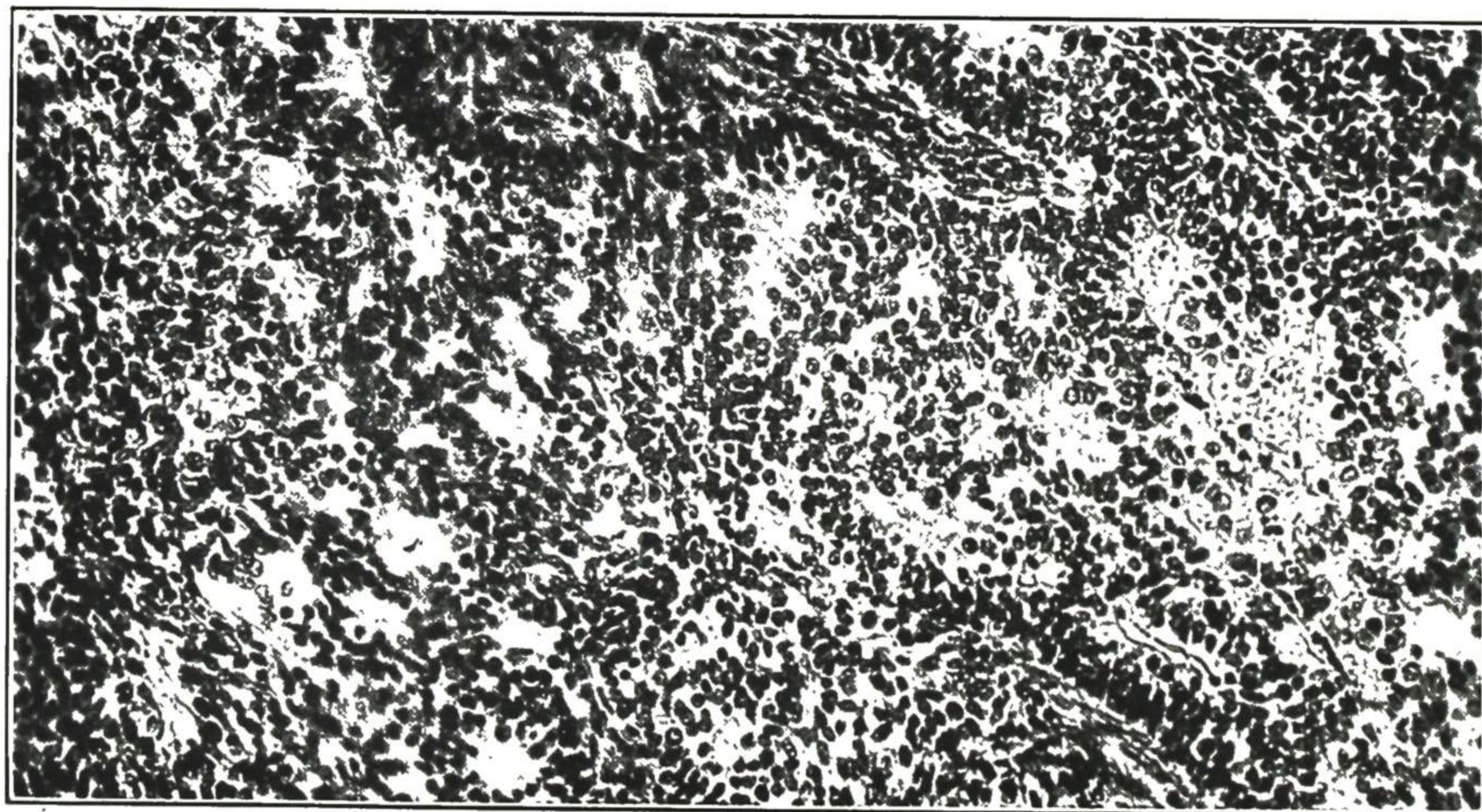


Fig. 827.—High power of Fig. 826. Gyn. Lab.

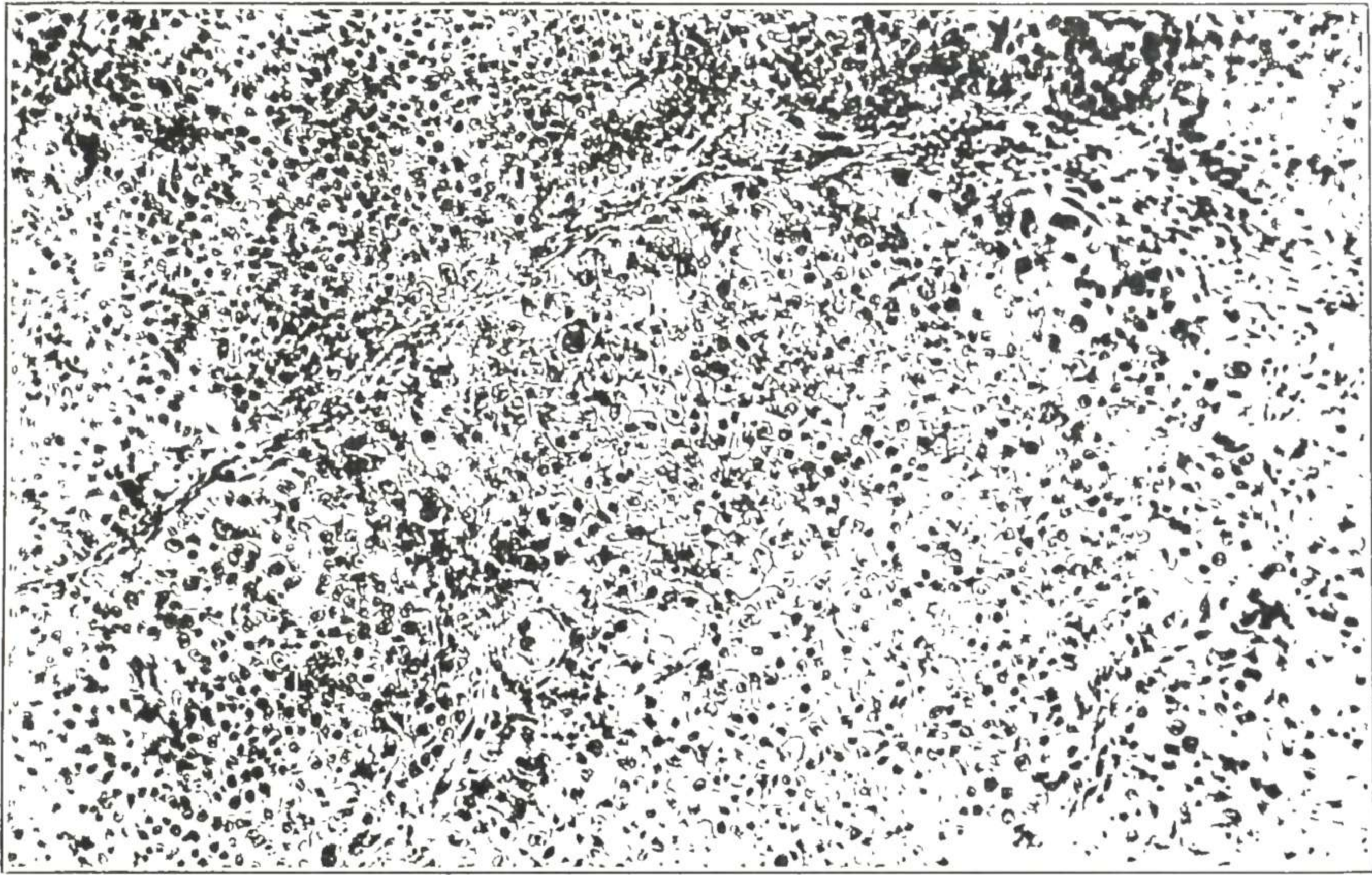


Fig. 828.—Endometrial carcinoma, Grade IV. The malignant cell change has advanced to the point of solid invasion, with only an occasional suggestion of gland tendency. Gyn. Lab.

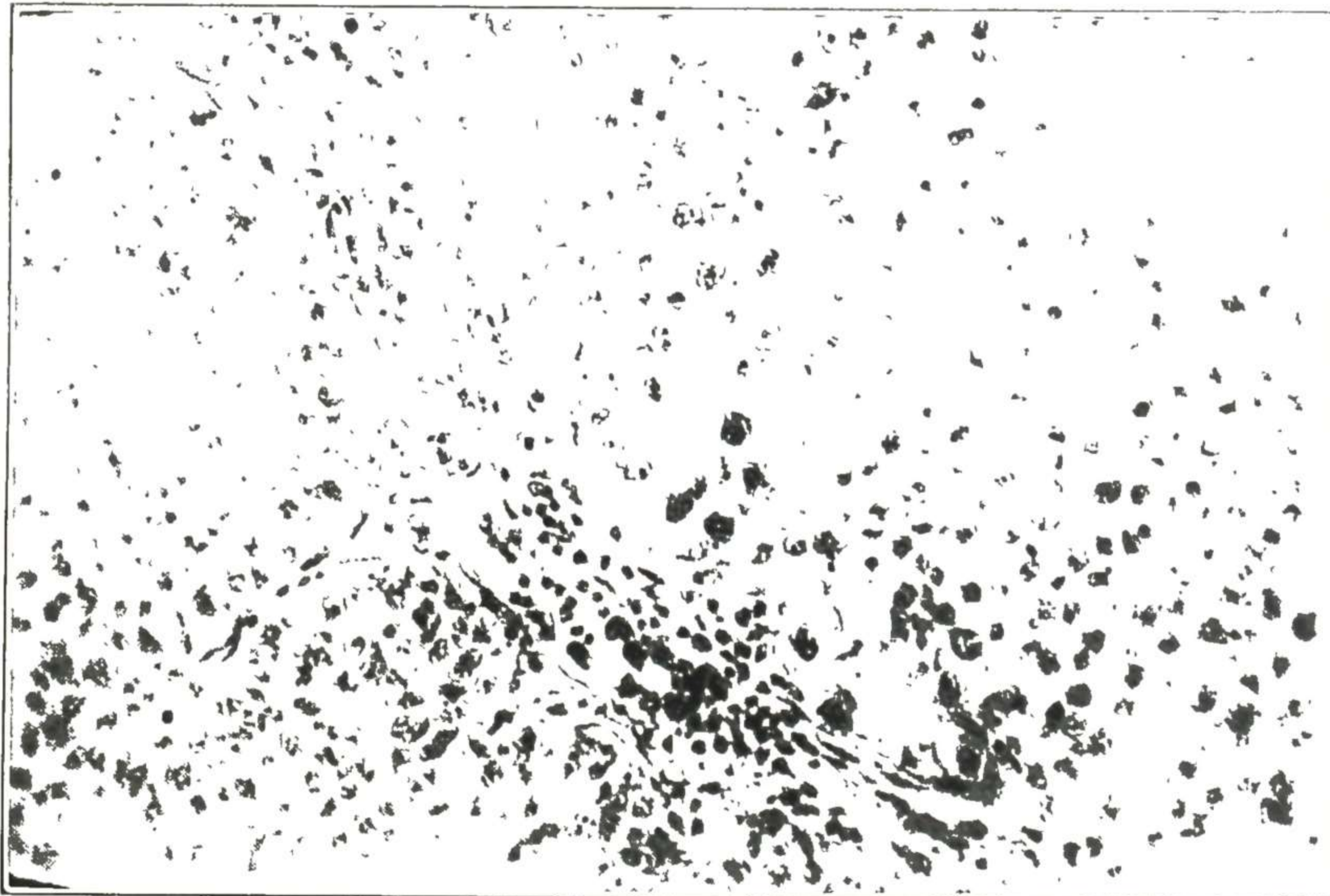


Fig. 829.—High power of Fig. 828, showing character of the cells.

closely packed, growing in sheets and cords. The nuclei are small and hyperchromatic and the cytoplasm is scanty. There are marked signs of anaplasia. There is complete loss of differentiation. Mitoses are very abundant. The histologic structure often closely resembles anaplastic epidermoid carcinoma of the cervix from which it may be difficult to distinguish microscopically. Fig. 830 shows mixed grades in carcinoma of the endometrium, Grades I and IV.

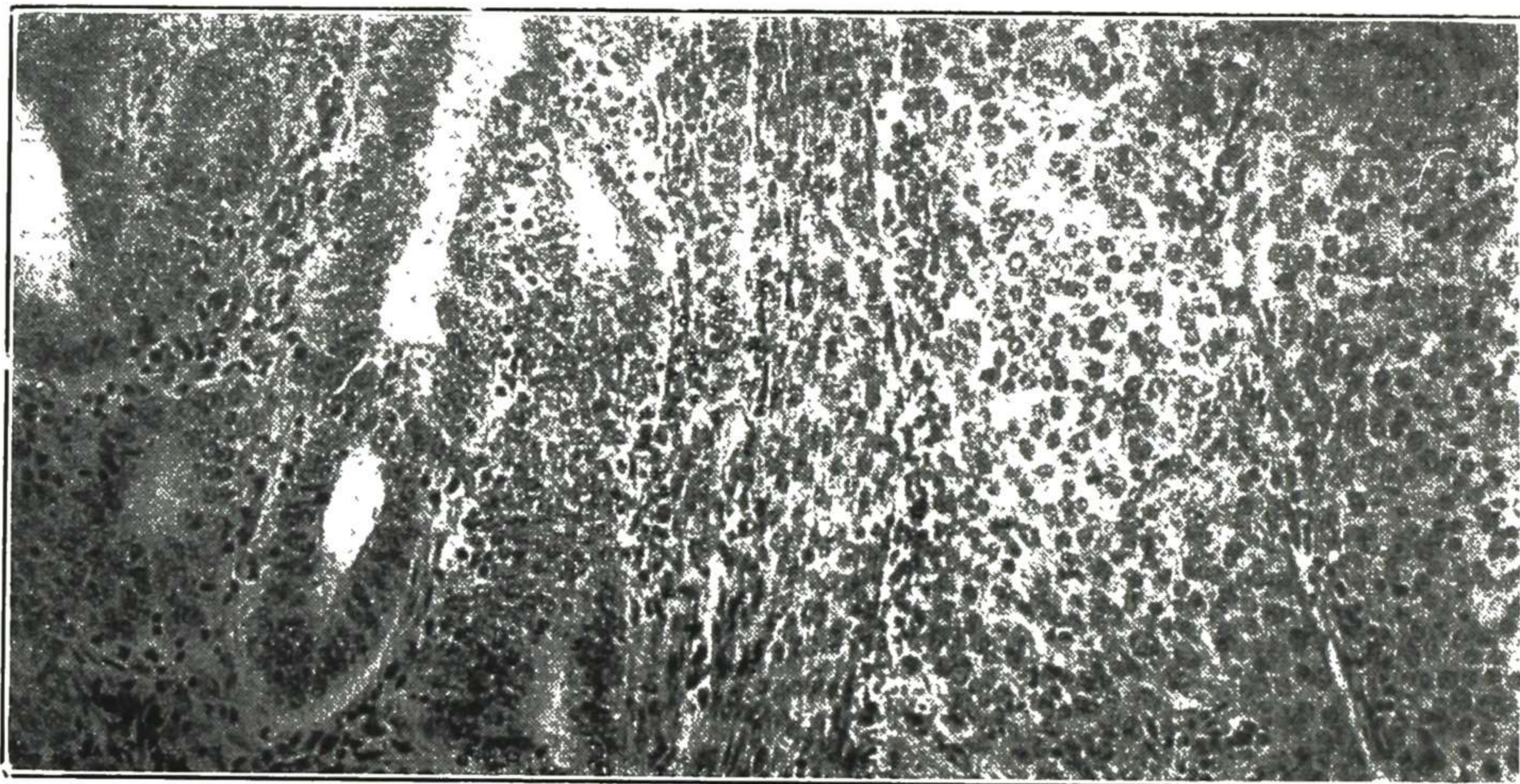


Fig. 830.—Adenocarcinoma of the endometrium, showing different grades in the same specimen. Grade I left and Grade IV right.

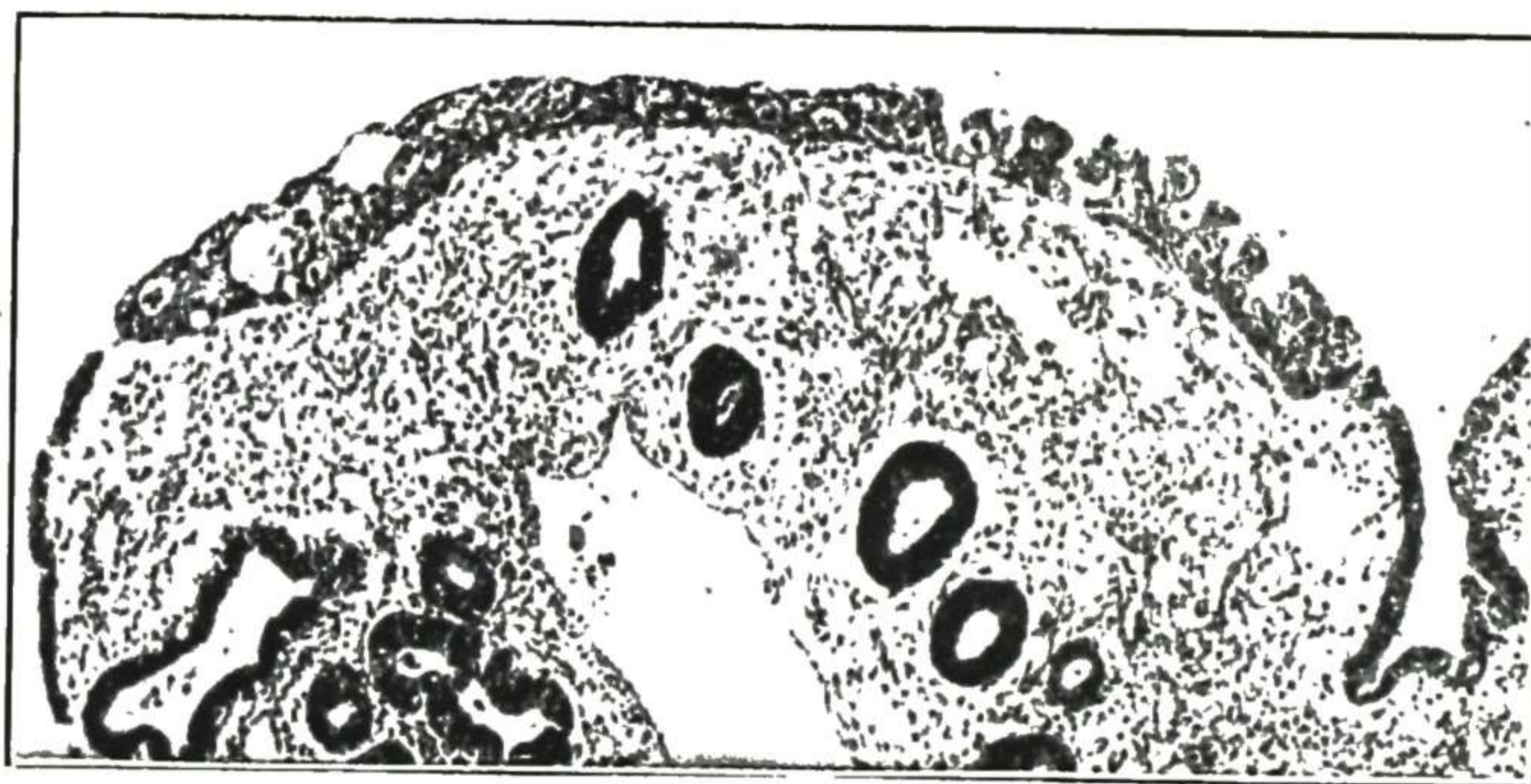


Fig. 831.—Squamous "metaplasia" or "epidermization" of the surface epithelium in a case of hyperplasia of the endometrium and adenomyoma. This is a purely benign change. (Novak—*Am. J. Obst. and Gynec.*)

The malignancy of these grades increases from group one to group four, and the response to radiation is in the reverse order.

Epidermization, described and illustrated in connection with the diagnostic problems of cervix cancer, occurs also in the endometrium. It is not frequent in this situation, and is probably due, as a rule, to metaplasia (Ruge) or to "rests" of embryonal cells which retain the power to develop into the squamous type (Meyer).

Fluhmann states that he found only six cases in the literature, including his own. Novak states that it is probably not so rare. Hintze reported nine cases.

Novak feels that the condition is essentially benign and states that seven of Hintze's patients were cured by simple curettage, and have remained well

from two to five years after operation. Fig. 831 shows surface epidermization of the endometrium overlying an adenomyoma, and Fig. 832 shows the epidermization in the deeper glands. Fig. 833 shows metaplasia in an adenocarcinoma.

Metastases.—The adenocarcinomas of the corpus are relatively slow growing as cancer goes, and they metastasize late from Grades I and II. Grades III and IV grow more rapidly, and the prognosis is much more grave.

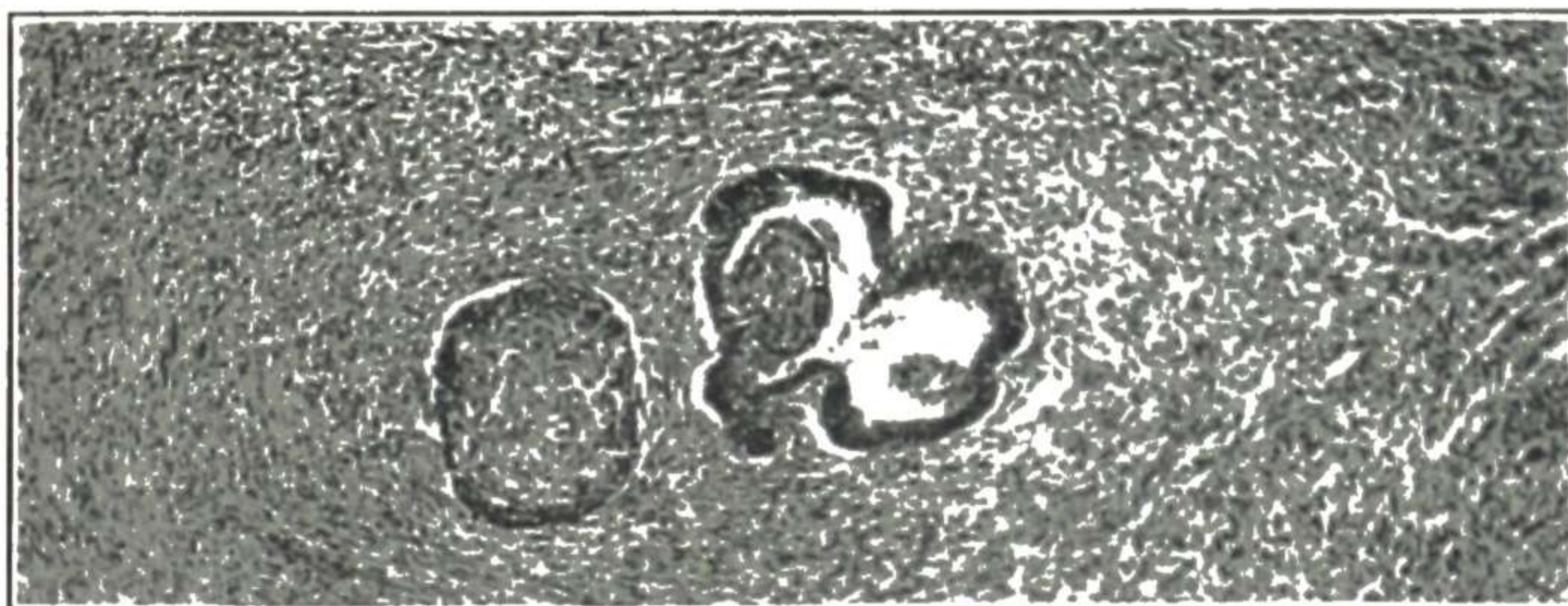


Fig. 832.—“Epidermization” of deeper lying gland epithelium of adenomyoma in same case. These changes, formerly considered as evidence of malignancy, are now looked upon as definitely benign (see text). (Novak—*Am. J. Obst. and Gynec.*)

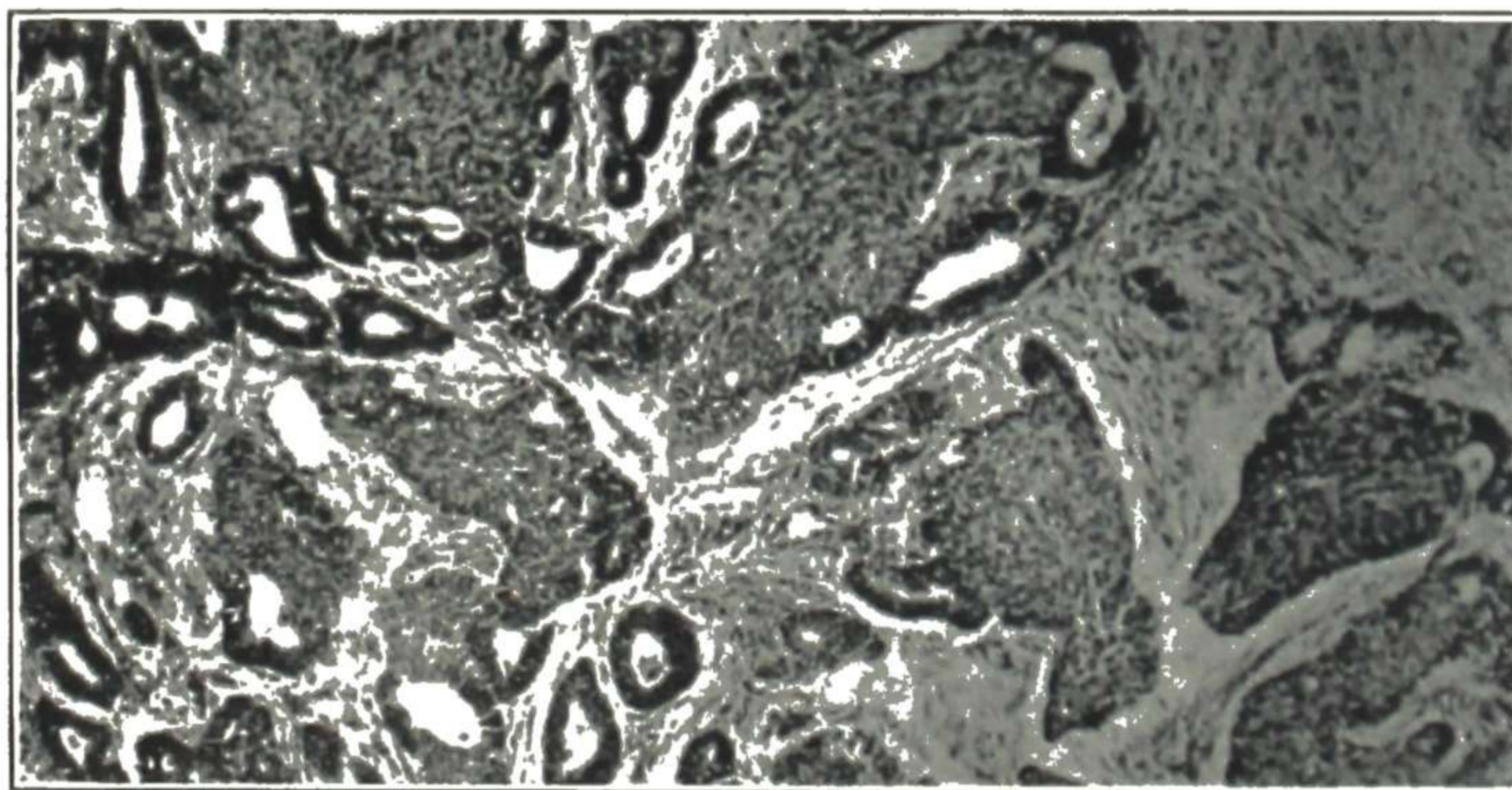


Fig. 833.—Extensive squamous metaplasia in an adenocarcinoma of the uterus. Here there is no doubt of the transition from a primary gland carcinoma, but in other areas the squamous change is so extensive that the primary character of the tumor is blotted out. Such cases have in the past often been wrongly interpreted as combinations of squamous cell and adenocarcinoma. (Novak—*Am. J. Obst. and Gynec.*)

Symptoms and Diagnosis

Carcinoma of the corpus starts in the endometrium, and hence gives rise early to excessive menstrual flow or spotting between periods. On this account the patient is likely to seek medical advice early in the disease, and if the physician recognizes the warning signal and acts accordingly a fairly early diagnosis results. The diagnosis depends on microscopic examination of curettings. Hence the importance of employing curettage when there is a bleeding tendency which does not yield promptly to medication, particularly if the patient is past thirty-five years of age. Very often in these bleeding cases there is also chronic cervicitis, which is an additional reason for urging the curettage, as the chronic cervicitis may be taken care of at the same time by conization. The curettage is effective treatment for the endometrial bleeding, and the conization removes the menace of chronic irritation

in the cervix. All tissue removed is subjected to microscopic investigation which gives definite information as to what process is going on in both cervix and corpus and whether or not there is any complicating malignancy. A point of importance is that the curetting should embrace all parts of the endometrial cavity, and then *all* curettings should be preserved and subjected to microscopic examination.

Uteroscopy with special endoscopic tubes has been used in these cases, as has also x-ray visualization of the endometrial irregularities by injecting opaque material. These measures combined with special instruments for clipping off specimens of such irregularities for cancer diagnosis, may have a strong visual and technical appeal to the uninitiated—so strong as possibly to obscure other important features of the situation. Hence it may be well to call attention to certain points in this connection. This method is *contraindicated* on account of the *danger* and also on account of the *inaccuracy* or inadequate handling of the diagnostic problem. The danger of the injected fluid carrying carcinoma cells into the peritoneal cavity has been mentioned. Sampson has demonstrated the transfer of cells from the endometrium through the tubes from slighter causes than injection, and in carcinoma such transportation by injected fluid might have serious results.

In regard to inaccuracy, this method seems to be a reversion to the old unsatisfactory plan employed in suspicious cervix cases, namely, excision of a small specimen and if no cancer is found then waiting and perhaps another specimen excision later as conditions develop. This has now been superseded by a more adequate method which consists of excision of the whole involved area. Thus all the involved tissue is secured for microscopic investigation, so that negative findings really exclude cancer, and at the same time there is effective treatment for the nonmalignant lesion which stops the chronic irritation. Fortunately, in corpus cancer gynecologists started with the thorough method of removing the whole diseased endometrium by curettage and submitting it all to microscopic examination. To do less would seem a backward step in diagnosis. Again, a bleeding uterus needs treatment as well as investigation, and removal of the diseased endometrium by curettage furnishes this.

Clinical Classification.—An item of diagnostic importance is the extent of the disease. While pathologic grading of carcinoma of the corpus according to cell type and arrangement is now on a firm basis and proving useful, clinical classification on a practical basis has been delayed. A dependable clinical classification of cases of carcinoma of the corpus into stages of progress is a complicated matter, much more complicated than appears on the surface. It has been delayed by difficulties not found in carcinoma of the cervix. In cervix cancer the location and extent of the marked infiltration can be determined by palpation, and the depth of the vaginal and cervical ulcerations are open to easy and accurate inspection. Not so in corpus cancer, where the various stages of extension into the thick uterine wall defy palpation and inspection, and can be outlined only after the uterus is removed.

Despite the difficulties, however, the attempt to work out a satisfactory clinical classification of these cases should be persisted in and vigorously pushed. The reliable and uniform grouping of these cases into clinical stages representing extent of growth is absolutely necessary for the evaluation of treatment results. In comparing the results of different methods of treatment, the comparison must be made between cases of the same approximate extent of involvement, i.e., early cases to early cases, medium advanced to medium advanced, and late cases to late cases. Otherwise there may be erroneous conclusions as to the efficacy of the different treatment methods.

Such classification requires careful examination and accurate recording of findings before operation, of gross findings at operation, and then of gross findings in the laboratory. This division into stages representing extent of growth must of course be founded on a solid *pathologic* basis. That is, the clinical stages cannot be defined by symptoms but must represent definite extent of growth as determined by examination at operation and in the laboratory. Hence, the stages of the classification to be made before operation as a guide to treatment must be defined in terms of pathologic extent which can be accurately determined only after operation. This paradox shows very well the vicious circle of difficulties encountered, and the reason why the solution of this important problem has been so long delayed.

Having identified the difficulties, we are in a better position to attack the problem successfully. In the first place, it is clear that the stage-classification made before operation cannot be accurate, only approximate. But by utilization of all the factors which help toward accuracy, the preoperative classification may be made to approximate so closely the actual extent as to be of material assistance in the selection of treatment for that patient. The first task is to define the stages in terms of pathologic extent, and the second and more difficult task is to devise a plan of recognizing the stages approximately before operation.

The Stages. The division of a continuous process into stages necessitates dealing with borderline areas about which there may be differences of opinion as to preferable assignment. The important thing, however, is not exactly where the lines of division are placed but that they should be placed definitely somewhere, and then that this definite classification be used in all clinical work and in all reports of cases. The following classification into stages is definite and practical, and stands the test of application in the examining room and at the operating table and in the laboratory. Each of these stages was selected with two points in view: first, to have its limits correspond with anatomic lines as far as practicable so as to be well defined and easily described, and second, to have it recognizable clinically before operation as far as possible with the various helps available. The six stages, each representing a definite extent of involvement, are as follows:

Stage I: Endometrium alone involved (Fig. 834).

Stage II: Definite involvement of the muscular wall, but not beyond its middle (Fig. 835).

Stage III: Extension to the outer half of the uterine wall, but not beyond the borders of the uterus (Fig. 836). This includes extension to the peritoneal coat with possible areas of adhesive peritonitis, but without carcinomatous involvement of the adhesions.

Stage IV: Extension to surrounding structures but not beyond removable ones, such as adnexa and adjacent portions of the broad ligaments (Fig. 837). There may or may not be extensive intestinal or other peritoneal adhesions, but no extension of carcinoma cells into such adhesions.

Stage V: Extension into structures not advisable to remove, but removal of the original tumor is still practicable. The carcinomatous extension may be into an adherent coil of intestine or an adherent area of bladder wall, or it may be along the broad-ligament lymphatics into the deep structures of the pelvic wall (Fig. 838).

Stage VI: There is such extensive involvement of surrounding structures that not even the main tumor mass can be safely removed (Fig. 839).

Clinical Recognition of Stages.—Clinical recognition or identification of the stage in a particular case is useful in two ways, namely, in accurate reporting of the case and in selection of treatment for the patient. Identification of the stage of involvement for case reporting is a comparatively simple matter, because the report is made after treatment, and hence, in most cases the uterus

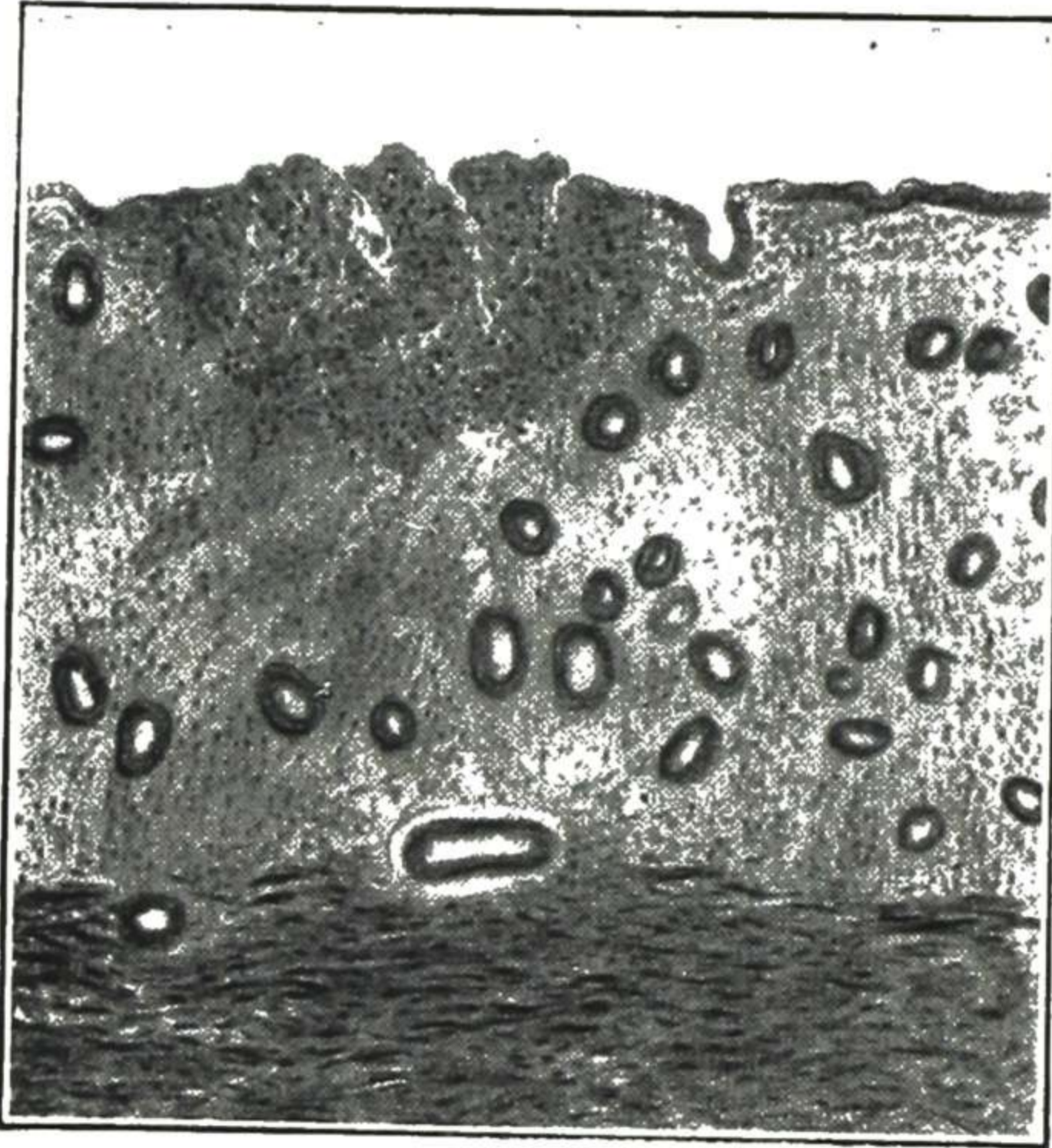


Fig. 834.



Fig. 835.



Fig. 836.

Figs. 834 to 838 show the clinical stages of corpus cancer, as detailed in the text. (Crossen and Crossen—*Operative Gynecology*.)

Fig. 834.—First stage. Endometrium only involved.

Fig. 835.—Second stage. The myometrium involved, but not beyond the middle.

Fig. 836.—Third stage. Myometrium extensively involved (past middle).

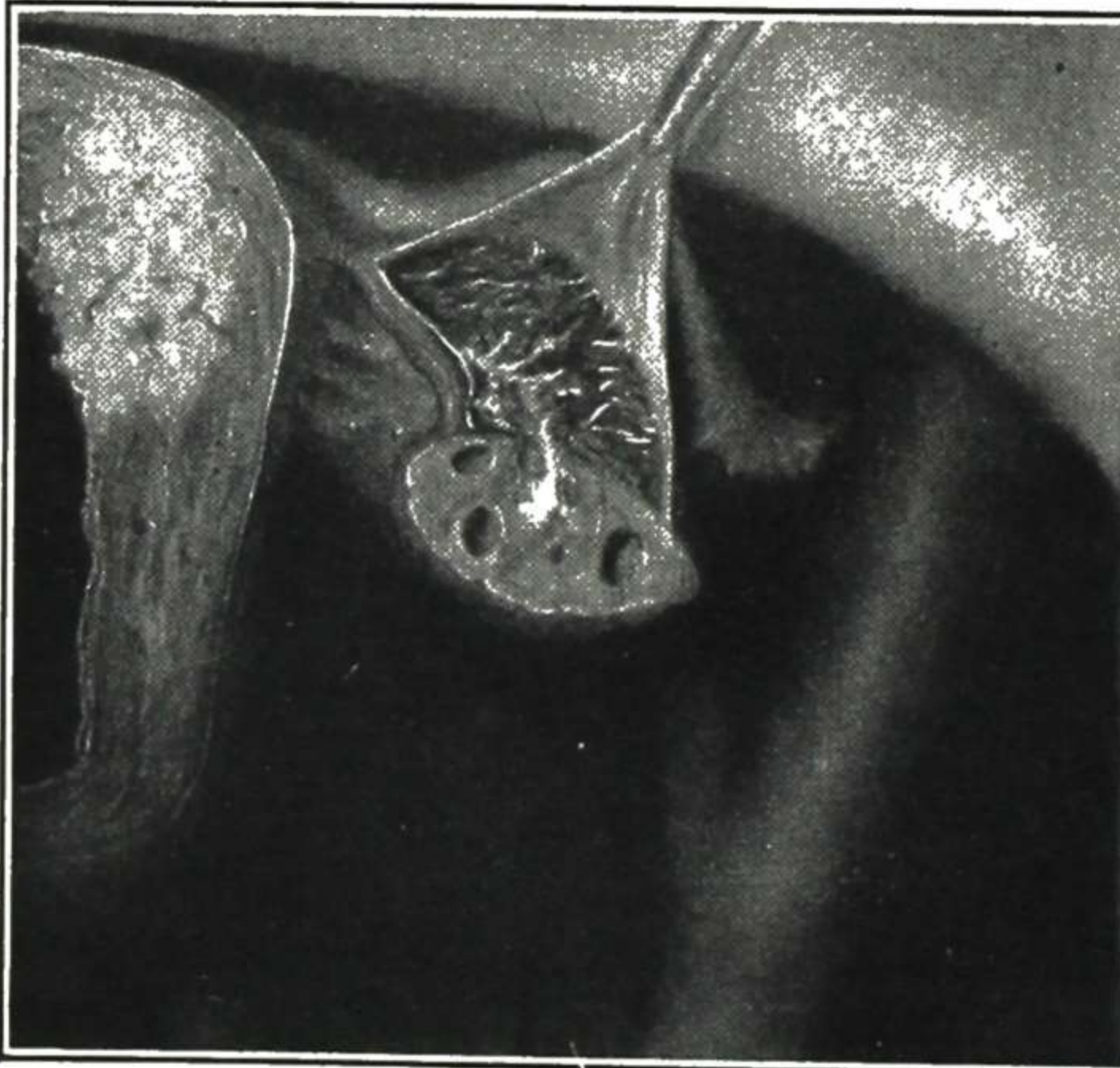


Fig. 837.

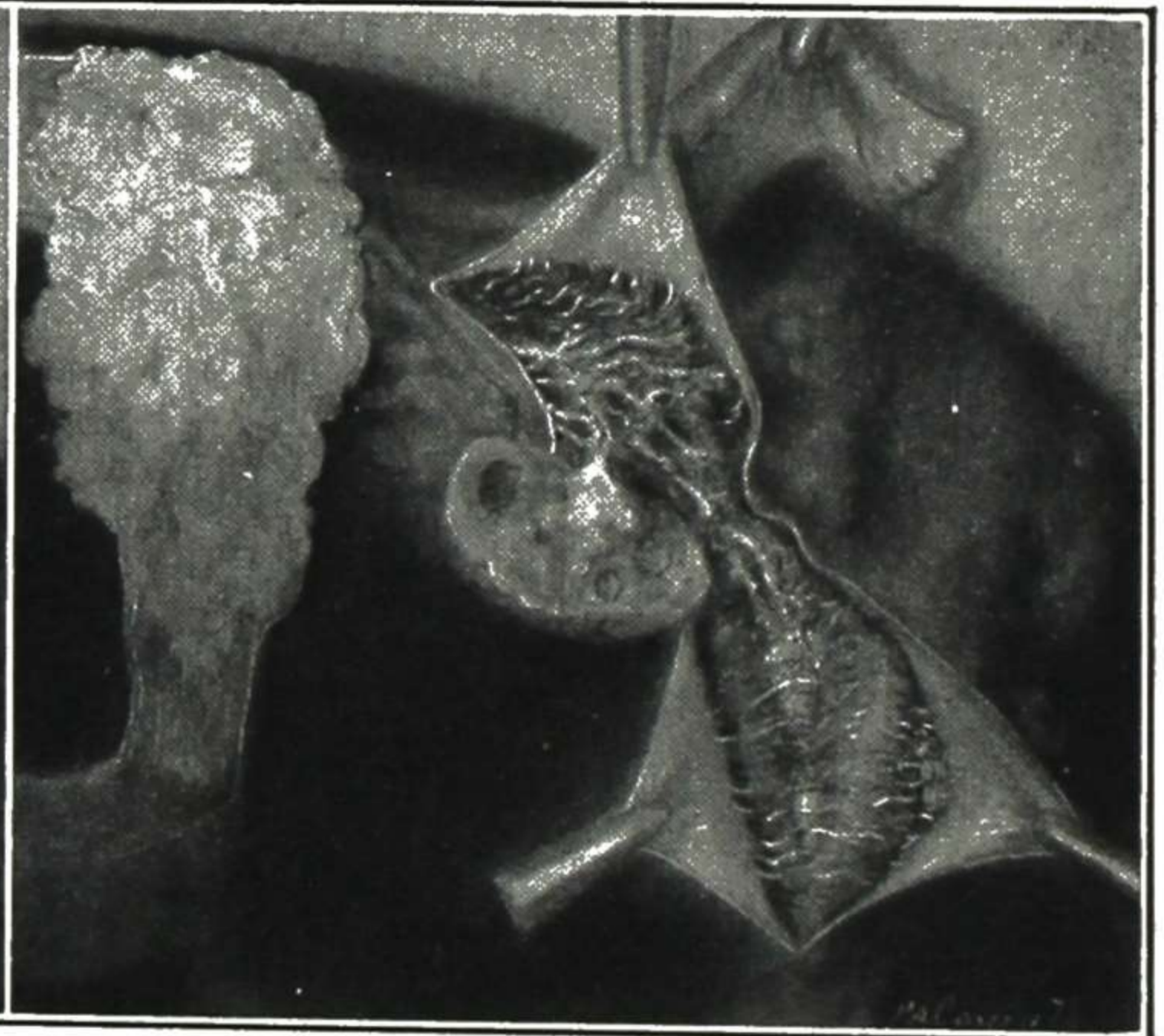


Fig. 838.

Fig. 837.—Fourth stage. Involvement of adjacent removable structures (in this case the ovary).

Fig. 838.—Fifth stage. Involvement of irremovable structures (in this case the deep pelvic glands), but the primary tumor-mass may still be removed.

is out and available for sectioning. Identification of the stage of involvement for the selection of treatment is a much more difficult matter, for it must be made before the uterus is removed.

There are a number of factors concerned in the early identification of the stage of involvement, early enough to be of assistance in deciding what treatment to give the patient. These factors are as follows: History of the case, pelvic examination, curettage exploration of cavity and deep pelvic palpation under anesthesia, microscopic examination of curettings, and special examination methods, including gastrointestinal x-ray and cystoscopic examination. Each of these factors is considered in detail in the article in which this subject is presented ("Clinical Classification of Cases of Carcinoma of Corpus Uteri"—see Reference List) along with the following summary. The grouping is into six stages, each stage representing an extent of involvement within fairly definite anatomic limits. The limits are capable of recognition and easy designation by the combination of operative and laboratory examinations. Stages III, IV, V, and VI may ordinarily be recognized at operation and Stages I, II, III, and IV may be recognized in the laboratory. The laboratory examination may identify even Stage V by critical examination of the gross specimen and selection of blocks at its margin where the cancerous extension to irremovable tissue was cut across in the operation.

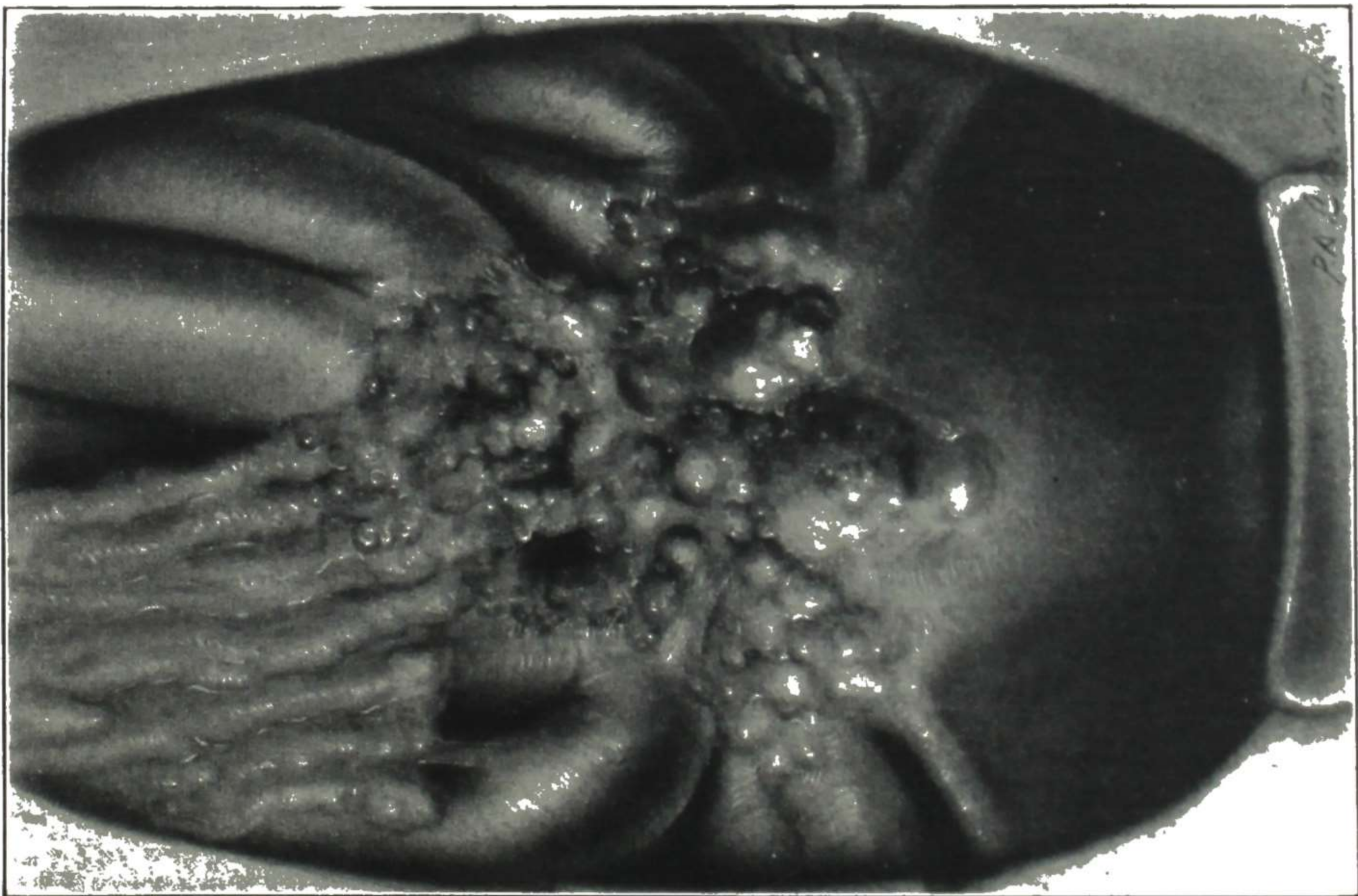


Fig. 839.—Sixth stage. Involvement of surrounding structures to such an extent as to preclude even palliative removal of the main tumor-mass.

Each stage has also a clinical significance of its own, bearing on treatment or prognosis, as explained in detail later when dealing with treatment for the different stages.

Why six stages? Six stages may at first thought seem a rather large number. It seemed so to us, and much study was given to trying to reduce the number. But carefully considered from the standpoint of accurate definition of each stage and the classification's usefulness in clinical and laboratory work, the six stages were found necessary. A reduction in number by combining any two of them was unsatisfactory. For example, if Stage I included I and II and the operator received a laboratory report stating "Corpus carcinoma, clinical Stage I," he would at once wish to know whether or not it had extended to the muscular wall, because of the difference in clinical significance. If Stage II were extended to include all muscular involvement, neither the clinician nor the pathologist would be satisfied with that broad designation, for each would wish to have stated clearly whether the cancer involved only a small part of the muscular wall or extended into the outer half. The same objection applies to any combination of two stages, and still more to any combination of three. Careful critical study of the six stages in practical application to clini-

cal and pathologic work shows that each stage represents a definite step in the progress of the cancerous infiltration and is of importance to the clinician in treatment and prognosis.

Treatment

The treatment of carcinoma of the corpus differs from that of carcinoma of the cervix in that the radical operation is still an important factor in the handling of corpus cancer. Radiation is used in all cases, and is our sole reliance in the inoperable cases. In the ordinary case, however, operation is added to the radiation. There are certain special features in corpus cancer which make operation more effective than in cervix cancer. For example, in carcinoma of the corpus the growth starts in the endometrium, hence bleed-

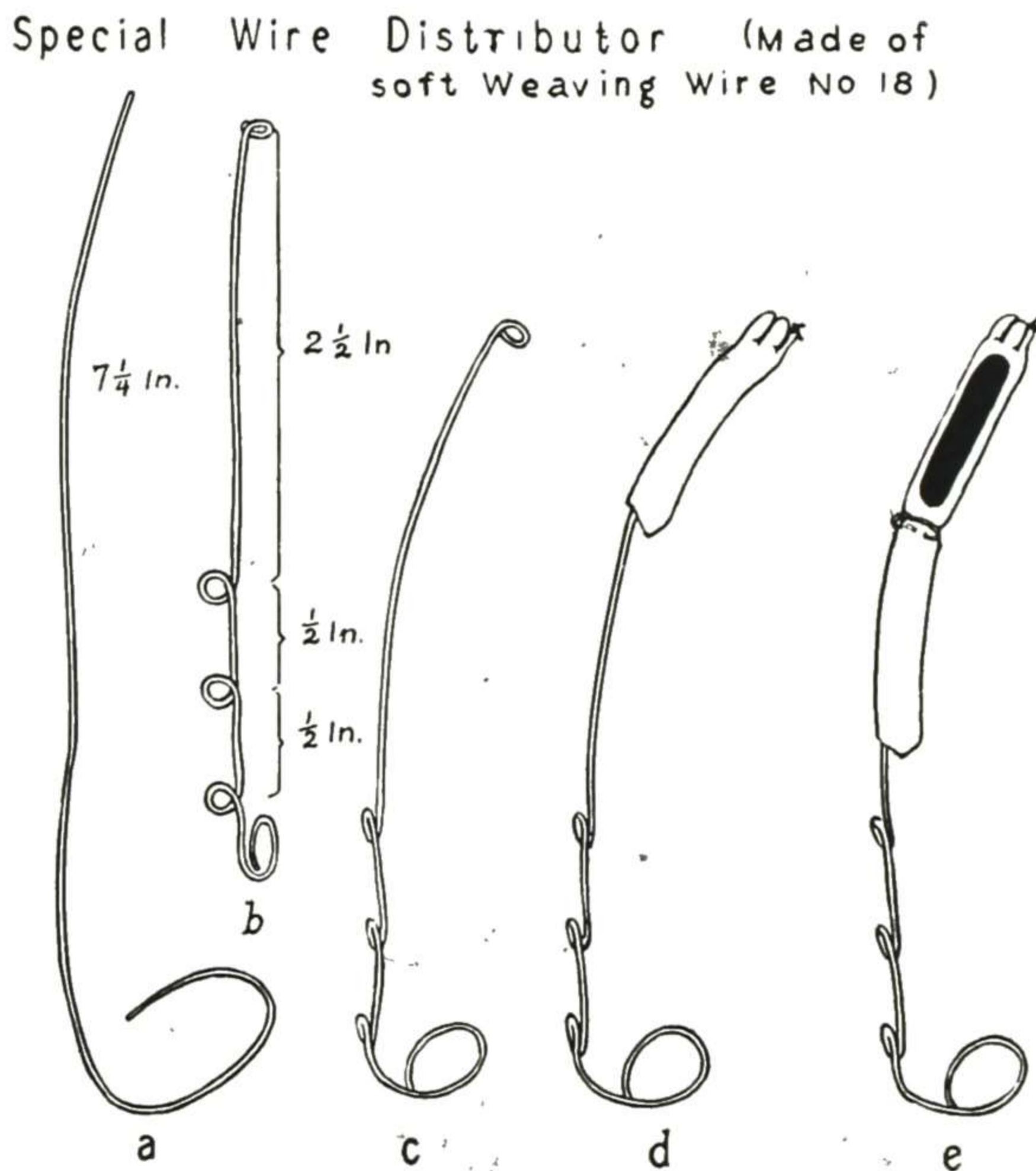


Fig. 840.—Details of the wire distributor devised by Crossen. a. The piece of pliable wire, $7\frac{1}{4}$ inches long, from which the distributor is made. b. The completed distributor turned so as to show the three eyes for adjustment to uterine cavities of different length. c. A general view showing the loop handle at right angle to the row of eyes and also the eye at the inner end to which the tubing is stitched. d. Rubber tubing for a single capsule in place and stitched securely to the eye at the end of the wire. e. A two capsule length of tubing in place and one capsule fastened in it. (Crossen—*J. Missouri M. A.*)

ing occurs early. This causes the patient to seek medical advice, leading to early examination and curettage and diagnosis of malignancy. Also, there is not the silent deep penetration of cancer cells to irremovable structures before outward clinical manifestation, as so often happens in carcinoma of the cervix. Again, the anatomical relations of the corpus uteri are such that the first lymphatic extensions of the growth may be easily removed, by excision of adnexa and associated portion of broad ligaments with contained vessels, while removal of the lymphatic extensions from the cervix necessitates deep dissection and removal of the parametrium beyond the ureters—a prolonged and exhausting operation with very high mortality.

In addition to the features rendering corpus cancer more favorable for operation than cervix cancer, there are conditions which render it less favor-

able for radium treatment. Its high location in the uterus puts it out of reach of direct palpation and increases the difficulties of determining the exact location of the malignant area and the extent and direction of its progress. These difficulties interfere with accurate application of the radium for safe maximum effect. This combination of conditions makes it advisable to employ operation in addition to radiation, except in cases where there is some serious operative contraindication.

Another principle of treatment is to secure radiation-devitalization of the cancer cells *before* the general tissue disturbance of operative removal. Such devitalization effect lessens virulence and diminishes the chance of cancer cell implantation-metastasis from the operation. It also eliminates the infective uterine discharge, and thus diminishes the danger of peritonitis following the hysterectomy. The elimination of the infective uterine discharge by the radium

Introducing and Fastening the Wire Distributor

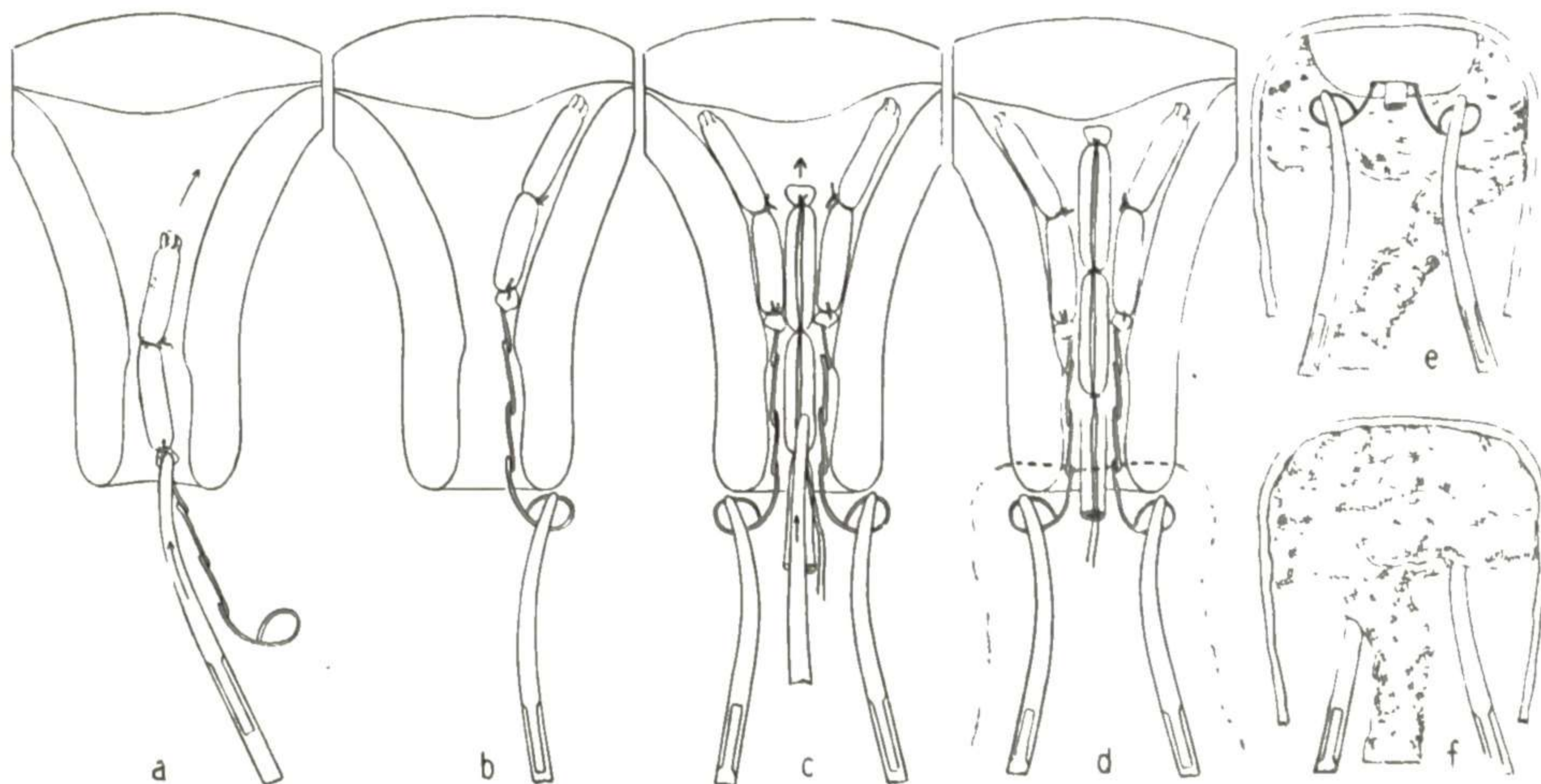


Fig. 841.—Details of the introduction and fastening of the distributor as explained in the text. a. The distributor is grasped about the middle with a strong Kelly forceps and introduced through the dilated cervix as shown. b. The distributor in place and held firmly by an assistant with the Kelly forceps clamped on the handle. c. The two distributors in place and held by the firm forceps hold on the distributors is maintained until the suture, which passes through the cervix and an eye of each distributor and the tandem tubing, is in place as in d, and also until the vaseline gauze packing is in place back of the cervix (e) and in front of the cervix and extends down beyond the distributor handles as in f. The forceps are then removed and the long suture is tied over the packing. (Crossen—*J. Missouri M. A.*)

radiation requires some weeks, and the process is hastened by giving the course of deep x-ray therapy in the interval, starting a week or two after the radium treatment.

An important technical feature in effective radium treatment for corpus cancer is distribution of the radium capsules in the uterine cavity and their maintenance in position and their certain removal. The reason for distributing the radium in several centers, instead of in a simple tandem as for myoma is to enable the heavier dosage required for carcinoma to be given without causing point-devitalization and sloughing. It is a difficult problem on which considerable work has been done.

The senior author recently devised a very satisfactory form of wire distributor for this purpose. The experimental and clinical details concerning it will be found in the article, "Advances in the Treatment of Cancer of the Corpus Uteri." The distributor is shown in Fig. 840, the method of introducing and keeping it in place in Fig. 841, and the recommended distribution in different types of operable cases in Fig. 842.

The vaginal packing of vaseline gauze is the same as that used in radium treatment for myoma, and the method of removal is the same (Figs. 752 to 757). The matter of insuring removal of all radium capsules placed in the uterine cavity is not as simple as may appear at first thought. In a reported case an overlooked radium capsule gradually worked through the uterine wall and penetrated the intestine, eventually causing death.

OPERABLE CASES OF CORPUS CANCER

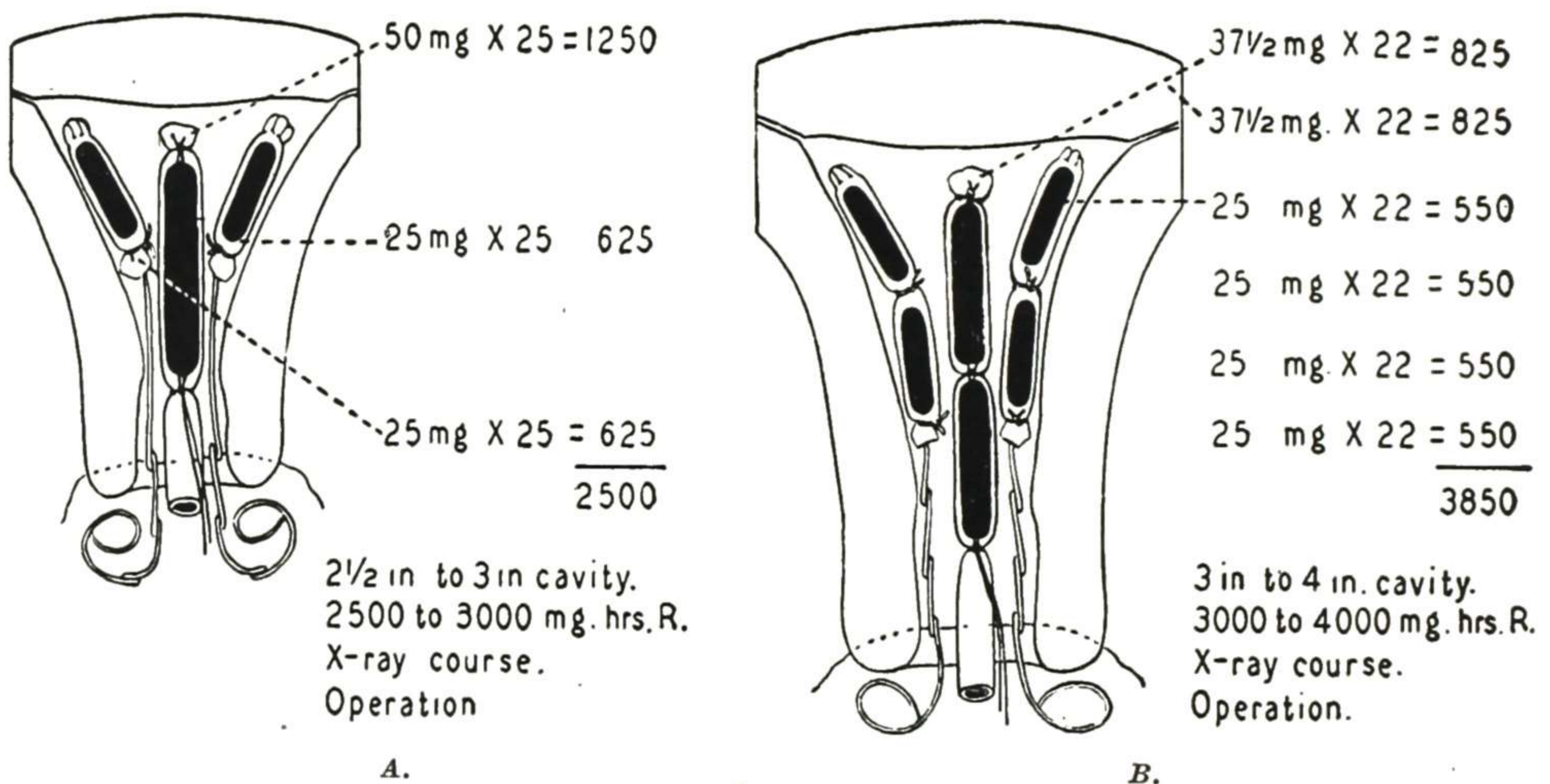


Fig. 842.—Distribution of radium and the unit dosages in operable cases of corpus cancer. A. A small uterus with three unit distribution. B. A large uterus with six unit distribution. (Crossen—*J. Missouri M. A.*)

Prevention of Corpus Cancer

Is there any factor entering into the causation of corpus cancer (endometrial carcinoma) which we can modify by treatment? There seems to be such a factor in association with delayed menopause. Delayed menopause or late menopause are terms used to designate that condition in which the permanent cessation of menstruation is delayed beyond the normal age. This delay is due to prolonged erratic ovarian activity and is frequently accompanied with endometrial hyperplasia.

The relationship of this undue endometrial activity in the age of declining function to the onset of endometrial carcinoma is an important subject. In this connection R. J. Crossen and J. E. Hobbs made an analysis of our cases of endometrial carcinoma and are investigating the subject in various directions. In a preliminary report (*J. Missouri M. A.*, 1935) they presented sufficient facts

to indicate that endometrial hyperplasia in delayed menopause may be taken as a sign of a definite tendency to endometrial carcinoma.

In the clinical analysis of bleeding at the menopause age it is necessary to consider all cases of late uterine bleeding, whether or not presenting the rhythmic character of menstruation. In giving the history, patients usually regard any recurring bleeding as menstrual flow and an appearance of blood after cessation as a return of menstruation.

Accepting this composite group for investigation, pelvic examination will show the cases in which the late bleeding is due to a demonstrable local lesion, such as carcinoma of the cervix or corpus, uterine myoma, ovarian tumor, or a tumor or inflammation of some adjacent structure. Further investigation will identify the cases presenting some extrapelvic disease which may be the cause of the bleeding, such as blood dyscrasia or cardiovascular-renal hypertension or thyroid disorder.

There remains a small group of cases presenting no evident genital lesion nor extragenital disease to account for the bleeding, and in which the bleeding simulates more or less the menstrual rhythm. This is a most interesting group, presenting unsolved problems in pelvic physiology and pathology. The patients are past the usual age for normal ovarian functioning and yet they present evidence of endometrial activity dependent on ovarian activity.

Are these cases simply examples of unusual disparity between the age in years and the age in physical changes, and consequently due to run a normal course to a later menopause? Are they, on the other hand, cases representing an irregularity of functional decline which may impose a pathological influence on the cell activity of the involuting endometrium? We have given considerable thought to this interesting problem and its practical bearings, and some features were presented in an article, as above noted. The ramifications of the subject are extensive and space consuming, but the practical conclusions from our study may be stated as follows:

1. Delayed menopause, especially when delayed to the age of fifty years, means some pathological condition, either in structural change or in cell activity. The influence of persisting irregular ovarian activity on the cells of the involuting endometrium tend to erratic cell activity, thereby favoring cancer development. In our series of 89 cases of cancer of the corpus uteri, there were 30 in which there was a definite interval between the menopause and the clinical appearance of the endometrial carcinoma. In these 30 cases the menopause occurred at the age of fifty years or later in 22 or 70 per cent, and at age of forty-eight years in 3 other cases.

2. Endometrial hyperplasia in the endometrium of involutionary age seems to represent a step in the pathological progress from normal endometrium to carcinoma. Hyperplasia is a very frequent finding at curettage for bleeding in this age-period when carcinoma is most common. In our series of cases of endometrial carcinoma a few of the patients had been curetted, in their home town or elsewhere, one or two years previously. In 3 such cases the slides of the previous curettings were available for study and each of them showed definite hyperplasia at that time. Here, in this one series of cases, there were 3 instances in which curetting showed benign hyperplasia and another curetting one to two years later showed endometrial carcinoma. There was also an interesting specimen of a double uterus in which one horn showed endometrial hyperplasia and the other horn endometrial carcinoma.

3. Delayed menopause, especially when delayed to the age of fifty years, is an indication of aberrant endometrial activity and a warning of a tendency to endometrial malignancy. Consequently, appropriate treatment should be employed to stop the aberrant endometrial activity.

4. Appropriate treatment consists usually of curettage (to stop the bleeding temporarily and to furnish tissue for microscopic study), conization of the cervix if needed for chronic cervicitis, and radium treatment to stop the erratic endometrial and ovarian activity. If there is no malignancy in the curettings or in the cervical tissue, the treatment outlined is usually sufficient to prevent further trouble. If the microscopic investigation of the curettings shows that endometrial carcinoma has already developed, then radical measures for that must be employed.

Chorioepithelioma*

Chorioepithelioma is a peculiar form of carcinoma arising from the fetal cells covering the chorionic villi. A striking feature is the early penetration of blood vessels resulting in the hemorrhagic character and appearance of the growth, as shown in Fig. 843. This blood vessel penetration leads also to early metastases to distant organs, which makes it an exceedingly fatal growth. It is nearly always preceded by abnormal pregnancy terminating in hydatidiform mole, but fortunately only a small percentage of such moles are followed by chorioepithelioma.

Care should be taken to exclude this type of growth whenever there is persistent bleeding coming on some weeks or months after confinement or miscarriage. It is especially liable to occur following hydatidiform mole. Such was the history of the specimen shown in Figs. 844 and 845. This patient was first seen some months after the expulsion of a large hydatidiform mole. The immediate cause of the consultation was repeated uterine hemorrhage, difficult to control. Curettage gave tissue that showed malignant disease of the corpus uteri. A hysterectomy was done, and sectioning of the removed uterus showed a typical chorioepithelioma.

As metastases occur early, one or more of the metastatic growths may overshadow the primary uterine trouble, causing it to be overlooked. In a suspected case of chorioepithelioma, x-ray examination of the lungs should be carried out to see if any metastases are there. Also, any disturbance of other organs should be investigated with the idea that it may be metastatic from a chorioepithelioma not yet large enough to produce pelvic symptoms.

Occasionally a metastasis to the vaginal wall will furnish a clew in diagnosis, as it did in the case shown in Fig. 846, reported by Wilson. This instructive case is of unusual interest because a year and a half elapsed after the removal of an hydatidiform mole before there was any evidence of chorioepithelioma. The Friedman test became negative promptly and remained so up to the time mentioned. The patient had periodic examinations and was in good health. About two months after the last examination she was admitted to the hospital, critically ill and with a history of cough and bloody sputum for the past week, and died in five days of generalized chorioepithelioma.

Microscopic Pathology.—The characteristic cellular features of chorioepithelioma are shown in Fig. 845. The difficult problem for the pathologist comes in the differentiation of benign hydatidiform mole from borderline conditions tending toward malignancy. The problem is further complicated by the fact that the site from which the specimen came is not of great significance, for bits of normal chorionic villi may be transported to distant parts of the uterus or

*"Chorionepithelioma" more definitely identifies the origin of this growth directly from the chorion, and this spelling may eventually prevail.



Fig. 843.—A Chorioepithelioma of the Uterus, showing the hemorrhagic character of the growth as it projects into the uterine cavity and penetrates into the uterine wall. Gyn. Lab.

even to distant organs of the body. Hence a diagnosis of malignancy requires cell characteristics beyond normal limits or clinical features which show destructive growth.

Diagnosis.—A large percentage of chorioepitheliomas are preceded by hydatidiform mole. Any bleeding in the weeks following labor or miscarriage should arouse suspicion of hydatidiform mole and investigation accordingly. This investigation includes (a) Aschheim-Zondek test to see if patient is excreting excess gonadotropic hormones, and repetition is necessary to see if it is increasing, (b) search of uterine discharge for the little cysts of hydatidiform mole (Fig. 847) which are sometimes broken off and discharged, (c)



Fig. 844.

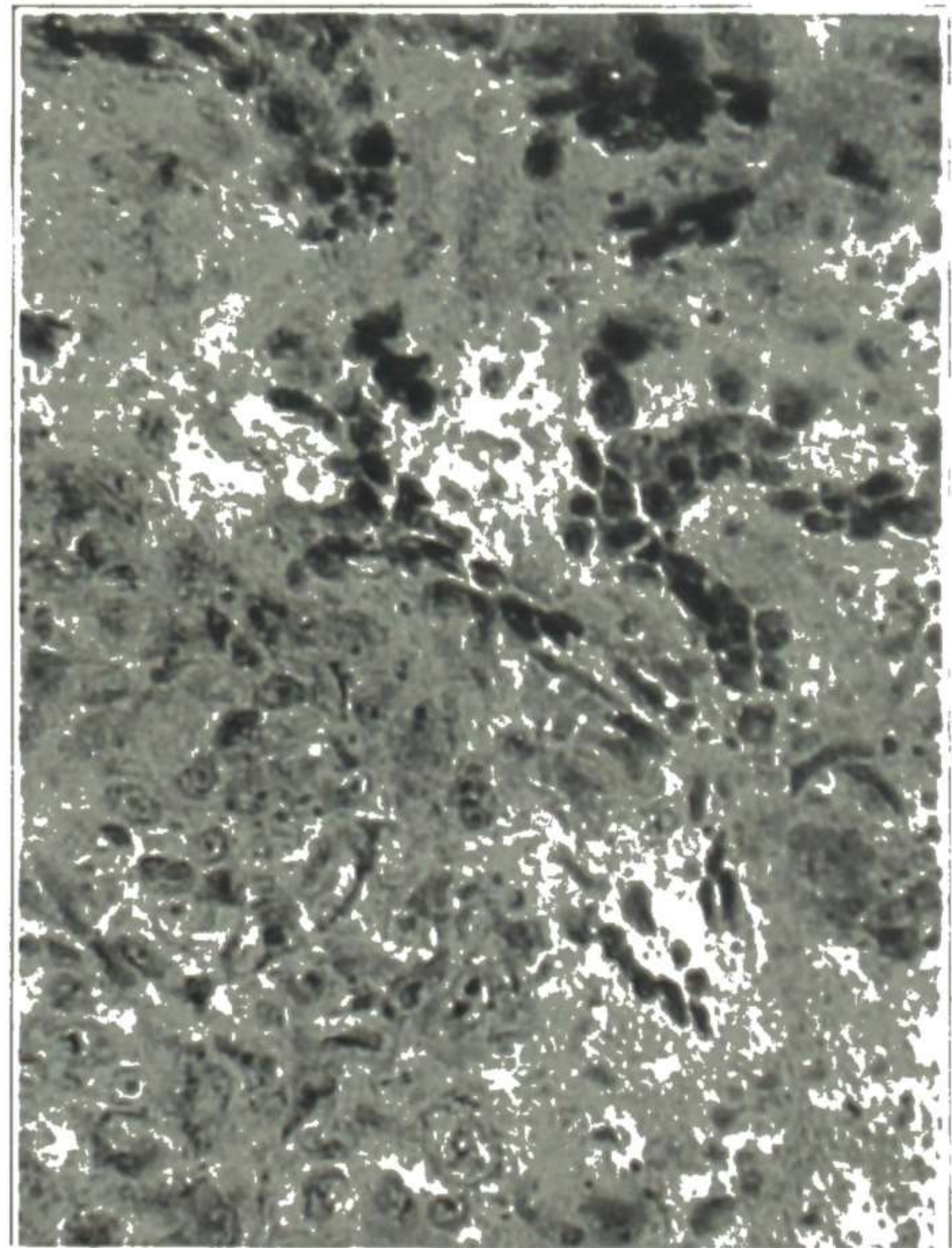


Fig. 845.

Fig. 844.—Another case of chorioepithelioma of the uterus, showing extensive involvement of the corpus uteri and a metastatic growth in the cervix. Gyn. Lab.

Fig. 845.—High power, from the specimen shown in Fig. 844. Shows syncytial cells and Langhans' cells. The latter are shown particularly well, as large light-staining cells in contrast to the darker syncytial cells. Gyn. Lab.

x-ray of lungs for metastatic nodules (Fig. 848), and (d) curettage if the bleeding tendency is not promptly stopped by medication. Though curettage must be employed with great caution and is of doubtful value in chorioepithelioma, in hydatidiform mole it is less dangerous and more certain to reveal the growth.

In chorioepithelioma, the Aschheim-Zondek test (with its modifications) assumes great importance in diagnosis. This test for excess hormones, when

strong, shows fetal elements growing somewhere, and if intrauterine and extrauterine pregnancy and hydatidiform mole can be excluded, chorioepithelioma is to be suspected. The suspicion becomes stronger as the excess of hormones increases, hence quantitative determination is helpful.

A most interesting case, in which the diagnosis and decision as to hysterectomy had to be based practically altogether on such quantitative analysis, was reported at the St. Louis Gynecological Society by Dr. Joseph A. Hardy, Jr.



Fig. 846.—A small chorioepithelioma deep in the wall of the uterus at the fundus, with metastatic nodules in the vaginal wall. (Wilson—*Tr. Am. Gynec. Soc.*)

A patient with hydatidiform mole removed by curettage continued for a period of several weeks to have about 100 mouse units of prolan, and then there was an astonishing rise to 40,000 mouse units. A second curettage showed the uterine cavity clear of any evidence of chorioepithelioma. As the high prolan excretion continued, abdominal operation for exploration of the pelvis was decided on. Fig. 849 shows the great rise in prolan excretion which brought the decision for operation.

Even with direct inspection and palpation of the uterus through the abdominal incision, there was no definite physical evidence of a uterine growth. But the great rise in prolan showed serious activity somewhere following the hydatidiform mole, and the uterine wall was the most likely place for it. Hence the uterus was removed, and on sectioning it showed a small focus of chorioepithelioma activity deep in the wall. The very early diagnosis and operation apparently forestalled metastasis, for the prolan output returned to normal in the course of a month and remained so.

Though the quantitative determination of the gonadotropic hormone output is the main reliance in the early diagnosis, the results of this test whether negative or positive must be *correlated* with the *history* and *examination findings*. In an instructive article on the subject, Mathieu makes the following observations:

Although all authorities agree on the value of the biologic pregnancy test in the diagnosis of mole and chorioepithelioma, it should be noted that there have been many misconceptions of the test—laboratory errors (2 per cent), too much reliance on a single test, and clinical and pathological judgment at variance with the test. The pregnancy test is always positive only if there is living chorionic tissue present or when the stored hormone has not been completely absorbed.

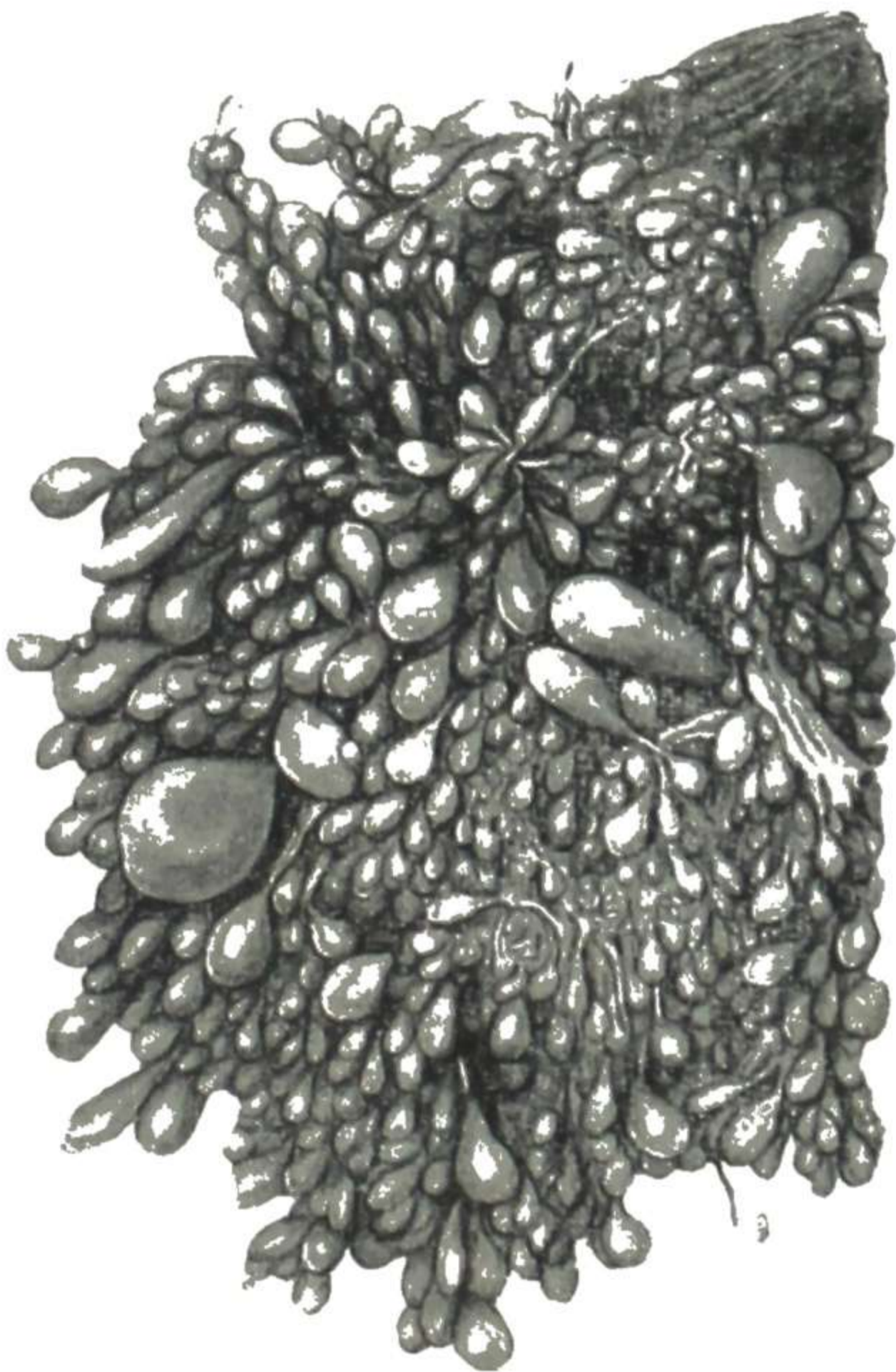


Fig. 847.

Fig. 847.—Showing the cystic character of an hydatidiform mole, from which most chorioepitheliomas originate. Vesicles may break off the mole and come away with the bloody discharge, which is often present, and search for them in a suspicious case may aid in diagnosis. Gyn. Lab.

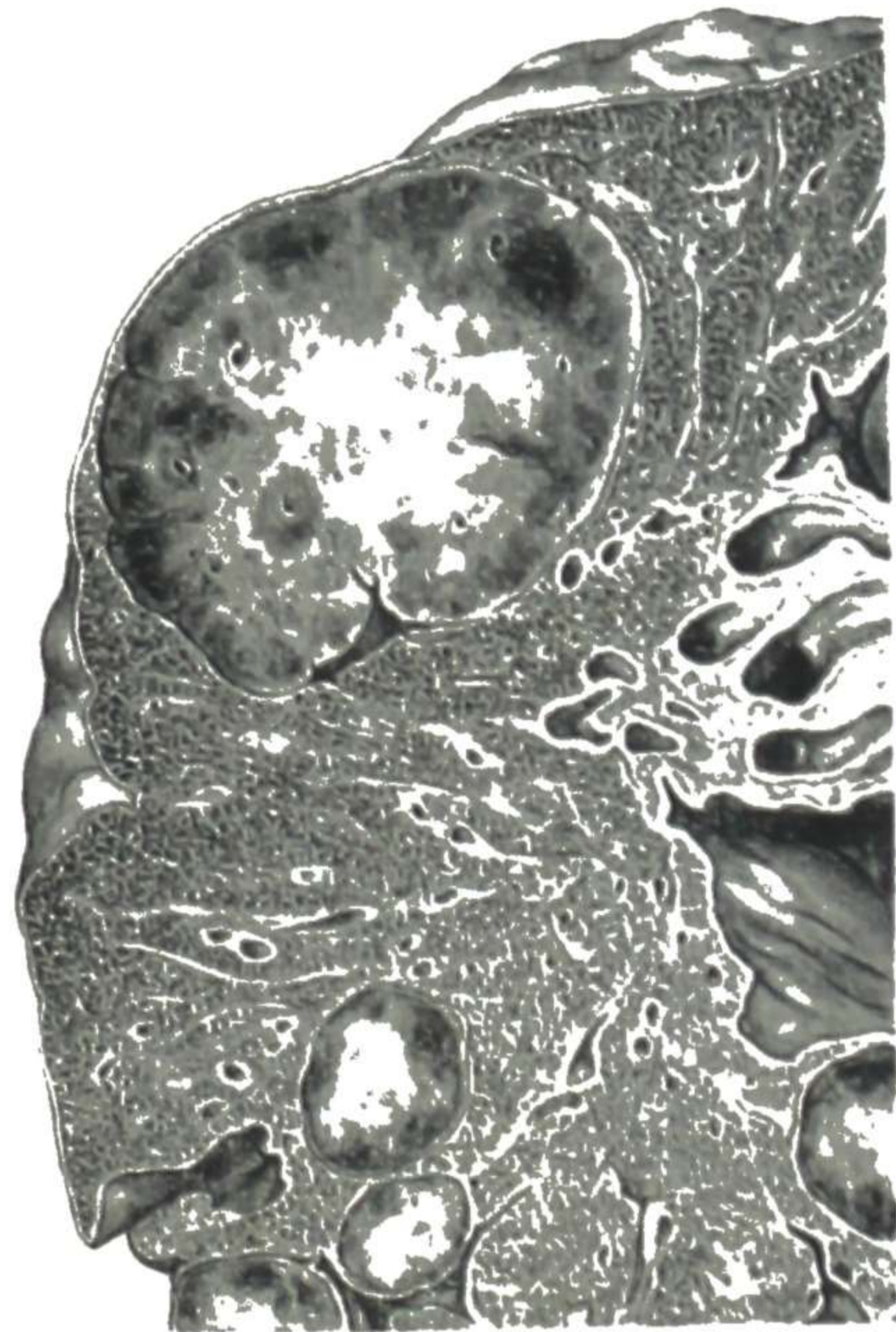


Fig. 848.

Fig. 848.—Lung metastases from a chorioepithelioma of the uterus. Gyn. Lab.

The qualitative test is not sufficient since the increasing amount of hormone associated with these diseases is detectable only by a quantitative assay. Nevertheless, one should not overlook the fact that at about the sixtieth day of normal pregnancy there is an enormous amount of the hormone. In the pursuit of mole and chorioepithelioma by means of biologic pregnancy tests, one must be certain that normal pregnancy is not present.

Quantitative tests are at times impractical, inexpedient, or even impossible. When only qualitative tests are used, one must be aware of the following facts: (1) the test is positive in the presence of living chorionic tissue, which includes normal pregnancy; (2) the test is also positive in hydatidiform mole, chorioepithelioma, or metastases of either disease; (3) the test may be negative in missed molar abortion; (4) the test may be positive for six weeks following the passage of a mole because of stored hormone in the body; (5) if a test is positive two months after the passage of a mole, and normal pregnancy has been excluded, it is likely that living molar tissue is still present or chorioepithelioma has developed; (6) in the presence of lutein cysts after all living chorionic tissue has been removed, the test will be positive until these cysts regress because the hormone is stored

in them; (7) a positive test one month after the removal of a chorioepithelioma is strong evidence of metastasis; (8) the spinal fluid gives a negative test in normal pregnancy and a positive test in mole or chorioepithelioma; (9) absolute reliance should not be placed on one test, and in questionable cases the test should be checked and rechecked; (10) the test should be used in all questionable conditions where the element of chorioepithelioma might exist.

In the discussion of Mathieu's paper, Novak called attention to the rarity of chorioepithelioma (only 8 or 9 in the 48,000 specimens at Johns Hopkins) and then emphasized the difficulties of pathological diagnosis and the chance of a mistake as follows:

Sometimes pathologic diagnosis is quite simple, in other cases difficult. In a borderline case it is difficult to say whether we are dealing with a benign hydatidiform mole, with marked trophoblastic proliferation or with a real chorioepithelioma. When we get large masses of trophoblast growing in bulk, with few or no villi, and destroying the uterine muscle, and with abundant evidence of anaplastic activity, there is little difficulty about the diagnosis. But in a perfectly benign hydatidiform mole if the sections are from the uterine wall, where the mole is getting plenty of blood supply, and not from the vesicles in the uterine cavity, we may be confused by the large masses of trophoblastic tissue,

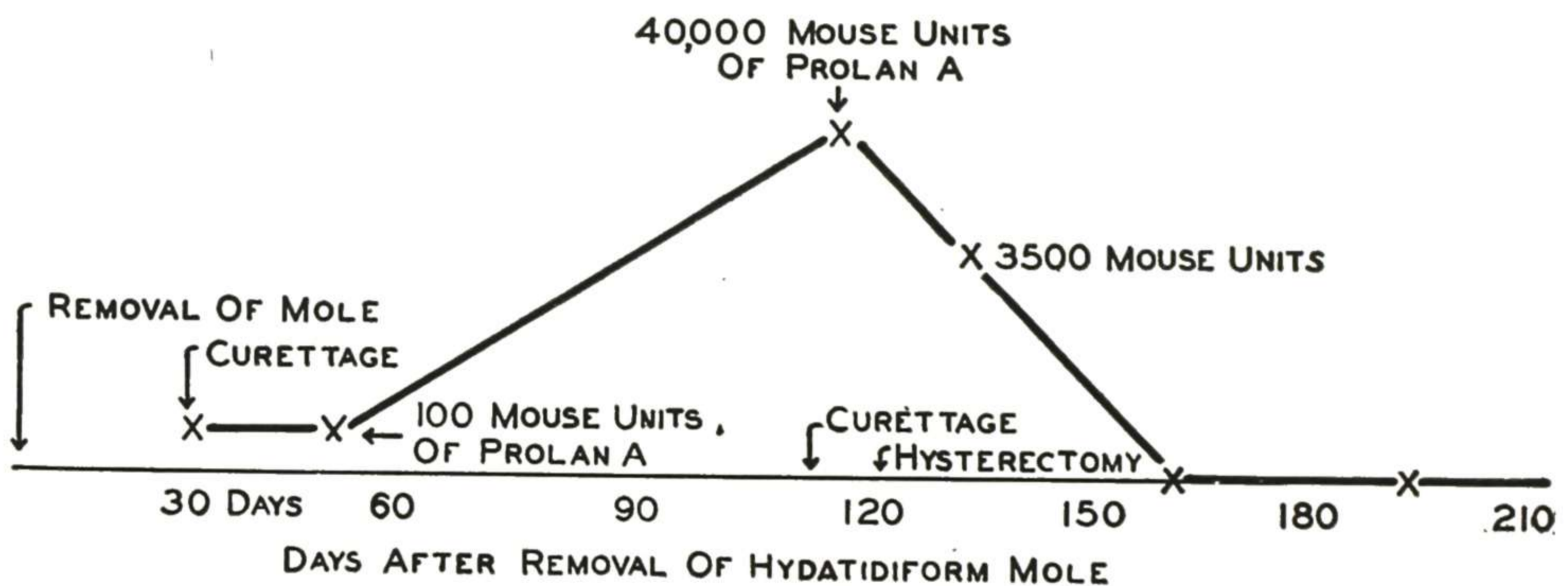


Fig. 849.—Graphic chart showing details of the case in which there was a rise of prolactin to 40,000 units, which led to hysterectomy and discovery in the uterine wall of a small chorioepithelioma which had not yet metastasized. (Case of Dr. Joseph A. Hardy, Jr., through whose courtesy this chart is reproduced.)

which nevertheless is not evidence of malignancy. I believe that many more mistakes of diagnosis are made in this particular field than in any other. Even normal pregnancy has often been mistaken for chorioepithelioma because of the frequent presence of numerous trophoblastic cells deep in the musculature beneath the implantation area, though this is entirely normal.

Cosgrove reported a series of cases of hydatid mole, the following quotation being from the summary:

This brief review of 15 cases of hydatid mole, including 3 cases complicated by chorioepithelioma, demonstrates that in all cases the behavior of the hormone tests has been consistent with the clinical history. In two cases the hormone tests have determined early radical treatment. In one of these positive diagnosis even by exploratory curettage would have been impossible, and failure to recognize the significance of the hormonal test would have deprived the patient of early and curative treatment.

As indicated above, laboratory findings must not be regarded as wholly determinative in these cases. If they are positive they confirm the significance of the clinical behavior. Negative findings, however, cannot be implicitly relied upon.

Concerning the troublesome and sometimes misleading variations in prolan output in hydatidiform mole and chorioepithelioma, the following conclusions were reached by Payne in a recent article on hormone studies in the presence of hydatidiform mole and chorioepithelioma.

The curve of prolan concentrations during normal pregnancy serves as a valuable standard for comparison in the interpretation of abnormal concentrations that are prone to occur in the presence of hydatidiform mole and chorioepithelioma.

Analyses of the clinical picture, the prolan values and the pathological findings of hydatidiform mole disclose that any of 4 types of molar activity may be encountered. Since each type presents distinctive clinical and hormonal characteristics, both aspects must be considered in its identification.

Following molar evacuation, regularly spaced hormone titrations for a year are necessary to differentiate between recovery and the development of chorioepithelioma. An increase in prolan values denotes the presence of malignant degeneration or intervening pregnancy, while a gradual decline or the lack of an increase, even over a considerable period of time, indicates the absence of chorioepithelioma.

In the diagnosis of chorioepithelioma, repeated quantitative prolan titrations are invaluable. The final decision does not rest upon a single qualitative or quantitative determination but upon the demonstration of increased values over a short period of observation.

Following treatment for chorioepithelioma, quantitative hormone studies are useful both as a prognostic aid and as a guide to subsequent treatment.

Treatment.—Though chorioepithelioma may metastasize early and run a rapid course to death, the operative treatment has not now the almost hopeless outlook of earlier years. There are two factors responsible for this improved outlook. Operative treatment has shown that some of the fairly advanced tumors are still localized and may be cured by hysterectomy.

The other factor, and the main one in the improved outlook, is the possibility of early diagnosis by careful watching and the employment of the means mentioned under Diagnosis. In reviewing this phase of the subject Mathieu remarks: "An analysis of the extensive papers written prior to 1930, including about 1,500 cases of chorioepithelioma and probably ten times as many moles, shows that the mortality rate of mole was approximately 12 per cent and that of chorioepithelioma 60 per cent. A review of the world's literature for the last three years, involving 576 cases of mole and 266 of chorioepithelioma, shows the mortality rate now to be approximately 2 per cent and 10 per cent, respectively."

A study of recent literature shows that the patient was almost invariably cured when the disease was diagnosed early and hysterectomy performed immediately.

We are inclined to think of chorioepithelioma as a pregnancy tumor only and confined to the female, but such is not the case. The bisexual nature of both male and female is emphasized by the occurrence of chorioepithelioma in the testicle and of arrhenoblastoma in the ovary. Two cases of chorioepithelioma of the testicle were reported, with review of literature, by Fortner and Owen.

SARCOMA OF THE UTERUS

A sarcoma is a malignant growth arising from connective tissue or connective tissue derivatives. Sarcoma differs from carcinoma in that it may

occur at any age (though more frequently between the ages of thirty and sixty), and furthermore it is not especially associated with childbearing. This form of cancer of the corpus uteri usually starts in a myoma which has begun to degenerate, though occasionally sarcoma starts in the connective tissue of the endometrium. It is in the larger myoma nodules that circulatory disturb-

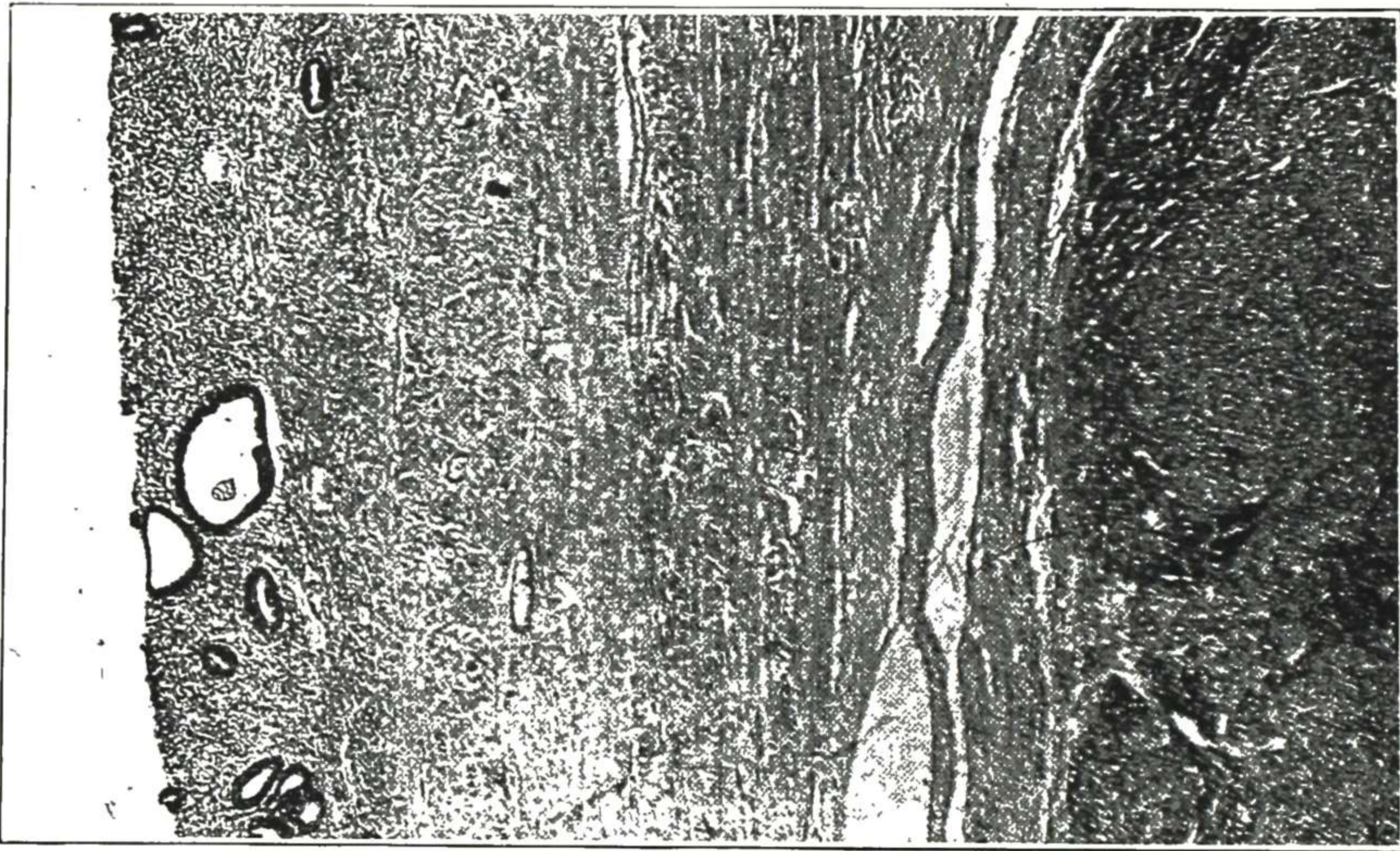


Fig. 850.—Sarcoma originating in an encapsulated intramural myoma about 8 cm. in diameter. At the left is the endometrium, in the center muscle tissue of the uterine wall and at the right the edge of the sarcomatous nodule. Gyn. Lab.

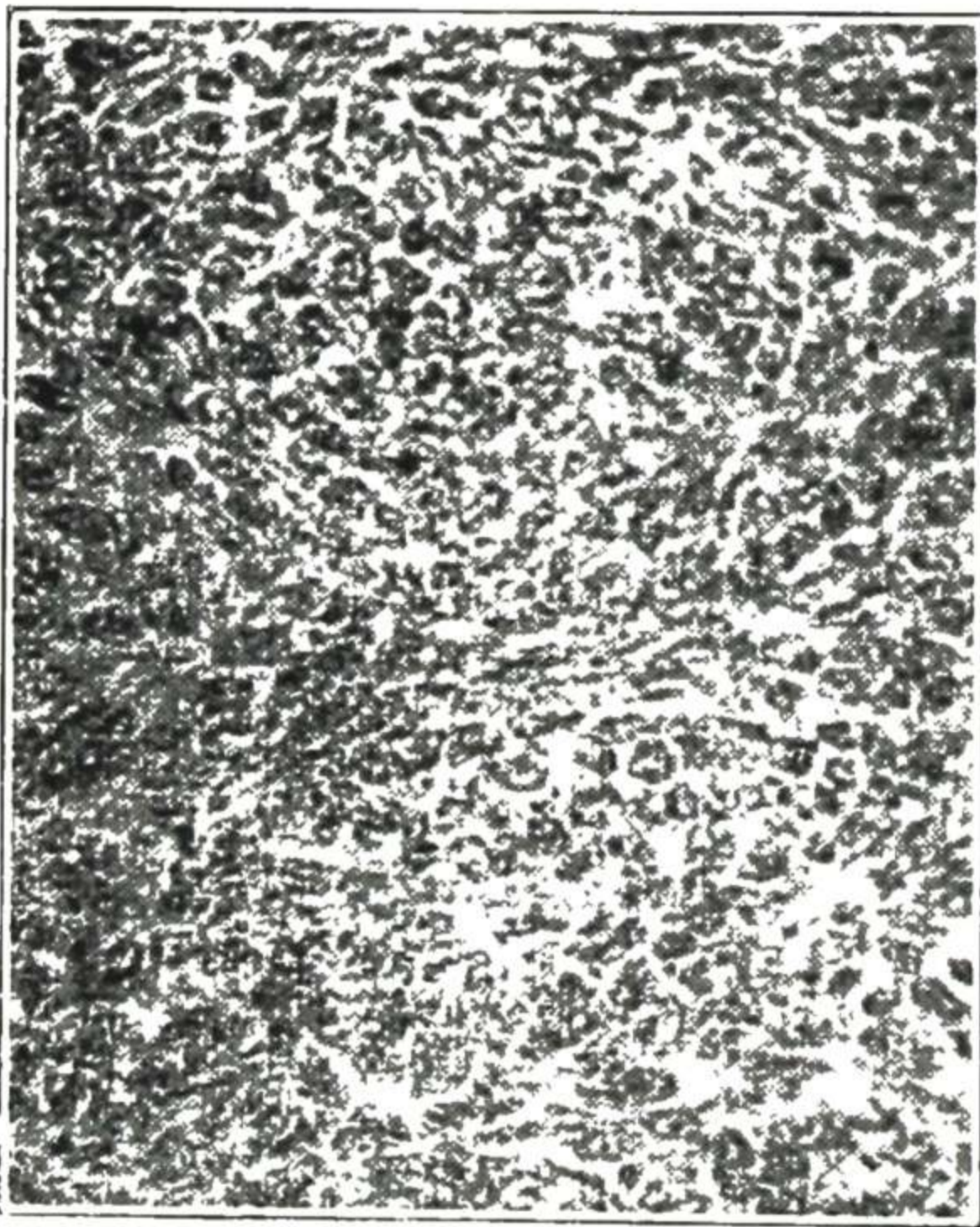


Fig. 851.

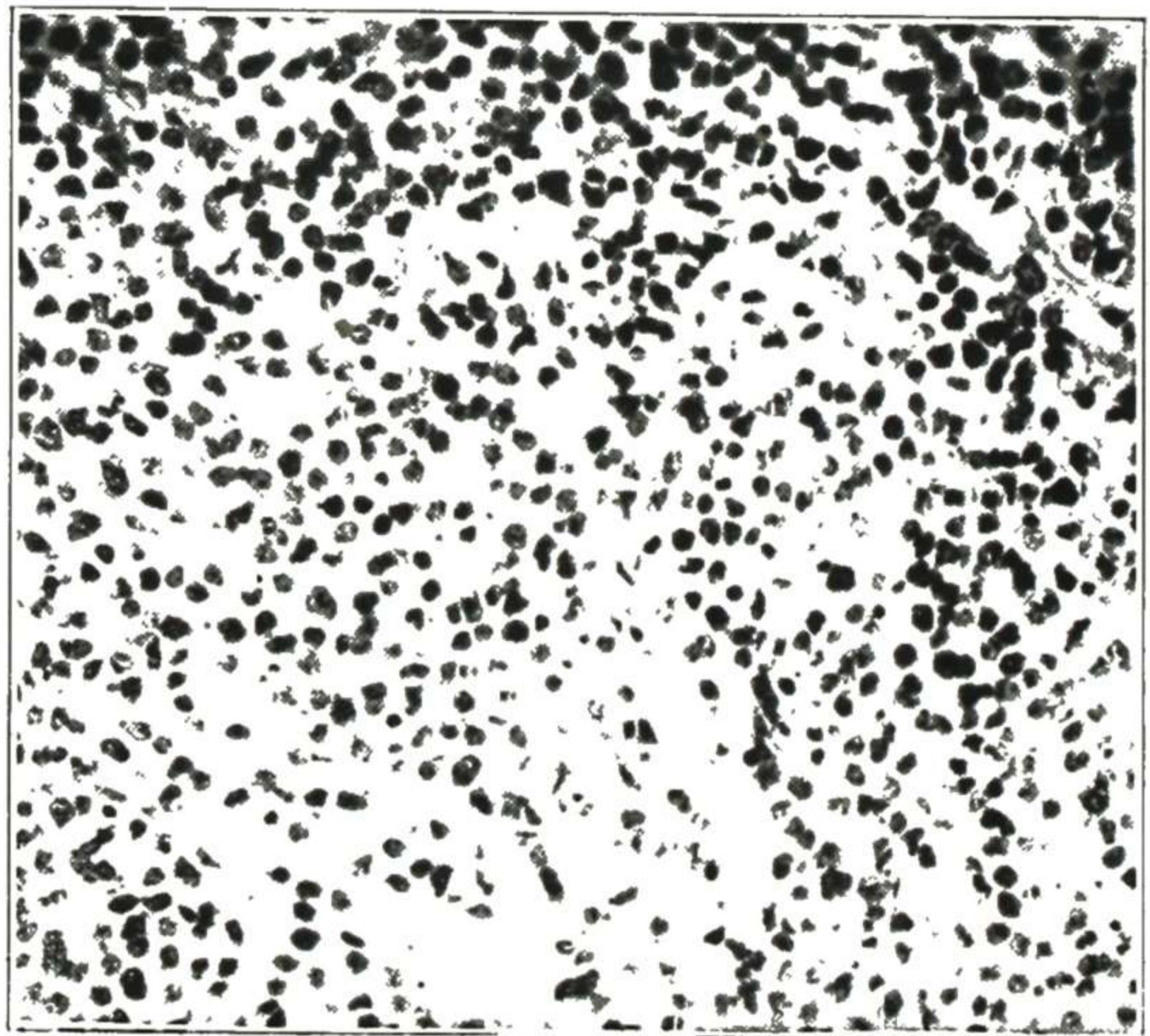


Fig. 852.

Fig. 851.—Sarcomatous change in submucous myoma. High power of Fig. 850. Large cells, chiefly spindle, occasional mitotic figure in field.

Fig. 852.—Photomicrograph of section from the tumor shown in Fig. 853. Gyn. Lab.

ance occurs with resulting degeneration of various types. It seems that the erratic cell activity of ordinary degenerative changes continued over a long period favors sarcoma development.



Fig. 853.—Section through a sarcoma originating in a myoma of the uterus. This specimen is unusual in that the sarcomatous change is so uniform throughout the large tumor. A cross-section of the uterus is seen at the lower right corner. Gyn. Lab.

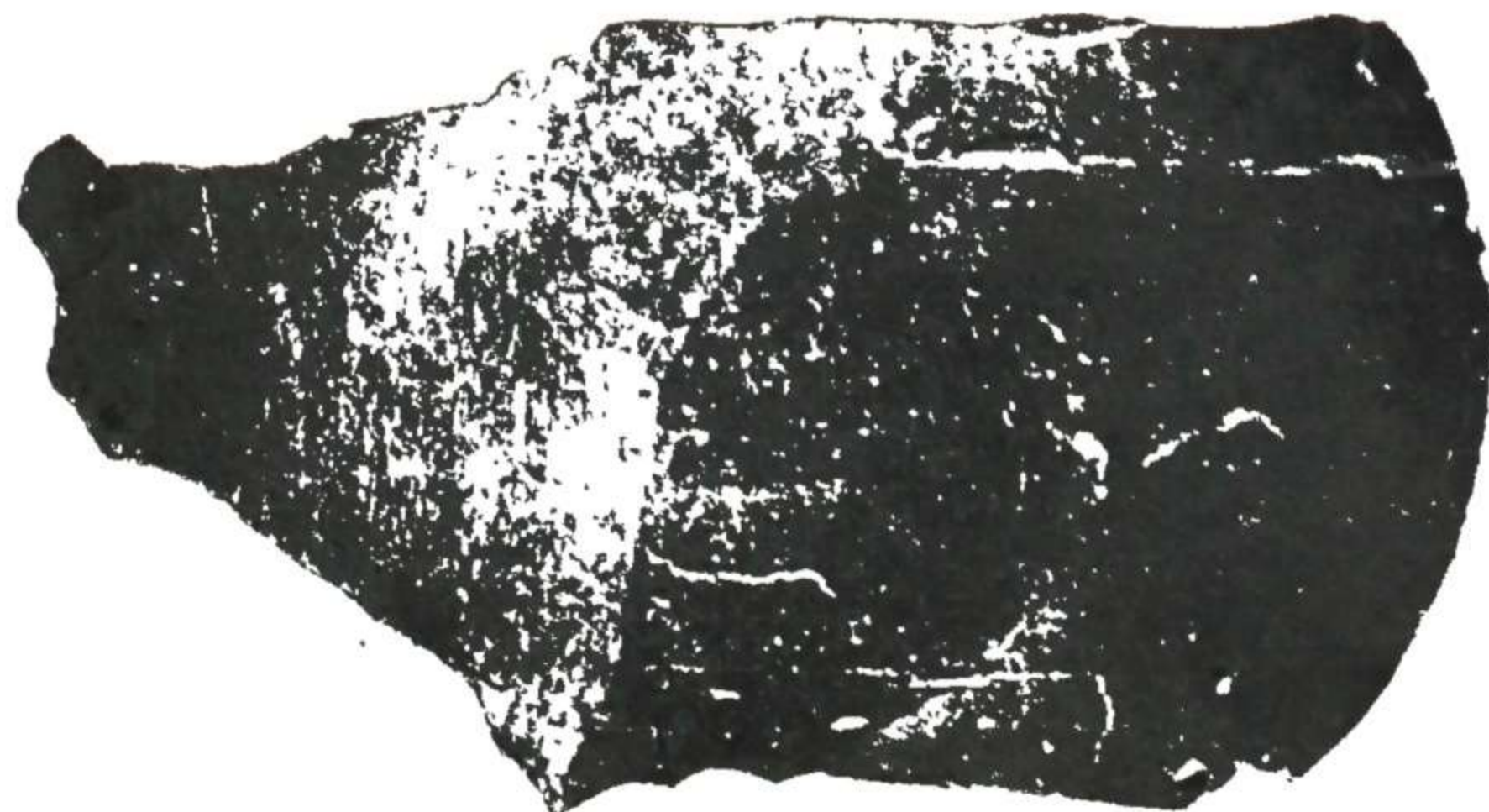
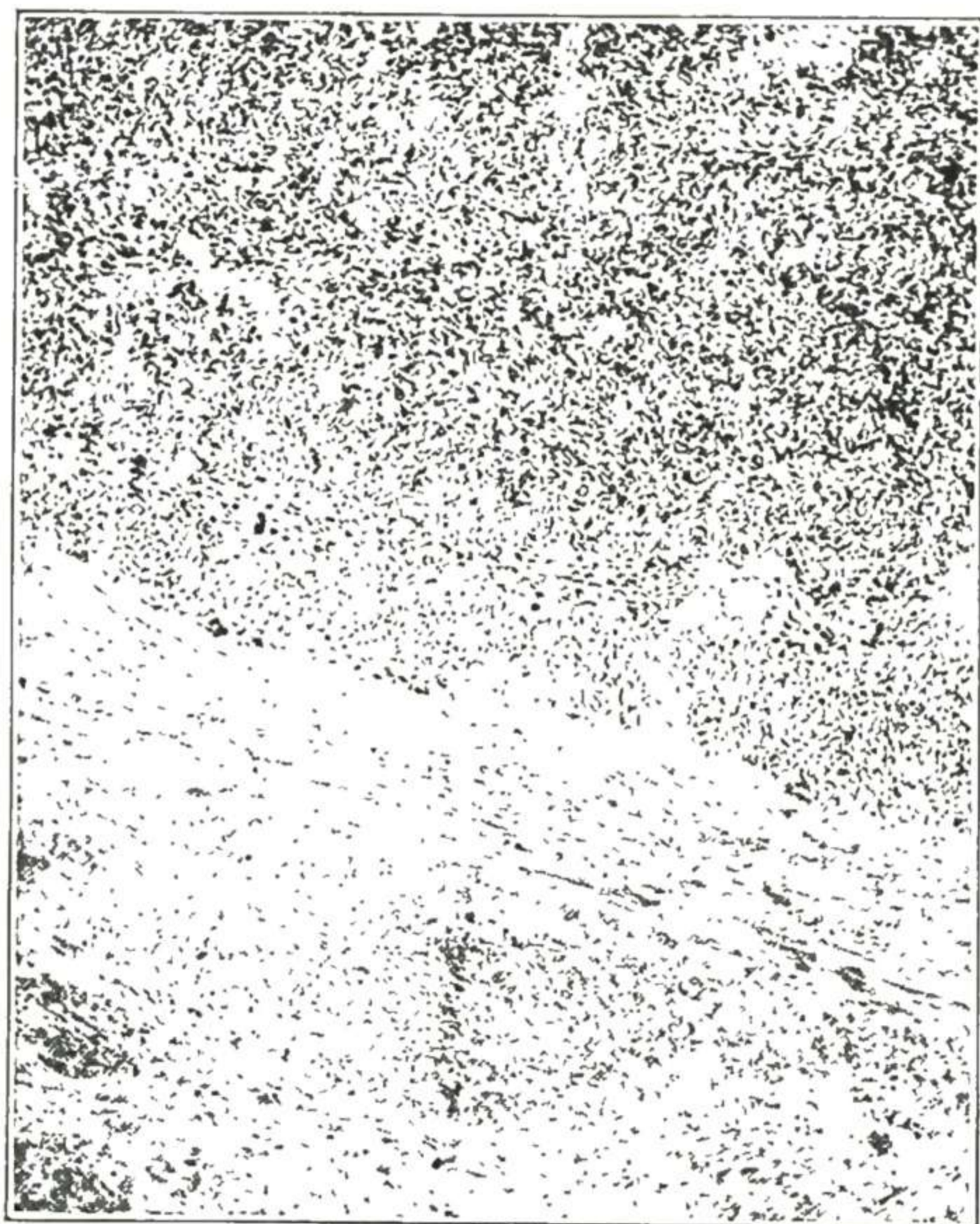
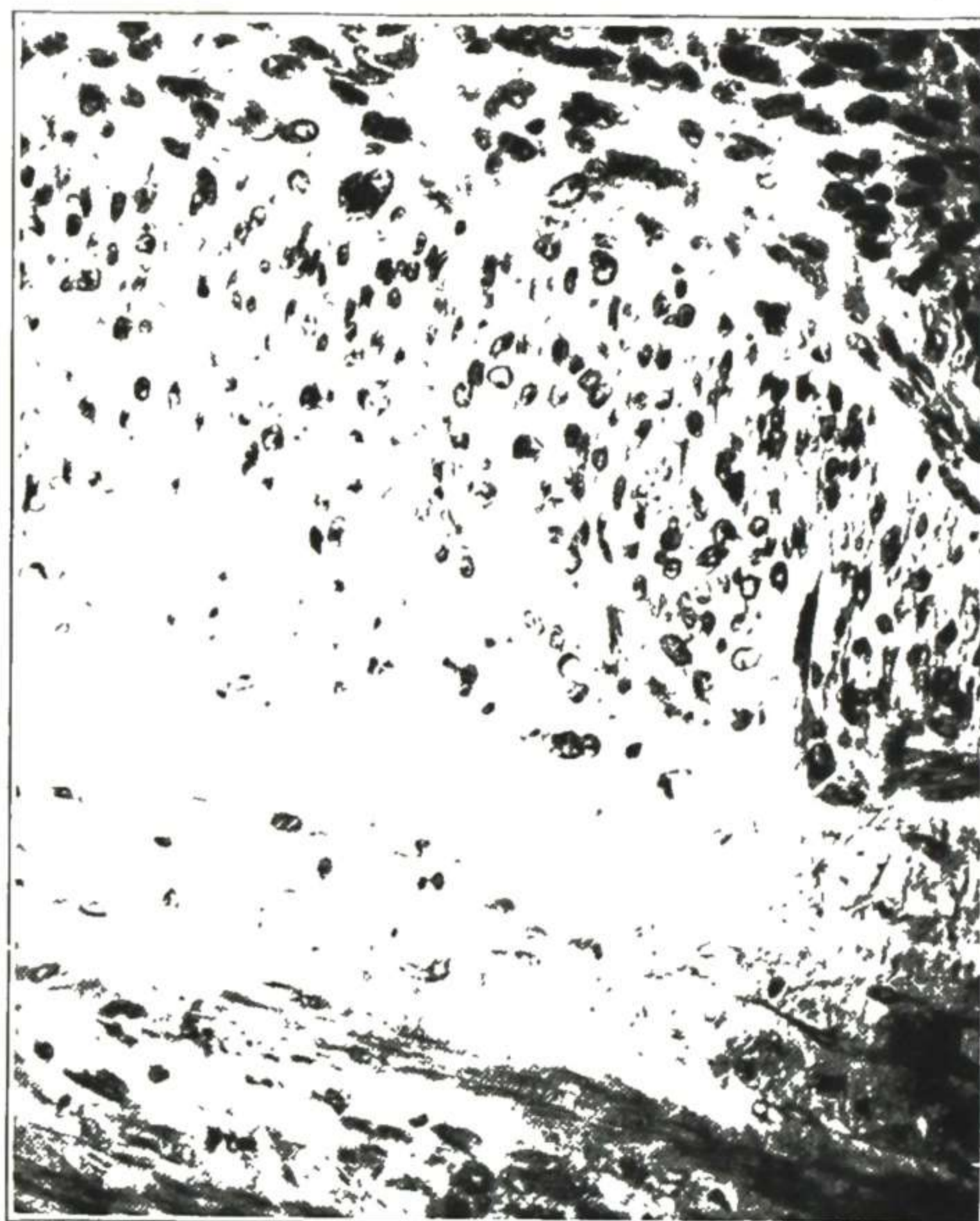


Fig. 854.—Sarcoma of the endometrium. The sarcomatous area is to the right. Notice the distinct line of demarcation between it and the normal portion of the uterine wall underneath. Gyn. Lab.



A.



B.

Fig. 855.—Sarcoma of the endometrium. Photomicrographs from the growing edge of the tumor shown in Fig. 854. *A*, Low power, showing the line of junction of the sarcoma (above) with the normal wall. *B*, High power of the contact area. Gyn. Lab.

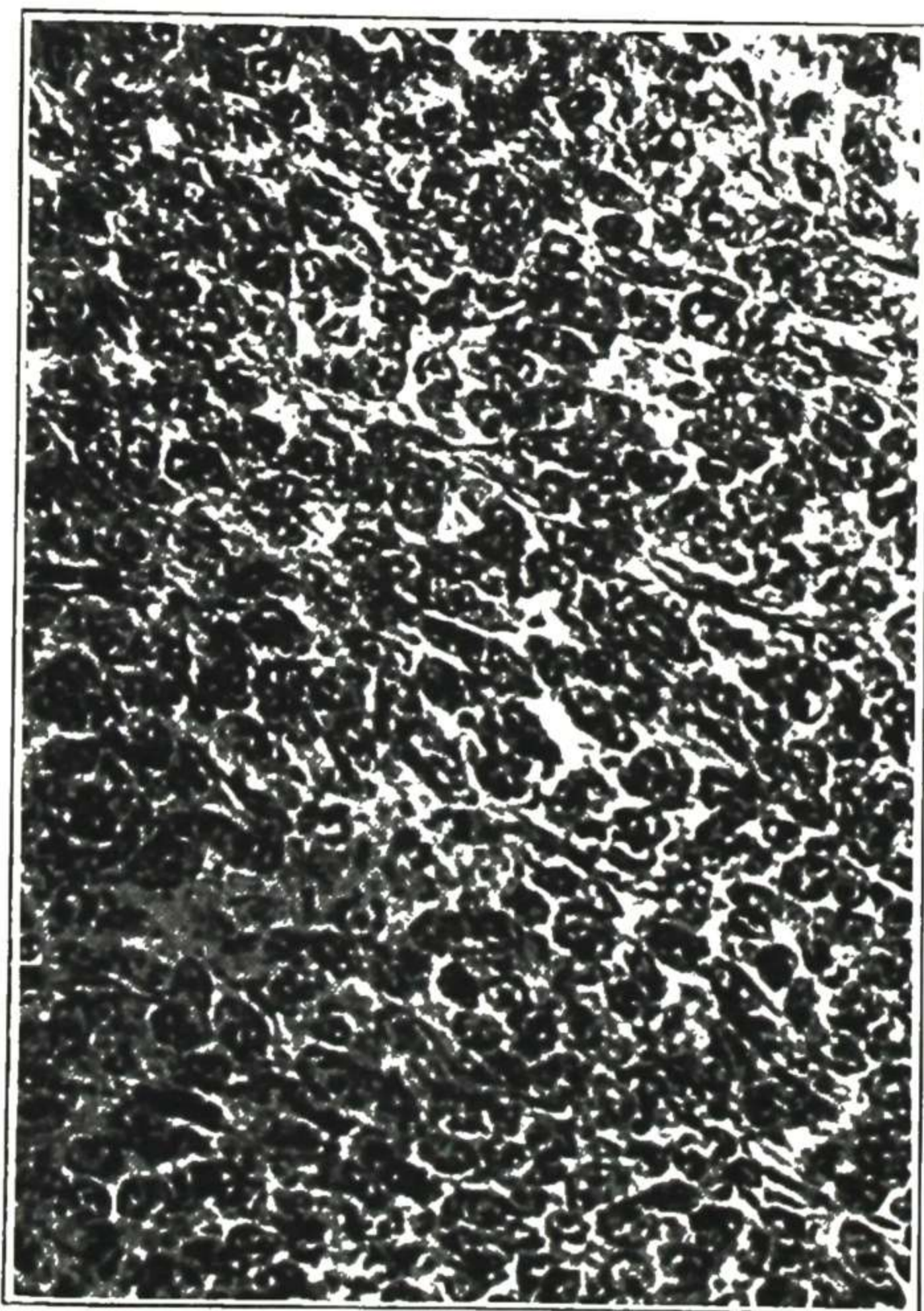


Fig. 856.



Fig. 857.

Fig. 856.—Sarcoma of the endometrium. High power, from the section shown in Fig. 854. This is the round-celled type of sarcoma. The appearance in the spindle-celled type of sarcoma is shown in Fig. 857.

Fig. 857.—Curetting. Sarcoma of endometrium. Spindle-celled type. Gyn. Lab.

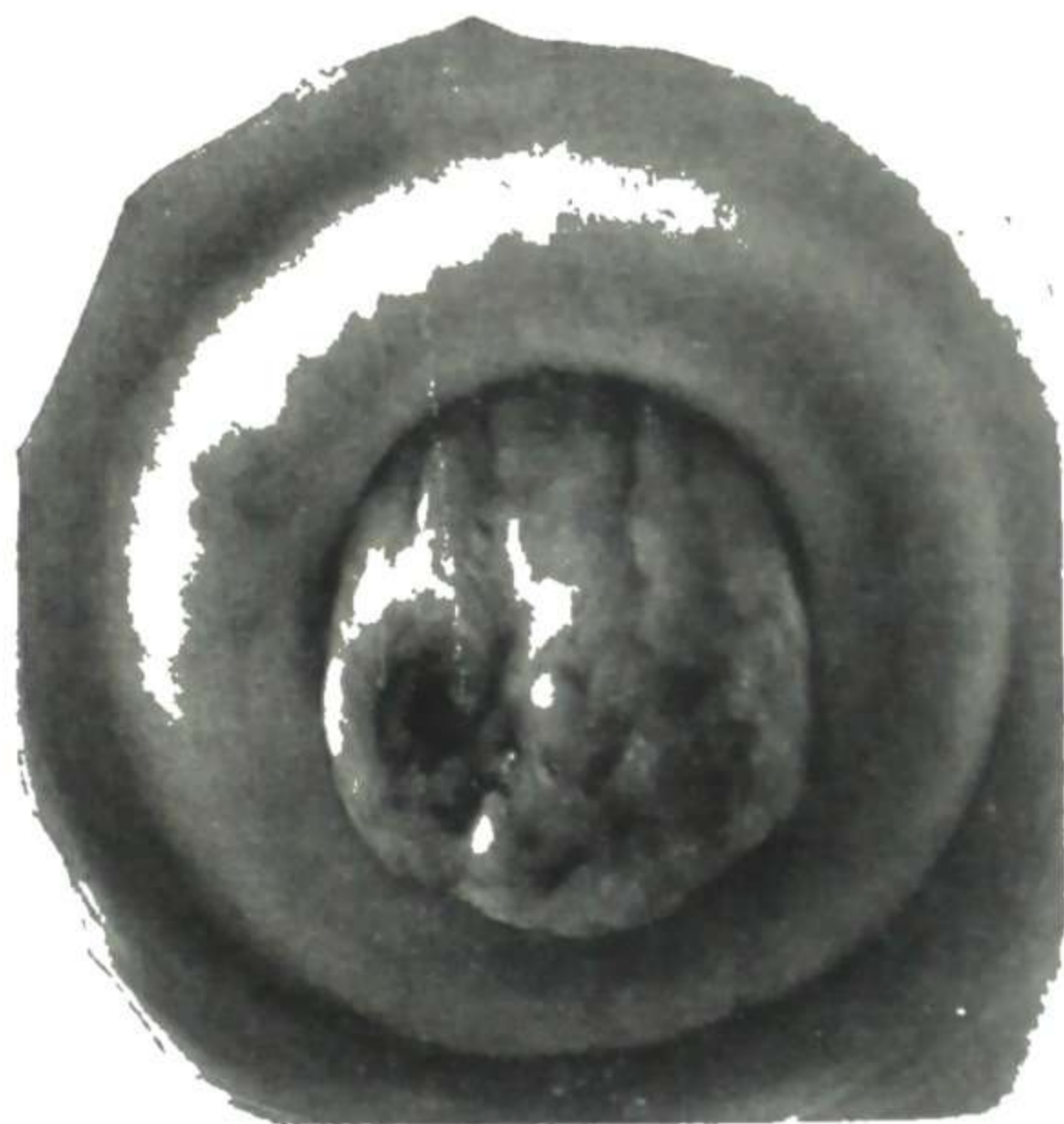


Fig. 858.—Polyp protruding from the cervix, which on removal and submission to routine microscopic examination proved to be sarcomatous. The uterus was then removed and when opened revealed the condition shown in Fig. 859. Gyn. Lab.



Fig. 859.—Extensive sarcoma of the corpus uteri originating in the endometrium. The exuberant growth formed polypoid masses which from time to time projected from the cervix (see Fig. 858) and were removed as simple cervical polypi. This happened several times before the patient came under the authors' care. Gyn. Lab.

Pathology

A sarcoma originating in a myoma is shown in Fig. 850, the point of contact with healthy uterine wall being shown. Higher magnification of the structure of this tumor is seen in Fig. 851. A very large sarcoma originating from a myoma is shown in the gross with uterus attached in Fig. 853, and the microscopic structure in Fig. 852. Sarcoma originating in the stroma of the endometrium is shown in Fig. 854. It has invaded the myometrium. Notice the distinct line marking the limit of invasion. This line is shown also in Fig. 855. This is the round-cell type as shown in Fig. 856. The microscopic appearance of the spindle-cell sarcoma of the endometrium is shown in Fig. 857, which is from a curetting resulting in diagnosis.

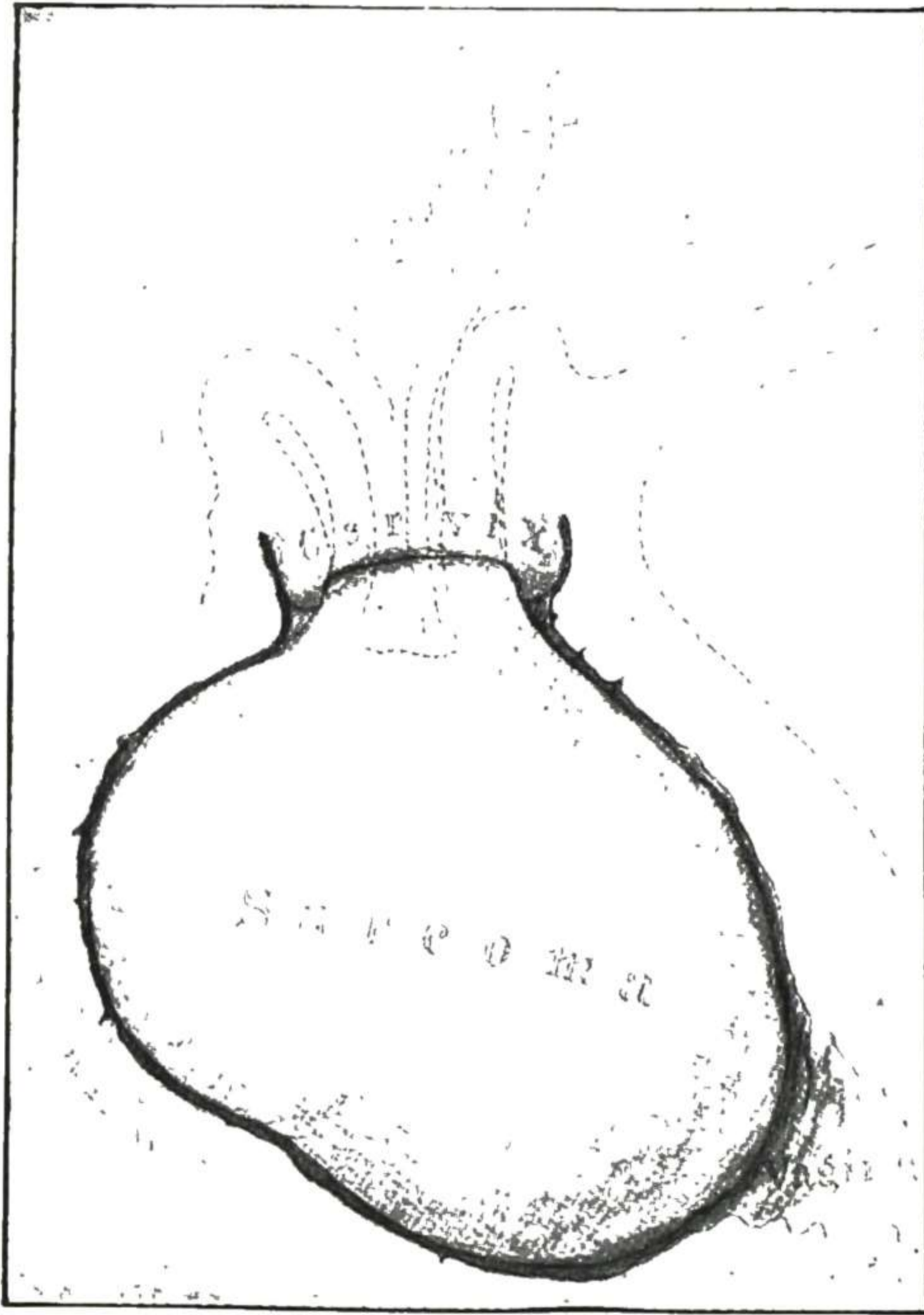


Fig. 860.

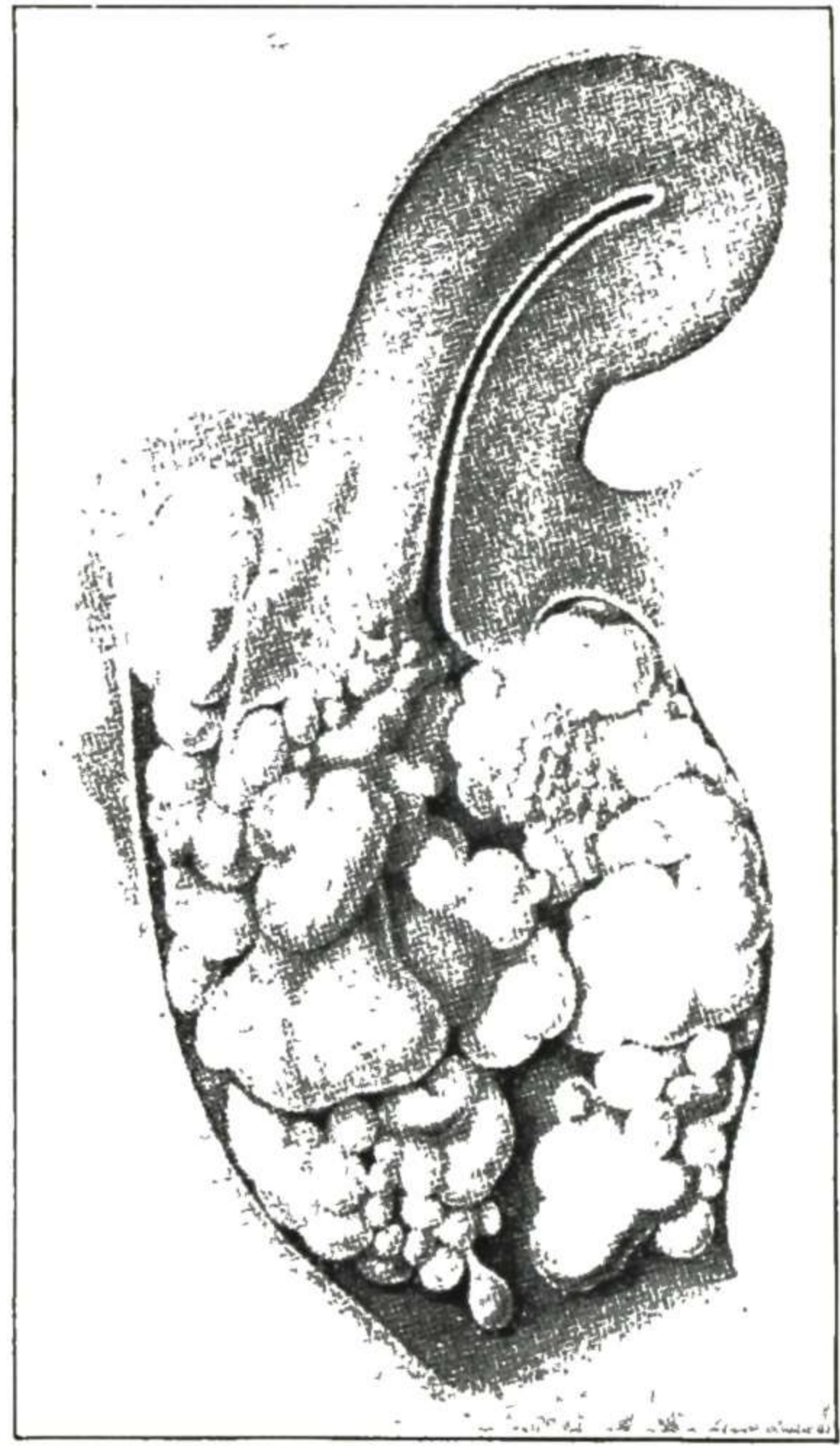


Fig. 861.

Fig. 860.—A sarcoma of the uterus projecting into the vagina and causing partial inversion of the uterus. (Kelly—*Operative Gynecology*, D. Appleton-Century Company.)

Fig. 861.—Grapelike sarcoma springing from the cervix uteri and forming a mass in the vagina. (Kuestner—*Kurzes Lehrbuch der Gynaekologie*.)

Sarcoma of the uterus occurs usually as a mixed cell sarcoma containing large spindle cells and giant cells. Rather characteristic of uterine sarcoma is the great diversity in size and shape of the cells. Large round-celled sarcoma is occasionally encountered and very rarely a tumor of the small round-celled type. The differential diagnosis from myoma is not always easy since non-malignant myomas frequently contain giant cells and mitotic figures.

Occasionally a sarcoma of the endometrium forms polypi which project from the cervix and may be mistaken for a simple mucous polyp of the cervix. Such a case is shown in Fig. 858, and it illustrates the importance of microscopic examination of all tissue removed from the cervix. The patient gave

a history of having had a "simple" polyp removed from the cervix twice. There was no microscopic examination. As the polyp returned, she decided to go to another physician for a more thorough investigation. Examination showed a soft polyp projecting at the external os. This was removed and sent for routine microscopic examination, and it showed sarcoma. The uterus was then removed, and it showed extensive sarcoma of the endometrium (Fig. 859), which had been growing all this time.

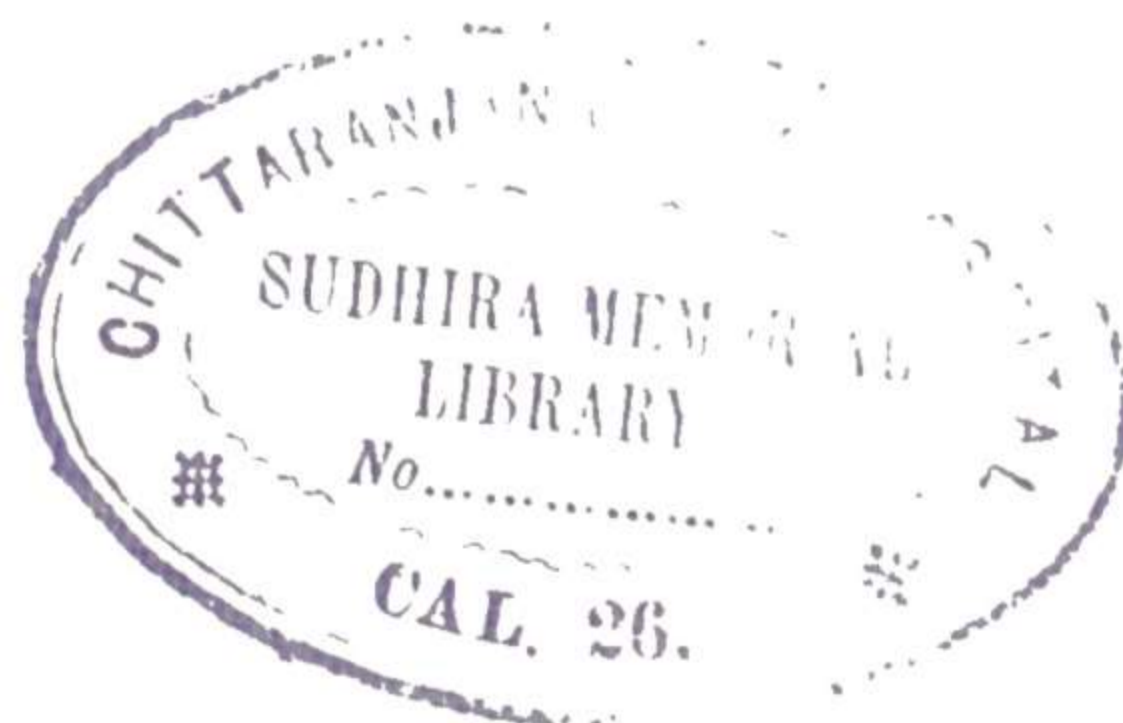
The fact that sarcoma usually originates in a myoma should be kept in mind in operations for myoma. On this account the opening of the uterus, as soon as removed at operation to see if there is any malignancy, should include the opening of all the large myoma nodules to see whether there is any evidence of sarcoma. If so, the adnexa and upper part of each broad ligament should be removed, and later deep x-ray therapy employed.

A pedicled sarcoma causing partial inversion of the uterus is shown in Fig. 860, and a grapelike sarcoma springing from the cervix, a rare type, is shown in Fig. 861.

Treatment

The treatment for sarcoma of the uterus is ordinarily prompt hysterectomy with removal of adnexa, followed by deep x-ray therapy. Special conditions may call for special modifications and in inoperable cases radiation is the main reliance.

McDonald, Broders and Counseller reported a series of 20 cases of uterine sarcoma, originating in the endometrium, with pathological and clinical analysis. The disease brought high mortality, both immediate from the operation, and later from recurrences. Three patients were cured (six-year check-up) and one was well at three years. Hysterectomy was employed in all but three cases, with radium and x-ray supplementing in some. The surviving cases all had hysterectomy.



CHAPTER X

PELVIC INFLAMMATION

Pelvic inflammation is the term applied to inflammation in the pelvis outside the uterus. The inflammatory process may be located in the fallopian tubes, in which case it is called "salpingitis," or it may be in the ovary, in which case it is called "oophoritis," or in the peritoneum, where it is known as "pelvic peritonitis," or it may be in the connective tissue, where it constitutes "pelvic cellulitis." The cause of these various forms of inflammation is the same—viz., infection—the symptoms are much the same, the treatment is in many respects the same, and two or three of the lesions are usually associated—in some cases so intimately associated that it is difficult to determine which is predominant. Consequently, it is convenient to group these lesions due to pus bacteria under the general term, pelvic inflammation, which at once identifies the type of process affecting the patient.

The continuous opening by which infection travels from outside the body into the peritoneal cavity is shown in Fig. 862. This continuous cavity is a large factor in the greater frequency of pelvic peritonitis in women than in men. There are narrowings which tend to check the upward progress of infection, for example, the external os and internal os and the uterine openings of the tubes. The mucus-filled cervical canal acts in the adult as an effective barrier to the upward extension of pathogenic bacteria, except the gonococcus, and even the gonococcus may be delayed and sometimes stopped by the protective qualities of the undisturbed canal contents. However, instrumentation in the canal interferes with this protective function and favors upward progress of any infection present. Hence, instrumentation within the uterus should be carried out only when indicated by conditions warranting the risk, and then under strict aseptic precautions.

The clinical differences between the acute and chronic forms of pelvic inflammation are greater than between the separate lesions, which fact indicates the two main divisions of the subject.

ACUTE PELVIC INFLAMMATION

The cause of acute pelvic inflammation is bacterial infection. The infection may be with the ordinary pus germs (staphylococcus and streptococcus) or with the gonococcus. Practically every case of primary acute pelvic inflammation in the adult can be traced to infection from **labor**, from **abortion**, from **instrumentation**, or from **gonorrhoea**. Secondary inflammation of the genital organs may be caused by extension from an inflammatory focus in some adjacent organ—e.g., the appendix or the bladder or from some general disease, particularly mumps or scarlet fever.