Pathology of tumours of the corpus uteri : being the Ingleby Lectures for 1910 delivered in the University of Birmingham / by R.F.C. Leith.

Prof. R. F. Leith with kind regards
R. F. Leith

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The Ingleby Lectureship was founded to encourage the study of the diseases of women and children. It has been a happy endowment. For many years the subject of diseases of women has flourished in this city. Its exponents, a succession of able workers, have succeeded in gaining a widespread and growing renown, not only for themselves, but also for the Medical School of Birmingham. The names of Lawson Tait, Malins, Savage (both father and son), John Taylor, Wilson, Martin, Purslow, Hewetson, Furneaux Jordan, Edge and others will occur to mind. The pathological museum, an educative instrument of the highest importance to every medical school, has benefited by their work and their gifts. Whilst all its departments—medicine, surgery, obstetrics and gynæcology—have made great progress of recent years, none has made more than the subject of diseases of women. Through the absorption of the old anatomical museum, it is now housed in more fitting and commodious quarters. Many new and valuable specimens have been added. Their preparation and description have entailed much time and labour, given unsparingly by the past honorary assistant curator in this department, Dr. Thomas Wilson, and by his successor, Mr. John Hewetson. Thanks to the public spirit and generosity of the many donors of specimens, and to the skill and zeal of the honorary curators, the pathology of diseases of women can be studied in this school under highly favourable conditions, which have become more or less known to recent students and to other workers within its academic walls, but are still largely unknown to the wider medical circle outside, whose interest in them is considerable. The delivery of the Ingleby Lectures seems to provide a fitting opportunity to

make this information more widely known. The subject of the tumours of the body of the uterus affords occasion for the discussion and illustration of some of the more important problems of an otherwise too comprehensive theme. It would be futile to attempt to cover the whole ground adequately within the limits of time available. Tumours of the body of the uterus are usefully divided into benign and malignant.

THE BENIGN TUMOURS.

The myoma, with its modifications, is the only benign tumour of any practical importance. It is commonly spoken of as a fibroid, but is more correctly designated a myoma or leiomyoma, or simply a leioma. It is occasionally called a hysteroma. Its frequency is so great that the uterus has become the commonest site in the body of the benign tumour.

I.—THE MYOMA.

General Characters. They are so well known that they require merely a passing notice. The great majority of these tumours grow in the body of the uterus, only some 4 per cent. to 6 per cent. occurring in the cervix. They vary greatly in size, many being quite small, almost pealike, and some of huge dimensions. The largest example in the museum of this university weighed over 60 lbs., but cases have been put on record where the weight exceeded 100 lbs. All intermediate sizes occur and they may be either sessile or pedunculated. In shape, vide Fig. 1, they tend to become rounded, though they occasionally assume a pear, heart, renal, saddlebag shape, leaf-like or lobulated appearance. The surface is smooth in most cases, though in a few it is rough, nodulated, or mulberry-like. In consistence they are firm and elastic, qualities which increase with their age and size. Small growths are thus soft as compared with large ones, but the softest are always firmer than the normal uterine wall. The terms soft and hard when applied to myomata are synonymous with small and large. Section, vide Figs. 2 and 7, reveals the most familiar and characteristic features of these tumours, the indefinite intermixture of muscle and fibrous tissue, the former in whorls and bundles of a dull grey or brown colour, everywhere interwoven with white glistening bands of the fibrous tissue. The muscle predominates in the smaller and the fibrous tissue in the larger growths. There is no distinct capsule, its place being taken by a small amount of loose fibrous tissue, which permits of the easy enucleation of the tumour from its bed within the uterine wall. In most instances, vide Fig. 3, this bed can be seen distinctly by the unaided eye, but sometimes it is so scanty as to be unobservable or absent. This is always the case in the variety known as the Adenomyoma, so that

all the latter as well as some of the ordinary myomata are not enucleable. The general pallor of the myoma is another of its striking characteristics. While it varies in degree, it is always less red than the uterine muscle, thus making it easy to distinguish between tumour tissue and uterine wall. The latter is fairly rich in blood vessels as is also the loose fibrous bed of the tumour, vide Fig. 3, but the body of the growth itself is scantily supplied with them.

Microscopic appearances, vide Fig. 4. (1) The muscular bundles run through the tumour in an irregular and indefinite way, quite unlike the orderly plan of the uterine muscle, their individual muscle cells are smaller and more closely packed together than those of the uterine wall, while their nuclei are larger. The nucleus varies even more than the cell. In the slowly growing and more typical tumours it is long and rod-like, but in those, which are young and of rapid growth, it is short and oval, more like that of an ordinary spindle-shaped connective tissue cell. Mitotic figures are very rare.

(2) The fibrous stroma has all the characters of ordinary fully formed white fibrous tissue. Elastic fibres are scanty. As already mentioned the fibrous stroma increases with the age of the tumour, so that in old growths, muscle cells may be very scanty.

(3) Blood vessels are markedly deficient throughout the substance of most fibroids, but many of them show large and prominent veins on their outer surface. In large growths they may exceed a $\frac{1}{4}$ inch in diameter. The corresponding arteries are seldom conspicuous. These veins form a plentiful plexus all over the tumour and empty themselves by many large branches into the utero-vaginal plexus of veins situated at the sides of the organ; from which, about the level of the internal os, the uterine veins, two on each side, arise and run outwards in the broad ligament. These superficial veins can be traced inwards through the uterine wall into the bed of the tumour, but rarely any further. Most of them seem to originate there, for they are very scanty throughout the body of the growth. Here and there small veins may be seen, either singly or in clusters, but numbers, comparable to those on the surface, are rarely met with. Arteries are scantier than veins, from which they are not easily distinguished owing to their exceptionally thin walls. Capillaries, both vascular and lymphatic, are more numerous. They are often the only vessels, with which large tracts of the growth seem to be provided. The lymphatics are frequently dilated into sinus-like spaces. Proliferative changes in the walls of the vessels are common and lead to the obliteration of many of them, particularly within the older and central parts of the tumours. The hindrances thus occasioned to the circulation within the tumour, aided by others consequent upon twistings of its pedicle, irregular uterine contractions and menstrual congestions, must lead to nutritional

changes and to hæmorrhagic and fluid exudates within the tumours, which in turn exercise an important influence upon their growth, life and histological characters. The freer blood supply of tumours entirely surrounded by uterine muscle (the so-called interstitial or intramural fibroids) enables them to grow faster than those surrounded partially in this way, viz., those which project into the cavity of the uterus (submucous fibroids) or from its outer surface (subserous fibroids).

(4) The lymphatic vessels, even more commonly than the veins, form conspicuous objects on the outer surface of the tumour, particularly in the neighbourhood of the broad ligament and in adhesions to the omentum, when they exist. These vessels appear as white tortuous tubes, sometimes exceeding half an inch in diameter and as bladder-like vesicles. They have very thin walls, which collapse when cut or punctured, hence they are difficult to see in the specimen after its removal from the body. Like the veins they form an abundant plexus beneath the peritoneal coat, within the uterine muscle and in the bed of the tumour. In the normal uterus, the lymphatics of the outer and middle muscular layers are large and numerous during adult sexual life; whereas during the earlier period and after the menopause, they are small and few. But, the existence of a fibroid favours their growth, so that they become larger and more numerous than in the normal mature uterus and do not atrophy after the menopause has set in. This plexus empties itself by means of several branches which pass to the sides of the uterus, where they unite to form 4 or 5 trunks which run outwards beneath the respective uterine cornua, accompanying the uterine artery and after joining the ovarian lymphatics beneath the ovary, ascend along with the ovarian vessels towards the lumbar region to enter the chain of lymphatic glands which lie near to and parallel with the aorta. A few of the lymphatics from the lower part of the body of the uterus do not take this course, but run outwards in the broad ligament at a lower level than the others and end in the inguinal glands. The course and distribution of these lymphatic vessels is of greater importance in malignant than in fibroid growths of the uterus. Within the substance of the fibroid there are only lymph sinuses and capillaries. They are most easily seen when distended, which is of frequent occurrence. Moderate distension gives a spongy appearance to the part, whilst great distension results in the formation of cysts often of large size. Hindrances to the free circulation of lymph within the tumour must be often at work. Not only may all the causes interfering with a free blood circulation retard the flow of lymph, but others, such as the mechanical pressure of the growth itself upon the thin walled lymphatic trunks within the pelvic cavity outside the growth must act in the same way.

(5) Nerves are not prominent. Though easily seen on the outer

surface of the growths they are traceable with difficulty into their substance, and consequently pain is rare. It is indeed remarkable that fibroids may grow to a great size without causing the patient more than a vague sense of discomfort. On the other hand there are some submucous fibroids in which pain is present. It is also of such common occurrence as to be of diagnostic importance in fibroids which have undergone the so-called "red degeneration" and in the variety known as "adenomyomata."

The effect of the growths upon the *size*, *shape*, and *position* of the uterus is of great practical importance. There is naturally an increase in size of the uterine mass, but the uterus itself may not take any part in this enlargement. It may indeed be smaller than normal even when the fibroids are large (vide Fig. 5.) In most cases, however, there is a true hypertrophy of the uterine wall causing some enlargement of the organ, due in all probability to stimulation by the fibroids, for it gradually subsides after their removal. The extent of this enlargement is never great, though, when it is uniform, it may simulate early pregnancy (vide Fig. 6). More commonly the uterus assumes an irregular shape, due to inequality of growth on the part of the tumours. The whole mass is confined for a time within the pelvis, but later pushes itself up into the abdomen. It not infrequently happens that the patient is first led to seek advice by the appearance of a smooth hard painless swelling in the pubic region. When the uterine body is distinguishable from the tumours, it is usually displaced, tumours situated in the posterior wall, pushing it forwards; in the anterior wall, backwards; laterally, sideways. It is only in cases in which several growths are scattered diffusely throughout its walls that it retains its shape. Similarly the cervix may be ante or retroflexed or displaced laterally or downwards.

The *uterine cavity* is usually enlarged, but in the case of some fundal and lateral tumours it is unaltered or occasionally even smaller than normal (vide Fig. 7). It is sometimes distended and may contain blood or pus. It is generally distorted, assuming all sorts of shapes, which interfere with the passage of a sound (vide Figs. 8 and 9). Occasionally it is partially obliterated. The mucous membrane may be pale, congested or marked by old or recent hæmorrhages. It may be thinned, thickened or raised into polypoid protuberances (vide Fig. 10), but it is often unaltered, even when the cavity is much distorted and encroached upon by the tumours. Microscopic examination, however, may show that it is considerably stretched and pulled out of place, the endometrial glands being parallel with, instead of more or less perpendicular to the surface (vide Fig. 11). The covering epithelium is generally preserved even when the whole endometrium is much thinned, but it may be flattened or even proliferated and form more than one layer. The veins are

often distended and may be thrombosed. The cellular tissue of the endometrium and the glands may be infiltrated with blood. Much granular blood pigment may be present either free or within leucocytes. No actual rupture of blood vessels can be made out, but their walls are in such cases looser and more spongy than usual, permitting of a general oozing of blood from them into the surrounding tissues and into the uterine cavity. It seems to be merely an exaggeration of the process which constitutes the menstrual flow and thus tends to increase the ordinary menstrual loss. It must be borne in mind that the great majority of fibroids have little or no influence in this direction. They do not affect the menstrual function. It is only when they encroach upon the endometrium and bulge into the uterine cavity, so as to be distinctly submucous, that the congestive and hæmorrhagic changes occur. Even then, they rarely cause loss of blood except at the menstrual periods, suggesting that they have to be aided by the physiologically produced congestion of the menstrual period before they can set up a menorrhagia. In a few cases, in which there is intermenstrual loss of blood, they may be capable by themselves of causing a hæmorrhagic discharge. The uterine glands may become blocked, as a result of pressure or displacement, and distended into pin head or pea like blebs filled with clear fluid, projecting from the mucous membrane. The epithelial lining of these cysts may remain unaltered, be flattened out, disappear or be proliferated into several layers. Atrophy of the glands is another result. Hypertrophy and active branching of the glands occasionally occurs and these new acini may grow out of the endometrium and penetrate for some distance into the muscular substance of the tumours. The muscle in rare instances may push its way inwards between the glands even as far as the epithelium. This penetration of muscle by the glands of the deeper part of the endometrium is observed to a certain extent in the normal uterus, but it occurs more frequently and to a greater extent when fibroids are present. It is the special feature of the variety known as adenomyoma. It has to be borne in mind in examining curettings in cases of tumours of the uterus for signs of malignancy. In all other situations, such an invasion of muscle by glands, belonging to a mucous membrane, is strongly presumptive of malignancy; but it has no such significance in the uterus.

Classification of Fibroids. The simple classification based upon their anatomical position is well known and has the merit of convenience. Those projecting from the outer surface of the uterine wall are covered by peritoneum and hence named *subserous*, those surrounded on all sides by uterine muscle, whether projecting outwards or inwards are named *interstitial* or *intramural*, those which bulge into the uterine cavity, remaining more or less covered by the endometrium, are named *submucous*, and those which push their

way among the tissues of the broad ligament are named *intraligamentous.*

Special characters of the varieties. The general characters already enumerated apply equally to all varieties. On the other hand certain special characters, determined largely by anatomical situations and relationships, apply particularly to certain of these varieties and are best dealt with separately.

The *subserous variety.* The outstanding special character of this variety and also, though less markedly, of the interstitial variety, is the tendency for adhesions to arise between the tumours and neighbouring organs and structures. The omentum, the Fallopian tubes, the ovaries, the intestine, both large and small, the vermiform appendix, the rectum, the bladder or the abdominal wall may be bound more or less firmly by fibrous adhesions to the fibroid uterus. These adhesions are the result of continued friction aided by toxic substances generated within the tumours on the one hand and within the viscus on the other hand. The toxins coming from the tumours are mostly the result of anæmic degenerations, whilst those from the viscus are often due to bacterial action. The adhesions are more or less freely supplied with blood vessels which thus provide an additional source of nourishment for the tumours themselves. In some cases this accessory blood supply continues to increase in volume as the natural supply diminishes and may come in time to be the only source of nourishment available for the tumours. This happens particularly in pedunculated growths. Owing chiefly to the persistent uterine contractions, the pedicle of some of these growths becomes progressively attentuated and may separate altogether from the uterus. Fibroids, which have thus become free, are called *parasitic* upon the bowel, other viscus or structure. The vessels running to them through the adhesions tend to keep degenerative and necrotic changes within them in check, but are prone to torsions, rupture and hæmorrhage from the sudden displacements to which these mobile tumours are liable. A short account of some of these adhesions taken separately will serve to make clearer these relationships and their consequences.

1. *The omentum.* Lying like a protective apron in front of the abdominal organs the great omentum comes in contact with the growing uterine tumours, whenever they rise above the pelvic brim and sometimes even earlier. Adhesions follow, particularly when the tubes or ovaries are the seats of active inflammation. It is naturally the upper parts of the tumours (vide Fig. 12) which acquire these adhesions, the very parts which, being furthest away from the ordinary source of blood supply through the pedicle, are most likely to undergo degenerative changes. But with the advent of these adhesions fresh blood is brought to the tumours, which serves not only to check degenerations, but also to favour growth. Microscopic examination

of the upper part of such tumours often discloses a considerable rind of young and growing cells enclosing degenerated and dead tumour substance deeper in. The adherent part of the omentum usually shows an interesting adaptation to its new nutritive function, in so far as it loses its fat, becomes thinned, fenestrated and breaks away from the tumour except at the places where the blood vessels enter it, so that all its available blood supply becomes concentrated for the better nutrition of the growth. During this adaptation, considerable obstruction to the lymphatic and venous returns may take place, particularly to the former, causing the formation of vesicles and cysts of varying size and number.

2. *The intestine.* Adhesions may unite the fibroid to any part of the bowel, the rectum, colon or small intestine. Adhesions to the rectum are not uncommon. They may help to imprison the growths within the pelvis, but even then rarely give rise to rectal trouble, unless aided by other adhesions, the result of antecedent or coincident pelvic peritonitis. Thus ovarian or tubal inflammations or abscesses or general pelvic inflammation or abscess, may cause such dense and extensive adhesions between the uterus and the general pelvic structures, that both vascular and rectal disturbances follow. Constipation and even intestinal obstruction may arise. Hæmorrhoids may appear and painful defæcation be complained of. But rectal mischiefs generally are more frequently met with in fibroids of the cervix than in those of the body. Adhesions to other parts of the intestine, such as the colon, cæcum, vermiform appendix or small intestine, form most readily after the tumours rise into the abdomen. They are greatly favoured by fixation of the viscus resulting from a previous oöphoritis or salpingitis. When thin and leaf-like they do not interfere with peristalsis. On the other hand when dense, close and at all extensive, constipation, partial or complete intestinal obstruction, may acutely or slowly supervene. Or the adherent intestinal wall may become necrosed and ulcerated, allowing of the escape of some of the intestinal contents into the substance of the tumour. Pus formation, necrosis and gangrene may follow. If an abscess be formed, it may discharge its contents into the bowel without much harm for a while, but it may suddenly become a source of danger. When the vermiform appendix is involved an acute appendicitis may be set up and require immediate operation. It does not complicate the case to remove the fibroid tumours at the same time. Whereas it is better not to interfere with an adherent appendix, in the absence of signs of acute inflammation, when it is met with in the course of a hysterectomy, on account of the added risk of infection, which this procedure entails.

3. *The bladder.* Troubles of micturition are not infrequent. Frequency is most often complained of, but there may be pain or discomfort from partial or complete retention and occasionally from

loss of control. Some displacement of the bladder, mostly upwards, usually follows adhesions (which may be very vascular), owing to the fibroid dragging it upwards in its growth. Cystitis is of rare occurrence.

4. *The tubes and ovaries.* These organs are frequently diseased in fibroid uteri. Many attempts have been made to form an accurate estimate of this frequency and though the evidence available is imperfect, it may be tentatively placed at about 10 to 12 per cent. at least of cases coming to operation. In the experience of some surgeons it is much higher. The lesions are inflammatory in origin except in a few cases, where they may be ascribed to the mechanical effects of the tumours. The tubal are more frequent than the ovarian lesions. Hydrosalpinx is the commonest of them, inasmuch as it may follow upon even a minor degree of inflammation, sufficient merely to seal the fimbriated end of the tube. It accounts for nearly a fifth of the tubal lesions, but pyosalpinx or at any rate active salpingitis, in the form of simple, œdematous, indurative or suppurative states, runs it close. Hæmatosalpinx is mostly an occasional incident of hydrosalpinx. A tubo-ovarian abcess forms about 2 per cent. of these lesions. Tubal tuberculosis, fibrous inflammation, and tubo-ovarian cysts are less, and a tubal pregnancy still less frequent. The adhesions resulting from these tubal lesions are dense and troublesome according to the degree and extent of the salpingitis. Among the ovarian lesions a cystic condition is the commonest; not the multilocular cystoma, for it is rare, but a Graafian follicle or corpus luteum cyst or some other form of simple cyst. It constitutes about one-third of all the ovarian lesions. Papillary and also dermoid cysts, the latter particularly, are of occasional occurrence. So is malignant disease, though less often than a dermoid cyst. Fibromata, interstitial oöphoritis and parovarian cysts are among the rarer lesions. Hypertrophy of the ovarian follicles and endarteritis are occasionally found. These tubal and ovarian diseases are in many instances antecedent to the growth of the uterine tumours and their simultaneous incidence is purely accidental. Blood vessels of considerable size, often tortuous and long, may pass between the tubes or ovaries and the tumours. Serious hæmorrhage may follow their rupture, a not unlikely event on account of the free mobility of many of these tumours.

It is not necessary to give more than a very brief account of the other complications of subserous fibroids. The round ligaments may be stretched or hypertrophied; the utero-ovarian ligaments cystic, hypertrophied or show tumour growth. The broad ligaments may show dilated vessels, be œdematously thickened or the seat of an abscess, a hæmatoma or a fibroid tumour. A varicose condition of the pelvic veins or thrombosis of the veins and œdema of the legs are occasionally seen. The ureters are most likely to be involved by

growths which invade the broad ligaments, but pressure effects may arise in other fibroids also and produce dilated ureters and hydronephrosis. This occurs with sufficient frequency to necessitate a careful examination of the urine prior to every hysterectomy. Ascites is a rare complication and when it does occur, is almost always due to some condition (*e.g.*, cardiac disease) entirely independent of the fibroid, though, in a very few cases, it may be ascribed to a torsion of the pedicle or other obstruction to the circulation caused by the fibroid.

Torsion of fibroids may arise at the cervix uteri when a fundal tumour grows upwards into the abdomen, lengthening and narrowing the cervix, so that a torsion of the fibroid uterine body upon the cervix is made easy, or it may occur in the pedicle of a subserous fibroid, the tumour itself in this case twisting upon the body of the uterus. The latter condition is more common than the former and minor degrees of it are in all probability fairly frequent.

The submucous variety. This variety, like the others, may be small or large, single or numerous. It alters the *shape* of the uterus less than the others. It is important to remember that it may cause the uterus to assume the shape, characteristic of pregnancy, particularly in its early months. Its rapidity of growth varies. When it ceases to be encapsulated by losing its covering of uterine muscle upon the side projecting towards the uterine cavity, its growth becomes slower but its protrusion towards the cavity becomes more marked. Its base of attachment may remain broad or become gradually pedunculated. In the latter case it may assume the shape of a polypus projecting into the uterine cavity (vide Fig. 13). When large it may be forced downwards, by uterine contractions, through the cervix into the vagina, where it may acquire fresh adhesions or become strangulated by the cervix and slough away (vide Fig. 14). Partial or total inversion of the uterus may attend its attempts at expulsion (vide Fig. 15). The necrosis is the result of the diminished blood supply and the sloughing of an invasion by germs. Owing to the fact that germs are rare within the uterine cavity, but common within the vagina, sloughing occurs, rarely in intrauterine compared with intravaginal growths, whilst necrotic changes occur not infrequently in both situations (vide Fig. 16). Intravaginal growths often assume a globular shape, a grey, green, red, brown, black or mottled colour, a rough surface (from erosion and deposit of fibrin) and either a tough, stringy or friable consistence. Their microscopic appearances vary with their duration, and the amount of inflammatory reaction which has taken place. In the main they consist of necrosed fibroid tissue showing bacteria particularly in their superficial parts and occluding some of the veins which are often thrombosed. In the more acute cases, fibrin on the surface, polymorphonuclear and other leucocytes invading the substance may be seen. In the

chronic cases, a definite amount of granulation tissue may be present in the deeper parts. Ulceration and sloughing of fibroids give rise to hæmorrhagic and offensive discharges. The loss of blood is occasionally so copious and sudden as to raise suspicions of abortion or of cancer. Actual pain, dysmenorrhœa, fever and indeed all acute symptoms are uncommon. It is more a condition of general ill-health, of semi-invalidism; an anæmic condition due to the repeated losses of blood, malaise and emaciation, caused by septic absorption along with cardiac dilatation, hæmic murmurs, dropsy and the other signs of the marasmic state.

Causation of fibroids. Nothing is definitely known of their cause. Several factors appear to have a relationship, more or less close, to their appearance, but whether it is merely fortuitous or causative cannot be determined. The following may be briefly noticed: (1) *Age.* Fibroids are practically confined to the period of adult sexual life, very rarely appearing before puberty and not often after the menopause. (2) *Heredity.* It has been held by some writers that the disease shows a tendency to run in families, but the weight of evidence does not support this contention. (3) *Race.* Fibroids are more common in black than in white people. (4) *Sterility.* The relationship between fibroids and sterility is a close one. They are undoubtedly a cause of sterility and it has been suggested that they may also be one of its results, on the ingenious hypothesis that, if the adult uterus is not kept relatively busy by repeated pregnancies, it may turn its activities to the formation of fibroids. (5) *Cell rests.* From the hypothetical standpoint, the origin of myomata, as of other tumours, from cell rests is, in a sense, satisfactory. But though a diligent search has been made by many writers in an immense number of uteri, no histological evidence of their existence has been forthcoming. Further, if the existence of cell rests be granted, is not a special irritant still required to rouse them into active growth? (6) *Irritation.* Like many other growths an irritation theory has been brought forward, but remains unproven. (7) *The vessels.* The whorled arrangement of the muscle cells in myomata and their general relationship to the blood vessels are suggestive of a genetic connection between them and much work has been done in this field ever since Klebs first enumerated the doctrine, that the growths take their origin in the muscular walls of the vessels. Young tumours are most suitable for investigation, but the histological methods so far available have not led to any general conclusion, for, though some of the workers have inclined to support the theory, others are against it. Most writers still adhere to the opinion that the tumours originate in the muscle of the uterine wall. (8) *Blood extravasations.* It has been suggested that small accidental blood extravasations may provide the stimulus, which starts the aberrant growth of muscle cells, but no evidence has been produced in its

support. (9) *Bacteria.* In a search into the possible causes of any disease, bacteria have always to be considered. But, though some speculations have been made, no proof has ever been forthcoming, that they have anything to do with the causation of myomata.

Growth of Fibroids. The rate of growth of fibroids is usually slow and progressive until the menopause, which they may postpone to some extent. Occasionally it is rapid, so that the tumours reach a large size in a few months. Sometimes they remain nearly stationary for months or even years. True growth is rare after the menopause, though increase in size is not uncommon. This is mostly due to degeneration and not to growth, except in sarcomatous reversion. This conclusion may be safely made when the increase in size is rapid and sudden. These degenerative and necrotic changes are of great importance both in the systematic study of the tumours, and in their practical treatment.

Influence upon Fecundity. The statistics, bearing upon the sterility of women who suffer from fibroids, show a high percentage of both complete and partial barrenness. In 50 per cent., approximately, pregnancy has never occurred, and among the remainder, the majority have borne only one child. Even in those with more than one child, the numbers of the children are fewer than those of mothers free from fibroids. It is, indeed, rare for the victim of fibroids to have a large family. These statistics no doubt over state the case, as in many of the patients other causes of sterility, such as diseased tubes or ovaries, are at work as well.

Influence upon Pregnancy and Parturition. Though fibroids prevent conception sufficiently often to be regarded as an important cause of sterility, they do not always do so. Conception frequently occurs and the subsequent pregnancy and parturition may run their normal course despite the presence of fibroids. When the fibroids are of moderate size there is every reason to hope that the course, both of the pregnancy and of parturition, will be favourable; and even if they be large, interference should not be resorted to, unless symptoms appear which make a favourable termination improbable.

It is sometimes said that pregnancy favours the growth of fibroids, and thus helps them to cause future trouble. But, though they may increase considerably in size with the advent of pregnancy and diminish in an equal way during the puerperium, it is doubtful if this is owing to a true growth. More likely it is due to the establishment and disappearance of an œdematous state. Fibroids also influence pregnancy in other ways. Both post partum hæmorrhage and septic infection occur more frequently when they are present than when they are absent. Moreover, congestive, degenerative and necrotic changes occur with greater frequency, probably from the greater mobility of the involuting uterus and the greater liability of the tumours to torsions.

Retrogressive Changes within the Fibroids. It is convenient to arrange them in two divisions according as they are attended by a diminution or an enlargement of the tumour mass. They are, however, not mutually exclusive, but overlap one another considerably.

A Diminution in Size. 1. *Atrophy.* The tumours may undergo atrophy at any time, and are particularly liable to do so after the menopause. But, though they may become greatly diminished in size, their complete disappearance is very improbable. The belief that they frequently disappeared spontaneously after the menopause was generally held until a few years ago. It led to the general adoption of the expectant method of treatment for all cases, and has thereby condemned many women to a life of semi-invalidism for years, only to face an operation in the end, when they are much less fitted for it. Good results have undoubtedly been obtained from it, and it should still be followed where the fibroids cause little or no trouble. On the other hand, whenever symptoms have become noticeable or at all troublesome, it is better for the patient to have recourse to operative treatment. She is in a fitter state of health for the operation and it will save her from a long period of chronic ill-health. The histological changes accompanying atrophy are arrived at largely from our knowledge of atrophy in general. It may be simple or degenerative, the fatty form being common. It affects the muscular more than the fibrous connective tissue. The latter may, indeed, show some compensatory hyperplasia, in the earlier stages at any rate, and by its subsequent contraction aid in the diminution of size of the tumour. A failing blood supply is, in all probability, the cause of the atrophy, but its manner of occurrence, whether by a vascular sclerosis, or compression by active uterine contractions or by other means, is largely a matter of conjecture.

2. *Fatty Degeneration.* Areas of fatty degeneration of sufficient size and degree to be detected by the unaided eye are not common. They form soft, yellow, irregularly shaped areas in one or more parts of the tumour, and are usually accompanied by other forms of degeneration. Occasionally the whole tumour shows this advanced fatty change. A more diffuse and less advanced degree of this degeneration is met with much more frequently. It usually requires the help of the microscope, and often of the special stains for fat, for its demonstration. In its early stages it takes the form of minute droplets of fat within the protoplasm of the muscle fibres.

3. *Calcification.* A slight degree of calcification, recognised by the grittiness experienced when the tumour is sectioned or by the intense blue colour it strikes with hæmatein when examined under the microscope, is not infrequent in many slowly growing tumours. More advanced stages are also met with in which the change is largely limited to the peripheral parts of the growth, constituting

a sort of shell, or distributed in regular patches or diffusely like a network throughout its substance (vide Fig. 17). It may be complete, converting the tumour into a rough mass as hard as a stone, the so-called " womb-stone " (vide Fig. 18). It must be remembered that this is not a primary change. It never arises except as a sequel to some other degenerative (*e.g. fatty*) or necrotic process. It is met with mostly in elderly patients, about 50 being the most likely age. It may appear in any fibroid, but is oftenest found in the peripheral parts of subserous tumours.

4. *Erosion, Disintegration and Sloughing.* Subserous fibroids, which have established a connection with the lumen of the bowel, are liable to lose some part of their substance by suppuration, disintegration and sloughing, but it is chiefly in submucous growths that these processes occur, either whilst still retained within the uterus (vide Fig. 16), or after extrusion through the cervix (vide Fig. 14), or outside the vulva. Large parts, or even the whole (though this is uncommon) of a tumour may be got rid of in this way, with both local and general relief to the patient, relief which is unfortunately temporary only in most cases, but one which may be experienced several times by a recurrence of the disintegrating processes. The subsidence of the acute stages may be followed by much fibroid induration, resulting in marked diminution in size. It is to be remembered, however, that these processes are largely hastened by the activity of pyogenetic, disintegrating and putrefying bacteria, and consequently attended by a varying degree of blood poisoning. They are responsible for the hæmorrhagic, purulent and other offensive vaginal discharges and for the fever, anæmia, malaise, emaciation, and general ill-health which will sooner or later undermine the constitution of these patients.

B. Increase in size. The enlargement in size, which accompanies the degenerative changes, is variable both in time and degree. It may be slow and progressive, but is more likely to be iregular. It is not infrequently sudden, particularly at the menopause, so much so that a sure diagnosis of uterine fibroid may be made when a pelvic tumour undergoes a rapid and painless enlargement at this period.

1. *Œdema.* An œdematous change may appear in any fibroid, but it is probably most common in the large, solitary, interstitial variety. It varies both in extent and rapidity of onset. While it may affect the whole of a solitary growth, though rarely of multiple tumours, it is often of sufficient extent to cause a noticeable increase in their size. There is reason to believe that it comes on fairly rapidly, sometimes suddenly, in many cases It is difficult to trace its method of production. At the best it is based upon speculative considerations referable to the failing circulation resulting from a sclerosis of the arteries, to torsions of the tumours, to irregular

uterine contractions, to an enfeebled cardiac action, and the like. Under the microscope the lymph spaces are distended and the individual muscular fibres separated from one another and rendered more distinct. Some of the spaces undergo considerable distension to form sinus-like and other irregular cavities or cysts (vide Figs. 19, 20). The distension may be great, constituting what is known as a "lymphangiectatic cyst," often of large size (vide Fig. 20). There may be only one or many such cysts (vide Figs. 24 and 25). Where they are very numerous and of varying size, the tumour may present a striking resemblance to a multilocular ovarian cyst, both in its clinical signs and in its general macroscopic appearances. The lining wall is usually smooth, showing a definite endothelial cellular layer, like that of a lymph cavity, but their lymphangiectatic nature is not negatived by its absence. Their increase in size is favoured by degenerative changes in the surrounding tissues. These changes advance more quickly in the muscular strands than in the older fibro-muscular bands, particularly around the blood vessels. The greater persistence of the latter may confer a sculptured appearance upon the walls of the cavities, not unlike the columnæ carneæ of the cardiac ventricles. The fluid itself is clear and colourless, or slightly opaque and pale yellow. Its composition is much the same as that of the lymph. It does not coagulate spontaneously within the body, though it occasionally does, after removal of the tumour and on exposure to the air. Immersion in formalin has the same effect (vide Fig. 21).

The explanation of the formation of these lymphangiectatic cysts is unsatisfactory. It seems to be clear that they are primarily due to retarded lymphatic outflow, but it is difficult to understand how the mere force of the lymph flow can lead to the formation of cysts of such large size. The pressure of the fluid within the cysts must surely soon rise above the pressure of the lymph in the various lymphatic vessels and spaces which drain into the cyst! An active secretion by the endothelial cells lining the cyst wall has been put forward, accordingly, as the probable explanation of these extreme cystic developments, whether met with in fibroids or in other situations such as the large, tense, fluid swellings in the submaxillary and neighbouring regions known as *cystic hygromata*, which are composed of a collection of large cysts, separated from one another by fibroid walls, lined by endothelium and containing clear fluid, like lymph. But, though there is some evidence in favour of an active secretion, it has not been proved to occur and the mode of formation of these large cysts, in the uterus as elsewhere, remains obscure.

Not the least interesting point in connection with œdema, is the possible influence upon growth exerted by the prolonged bathing of the tumour cells in an excess of nutritive fluid, and by their comparative freedom from mutual pressure. It is true that the fluid, being some-

what stale, has a diminished nutritive value, and contains a greater amount of effete products than does the ordinary lymph, and that active growth is not a characteristic of a dropsical condition of tissues generally. Nevertheless it may stimulate growth in a fibroid, whose vegetative activities are naturally more active than those of the adult tissues, but whether it can ever heighten them to the standard usually recognised as sarcomatous, may well be doubted (vide Figs. 66 and 67). If it could start in this way, mitotic figures ought to be commoner in the cells of an œdematous part than elsewhere in fibroids, and this has certainly not been the writer's own experience, except in cases where other important influences have been present at the same time.

2. *Myxomatous Degeneration.* Fibroids often show, in many parts, a structure characteristic of a myxomatous tissue, viz. branched cells in a jelly-like or sparsely fibrous matrix. It is a condition which is seen in other tumours, and in many inflammatory growths whose return circulation is interfered with. The mucous polypus of the nose is an illustrative example. All the indications go to show that the myxomatous appearance of fibroids is really explainable by a similar œdematous change and not by a true myxomatous degeneration.

3. *Hyaline Degeneration.* The conversion of portions of a fibroid into a smooth, glassy homogeneous substance is spoken of as a hyaline change, one of the most characteristic alterations met with in these tumours. It is common in minor degrees, recognisable only with the aid of the microscope, being present in most if not in all fibroids. But it is not nearly so common in major degrees, sufficiently pronounced to be detected readily by the unaided eye, its frequency being about 5 per cent. It occurs in patches or large masses of varying shape, though often rounded, having a white, grey or pale yellow colour, sometimes tinged with shades of pink, red, brown or blue (vide Figs. 21, 24, 25 and 26). They have a firm consistence, and cut like cartilage. They are best marked in large tumours, particularly towards their centre, and also in the distal peripheral parts of subserous growths. Under the microscope they exhibit a homogeneous or slightly fibrous and structureless appearance (vide Figs. 22 and 23). Selective stains such as Van Gieson's, which pick out muscle from fibrous tissue, are preferable to non-selective stains such as eosin for its study. The former stains it red when it is young, and yellow when it is old, whilst the latter always colours it red. It is difficult to trace the evolution of the change. In its early stages it appears to affect only the interstitial fibrous tissue, and not the muscle fibres. The latter can often be shown to contain fat globules. The early changes thus suggest a coincident fatty degeneration of the muscle, and a hyaline transformation of the connective tissue fibres. As the process advances, it is difficult

even with the help of the best selective stains to say whether or not the hyaline transformation spreads to the muscle and several writers assert that it does, but the appearances seem to the present writer to favour the opinion that the muscle only undergoes a degenerative atrophy. Its final disappearance is helped by the pressure of the increasing hyaline substance, in the formation of which it plays therefore only a passive part (vide Fig. 23). It is noteworthy that the hyaline transformation usually affects the parts of the tumours most remote from a free blood supply, though it is occasionally well marked in the walls of the blood vessels themselves. A similar hyaline change is common in the fibrous stromas of other tumours, in enlarged lymphatic glands, in the renal glomeruli in chronic nephritis, in scar tissue generally and the like. It affects only abnormal fibrous tissues, not muscle, and is closely related to a deficient blood supply. It is more of the nature of a necrosis than of a degeneration, and its appearanecs are probably the result as much of a physical as of a chemical change. It is, therefore, probable that the so-called "hyaline degeneration" of fibroids is secondary to some degenerative process, primarily affecting the muscle as a fatty or allied change, and that the hyaline swelling affects only the physical or otherwise altered interstitial connective tissue, and never the muscle. It is certainly the case that other degenerative changes both accompany and follow upon it. Œdema is frequent, both as a forerunner and a contemporary. Fatty degeneration is sometimes prominent. True amyloid or waxy degeneration has been observed. Soft, or even liquid, foci appear within the hyaline mass, giving rise to pseudocysts (vide Figs. 21 and 24). They have been ascribed, on somewhat insufficient evidence, to a form of mucinoid softening, sometimes wrongly termed colloid. Hæmorrhage may arise into the cavity of a true or false cyst. Occasionally it is very free and forms a hæmatoma filling a large cyst and at times constituting the main bulk of the tumour.

4. *Necrosis and Softening.* Necrotic and disintegrating foci of varying size and number occur with moderate frequency within fibroid tumours of all varieties, particularly in large ones. They vary in colour and consistence, and lead to the formation of irregular cavities containing pigmented debris and fiuid (vide Figs. 26, 27, 28, and 29). They may resemble an abscess macroscopically, but when examined under the microscope, the characteristic signs of inflammation are absent. There are neither polymorphonuclear leucocytes nor bacteria to be seen, except occasionally, and in such small numbers as to indicate a secondary and accidental invasion. Strands of fibrin are sometimes present, but they can be traced to hæmorrhages or thromboses. Autolytic and not bacterial ferments must be the cause of this softening. The degenerative and necrotic

processes, which precede the softening, bring about the liberation of these ferments. In the walls of cavities and in the surrounding tumour substance various retrogressive changes are visible, viz., œdema, hyaline, a fatty degenerative, coagulative, and colliquitive necrosis. Blood may be poured out into the cavities and infiltrate the surrounding walls. Torsions and other influences which lessen the blood supply and disturb the circulation may lead to necrosis within fibroids similar in character to the anæmic, and occasionally to the hæmorrhagic, infarcts of the organs supplied by the so-called "end arteries." The uterine arteries are not "end arteries," but fibroids are much less vascular than the uterine muscle, and much more liable to circulatory disturbances, and patches of necrosis, suggestive of this method of causation, are not infrequent. Both macroscopically and microscopically these tumours, particularly the submucous forms, may present all the features of a bland hæmorrhagic infarct (vide Figs. 29, 30, 32, 33, and 34). Some of the cases described as showing angiomatous degeneration of a fibroid, may possibly be of this nature. Moreover in many fibroids there are varying sized areas of a deep red colour, which show similarly distended vessels, containing thrombi or blood separated by degenerations or necroses. These areas are often spoken of as being due to the presence of thrombosed and distended veins, but they may really be small infarcts.

5. *Suppuration and Gangrene.* Suppuration may occur within either a perfectly healthy or a degenerating fibroid after invasion by pyogenetic germs. These germs may enter from the vagina, the intestine, the Fallopian tubes or ovaries, the bladder, or by the blood stream, and the abscess may discharge itself by any of these paths, or into the peritoneal cavity. Gangrene is a common sequel.

6. *Angiomatous Degeneration.* Though fibroids as a class are poorly supplied with blood vessels, it occasionally happens that blood vessels become so numerous as to impart an angiomatous character to growth. This change is regarded as degenerative in nature, since it is only found in tumours showing other retrogressive features.

7. *Red Necrosis.* When a fibroid exhibits a red colour of its necrosed parts, it is said to have undergone red necrosis (vide Fig. 35). This retrogressive change has long been a subject of interest and discussion. The shade of colour varies from a pale to a dark red hue. While it often involves the whole substance of the tumour, more or less equally, it may appear in patches only, and is particularly likely to begin and be most marked at the periphery. Its consistence is firm, and it is less elastic than the normal fibroid tissue. Under the microscope it exhibits the architectural structure of a fibroid. The fibro-muscular bundles and the blood vessels apparently preserve their normal relationships and grosser structure, except that they are dead and do not stain with the ordinary dyes.

Fat globules and pigment granules may be abundant. Hæmorrhage may be present, but not in sufficient amount to account for the colour, which appears to be due mainly to a solution of hæmoglobin. Thrombosis within both arteries and veins may be seen, especially at the periphery, but it is not clear whether it is of primary or secondary occurrence. Poisons allied to the amines have been found, and they, along with a tendency to bacterial infection, may account for toxæmia or sapremia, which may become pronounced in these cases. Though the causation of this peculiar form of necrosis has been much discussed, it has not been successfully explained. It is probably produced more rapidly than other forms of necrosis, since pain is frequently a prominent symptom. It seems also to be related in some way to pregnancy, for it occurs oftener during pregnancy and during the puerperium than at other times. This relation is not essential, however, for it is met with in women who have never been pregnant. Bacteria have been sought for most diligently of late years, by many workers. Staphylococci and bacilli have been found in a few cases, but only in such numbers and surroundings as to suggest their secondary and accidental advent. In most cases, on the other hand, no bacteria have been found, and the question remains for future settlement. No parallel condition to red necrosis occurs elsewhere, and the rapid hæmolysis which gives the special character to it is still unexplainable. A rapid bacterial invasion might produce the red colour either by hæmolysis or by special pigment formation, and as rapidly disappear as a result of bacteriolysis. Investigation, if undertaken early enough, may help to solve this question.

8. *Sarcomatous Degeneration.* The consideration of this obscure and interesting form comes more conveniently under the heading of malignant tumours.

II.—THE ADENOMYOMA.

The pathological features of the adenomyoma differ from those of the myoma in two main characteristics. It is a diffuse and not a circumscribed growth, and it contains islands of endometrial tissue throughout its substance. The former character prevents it from being easily shelled out. It is devoid of the loose cellular bed which bounds the myoma, blending at its margins insensibly with the uterine muscle (vide Fig. 36). This character becomes more obvious when adenomyomatous and discrete myomatous growths co-exist in the same case (vide Fig. 37). The adenomyoma may occupy the anterior, posterior, or lateral walls of the uterus and always reaches the endometrium internally. It is generally of moderate size. The second characteristic, viz., the presence of islands of endometrial tissue within the muscle, presents the appearance of spaces or chinks within the substance of the growth, impart-

ing to it a sponge-like appearance when the chinks are close together. A muscular variety with few and a glandular variety with many tubules occur. Under the microscope these spaces, often branching in a comb-like fashion, are seen to be lined by columnar epithelium, possessing glands and usually also a certain amount of cellular tissue, all exactly like that of the endometrium. They appear to be minute uterine cavities, the tubules showing no signs of active growth (vide Figs. 38 and 39). In all other respects the minute structure of the tumour is the same as that of the myoma, and if these interstitial endometrial spaces occurred only in the near neighbourhood of the uterine mucosa, it would appear natural to regard them as merely prolongations of it, but they may occur everywhere throughout the tumour, even so far as the peritoneal coat. Notwithstanding this, writers are now mostly agreed that they take their origin in this way. By means of serial sections even the most distant spaces can be shown to be in direct continuity with prolongations from the uterine cavity, and in instances where this can no longer be demonstrated, it is easy to understand how they may have got cut off in the course of the growth of the muscle bundles of the tumour. Even in the normal uterus the mucosa may dip in for some distance into the muscular coat and the adenomyoma may, unlike the myoma, always begin close to the mucosa, when it would be easy for portions of the latter to become entangled within the growing muscular fibres. In the prolongations closest to the mucosa, the tubes run perpendicularly to the uterine cavity, but they soon get pushed out of position by the growing muscle bundles, whose course they follow as the way of least resistance. They run parallel with them for a time, but owing to the irregularity of the course of the muscle bundles, they come to get nipped off and pushed further out until they may be found in any part of the substance of the tumour. Some of these isolated spaces may become distended into cysts. Fig. 39 shows the beginning of this process. Lymphangiectatic and telangiectatic cysts also occur occasionally in these growths; hence the names adenomyoma cysticum and adenomyoma telangiectaticum. Whilst this method of origin of these interstitial spaces is gaining adherents among pathologists, Recklinghausen's theory of origin, enunciated some years ago, is still supported by several writers. This distinguished pathologist, noting the resemblance of the tubes within an adenomyoma to the comb-like appearance of the Wolffian body within the broad ligament, suggested that these tumours represented the inclusion within the uterine wall of the upper end of the Wolffian duct, whose muscular coat had undergone overgrowth. He failed to explain why these tumours should be so much more common in the body of the uterus, above the site of entrance of the Wolffian duct into the uterine wall, than in the cervical region below it. But the later evidence obtained by

means of serial sections has done more than such theoretical objections to upset Recklinghausen's theory. Moreover, altered blood and blood pigments have been found within these interstitial spaces, suggesting that they function as miniature uterine cavities and participate in the menstrual congestions and swellings, thus explaining the pain so often experienced by the patients at the menstrual periods. A somewhat parallel condition, as shown by Aschoff, occurs in some subserous myomata, in so far as peritoneal down growths may invade the substance of myomata and take on glandular characters. Increase of the ordinary menstrual discharge is another feature often present in these tumours, and it is explainable on the supposition that many of these spaces are still in communication with the uterine cavity. Though intermenstrual discharge is rare, it occurs more frequently in adenomyomata than in myomata. In still another point do the former differ from the latter in so far as they do not appear to offer any hindrance to conception. Again, while both are essentially benign growths, they (particularly the adenomyoma) are so often accompanied by malignant disease within the uterus, ovary or tubes, that it is difficult to regard the association as entirely accidental in character. Fig. 36 shows the co-existence of an adenomyoma of the uterus and of a sarcoma of the ovary. Cases of cancer arising in the mucosa covering an adenomyomatous tumour are on record, in some of which the benign tubes of the latter seem to run up to and even among the malignant tubes of the former. The juxtaposition is such, that it naturally suggests the transformation of the simple into the malignant adenomatous tubes. Fig. 40 shows a surface cancer growing superficially to an island of simple adenomatous structure within the substance of a diffuse fibroid at some distance from it. In this case no direct continuity could be demonstrated between the two orders of tubes. They appear to have originated independently of one another and all the evidence seems to the writer to point in the same direction, even when a topographical continuity can be shown to exist. There is no reason to believe that the simple growth ever originates the malignant one, but there may be some unknown underlying factor connected with both the myoma and the adenomyoma which favours the subsequent development of a cancer. It is difficult to account for the frequency of the co-existence of fibroids and of cancer, which will be referred to again, except upon some such hypothesis. Although a begnign tumour, the adenomyoma often causes more active symptoms and becomes more dangerous to the general health than the myoma.

III.—Other Benign Tumours.

The practical importance of the other benign growths of the uterine body is slight. Myxomas, fibromas, chondromas, osteomas, and adenomas have been described, but they seem mostly to have

been altered and degenerated myomas. The lipoma occurs in the cervix as a polypus, not in the corpus uteri, and the dermoid cyst occasionally occurs in the form of polypoid outgrowths. The placental mole is in most cases (about 70 per cent.) a benign uterine tumour, but its consideration is deferred until the chorioepithelioma is described.

Short Synopsis of Fibroids.

1. The vast majority is entirely innocent.
2. A large proportion of them impairs the general health.
3. All are potentially dangerous, either by (1) retrogressive changes which are liable to appear as soon as even a moderate size is attained; (2) the acquisition of malignant characters, which occurs in 2 per cent. approximately; or by (3) coincident inflammatory states of the uterine adnexa.
4. Atrophy and diminution in size may occur at the menopause, but spontaneous disappearance is doubtful.
5. Surgical removal is the only certain means of cure, and should be adopted whenever symptoms become marked. The mortality is less than 2 per cent.

B.—MALIGNANT TUMOURS.

I.—Sarcomatous Degeneration in Fibroids.

A certain proportion (probably under 2 per cent.) of fibroids, which come to operation, shows histological changes apparently indicative of malignancy. They are referred to by writers under various names, of which sarcomatous degeneration or transformation seems to be the most convenient. Their presence can never be determined with certainty until the tumour has been submitted to minute histological examination, though various signs, such as a rapid increase in the size of the tumour, a hæmorrhagic or offensive vaginal discharge, or onset of pain, may arouse suspicion in the mind of the clinician. The nature of these changes, their time, method of evolution and their cause are imperfectly known at the present time, and are deserving of further study. Sarcomata in general vary greatly in their degree of malignancy. In the absence of metastases, this rests upon their histological characters, and their behaviour to the tissues surrounding them. Of these, the vegetative nature or the grade of vegetative power of the cells is the most important. The comparative absence of matrix, the rudimentariness of the vessel walls, the tendency to central degenerative and necrotic changes, are useful additional signs, though merely the natural outcome of the first. Fibroids in which sarcomatous degeneration has occurred rarely give rise to metastases, and their degree of

malignancy must be determined in most cases by their histological characters.

But when recurrence does arise all doubt as to malignancy ceases. Figs. 41 to 44 are from a case of this kind. The patient was 55 years of age when she began to suffer from attacks of abdominal pain. The menopause, which occurred at the age of 47, was uneventful, and the health was good until the attacks of pain began. They continued during the next two years, becoming worse during the last three months. During the last six weeks of this time she noticed a swelling in the abdomen, which had steadily increased. She was then 57 years of age, and had the appearance of a fairly healthy, well-nourished woman. Mr. Hewetson, whom she consulted, found that she had a large, smooth and firm tumour of the uterus, extending upwards as high as the umbilicus, where it was of a soft and almost cystic consistence. He removed it by abdominal total hysterectomy, and the patient did well. She enjoyed good health for about six months, when she again began to suffer from pain, swelling and other symptoms. Mr. Hewetson then found that large and numerous secondary tumours had arisen, not only in the pelvis, but within the abdomen, and to these she presently succumbed. It seems certain therefore that the primary tumour was malignant, either from the start or from a later date. Examination of the tumour itself, a section of which is seen in Fig. 41, discloses a suspicious-looking softened area towards its upper part, whilst the rest, constituting about four-fifths of the whole, presents the appearances of an ordinary fibroid, except for some œdema and hyaline degeneration. This was corroborated under the microscope, for sections taken from different parts of this fibroid-looking tumour, presented the usual histological characters of an old fibroid of the ordinary kind, whereas the structure of the apical softened area was different. It consisted almost entirely of cells of varying size and shape, with little or no matrix and rudimentary blood vessels, as disclosed in the Figs. 42 to 44; in short, of the vegetative features, so characteristic of a sarcoma. The subsequent history of the case establishes the correctness of this interpretation. In such cases, a small minority, a sarcomatous reversion seems undoubted. But in the great majority it is not so clear, since recurrence does not arise, for it is rarer in the case of fibroids than in ordinary sarcomata, partly, no doubt, due to a low degree of malignancy, but partly also, to a difference in the anatomical relationships in the two cases.

Removal is wider and freer in the fibroid than in the sarcoma elsewhere. In the former the sarcomatous growth lies within the fibroid, a condition of *tumor in tumore*, as it were, which, in turn, lies more or less within the uterine wall. Hysterectomy, therefore, removes the sarcoma with a freedom which it is difficult to secure

in other situations. Moreover, removal is accomplished earlier than in the case of other sarcomata, operation being undertaken with the object of getting rid of the fibroid. A sarcomatous growth within it, though at times suspected beforehand, is only determined after a minute histological examination. It appear to occur in fewer cases than formerly, probably because removal of fibroid tumours is now undertaken both earlier and oftener. It gives rise to one or more patches often sufficiently distinctive to be picked out by the unaided eye. They vary in size and shape. The whorled and fasciculated appearance typical of the fibroid is replaced in them by a homogeneous or slightly granular white, pale grey, or yellow substance, likened sometimes to raw pork. Recent and old hæmorrhages appear within them. Their consistence is often firm, but is liable to become soft, spongy or cystic from the intervention of œdema, degeneration or necrosis. Pseudo-cysts and true cysts (both lymphangiectatic and telangiectatic) may be present. Hæmorrhagic foci, which at times reach a large size, are not uncommon.

These appearances, whilst they are suggestive, are not distinctive of malignancy, for closely similar changes are met with in some of the benign degenerative changes, and it is only when they are examined under the microscope that the difference in their character can be determined. Figs. 45 to 48. are taken from a case which serves to illustrate this difficulty. There was nothing in the clinical history of the case to suggest to the surgeon that the growth was not in its entirety an ordinary simple fibroid, but on sectioning the tumour (vide Fig. 45) he noticed one or two areas of a darker and more homogeneous appearance than the rest, and sent it to the writer for examination. These foci were found to be cellular in structure (vide Figs. 46 to 48), presenting the main histological characters of sarcomatous tissue. The subsequent history of this case could not, unfortunately, be obtained. The foci thus met with in fibroids are essentially cellular in structure with scanty intercellular substance and rudimentary blood vessels, recalling at once the appearances presented by a typical sarcoma. The cells vary so much in different cases and even in different parts of the same tumour, that it is difficult for any general description to give a satisfactory picture of them, and it will be found necessary to supplement the account herein given by a reference to the accompanying illustrations and to other cases published in gynæcological literature. The cells conform in many cases to two types—the one a non-striped muscle cell, and the other a connective-tissue cell type.

In the former or myoblast type, the cells are rather large, elongated in shape, with large oval or elliptical nuclei and a good deal of protoplasm. By close superimposition they form bundles which interlace in every direction. There is little or no intercellular substance, and the blood vessels are fairly numerous and capillary-

like. The general appearance is strikingly like a young actively growing part of a pure myoma, but the texture is opener in places, and the cells at times are large and may possess two nuclei (vide Figs. 49 and 50). Multinucleated cells or cell masses occur occasionally, but mitotic figures are rare. There may be several such cellular foci within a fibroid whose structure otherwise is constituted by old well-formed fibro-muscular tissue, into which the young growth seems to fade insensibly. In the other, or fibroblast type, there is greater irregularity in the size and shape of the cells. They are not superimposed upon one another, but are scattered, or at times clustered together, in a more or less plentiful granular or finely fibrillated matrix. Cells with more than one nuclei are common, and multinucleated cells or giant cell masses and mitotic figures are met with more frequently than in the myoblast type. The nuclei stain irregularly and often very deeply (vide Figs. 51 and 52). The blood vessels may have a single layer only of flattened cells or many layers of cells similar to, and contiguous with, those of the tumour; arranged at first concentrically around the lumen, they soon open out and straggle irregularly, becoming indistinguishable from the rest of the tumour cells. A study of these cells may disclose signs indicating that those nearest the lumen are younger than those further away, thus suggesting a genetic relationship between them, and a mode of origin and spread of the tumour growth; new blood vessels being first formed as buds from the pre-existing vessels, and thereafter that the new tumour cells are the offspring of the vegetative activity of some of the cells which form the walls of these new vessels, vide Fig. 53. When hyaline and other degenerative conversions supervene, they naturally affect the older parts of the growths, and may spare the younger cells immediately around the vessels. In this way the latter may present a picture of cellular cylinders running through a homogeneous matrix, a form of sarcoma often spoken of as a *cylindroma*. This is exemplified by the case from which Figs. 54 to 57 are taken. The uterus is the seat of a tumour growth, which has caused considerable, though uniform, enlargement of the organ, and has eaten its way through its lateral wall, forming an irregular tumour mass, which infiltrated the pelvic structures. The main body of the tumour (vide Fig. 55) had all the appearances of an ordinary old fibroid, but that portion of it which had eroded the uterine wall and formed the extrauterine growth was different. It presented (vide Figs. 56 and 57) the characters of a sarcoma of the cylindromatous type. The subsequent history of this case is not available, but there can be little doubt, from its histological characters and locally destructive nature, that it is a case of a fibroid which had taken on sarcomatous characters.

Whilst it is probably true that sarcoma in fibroids belongs either

to the myoblast or fibroblast type, or, as will presently be explained, to a still more primitive type of cell, it cannot be claimed that individual cases can be easily ascribed in practice to either of these types. There are indeed many cases in which the structure departs so little from that of a benign fibroid that some slight degree of malignancy is only a remote possibility, and others in which the departures are so much greater, that malignancy becomes correspondingly the more and more probable, until we can assert it with considerable assurance, when the vegetative characters of growth, associated with sarcomatous tissue generally, are present.

Figs. 58 and 59 are taken from a case of considerable interest in this relationship. The patient was a married woman, æt. 62, who had had ten children, the youngest being 20 years old. Her menopause occurred at the age of 53, and for three years afterwards she had no menstrual loss or other symptoms, but thereafter a menstrual discharge again appeared and continued every three weeks until a year ago, when it began to be more frequent and has occurred every few days for the last year. She first noticed a lump in the lower abdomen about a year ago, reaching as high as the umbilicus. She had become somewhat thinner, but had suffered no pain, and seemed a fairly healthy woman at the time she consulted Mr. Hewetson. He found that the tumour, which was connected with the uterus, now filled the whole abdomen. He therefore removed it by abdominal total hysterectomy, experiencing considerable difficulty owing to the extensive adhesions to the omentum, bowel and other structures. The mass weighed 26 lbs. There were several tumours, one, of moderate size, being submucous, and two or three smaller being interstitial, whilst the largest, measuring $12\frac{1}{2}$ inches by $10\frac{1}{2}$ inches by $8\frac{1}{2}$ inches, was subserous (vide Fig. 58). It was this large tumour which had formed the main part of the abdominal swelling and had increased in size during the last year with such alarming rapidity. Its appearances on section suggested a considerably degenerated fibroid rather than a sarcoma, but its fasciculation was indistinct. There were extensive œdema, hyaline degeneration and pseudo-cyst formation, but, in addition, just beneath the capsule, there were scattered areas of a pale, homogeneous, fleshy appearance, which were suggestive of a sarcomatous change. Under the microscope the main bulk of the tumour was shown to be a fibroid of some standing, which had undergone extensive degenerative changes, and it was no doubt largely to them that the recent rapid increase in size of the tumour was due; but the pale, fleshy areas showed a different structure (vide Fig. 59). They were distinctly young and actively growing centres, fibrocellular in structure, with many capillary blood vessels. There can be no doubt that their vegetative activity had contributed considerably to the recent rapid increase in the size of the tumour. Their nature was therefore of grave importance in the

prognosis. From their histological characters alone they cannot be unhesitatingly pronounced to be either benign or malignant. From a consideration of all the clinical and histological facts, which should always be done, a possibility of malignancy must be admitted, though the balance of evidence may be largely in favour of innocency. The patient was quite well at the time of writing, fully four months after the operation.

It is difficult to estimate the proportion in which these different degrees of malignancy occur in fibroids, owing, among other things, to the different interpretations of the histological features of individual cases, which it is possible for even competent authorities to hold. But when due allowance is made for doubtful cases, it is probable that the proportion of fibroids coming to operation, in which a sarcomatous change has occurred, is not far from 2 per cent. of the whole. The alterations in structure, which thus occur, are considerable. They give rise to growths of a cellular character such as are met with in sarcomata of a few weeks or months growth, and they are present within the substance of tumours, whose histological characters and clinical history suggest an existence often of years. They may make their appearance in fibroids, long after the menopause, in women of 60 years of age or more. When did these fibroids arise? Were they present before the menopause? Did they, after undergoing a certain degree of atrophy at that period, become quiescent until the sarcomatous growth developed within them, or did they arise themselves long after the menopause, and not so very long antecedent to the sarcomatous foci? It is difficult to answer these questions. It is the occurrence of bleeding or of a tumour undergoing increase in size, or of some other symptom which induces the surgeon to perform hysterectomy. He can seldom say from his knowledge of the clinical history that the fibroid has been present at or before the menopause. A history of trouble at or before that period has been given in some cases, making it probable that the fibroids were then existent. But the general anatomical and histological characters afford better evidence. They are similar to those of tumours which, there is good reason to believe, have been in existence for years. Such as it is, then, the evidence points to the sarcomatous foci arising as recent growths within very much older tumours, as a result of the vegetative activity in certain hypothetical cell rests, or of an anaplasia, or reversion to embryonic type of certain cells of the fibroid, not any of the fully formed muscle or fibrous tissue cells, for that does not seem possible, but of young, developing myoblasts or fibroblasts. Instead of proceeding to functionate as fully formed supporting tissue cells, after the fashion of ordinary young cells of this class, they revert to their earlier anatomical shapes, and expend their energies in vegetative reproduction. Not only do the two histological types find an explana-

tion on this hypothesis, the reversion affecting the young myoblast in the one case, and the young fibroblast in the other, but the aberrant instances which do not seem to belong to either type, may be referred to a still earlier mother cell, and be looked upon as the result of a reversion to the primitive undifferentiated cell from which the other two types spring. The fixing and staining solutions hitherto used by the pathologist in studying these embryonic foci have not been sufficiently selective to enable him to differentiate these types from one another with any degree of certainty. More success has followed the use of selective stains such as picrocarmine and picrofuchsin (Van Gieson's), than of non-selective stains such as eosin, but the greatest success of all has been obtained by Mallory by fixation in Zenker's fluid and staining with a modification of his aniline blue connective-tissue method. It enables the observer to trace the sarcomatous cells to their myoblastic or fibroblastic progenitors with apparent certainty, and has added the proof hitherto wanting to the opinion, which has long been maintained by pathologists, that the sarcomatous foci which appear in fibroids, might take their origin either in the muscular or the connective-tissue of these tumours. From an examination of the considerable number of cases which have come before him, the writer is inclined to believe that the myomatous origin and nature of such sarcomatous growths are more common than has hitherto been believed. Up to the present time only a small number of cases have been put on record, in which the myomatous nature and origin of both the primary sarcomatous focus and of such metastatic deposits as have occurred, have been clearly established. Another point which has appeared to him to evolve from this examination is the frequency with which the tumour cells could be traced to a development from the walls of the blood vessels, the mesothelium in some cases, the endothelium or perithelium in others, the entire tumour being the product of the endothelium, of the mesothelium, or of the perithelium of the vessels in each case. The first constitutes that form of sarcoma known as an *endothelioma*, the second a new type unknown in other situations, and the third that form known as *perithelioma*, in which the sarcomatous cells spring from the endothelium lining the lymph spaces of the outer coat. It is theoretically possible that the embryonic fibroblasts of the outer coat may, like those of the general substance of the growth, revert and constitute an ordinary round, spindle or irregular celled sarcoma, called, because of its position within the fibroid, a *myoma sarcomatodes*. The new type of sarcoma springing from the myoblasts of the middle coat of the vessels or from other myoblasts throughout the growth is conveniently spoken of as a *myosarcoma*. The name *mesothelioma*, which is naturally suggested by those of *endothelioma* and *perithelioma*, is not available for this variety, as it has already been appropriated for the malignant

growths springing from the endothelium of serous membranes, *e.g.*, the pleura, peritoneum, etc. We thus have a variety of sarcomatous growths arising within fibroids, the *endothelioma*, the *perithelioma*, the *myosarcoma*, and the *myoma sarcomatodes*, which may be the explanation of the relatively low degree of malignancy exhibited by most of these growths. Those originating in fibroblasts, though varying greatly in malignancy, show it in greatest degree, whilst the myosarcoma is the least malignant of all, the other two forms showing varying intermediate degrees.

The following case, from which Figs. 60 to 65 were taken, is an example of this endotheliomatous origin :—

The patient, a married nullipara, whose menopause had occurred two years before, consulted Dr. Wilson in 1903, when she was 44 years old, complaining of an increasing abdominal swelling and of incontinence of urine. She had an interesting previous history of tumour, having undergone two operations by different surgeons. At the first operation, five years previously, a cystic tumour, about the size of a fœtal head, was tapped per vaginam; at the second, 13 months later, a cystic tumour was attacked by abdominal section, but not removed owing to dense adhesions and the collapsed condition of the patient. Dr. Wilson, in 1903, found that the uterine tumour filled the pelvis and extended upwards to the umbilicus. He removed it along with the tubes and ovaries, though the operation was attended with much difficulty owing to the dense and extensive adhesions to the surrounding structures. The patient made an uninterrupted recovery, and was well when last heard of, six years after the operation. The uterus contained three tumours (vide Figs. 60 and 61); the largest, in its anterior wall, was almost entirely converted into a cyst (vide Fig. 62), whilst the other two were solid. The wall of the cyst contained a soft, shiny, homogeneous, waxy-looking material, and the solid tumours contained masses of the same substance between strands of fibro-muscular tissue of varying thickness. This substance has the vegetative histological characters of a sarcoma (vide Figs. 63, 64 and 65), invading, in the case of the two solid tumours at any rate, a fibroid; though in the case of the large cystic growth no fibroid tissue remains. This large cystic growth was probably the primary tumour, since no extirpation was undertaken at the previous operations; but, since no fibroid structure is present in it, the case cannot with certainty be classified under sarcomatous reversion in a fibroid tumour. Extensive telangiectatic and liquefying changes had occurred, and from the presence of other fibroids and a similar sarcomatous invasion of them, it seems probable that this is the interpretation of the case. From the characters of the cells and their relationship to the blood vessels (vide description of Fig. 64), it is probably an example of the peritheliomatous variety of sarcoma.

What is the cause of this sarcomatous reversion? Certain factors seem to favor its occurrence. The menopause is one of these, for the sarcomatous degeneration occurs most frequently about that period, though it may occur both earlier and later. Again, it is more common in multiple fibroids (though it does not often affect more than one of them), than in the solitary tumour. It is equally common in all varieties of fibroid. Earlier writers claim a predominance for the submucous variety, but operative interference was not then resorted to so early as now, and hence many of the really intramural may have been reckoned as submucous tumours. It has been suggested that the œdema or hyaline degeneration, so frequently present in the parts of the fibroid surrounding the sarcomatous foci, may precede and help to bring about the embryonic reversion. It is difficult to see how the hyaline degeneration, being a necrotic process, can have any such influence, and though the œdema may bring about a relief from mutual cell pressure, and a freer supply of nutrient fluid, it can hardly, as already explained, be regarded as able to originate vegetative activity of this kind (vide Figs. 66 and 67 and their descriptions). There is one particularly interesting point in these sarcomatous foci which deserves mention in discussing their causation, and that is the frequency with which a number of them are met with in the same fibroid tumour, and apparently as entirely separate growths, and not outlying parts of the one growth. Are all of them primary and independent centres of growth? But primary sarcomatous growths in other situations are single, and not multiple, the latter being a characteristic of secondary growths. It seems probable then, though practically incapable of proof, that only one of them is primary and that the rest are metastases. Some disturbance of the natural course of growth is all that is necessary to explain the production of this primary focus; something which upsets the (probable unstable) physiological balance of cell activities, directing the whole cell energy, into vegetative growth and multiplication.

II.—Sarcomata.

Tumours with the characters of sarcomata throughout, also occur in the body of the uterus. They are sarcomata from the beginning, comparable to the sarcomata occurring in other situations, though they may present many of the macroscopic appearances of a fibroid, particularly of the intramural variety. They are much rarer than sarcomatous foci within fibroids. They occur either as submucous or as intramural growths. The former originate in the endometrial stroma, and form either a diffuse or polypoid submucous tumour. They may give rise to sudden and profuse hæmorrhage, and are liable to be mistaken either for a simple polypus in younger,

or for a cancer in older patients. The histological examination of curettings will assist the diagnosis in most cases, but it is to be remembered that, even when the whole growth is available for such examination, it is difficult in some cases to say whether the growth represents a benign fibroid or a sarcoma.

Figs. 68 to 72 are taken from a case which could only be diagnosed as a sarcoma from curettings, but which, on fuller investigation, shows an undoubted cancerous growth. The clinical history of the case has not been preserved, but the uterine cavity is completely filled with a large submucous tumour (vide Fig. 68), which on section presents a dull grey fleshy appearance relieved by numerous darker areas of degeneration and hæmorrhage (vide Fig. 69). The remains of the uterine cavity are seen below, and there is a small discrete fibroid in the wall of the uterus to the left. The large size of the tumour is in favour of a fibroid or a sarcoma and not a cancer, which very rarely reaches such dimensions. On microscopic examination all the inner part of the growth presents the characters of a sarcoma, while the outer part which includes the uterine wall shows the structure typical of a columnar-celled epithelioma (vide Figs. 70, 71, and 72). The tumour is thus, apparently, composed of a coexistent sarcoma and cancer, both of which originated in the endometrial tissue.

One variety of sarcoma, the so-called *sarcoma botryoides* forms cyst-like masses, presenting a resemblance to a hydatid mole. It consists of round, spindle and irregular cells in a matrix of clear spaces traversed by a network of fine fibrils and delicate blood-vessels. The intramural variety of sarcoma occurs also as a diffuse and as a localised tumour. Both are indistinguishable clinically from the fibroid, though the rapid increase in size of the uterus may arouse suspicion. They may break through the walls of the uterus, invade the surrounding structures, and cause metastases. The localised form is often strikingly like a fibroid, and the microscope has to be used before its sarcomatous character is revealed. This discloses a picture not unlike that which is found in the sarcomatously degenerated foci already referred to, suggesting an origin either in young fibroblasts or in young myoblasts of the uterine wall.

Fig. 73 gives the appearances on section of a localised intramural tumour, apparently of this class. It is not at all unlike a degenerating fibroid, but on microscopic examination it presented the histological characters, in all parts examined, of a sarcomatous growth originating in the walls of the blood-vessels (vide Fig. 74). The clinical history of this case was not preserved. In another case the growth, though still localised, was more diffuse. It was an imperfectly circumscribed interstitial tumour in the anterior wall of the uterus, which had become submucous, bulging into the uterine

cavity. It measured 4½ inches in diameter. On section it had an indefinitely fasciculated appearance not unlike an ordinary fibroid which had undergone considerable degeneration throughout and much cystic change, particularly in its upper parts (vide Fig. 75). Under the microscope it presented, both in its upper cystic parts (vide Fig. 76) and in its lower solid portions (vide Fig. 77), many of the characters of sarcoma. The cells, which constituted the chief part of the growth, were spindle and irregular shaped, the interstitial substance mostly scanty, and many of the blood-vessels rudimentary. At the same time there were many thick-walled blood-vessels and some well formed fibroid strands, and it might be regarded as a border line tumour, or a fibroid in which a change suggestive of sarcoma had arisen. The patient was a young woman, æt. 27, under the care of Mr. J. Furneaux Jordan, who himself regarded the case as one of primary sarcoma of the uterus. She had been married for two years and had no children. She suffered from some menorrhagia with dysmenorrhœa for 8 months, but had not lost flesh. The tumour reached to the umbilicus and was movable. The operation was successful and the patient was in good health when last heard of, about a year afterwards. The appearances and structure of the diffuse form of intramural sarcoma are similar, though in the writer's experience primary sarcoma of the uterus in all its forms is rare. There is considerable risk of classing a sarcomatously degenerated fibroid as primarily a sarcoma of the uterus, unless the whole of the growth has been carefully investigated.

III. The Co-existence of Fibroids and Cancer of the Body of the Uterus.

Fibroids and cancer of the body of the uterus are so often found within the same uterus, that it is difficult to resist the conclusion that the former favours the development of the latter. On the other hand, fibroids rarely co-exist with cancer of the cervix. Apart from fibroids, cancer of the cervix uteri is about twelve to fifteen times more frequent than cancer of the corpus uteri, but when fibroids and cancer are co-existent in the same uterus, cancer of the body appears to be as frequent as cancer of the cervix. Therefore, when the presence of a fibroid has been definitely ascertained, the possibility of the concurrence or future onset of cancer has to be borne in mind. It may disclose itself by the appearance of, or a considerable increase of, bleeding or by a profuse discharge, especially at the climacteric (vide Figs. 78 and 79).

IV. Cancer.

Cancer of the body of the uterus is a malignant epithelial tumour of the uterine mucosa. It has its origin in the epithelium, either of the surface or of the endometrial glands, and consequently

encroaches early upon the uterine cavity. Symptoms, of which the most characteristic is an abundant hæmorrhagic discharge, appear much earlier than in the case of submucous fibroids, and even earlier than in endometrial sarcomata.

Macroscopic appearances. A more or less circumscribed tumour of varying size, projecting into the uterine cavity, is the form which this growth takes most frequently (vide Figs. 80, 81, and 82). Its surface is mostly rough, eroded, and sometimes cystic, villous or papillomatous, its consistence soft and friable, and its colour white or grey, and often red in places from recent or old hæmorrhagic foci. The projecting part of the growth may become polypoid or break down and escape under the influence of necrotic and disintegrating processes of either a bland or infective nature, leaving an ulcerated surface, which has at first sight little or none of the appearances of a tumour (vide Fig. 82). Similar malignant ulcers are met with in the stomach, intestines, etc., and their true character is discerned by the extent to which the growth involves the uterine wall as well as by their microscopic structure. Invasion of the deeper parts of the endometrium and to a certain extent also of the muscular coat, has occurred in all the tumours by the time they come under observation. Extension in this direction is slow, much more so than towards the uterine cavity, and it may take a long time before it completely penetrates the muscular coat and reaches its peritoneal covering. Rapidly growing cases may accomplish this in about a year, but most cases take longer, two to five years, or even more. As is but natural, growth inwards and outwards is attended by growth in other directions as well, and a tumour, at first circumscribed and local, may come to implicate the whole uterine cavity and the greater part of that wall of the uterus in which it is growing. A *circumscribed* (vide Figs. 80, 81, and 82) and *diffuse* (vide Figs. 83 and 84) form of cancer are thus recognised; the latter being mostly an extension of the former and occurring particularly in tumours of quick growth. Parts, even to almost the whole of a tumour, may undergo a coagulation necrosis without breaking down and become converted into a cheesy-looking substance suggestive of caseation (vide Fig. 85). One or two cases in which this caseous-looking change has occurred extensively have been put on record. The uterus remains freely movable for a long time. It sometimes becomes fixed by simple inflammatory adhesions in advance of the extension of the growth, but this fixation becomes at once greater and more serious when the growth has penetrated the peritoneal coat and invaded neighbouring structures. This invasion and fixation are of late occurrence, rarely, if ever, occurring until after well marked symptoms have been present for some time, sufficiently marked at any rate to arouse suspicion. Hysterectomy can be successfully undertaken up to this time, and the importance

of an accurate knowledge on the part of practitioners of medicine of the symptoms of this disease can hardly be over estimated. Moreover neither lymphatic nor vascular metastases arise readily. They may not occur till some time after fixation of the uterus has taken place, and it is therefore possible to eradicate the growth completely. Unfortunately, it is not possible here, as it is in some other situations, to say whether lymphatic metastases has already arisen, when the operation is made; for the lymphatic glands affected lie beyond the reach of exploration, as has been explained in describing the relationship of the uterine lymphatics.

Microscopic appearances. The microscopic appearances of the growth are similar to those of an ordinary columnar epithelioma, presenting tubes and spaces lined by epithelium in a fibro-cellular stroma (vide Fig. 86). The cells are mostly of the columnar type when only one layer thick, but tend to become polymorphous when there are several layers. They are not separated from the stroma by any basement membrane. They are larger and their nuclei stain more deeply than the cells of the normal mucosa and utricular glands. Moreover they are placed more irregularly within the cells, occupying different levels within adjacent cells. The cancerous tubes thus assume, even when they resemble the utricular glands in shape, a more distinct and prominent appearance (vide Figs. 70, 72, 86, and 87). But they rarely resemble them even in shape. The glands form regular tubes which run at right angles to the surface epithelium, into the endometrium as far as, or even a short distance within, the muscular coat of the uterus, where they end in blind extremities, sometimes branching into two just before doing so. They do not give off branches in their course, except under the influence of endometrial inflammations, when a certain amount of branching may occur. The malignant tubes on the other hand run in every direction within the growth, branch freely and assume all kinds of shapes, so that it is impossible to trace any single tube for any distance in any section, as can be so often done in the normal or even in the inflamed mucosa (vide Fig. 88). They invade the muscular wall freely and can be traced outwards for varying distances towards the peritoneal covering of the uterus, occupying the distended lymphatic spaces between the muscular bundles. The outline of individual tubes and spaces may become irregular and complicated by ingrowing papillary processes. The epithelium lining the spaces may multiply and fill the lumen with a solid mass of cells. When this is a feature of many of the spaces in any microscopic field, the term *adeno-carcinoma* is often applied to the growth (vide Fig. 90). This filling of the spaces with cells is sometimes followed by a degeneration of the lining layer of cells, so that these spaces now present the appearance of an ordinary alveolar carcinoma, in which a mass of cells, united only by their cement

substance, lies free within the alveoli, a stage which is sometimes referred to as a *spheroidal celled* carcinoma (vide Fig. 90); a refinement of nomenclature which is equally applicable to many columnar celled epitheliomata in other situations, and is of doubtful utility. The same thing may be said of the differentiation of this cancer into two types; an *everting* type, in which the tubes preserving somewhat their tubular shape, grow and branch outwards into the stroma (vide Fig. 88), and an *inverting* type, in which the tubes become dilated into irregular shaped spaces, giving off papillomatous ingrowths into their interior (vide Fig. 88). Mitoses within the epithelial cells are not uncommon in several parts of the tumour. The stroma of the tumour consists of rounded and slightly irregular shaped cells resembling those of the endometrium, with little or no fibrillation and numerous blood-vessels. In the inner parts of the tumour it is the product of the stroma of the endometrium, consisting partly of the pre-existing and partly of newly-formed endometrial tissue. In the deeper parts of the tumour which invade the muscle, it is the product of the intermuscular fibrous tissue, and is more fibrous than elsewhere. The muscular bundles undergo atrophy from pressure and erosion, but show no signs of reactive reproduction. There may be considerable œdematous, myxomatous, or hyaline change within the uterine wall, in the neighbourhood of the cancerous growth, and sometimes cancerous emboli may be detected within dilated lymphatic spaces within the muscular wall at some distance beyond the margin of the tumour (vide Fig. 89). But the most striking feature of the stroma in great parts of the tumour, particularly towards the uterine cavity, is its scantiness. It is frequently reduced to the smallest limits, consisting of no more than the thickness of a single cell separating the cancerous spaces from one another (vide Fig. 91). The blood vessels lie within the stroma, and many of them have very thin walls, so that hæmorrhages are common. Clusters of leucocytes are often seen around the blood-vessels, and invading the tubes. They are due to secondary inflammatory processes (vide Fig. 91).

Retrogressive Changes.—Degenerations and necroses are common within the central parts of the tumours, and may arise elsewhere. They are due to loss of blood supply and are comparable to similar changes within cancers in other situations. A mucoid or mucinoid change may convert portions of the cancer into a structureless jelly-like substance. Droplets of a mucinoid substance appear within the protoplasm of the epithelial cells, which coalesce and cause the disappearance both of the protoplasm and of the nucleus. The intervening stroma suffers the same change a little more slowly. But perhaps the most interesting change is that which occurs within the centre of some of the cell masses filling the spaces in certain of the cancers. The most central and hence the oldest of these cells

become glassy looking and compacted together, so that the whole cell mass comes to resemble the cell nests of a squamous epithelioma more or less closely (vide Figs. 92 and 93). Several cases of so-called squamous epitheliomata of the body of the uterus are on record, which are reported to resemble the histological appearances characteristic of a squamous cancer of the cervix uteri, and the production of the cell nests is explained in the usual way as the result of a similar hyaline or keratinous process. The horny change which characterises the stratum squamosum of the normal skin, and to a less extent the central cells of a cell cluster of a squamous epithelioma, is the natural result partly of a physiological adaptation and partly of a lack of nourishment and a loss of moisture. The term hyaline is applicable to it only in so far as it assumes a more or less glassy appearance. The cast-off columnar cells of a cancer of the uterine body have no natural tendency to a keratinous change, and the assumption of the cell nest appearance is probably due to some mucinoid degenerative change, followed by a loss of moisture.

Curettings. An accurate knowledge of the minute histological appearances found in these cancers is essential for a correct interpretation of curettings. While exceptional difficulties sometimes present themselves, it most frequently occurs that a decision has to be made between cancer and a benign endometritis. In the latter, the tubes resemble the normal utricular glands, and there is a plentiful intervening stroma; in the former, the tubes are aberrant and the stroma is scanty (vide Fig. 94). These leading distinctions are often sufficient to enable a diagnosis to be made with certainty, but all the cancerous characteristics should be kept in mind and applied to the solution of more difficult cases. It must not, of course, be forgotten that the histologist can only express an opinion upon the nature of the curettings submitted to him. The clinician who knows all the history of the case, and has explored the uterine cavity, can best apply the histologist's findings to the individual case. But too much stress cannot be laid upon the importance of an early recognition of the disease. A great improvement in the outlook has occurred within recent years as the result of a combination of a better knowledge and a greater alertness on the part of the general practitioner, and of a readier resort to uterine exploration, histological examination and operation on the part of the specialist. It is computed at present that about one-third of the cases are curable by operation, and it is at least possible that the proportion may be increased in the future.

Cause and Origin. It is a disease of old age, the average age being nearer 60 than 50. There is usually a definite interval of years, sometimes only of months, between the menopause and the first appearance of symptoms. It may, but rarely does, come before the climacteric. Many of the patients are unmarried, and

among married women it is commoner in those who have had few, than in those who have had many children. It starts in the epithelium, either of the utricular glands or of the surface, more often the former, it is thought. Its origin in the surface epithelium has been traced by some to a preliminary proliferation, whereby this epithelium comes to consist of several layers thick, a condition known as *leucoplakia* or *ichthyosis*. After a time definite ingrowths from these layers invade the endometrium in the form of tubes, and constitute a definite cancerous condition. It is cancers of this nature which may show the so-called cell nest formation. It is a curious method of growth, for it must be the result of a special vegetative activity at one point of the surface epithelium and not at many; multiple points of origin of primary cancer being contrary to experience. But whether the cancer starts in the surface epithelium or at some point in the utricular glands, all the evidence goes to show that the new cancer cells and tubes are entirely the offspring of those first formed, though delusive appearances may sometimes suggest a direct conversion of the normal epithelium into cancerous cells at the advancing margin of the growth. The influence which starts the excessive vegetative activity is here, as in cancers elsewhere, unknown. It is interesting, however, to note that the body of the uterus is far less liable than the cervix to both irritation and to cancer.

Comparison between Cancer of Body and Cervix. A short comparison of the chief differences between cancer of the body of the uterus and that of the cervix is interesting. (Thesis on Cancer of the Body of the Uterus, by Dr. Thomas Wilson).

1. Frequency. Cancer of the body is twelve to fifteen times rarer than that of the cervix.

2. Age Incidence. Cancer of the body is commonest between 50 and 60; of the cervix between 35 and 45.

3. Influence of Childbearing. Cancer of the body is not related to childbearing, while cancer of the cervix appears to be. At any rate cancer of the body occurs oftenest in the unmarried, or in women who have borne few children; while cancer of the cervix occurs in women who have borne large families, or at least the average number of children.

4. Malignancy. Cancer of the body is much less malignant, both locally and generally than cancer of the cervix, and is less prone to recur after removal.

5. Fibroids. The co-existence of fibroids and cancer of the body is common; of fibroids and cancer of the cervix is rare.

6. Pyometra. Cancer of the body is less commonly followed by pyometra than is cancer of the cervix.

V. Chorio-epithelioma Malignum and Placental Mole.

The former name is now generally adopted for the malignant epithelial tumour, which springs from the ectoderm cells of the villi of the chorion. It was formerly known as a deciduoma or syncytioma malignum or malignant serotinal tumour. It is a growth, which stands in a class by itself, inasmuch as it springs from fœtal cells, invading and destroying the tissues of the mother, instead of undergoing involution, atrophy and disappearance at the end of its normal physiological cycle.

Macroscopic Appearances. It forms a mottled or dark red, maroon coloured, soft, friable spongy mass of varying size, mostly localised and definite in outline, but occasionally diffuse. It projects into the uterine cavity, often only to a slight extent, forming a rough nodular surface (vide Figs. 95, 97, and 98), but sometimes filling it more or less completely, its free surface being generally rough and much broken, rarely smooth. It is fixed to the uterine wall, which it always invades, by a broad base (vide Figs. 96 and 99). Some part of the growth is almost always within reach of the finger when digital exploration of the uterus is undertaken (vide Figs. 98 and 99). The extent of this erosion varies, but it always involves the muscular coat to some extent at least. The penetration of the muscular coat may be slight as in Figs. 96 and 99, so that the growth may be localised and superficial, or it may be great, sometimes eating through the uterine wall and invading any of the pelvic viscera, intestines or other neighbouring structures. The neighbouring mucous membrane of the uterus is either healthy-looking, inflamed, or shows some decidual membrane. The growth directly or indirectly extends to the vagina in about half of the recorded cases, this being the site in which secondary metastatic growths most commonly appear. On section the most striking additional feature is the prevalence of hæmorrhages of all ages, old and recent blood clots forming, in some cases, more than three-fourths of the whole tumour.

Successive sections, passing through the base of the tumour, show that the deeper parts of the growth send out branching processes of varying size into the neighbouring part of the myometrium which in different sections of the latter appear as separate growths (vide 96, 99, and 100). Many of them are merely outlying extensions of the primary tumour, though some of them are distinct centres of secondary growth. The *placental mole,* in cases of blighted ovum where the placenta and membranes (being the sole product of conception) form an irregular fleshy mass (the *fleshy mole*) sometimes imbedded in blood clot, (the *hæmorrhagic mole*) may present certain resemblances to the chorio-epithelioma; but in its more usual form (in relation to premature birth) that of

the vesicular or hydatidiform mole, it constitutes a much larger growth, always distending the uterus to a greater extent than a normal pregnancy of a like date or than a full term fœtus. The vesicular grape-like masses of this growth differ entirely in appearance from a chorio-epithelioma, though they may likewise be infiltrated with blood clot. Figs. 101 and 102 show the appearances (opportunities of seeing such specimens being infrequent) of such a mole with hæmorrhage *in situ*.

Microscopic Appearances. An appropriate piece must be selected, preferably from the white marginal part of the growth which has not been invaded by either the prevalent necrosis or by hæmorrhages. The structure is essentially cellular, the cells being of the epithelial type. It is true that in the majority of cases there is a certain amount of a fibro-cellular connective tissue which in places may run out into finger-like processes, on the outside of which the cells lie, presenting a picture similar to that of a normal chorionic villus (vide Fig. 104). But this fibrous basis or core, though present in most instances of this tumour, may be altogether wanting in other cases (vide Fig. 111). It is in one sense a fortuitous constituent, the last to come and the first to go. It is nature's device for the rapid conveyance of nutriment from the mother to the fœtus inasmuch as it supports the allantoic vessels which it carries. Its presence in the chorio-epithelioma depends upon the particular stage in the cycle of gestation at which the tumour began to grow. This fact will become clearer, when the evolution of the growth is traced a little later on; meanwhile let us return to the cells, which comprise the real and essential tumour. It has no stroma and no blood-vessels, nothing but cells. These cells are of two kinds, plasmodium or giant cell masses, the *syncytial cells*, and smaller polyhedral cells, the *Langhans' layer cells*. The syncytial elements are large, elongated or irregular masses of finely granular protoplasm, containing many nuclei rich in chromatin and often also vacuoles. The outlines of the masses are generally well defined and distinct, but they show no lines suggestive of cell division (vide Fig. 112). They recall the giant cell masses met with in sarcomata of the suprarenal and some other parts. The Langhans' layer cells are of moderate size, mostly polyhedral in shape, but may be spherical, irregular or spindle-shaped; their protoplasm stains less darkly than that of the syncytial elements, and contains globules of glycogen, their nuclei (usually only one in each cell) have a moderate amount of chromatin and often show mitoses (vide Fig. 113). The proportion in which these two kinds of cells exist, is capable of great variation in different tumours and in different parts of the same tumours. Sometimes the one and sometimes the other greatly predominates, and whilst they may appear often to be mixed up together, the prevailing relationship is syncytial cells outside and polyhedral cells inside (vide Figs. 104

and 107), in more or less parallel rows, or forming irregular alveoli filled with blood, or the latter are grouped around the former in masses. They invade the uterine mucosa extensively, filling and often distending its vascular spaces. They extend into the muscular wall, eroding and lying between the muscular bundles (vide Figs. 107 and 109), often continuing for long distances outwards. They are most frequently seen around the veins and other vessels of the muscular coat, often running for some distance within the outer coat or dissecting a way between the inner and middle coats, and always reaching, sooner or later, the vascular lumen, which they proceed to fill. They penetrate the uterine wall much in the same way as the roots of a tree grow into the ground. The syncytial cells are more actively erosive and phagocytic, and are often found alone or much in advance of the polyhedral cells. It can be determined by means of serial sections that many of these far outlying cell masses are really far reaching rootlets, though in other cases they are emboli, which have become detached from the growth and lodged within some vein further out, either within the wall of the uterus (vide Fig. 114) or broad ligament (vide Fig. 115), or elsewhere.

Mode of Evolution. It is difficult to obtain a clear conception of the mode of growth of this tumour without tracing the main steps in the development of the villi of the chorion. In the earliest embryo known to us (Bryce's), which is about 14 days old, both the syncytial elements (outside) and Langhans' cells (inside), products of the ectoderm of the trophoblast, are well developed. The differentiation between them occurs therefore at a very early date and there is no proof, in the subsequent stages of either normal or abnormal pregnancies, that the cell elements of the two layers are interchangeable. In other words all subsequent growth of syncytium or of Langhans' cells springs by direct lineal descent from the respective cells of their own class, viz., syncytium from syncytium and Langhans' cells from Langhans' cells existent at this early period. Both have extremely active vegetative properties, whilst the syncytial elements possess also strongly erosive and phagocytic qualities, which enable them to penetrate the decidua, and reach the venous sinuses. The Langhans' layer cells are probably nutritive, but they may also, under certain circumstances exert erosive or destructive properties. With the development of the allantois a vascular fibrous tissue core appears within the primitive and previously cellular representative of the villus, in order to transfer nourishment more effectually from the mother to the fœtus. The young villi continue to penetrate into the venous sinuses of the decidua serotina during the period of formation of the placenta, the syncytial cells being generally prevented from invading the uterine muscle by the deepest layers of decidual cells (vide Figs. 105 and 106). With the approach of the end of the

period of normal gestation, the villi begin to atrophy, the fibrous core first disappearing, followed by the syncytial elements, and, lastly, by the Langhans' cells. The attachments of the villi are thus loosened, so that they readily slip out of the venous sinuses at the birth of the fœtus. But under certain pathological conditions, imperfectly known at present, the epithelial elements of the villi may retain their inherent vegetative properties, continue to grow, and form actual tumours. Interferences with the normal period of gestation, such as early abortion or a blighted ovum, in which no fœtus is formed or at any rate found, apparently favour this growth. It thus seems to be probable that the fœtus, by its metabolism, exerts an inhibitory, regulative or restraining influence upon the vegetative activity of the cells of the villi and that the premature withdrawal of this influence results in over-growth. It is also possible that the character of the overgrowth may be influenced by the date or stage of the gestation cycle, at which this withdrawal occurs. An attempt has been made to explain in this way the differences in histological structure which individual cases of chorio-epithelioma may present. Thus in some of them the villi are represented by cellular outgrowths similar to the primitive kind, and never come to possess any mesoblastic core. It is thought that the abnormal influences, which result in a loss of normal restraint, arise at a later date in these cases than in the more common examples, in which the villi show some trace of the mesoblastic core, inasmuch as this core is the first part of the villus to disappear (vide Fig. 110). In the same way the sarcomatous looking chorio-epitheliomata, of which a few have been described, may start at a still later date, after the syncytial elements have also had time to disappear. The chorio-epithelioma then is a tumour of high local and considerable general malignancy. It is the result of the retention of their vegetative properties by the fœtal ectodermal cells, after the termination of the normal period of gestation. But there is another and commoner result in the formation of the placental mole, a growth of low local and very slight general malignancy.

Relations to Placental Mole. The latter tumour is of great interest. It consists of an altered embryonic sac, with no sign of an associated fœtus in most cases. Two types occur—the *fleshy* and the *hydatidiform*. The former is the rarer. It starts earlier, arising chiefly in cases of blighted ovum, the fœtus being absent or dying and becoming absorbed, whilst the placenta continues to grow, and fills the uterus with a large fleshy mass prone to hæmorrhage and putrefaction. The *hydatidiform mole*, on the other hand, arises mainly in cases of premature birth, in which after expulsion of the fœtus, portions of the placenta remain behind, whose chorionic villi continue to grow, and at the same time become swollen by a mucoid

change, which converts them into masses of grape-like clusters, having a superficial resemblance to hydatid cysts, hence the name. Whilst in most cases the fœtus is no longer present, in a few a dead one has been found, and in still a few others, in which the hydatid change has affected only a portion of the placenta, a living child has been born. The hydatidiform, like the fleshy mole, is liable to hæmorrhages, which, added to its increase in size by growth, stimulate the uterus sooner or later to extrude it. Opportunities of ascertaining exactly how far into the uterine wall the villi penetrates in these cases have so far been few in number, and the prevailing opinion that their growth, though continuous, is restricted to the limits of the normal placenta, is rather of the nature of an inference, founded upon an absence of subsequent growth after evacuation in the majority of cases, than of actual knowledge. In a proportion of the cases, put by some as high as 30 per cent., a deeper local erosion occurs, so that neither spontaneous extrusion nor artificial evacuation followed by curetting, can free the uterus from all the invading fœtal cells. Both local recurrence and metastases remain possible, and have occurred in a few cases. The depth of uterine wall erosion varies somewhat in these cases, but it may involve the muscular coat to some extent in a certain proportion of them.

This raises an important point which may serve to explain the frequent sequence of the chorio-epithelioma to a previous placental mole, abortion or otherwise disturbed pregnancy. As shown by the Figs. 117 and 118, Mr. Hewetson demonstrated to the writer in a part of this particular case of hydatidiform mole after the removal of the uterus, that neither natural nor artificial evacuation by means of finger or curette (as complete as any that could be used upon the uterus *in situ* in a living case) could suffice to free the uterus entirely from the invading fœtal villi. It is therefore a reasonable assumption that if the uterus had been merely emptied out in this case and not removed, a chorio-epithelioma would subsequently have developed. It is hoped that the extent of penetration of the muscular wall by the fœtal elements will be determined as far as possible in any similar cases of placental mole which become available. Two possibilities present themselves, first a varying degree of inherent vegetative activity on the part of the invading fœtal elements, and second a varying depth of penetration by them of decidua and uterine wall. The latter is probably the chief factor, though the former may play a part. In the great majority (over two-thirds) of cases of placental mole the penetration of the maternal tissues by the fœtal elements may be so slight as to permit of complete evacuation, whereas, in the minority, fragments remain behind, whose inherent vegetative activity overcomes the resistance of the maternal tissues and by active growth constitute the tumour known

as a chorio-epithelioma. Indeed this theory would account in a satisfactory way for the differences in histological structure presented by chorio-epitheliomata. In most cases, as in Figs. 117 and 118, portions of a complete villus with fibrous core and epithelial covering would remain within the uterine wall and the resulting chorio-epithelioma would therefore show villi of a similar structure; but occasionally only syncytial elements or Langhans' cells or both would remain and result in a chorio-epithelioma with a corresponding histological structure.

Metastases. Considering the freedom with which these growths and outlying cells from them penetrate into the blood stream (vide Figs. 119, 120, 121, and 122), it is surprising that metastases are not more frequent. But it is to be remembered that the connection between the growing fœtal cells and the blood-vessels of the mother is hardly less free, even in normal pregnancy. It has been shown in eclampsia, where the violent muscular contractions may favour separation of some of the cells and their passage into the circulation, that syncytial elements may be present in the capillaries of the lungs and other organs, and it is at least possible that their escape into the blood stream may sometimes take place in ordinary pregnancy, particularly towards its termination. But it is to be remembered that these fœtal elements have in all probability lost much of their inherent power of reproduction and thus may fall an easy prey to the phagocytic action of the vascular endothelium and other cells. The frequency with which clinical signs of pulmonary apoplexy occur compared with metastases in the lungs in chorio-epithelioma is cited as a proof that many of these emboli die after impaction without starting a metastatic growth. There may be something in this contention, though it must not be forgotten that thrombosis, within the placental and other vessels invaded by the growth, is of frequent occurrence, and that the resulting emboli may consist of blood clot only, and be devoid of any of the fœtal cell elements. That some of the malignant emboli may be fairly large, and contain not only epidermic elements, but mesodermic as well, is shown by some of the metastases, *e.g.*, in the lung, exhibiting a more or less typical villous structure, with central fibrous core, surrounded by both Langhans' cells and syncytial elements (vide Fig. 116). It is easy to understand that this kind of separation should occur more readily in the loosely built and rapidly growing villous outgrowths of the chorio-epithelioma than in the more compact villi of normal pregnancies; but Schmorl maintains that portions of chorionic villi may be detached and become emboli, which, after impaction, form a primary chorio-epithelioma in some extra-uterine situation. Whether this be true or not, it is certainly not the explanation of the origin of the instances of this primary growth which have been met with

in the testicle, mediastinum, and cranium. These are true teratomata and independent entirely of any uterine pregnancy. Secondary chorio-epitheliomata in cases of the primary uterine form are met with often in the vagina, not uncommonly in the lungs (vide Fig. 116), and sometimes in the liver, spleen, and ovary. It also occurs as a primary growth in the ovary.

Cause. It follows from the mode of evolution of both the placental mole and the chorio-epithelioma, that, in a sense, the same cause operates in both cases, viz., the preservation of inherent vegetative characters by the fœtal ectoderm cells of the trophoblast and the continuance of their physiological manner of growth within the maternal tissues, when freed from the control and restraint of certain governing physiological laws. These laws operate in normal pregnancies either through the living fœtus or in some other way, so as to weaken and destroy the inherent vegetative endowment of these fœtal ectoderm cells and secure their extrusion from the uterus, when the end of the period of normal gestation has been reached. On the other hand in abnormal pregnancies, these laws are either inoperative or inefficient during part or the whole of the period of maturation of the ovum and the resulting (usually premature) extrusion of the fœtal elements from the mother may be imperfectly accomplished. Some of the ectoderm cells of the trophoblast, still retaining their natural endowment of vegetative activity, remain behind within the uterus and by continuance of growth produce a chorio-epithelioma. This retention is more likely to occur in the graver cases of disturbance of maturation of the ovum, *i.e.*, of abnormal pregnancies such as placental mole, abortion and the like, and the records of published cases of chorio-epithelioma show that in fully one half of them there has been a preceding placental mole and that in the remainder there is a more or less complete history of some other form of previous abnormal pregnancy. In the very few cases which are said to have followed normal pregnancies, it is reasonable to suggest that the histories are incomplete, all the more so since it is not usually recognised that the "latent" period intervening between the preceding pregnancy and the resulting chorio-epithelioma may vary from a few weeks to months or occasionally even years. Similar prolonged periods of "latency" have been met with in connection with metastases both in sarcomata and cancers, when secondary growths in other situations have appeared many years after the date of extirpation of the primary tumour in various sites. The origin and cause of chorio-epithelioma seem to be clear. It is unnecessary to assume the existence of an internal secretion or the appearance of any other new stimulant to growth. Since Leo Loeb put forward the theory, based upon his experiments, that the ovary furnishes an internal secretion, possibly in connection with the corpus luteum, which stimulates the formation both of the

decidua and of the ectoderm of the trophoblast when the placental growths under consideration arise, much attention has been given by gynæcologists to the lutein tissue and to co-existent lutein cysts of the ovary, without however disclosing any genetic relationship between them and the placental growths. Neither increase of lutein tissue nor lutein cysts have been present in the great majority of such growths, though appearing in a few of them (vide Fig. 99). The natural inherent endowment of vegetative activity of the ectoderm cells of the trophoblast unrestrained by the normal laws usually in action, is sufficient to account for their continuance of growth and the production of the chorio-epitheliomatous tumour. Multiple primary centres of growth, which have apparently been present in some cases, are thus easily accounted for. It is the same explanation as underlies the production of all teratomata.

When cells representative of one or more of the embryonic layers of one individual are included within the tissues of another individual they grow as a parasite upon the latter, and form a monster or a tumour. Their inherent tendency to grow is merely exerting itself. No other cause of growth is necessary. The nature of the resultant growth depends entirely upon the type of the cells enclosed; if all three types are represented, an attempt may be made to produce a more or less complete individual; if one only, the resulting growth can show only tissues derivable therefrom. In the chorio-epithelioma the included cells are representative only of the sac, in which the embryo is developed. They are unipotential, and capable only of producing their own type of tissue. Consequently their activities, however great, never give rise to an individual.

The cause or causes which underlie the onset and production of disturbances of the normal maturation of the ovum and result in the formation of a placental mole, in an abortion and the like are imperfectly known, but they have nothing directly to do with the causation of the chorio-epithelioma, further than that they lead to the retention within the maternal tissues of potentially dangerous fœtal ectoderm cells, without which the chorio-epithelioma cannot arise. Moreover it is easy to see how in some cases of placental mole, in virtue either of less restraint upon the ectoderm cells or of undue retention of the mole, the fœtal invasion of the tissues of the mother may take on the characters of the chorio-epithelioma. In other words, a chorio-epitheliomatous growth would result before instead of after the extrusion of the mole. In this way the few cases of malignant placental mole recorded by Pestalozza and others find an easy explanation.

DESCRIPTION OF PLATES.

All the illustrations are taken from specimens in the Pathological Museum of the University of Birmingham. They are photographs and photomicrographs taken by the writer with the assistance of certain members of his staff, particularly Drs. Wilson and Hewetson and Mr. J. F. Brailsford. They are all new, not having been previously published, except in the case of Figs. 95, 96, 108, 109, 112 and 122.* A short clinical history has been added, wherever possible to the anatomical and histological features so as to increase interest in the cases and relieve the paper itself from many details.

GENERAL CHARACTERS OF FIBROIDS.

Fig. 1. The uterus is greatly altered in size and shape by many nodular fibroids. About one-quarter natural size.

Fig. 2. Section of body of uterus (cervix not present) and fibroids about half natural size. The whorled and fasciculated appearance is well seen. The endometrium is thickened, being 2 to 3 mm. in thickness. From a single woman æt. 37 who complained of severe bearing down pains of 3½ years' duration in the lower abdomen and back, increasing dysmenorrhœa, no menorrhagia.

Fig. 3. Section of uterus with interstitial fibroid less than half natural size, shewing the loose bed of the tumour with many large vessels, the substance being devoid of visible vessels except at an opaque area towards the centre, in which there are two. This area shews hyaline degeneration. From a single woman æt. 31, of an irregular menstrual history till 29, who had menorrhagia for 2 years, increasing during last 3 or 4 months, as well as much sacral and lower abdominal pain.

Fig. 4. Section of a typical young fibroid x 25 shewing irregular interlacing of muscular bundles, small amount of intervening fibrous tissue, many capillary blood vessels and lymphatics.

Fig. 5. Uterus only slightly enlarged with large fibroid growing from the posterior surface of its body, also several small ones and two small inflammatory polypi, less than half natural size. The fibroid has been sectioned and the halves spread out.

Fig. 6. Uterus with many fibroids shewing uniform enlargement similar to that of pregnancy about one-quarter natural size. From a widow æt. 42, who had had two pregnancies, one ending at full term and the other in a 3 months' abortion. She was anæmic and wasted and had suffered from pain in back, leucorrhœa and menorrhagia for 2 years.

* Some of the illustrations of cancer have been taken from a thesis by Mr. Thomas Wilson, entitled "Cancer of the Body of the Uterus," University of Birmingham, to whom the writer desires to express his thanks for valuable help in this part of the subject.

Fig. 7. Uterus of unaltered size and cavity with interstitial fibroid (about size of goose's egg) becoming subperitoneal at its apex, having for its base the whole posterior wall of uterus. The endometrium is thickened (about 4 mm.). From woman æt. 38 who had had 1 child only, 9 years prior to the hysterectomy. She complained of bearing down pains, worse before the menstrual periods, of 3 years duration and pain on defæcation of 1 year's duration. No menorrhagia.

Fig. 8. Uterus with several fibroids causing distortion of uterine cavity and retroflexion of cervix, about half natural size. From a single woman æt. 47, who was anæmic and wasted. She had suffered from much menorrhagia, offensive leucorrhœa and pains over lower abdomen and sacrum for last 4 months.

Fig. 9. Vertical antero-posterior section of enlarged uterus with many fibroids shewing two sharp bends in uterine cavity, which is 11 cm. long; less than half natural size. From a single woman æt. 33, who had srffered from much loss of blood.

Fig. 10. Section of part of distorted uterine cavity showing resulting polypoid formation ×20. There is localised œdema of the fibroid above and a patch of hyaline degeneration to the left of the cavity (the reader's right).

Fig. 11. Section of endometrium ×30 in a case of distorted uterine cavity, showing dragging of mucosa and displacement of glands.

Fig. 12. Omental adhesions. Anterior view of a large lobulated mass consisting of several tumours, which have grown from the posterior wall of the body of the uterus; less than one-quarter natural size. The elongated cervix (into which a glass rod has been inserted) is seen at the upper left angle. The lower part of the mass filled the pelvis, the upper and larger rose into the abdomen. The peritoneal surface showed many large veins. A large mass of the omentum, in which were several lymphatic vessels about the thickness of the little finger, was adherent to the anterior and upper surface of the tumour and to the right tube and broad ligament. From a single woman æt. 34, in whom Dr. Thomas Wilson tried a double öophorectomy 5 years previous to the hysterectomy. For the first 3 years the periods continued regularly each month without any change, but during the last 2 years there has been complete amenhorrhœa. Flushes were severe day and night since the öophorectomy and for the last 6 months the tumour has been again slowly enlarging and a ventral hernia had appeared.

Fig. 13. Submucous fibroid about $1\frac{3}{4}$ inches in diameter attached by broad base to posterior wall of body of uterus, shewing a tendency to become polypoid. The cervical canal is taken up into the body as occurs at the beginning of labour. The tumour was of a dark plum colour with a smooth surface, except in its upper part where it is irregularly eroded and partly covered with lymph. The lower surface is partially denuded of mucosa and shows an acute inflammatory change extending for a little distance into the substance of the growth; rather less than half natural size.

Fig. 14. Section of uterus containing a large interstitial fibroid. A soft friable mass which caused bleeding and offensive discharge projected through the cervix into the vagina. This was removed by Dr. Purslow and found to consist of fibroid tissue undergoing sarcomatous change; see figs. 51, 52, and 53 for the appearance under the microscope. Dr. Purslow thereupon removed the uterus. The great bulk of the fibroid is benign but sarcomatous-looking characters begin to appear towards the lower part where the growth was gripped by the cervix. Less than one-third natural size.

Fig. 15. Postmortem specimen showing large fibroid attached to body of uterus protruding through the vulva. The prolapsed uterus is partially inverted. The specimen has been bisected and thrown open; about one-quarter natural size.

Fig. 16. Enlarged uterus opened by a T-shaped incision to show a submucous fibroid which is undergoing suppuration and sloughing in its lower part due to pyogenetic and putrefactive germ invasion. The substance of the tumour is œdematous and shows a few large thrombosed veins in its upper part; less than half natural size.

BENIGN DEGENERATIONS IN FIBROIDS.

Fig. 17. Section of 2 fibroids, the larger being of irregular shape and showing a well marked shell and nodules of calcification; about natural size.

Fig. 18. Two fibroids which have undergone complete calcification; about one-third natural size.

Fig. 19. Œdema. Section of fibroid ×25, shewing dilated lymph spaces and œdematous condition of surrounding tissue.

Fig. 20. Large lymphangiectatic cyst within fibroid; less than half natural size.

Fig. 21. Section of a large hourglass-shaped, subserous fibroid about one-quarter natural size, which was attached to the uterus by a slender, chiefly membranous, pedicle. In its upper part is a large irregular pseudo cyst, formed partly by œdema and partly by bland liquefactive necrosis of the tumour substance. The omentum carrying several large vessels was adherent to the upper part of the tumour. Smaller softened and liquefied foci are scattered through the tumour. The fasciculated appearance is largely replaced by granular material; œdema, fatty and hyaline degeneration being abundant. There are also two calcareous nodules in the narrowed isthmus. From a single woman æt. 47, who had known of the existence of a slowly increasing abdominal tumour for 10 years. Two attacks of severe pain 6 years and 2 years ago; menorrhagia during the last few months.

Fig. 22. Section of fibroid ×20, shewing well defined patches of hyaline degeneration, some of them in the walls of blood vessels.

Fig. 23. Section of fibroid ×50, shewing extensive, but incomplete, hyaline degeneration below, passing gradually into an œdematous condition above. The remains of the muscle fibres and their nuclei are still visible in the hyaline part.

Fig. 24. Œdema lymphangiectasis and hyaline degeneration. Section of fibroid less than half natural size shewing extensive degenerative changes. The contents of the spaces are coagulated by formalin. Hyaline and myxomatous changes are abundant, particularly in the dark coloured areas near the spaces.

Fig. 25. Section of a fibroid less than one-third natural size. The smooth lined cavity at the lower end of the tumour contained about 1½ pints of clear yellow fluid. Immediately above and to the right is a similar small cavity. No epithelial lining could be demonstrated in either of them, but they are probably lymphangiectatic. The solid part of the tumour shows œdema and myxomatous change. From a widow æt. 42, who had never been pregnant. Her only complaint was the steady increase of the swelling in her abdomen which she had noticed for fully two years. At the time of the operation the tumour extended to 4 inches above the umbilicus.

Fig. 26. Section of a large fibroid a little over one-quarter natural size shewing a necrotic cyst which contained clear gelatinous fluid, in its upper part, and much œdematous, lymphangiectatic, fatty and hyaline change in the upper solid part of the growth. From a single woman æt. 43, who had menorrhagia for about 1½ years and had noticed a swelling in abdomen for over a year.

Fig. 27. Section of an interstitial fibroid under half natural size, which has almost completely broken down into an irregular cyst with rough sculptured walls lined by a brownish-yellow waxy looking substance. It was filled with dark chocolate coloured thick fluid, and there was a deposit of fibrinous material in many places. The walls under the microscope shewed myomatous tissue much altered by œdematous and hyaline changes. From a woman æt. 52, who had had 3 children, the last 25 years ago. Menstruation regular until 14 months ago, then only two periods in next 8 months, and during last 6 months, red discharges with sharp shooting pains of several days duration have occurred at frequent intervals, the longest lasting about a week; abdomen gradually getting larger, retention of urine a fortnight ago.

Fig. 28. Left half of uterus with several fibroids about one-third natural size. The largest situated in posterior wall, has undergone almost complete necrosis, the wall being in no place more than 11 mm. thick and showing many projections, and tags of tumour remains. The posterior wall of uterus shows many large vessels. From a married nullipara æt. 40, who began to suffer pain and difficulty in micturition 12 months ago, which culminated in retention 3 weeks ago. There had been copious leucorrhœa before and increase of loss during the periods of late.

Fig. 29. Section of an interstitial fibroid about one-third natural size, showing a solid part of a dark red colour suggestive of a hæmorrhagic infarct and a cavity which contained dark coloured fluid, probably derived from a colliquative necrosis of part of the fibroid.

Fig. 30. Section of a submucous fibroid about half natural size, shewing appearances in its lower part, next to the uterine cavity, suggestive of a hæmorrhagic infarct.

Fig. 31. Section of this fibroid at its base ×30, shewing distended lymph spaces and some hyaline change.

Fig. 32. Section of same tumour at junction of pale and hæmorrhagic parts ×30, shewing partially necrosed fibroid and many distended blood vessels.

Fig. 33. Section of same tumour in the middle of the apparent infarct ×30, shewing greatly distended blood vessels and more extensive necrosis.

Fig. 34. Section of surface part of apparent infarct ×30, shewing distended blood vessels separated only by necrosed septa of tumour tissue.

Fig. 35. Section of fibroid in anterior wall of uterus about half natural size. It had undergone "red necrosis" and was of a dark red colour, darkest at periphery. From a married woman æt. 26, who had had 2 children. The tumour was discovered at the time of birth of the second child, which required forceps, and hysterectomy was performed about 2 months later.

ADENOMYOMA.

Fig. 36. Section of uterus containing an adenomyoma partially submucous, about one-third natural size, associated with sarcoma of ovary. The tumour is situated in the upper part of the uterus and also forms a submucous growth. There is no loose bed and there are many chinks filled with endometrial tissue, scattered through the tumour.

Fig. 37. Section of uterus containing an adenomyomatous growth and one discrete myoma about half natural size.

Fig. 38. Section through the highest part of this growth at a considerable distance from the uterine cavity ×30, shewing miniature uterine cavities.

Fig. 39. Section of this adenomyoma ×30, shewing miniature uterine cavities in the substance of the growth undergoing distension.

COMBINATION OF ADENOMYOMA AND CANCER.

Fig. 40. Section of the edge of a cancer ×30, shewing simple endometrium to the left, cancerous growth to right and an island of simple adenoma deep within the muscle. There were several other similar islands, within the thickened uterine muscle, all separate from one another, whose connection with the normal endometrium was no longer traceable, except in the case of one of them. They were all independent of the malignant adenomatous or cancerous growth of the mucosa. From a single woman æt. 57. Menopause at 49, thin red discharge for last year, was emaciated and felt ill. Uterus explored and removed.

SARCOMATOUS DEGENERATION IN FIBROIDS.

Fig. 41. Section of large fibroid about one-sixth natural size, shewing a dark softened sarcomatous area at its apex. Other parts of the fibroid show œdema and hyaline degeneration. From a woman æt. 57, in whom menopause had occurred at 47. Had suffered for 2 years from attacks of abdominal pain, which had become worse during last 3 months. She first noticed the tumour 6 weeks before consulting Mr. Hewetson. It then reached the umbilicus and felt cystic in its upper part. She enjoyed good health for some time after the operation, but died from multiple recurrence about 6 months thereafter.

Fig. 42. Section of sarcomatous area ×30, shewing cellular structure.

Fig. 43. Similar section ×100.

Fig. 44. Similar section ×250, shewing irregular cells.

Fig. 45. Section of tumour which clinically and microscopically looked like an ordinary fibroid about one-third natural size.

Fig. 46. Section of a part of the middle of the tumour (vide Fig. 45 for part taken) ×50, shewing suspicious cellular focus in typical fibroid tissue.

Fig. 47. A similar focus ×250, shewing cellular mass bordering on and merging into myomatous tissue.

Fig. 48. A similar focus ×250, near the last, shewing a structure still more closely resembling sarcomatous tissue.

Fig. 49. Section of a sarcomatous looking focus in a fibroid ×250, shewing the myoblast type of change. The individual cells are visible, running loosely in bundles. Some of them have two nuclei and there is little or no intercellular substance.

Fig. 50. Section of a similar focus ×250, shewing the individual myoblasts, some with deeply stained nuclei.

Fig. 51. Section of sarcomatous area in cervical region of uterus in case Fig. 14 ×250, shewing multinucleated cells and growth of fibroblast type.

Fig. 52. Section of a vaginal portion of the growth in the same case, shewing multinucleated fibroblast cells and much œdema of the sarcomatous growth ×250.

Fig. 53. Section of a sarcomatous focus suggesting the origin of the cells from the walls of a blood vessel ×200.

Fig. 54. A uterus enlarged by a tumour growth which has eaten its way through the uterine wall and formed a large irregular mass on its outer surface about one-third natural size.

Fig. 55. The same uterus bisected, the cut surface presenting the usual appearances of an ordinary fibroid.

Fig. 56. Section of the tumour at the site of perforation ×50, shewing cells clustering round the blood vessels suggestive of an origin from the vessel sheaths,

the older and external cells gradually undergoing a form of hyaline degeneration, the so-called cylindroma.

Fig. 57. The same section ×250, shewing one of the cellular cylinders cut transversely. The cells immediately around the vascular lumen are larger and more vegetative looking than those further out. Remains of cells and nuclei are still visible here and there in the general matrix.

Fig. 58. Section of uterus shewing one submucous and a very large subserous tumour, the latter measured 12½ inches by 10½ inches by 8½ inches. Several small interstitial fibroids were present which are not shown in the photograph, about one-sixth natural size. The submucous tumour was an ordinary fibroid, but the larger subserous tumour, though mostly resembling a fibroid, had several suspiciously sarcomatous areas, particularly in the cortex. From a woman æt. 62, who complained of a hœmorrhagic discharge, recurring every 3 weeks for the last 6 years and every few days during the last year of this time. About a year ago she noticed a swelling in the abdomen which reached as high as the umbilicus and had greatly increased in size since then. When she consulted Mr. Hewetson, it filled the whole abdomen. She had the appearance of a fairly healthy woman, but had lost some weight. She had no pain.

Fig. 59. Section of one of the suspiciously sarcomatous areas above mentioned ×250, shewing the largely cellular structure, the finely fibrillated matrix and the rudimentary blood vessels. There were many such areas scattered through the tumour which otherwise presented the characteristic appearances of a fibroid of considerable standing, extensively degenerated in places. The cells in the cellular areas were very irregular in shape, with deeply staining nuclei and the appearances were suggestive of a fine fibro sarcoma.

Fig. 60. Anterior view of uterus enlarged by tumours, a little less than ¼th natural size. The mass measured 14×10×9 cm. The largest tumour is irregularly rounded and growing in the anterior wall. Another smaller tumour about 6 cm. in diameter is seen at its lower end.

Fig. 61. Posterior view of same, shewing a third and rounded tumour attached to the second and continuous with the round ligament, which appears to swell out into it.

Fig. 62. Section of the same uterus and of large tumour in its anterior wall, less than one-third natural size, shewing the latter hollowed out into a large cyst, whose walls, thin above but thick below, where both tumour substance and uterine muscle is seen, still show thickening and projections, the remains of former septa. The tumour substance inside the uterine muscle is smooth, shiny or waxy looking, homogeneous and comparatively soft, with some resemblance to raw pork in appearance. It contains smaller cysts of varying size some of which have no connection with the cavity of the large cyst. Similar masses of waxy looking material permeated the substance of each of the smaller solid tumours.

Fig. 63. Section of one of these solid tumours ×50 shewing that the waxy material consists of a cellular growth, the remaining tissue of the fibroid being seen as strands of muscle separating the cellular masses.

Fig. 64. The same section ×250. The growth permeating the fibroid is seen to be cellular with a small amount of a fine fibrous matrix. The cells are irregular in shape and size and of an active vegetative type. Some of them have several nuclei, particularly those bordering upon the walls of the numerous capillaries. The frequency with which clusters of young rounded cells are seen close to the endothelial lining of the capillaries, sometimes indeed replacing the latter, is suggestive of an origin from the endothelial cells either of the vascular lumen or of the perivascular lymphatics and thus that the growth is either an endothelioma or a perithelioma.

Fig. 65. Section of wall of large cyst ×250, shewing the same sarcomatous tissue inside and fibro-muscular tissue outside.

Fig. 66. Section of myomatous part of a vascular and œdematous adenomyoma ×50, shewing the presence of many large, irregular cells with 1, 2 or more deeply staining nuclei lying close to the capillaries and between the muscle cells. They are most abundant in the neighbourhood of the endometrial islands, which are mostly large with a good deal of cellular mucosa around the glands. No distinctly sarcomatous foci were found anywhere in the somewhat enlarged uterus, which was removed owing to the patient having suffered from menorrhagia of 12 months' duration, becoming more severe of late. Pain had also been severe, generally beginning a day or two before the flow. Curetting improved but did not cure matters.

Fig. 67. Part of the same section ×250, shewing many of these large vegetative cells. Are they merely dropsical or inflammatory developments or do they indicate the beginning of a sarcomatous growth?

SARCOMA OF UTERUS.

Fig. 68. The uterus opened to show a large fungating tumour filling up the whole of its cavity; about one-third natural size.

Fig. 69. Section of the tumour shewing its incorporation with the uterine wall and the almost complete filling of the uterine cavity. The section shows a dull grey, homogeneous surface, darkened in many places by various degenerations and by old hæmorrhages. There is a small discrete intramural fibroid in the lower part of the uterine wall.

Fig. 70. Section of the tumour at its base of attachment to the uterine wall ×40, shewing sarcoma to right (the reader's) and cancer to left among the muscular fibres.

Fig. 71. Part of this sarcomatous area ×250.

Fig. 72. Part of the cancer ×250, shewing the typical gland acini of a columnar celled epithelioma.

Fig. 73. The uterus sectioned and thrown open, so as to show the two halves of a large, localised, intramural tumour, presenting many of the appearances of a degenerating fibroid but found on microscopic examination to be a sarcoma (?) about half natural size.

Fig. 74. A section of this tumour ×40, fairly representative of the whole. There are clusters of young cells around the blood vessels, suggesting an origin from their walls. The growth is largely cellular and suggestive of a sarcomatous condition.

Fig. 75. Section of an intramural tumour growing in the anterior wall of the uterus. It was imperfectly circumscribed and bulged into the uterine cavity, which was elongated. It measured 4½ inches in diameter and was not unlike a greatly degenerated fibroid. It had undergone much cystic change, particularly in its apical parts; just under half natural size.

Fig. 76. Section of a portion of this tumour taken from its cystic apical part.

Fig. 77. Section of a portion of the solid lower part of the tumour ×250.

COEXISTENCE OF FIBROIDS AND CANCER.

Fig. 78. Outer surface of uterus with appendages, shewing several small fibroids less than half natural size. There is no appearance of the cancer on the outer surface.

Fig. 79. Section of the same uterus about ½ natural size, shewing a cancerous growth in the fundus. From a single woman æt. 47, who complained of irregular and excessive hæmorrhage of about 18 months' duration, attributed to a fall from a bicycle. The discharge had recently become offensive and a granular red mass was passed lately. There was no pain or other local symptom. The uterine cavity

was explored by Dr. Thomas Wilson and the curettings found to be cancerous (vide fig. 94. The coexistence of cancer and fibroids was diagnosed and the uterus removed by him, the patient being well when last heard of, namely 2½ years after the operation.

For microscopic sections of cancer in this case see Figs. 91 and 94.

CANCER OF THE UTERUS.

Fig. 80. A localised nodular cancer of considerable size in the upper posterior wall of the uterus about half natural size. Post mortem specimen.

Fig. 81. A localised papillary cancer in the lower part of body of uterus about half natural size. The growth had well defined overhanging margins, but did not project much into the interior of the uterus and seemed to invade the muscle only to a moderate extent. At a little distance above it there is a simple glandular polypus. From single woman æt. 67, who complained of a constant watery blood-stained discharge of 5 months' duration. Menstruation had ceased 3 years before. No pain, anæmia or wasting, uterus movable. For microscopic section see Fig. 90.

Fig. 82. A localised cancer taking the form of a malignant ulcer with a granular or villous surface in lower part of body of uterus, just above internal os; about two-thirds natural size. Another small but malignant ulcer is seen at the fundus near one of the cornua. The uterus has unusually thick walls. From a married woman æt. 55, who complained of a constant green discharge of 2 years' durations, which stiffened the linen; also of pain at intervals in right groin. Menstruation had ceased two years before. She was well nourished and of a good colour, though she had recently begun to lose flesh. The uterus with appendages were removed by Dr. Thos. Wilson, after curettings had been pronounced to be cancerous by the writer to whom they were submitted by Dr. Wilson.

Fig. 83. Localised cancer with smooth surface filling up large part of body of uterus, almost diffuse; about two-thirds natural size.

Fig. 84. A diffuse cancer invading the whole uterus and cervix about half natural size. There is also a small discrete fibroid in the anterior uterine wall. The cancer had penetrated the wall of uterus and invaded that of the bladder and caused partial fixation of uterus. From a married woman æt. 47, who complained of a watery and sanious discharge of 12 months' duration and of pain for five years. There was a profuse loss of blood at the time that the pains began, but patient was neither anæmic nor emaciated at the time of the operation.

Fig. 85. Localised cancer in upper part of body of uterus which had undergone extensive necrotic changes; about two-thirds natural size. In great part it had a white or pale yellow appearance suggestive of caseation.

Fig. 86. Section of margin of cancer ×50. Cancerous tubes and spaces are seen to left (the reader's) and below, and normal tubes to the right, the former being more prominent and active looking than the latter.

Fig. 87. Section of margin of cancer ×50, shewing invasion of muscular wall by cancerous tubes to the right of the uterine cavity, and atrophied but otherwise normal endometrium, becoming slightly cystic, to its left, illustrating the same differences in structure and prominence between the two kinds of tubes.

Fig. 88. Section of a cancer ×50, shewing typical tubes lined by columnar epithelium, the structure characteristic of a columnar epithelioma. Most of it is of the so-called inverting type, though the nodule at the upper right corner is of the everting type.

Fig. 89. Lymphatics of the outer layers of muscular wall of uterus distended by cancerous cell growths, the result of cell emboli, ×50.

Fig. 90. Section of cancer ×50, shewing columnar celled spitheliomatous struc-

ture to left and below, and adeno-carcinoma and spheroidal celled carcinoma elsewhere. Taken from case Fig. 81.

Fig. 91. Sections of free surface of a cancer ×250, shewing the typical appearance of villous or papillary processes, which grow out from the free surface of the cancer or into the interior of alveolar spaces. Taken from case Figs. 78 and 79.

Fig. 92. Section of a cancer shewing the so-called keratinoid change in the epithelial cells of the cancer ×30.

Fig. 93. Section shewing the same change; apparent "cell nest" formation ×250.

Fig. 94. Curettings ×30 from case Figs. 78 and 79, shewing irregular alveoli much branched tubes and scanty stroma characteristic of malignancy.

CHORIO-EPITHELIOMA AND PLACENTAL MOLE.

Fig. 95. The uterus has been laid open in front to show the chorio-epitheliomatous growth forming only a small circular projection (about 3 mm. in diameter) into the cavity of the uterus.

Fig. 96. Sagittal section of the same uterus passing through the middle of the chorio-epithelioma. It forms a wedge-shaped growth penetrating nearly half way through the uterine wall. In the fresh state it was of a maroon colour, soft and friable. Above it another smaller but similar area is seen. They are two outlying parts of the same tumour. The uterus measured 11 cm. long, 7 cm. broad and the uterine wall 2 cm. thick. It was removed by Dr. Smallwood Savage by vaginal hysterectomy from a patient æt. 50, whose history disclosed that she had had 8 children, the last 7 years before, a hydatidiform mole extruded 11 weeks before and reappearance of hæmorrhagic discharge, which had begun 7 weeks before and had got worse of late. The patient was quite well when last heard of.

For full description of this case see paper by Leith and Smallwood Savage, "British Med. Journal," 1904, vol. 2, pp. 1391 to 1395.

Fig. 97. Uterus opened from the front shewing nodular, chorio-epitheliomatous growths projecting into the uterine cavity and infiltrating the underlying muscular wall as soft friable dark brown areas. From a woman æt. about 32, who was admitted to the General Hospital, Birmingham, suffering from high fever, rigors and a brown offensive uterine discharge. Chorio-epithelioma was suspected but she was too ill to undergo an operation and died of septicæmia within 24 hours of admission. There was an indefinite history of a miscarriage about 2 months before the date of admission but none of a vesicular mole. The uterus was removed post mortem and the lungs showed numerous small secondary growths: vide Fig. 116.

Fig. 98. Uterus laid open from front shewing a rough nodular growth on posterior wall, a chorio-epithelioma.

Fig. 99. Sagittal section of the uterus with coronal section of both ovaries in the same case. The uterus shews dark maroon coloured, soft, friable masses situated in muscular wall, just external to the endometrium and penetrating only for a short distance into the muscle. The growth is localised to the posterior wall and the apparently separate masses are outlying parts of one growth. Both ovaries shew numerous cysts varying in size from a pea to a Tangerine orange, which were found to be lutein and follicular in nature. From a woman æt. 28, who had been married for 14 months. She had had amenorrhœa of 2½ months' duration, followed by a smart flooding. A month later the uterus reached midway between the umbilicus and the ensiform cartilage. Flooding recurred and a large vesicular mole was evacuated. Intermittent hæmorrhage continued for 1 month when she was admitted to the Women's Hospital, Birmingham, under the care of Mr. Hewetson. The uterus was explored and a chorio-epithelioma accompanied by cystic ovaries was diagnosed. Abdominal hysterectomy was performed and the patient was in good health when last heard of, over two years afterwards.

Fig. 100. Sagittal section of uterus shewing several areas of chorio-epitheliomatous growth in the uterine wall just external to the endometrium. In the fresh state they were soft, spongy and maroon coloured. There were many others, varying in size from a pea to about that of a filbert nut, scattered throughout the myometrium. The cavity is empty owing to a previous curetting. The peritoneal surface, ovaries and tubes were normal. From a married woman æt. 43 who had had neither children nor miscarriages, who was admitted to the General Hospital, Birmingham, because of œdema of legs and abdomen and albuminuria complicating early pregnancy. The uterus was about the size of a 4 months' pregnancy. There was amenorrhœa of 2 months' duration. After being in hospital for about one month, she began to suffer from uterine hæmorrhage and a vesicular mole was expelled. About 4 weeks later irregular uterine hæmorrhage recurred and continued for 6 weeks, when she was readmitted to hospital, curettage was performed and a diagnosis of chorio-epithelioma established, when abdominal hysterectomy was performed. The patient was well when last heard of two years later.

Figs. 101 and 102. Sections of uterus about one-quarter natural size, containing many interstitial fibroids in its wall and a hydatidiform mole and blood clot in its cavity. From a married woman æt. 42, who reported that she had had a fleshy mole removed one year after her marriage 5 years before the hysterectomy. Menstruation thereafter was regular for a period of 6½ months, when after amenorrhœa for 2 months, a severe hæmorrhage occurred, which was followed by a more or less persistent loss of blood and occasional escape of a currant jelly like substance, for the next 4 months. The uterus was removed by Dr. Smallwood Savage in April, 1909, and the patient when last heard of, considerably more than a year after, was enjoying good health.

Fig. 103. Villi of hydatidiform mole ×30, extruded in case of Fig. 100, shewing the mesoblastic core and epithelial covering, though the differentiation into Langhans' layer cells and syncytial elements is not obvious owing to the low magnification.

Fig, 104. Part of a villus from the same case ×50, shewing the mesoblast core with epithelial covering, plainly differentiated into Langhans' layer cells inside and syncytial elements outside. These are the characteristics of a normal villus.

Fig. 105. Section taken from junction of mole and uterine wall in case Figs. 101 and 102 shewing blood clot below, immediately above which is a villus, penetrating the decidua, running horizontally across the field from right to left and reaching about half way across. Immediately above this is a great thickness of decidua between the villus below and uterine muscle above.

Fig. 106. The same villus ×50, shewing mesoblast core and epithelial covering, blood clot and decidua below and decidua above.

Fig. 107. Villus ×100 of the chorio-epithelioma in case Figs. 98 and 99 seen to be invading the muscular wall of the uterus. The mesoblastic core and both epithelial elements are visible.

Fig. 108. Section taken from near the margin of the large maroon coloured area in Fig. 96, shewing a villus of chorio-epithelioma, possessing fibrous core and epithelial covering, occupying a wide channel below and to the left, surrounded by a mass of blood clot and fibrin, above and to the right ×40.

Fig. 109. Section taken from the same area closer to the muscular wall, shewing a villus, possessing fibrous tissue core and epithelial covering (chiefly of Langhans' cells) penetrating the muscular wall of the uterus ×40.

Fig. 110. Apex of villus ×100 of the chorio-epithelioma in case Fig. 100 shewing the mesoblastic core commencing to degenerate and the epithelial covering still actively vigorous..

Fig. 111. A solid epithelial villus ×30 of the chorio-epithelioma in case Fig. 100. Both epithelial elements are present but there was no trace of a fibrous core. Other villi near it showed cores partly degenerated.

Fig. 112. Section of the tip of a villus ×300 taken from case Figs. 95 and 96 shewing both cellular elements, the syncytial predominating. The latter are seen as large irregular granular masses containing several nuclei and sometimes vacuoles. The Langhans' cells are polyhedral uninucleated usually and stain less deeply.

Fig. 113. Apex of a villus tipped with a little white thrombus invading a large venous sinus in the muscular coat of the uterus. The villus is chiefly composed of Langhans' layer cells. From case Fig. 100.

Fig. 114. Cellular embolus composed mainly of syncytial elements ×20 lying free in cavity of a vein within the muscular wall of the uterus. The tongue of muscle to the right (reader's) between the forked branches of the vein is lined in part by similar fœtal cell penetrating the muscular wall of the uterus ×40.

Fig. 115. Cellular embolus lying free in a vein in the round ligament as far out as the ovary ×250. It contains both syncytial and Langhans' cells. From case Fig. 100.

Fig. 116. Embolus within a branch of the pulmonary vein within the lungs ×50 shewing both mesoblastic core and epithelial elements, proving that portions of the whole thickness of a villus may be detached from the original uterine growth and deposited in a distant organ. From case Fig. 97.

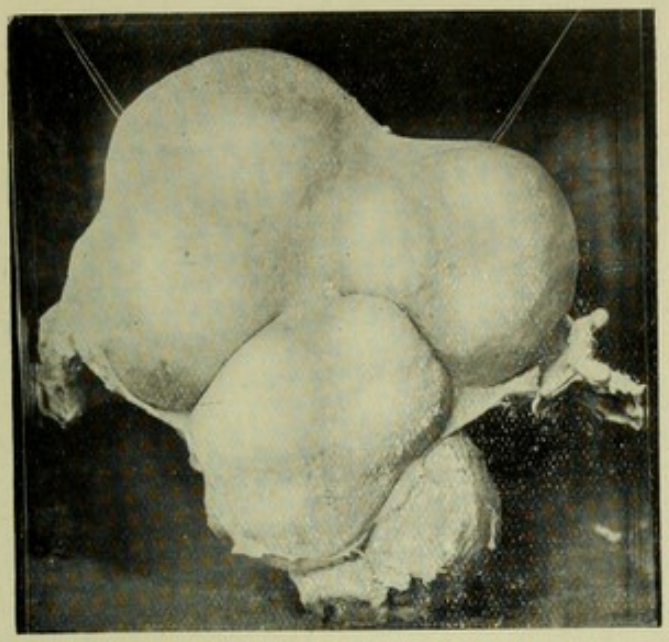
Figs. 117 and 118. Sections taken from two parts of the muscular wall of the uterus in case Figs. 101 and 102 after they had been thoroughly scraped with the finger and the curette by Mr. Hewetson, with the object of determining whether artificial evacuation of a mole with the finger followed by a thorough curetting of the same area could be depended on to free the uterine wall from the invading fœtal elements. In both cases considerable portions of villi, containing both fibrous cores and epithelial coverings, are seen to have been left behind, showing that in some cases of hydatidiform mole, at any rate, the fœtal elements invade venous sinuses within the myometrium too deeply to allow of either natural extrusion or artificial removal. These fœtal remains may be the origin of the chorio-epitheliomatous growths which follow after the extrusion of a hydatidiform mole.

Fig. 119. Section of a chorio-epithelioma ×100 taking from a part of the muscle wall of the uterus beyond the apparent base of the growth shewing syncytial elements (fine rootlets of the growth cut across or emboli) burrowing among the muscle in making their way to the veins.

Fig. 120. Section of a similar part of a chorio-epithelioma ×150 shewing syncytial elements burrowing in the walls of the veins and making their way into the lumen.

Fig. 121. Section of a similar part somewhat further into the uterine wall ×150 shewing syncytial elements in the process of penetrating the left end of the vein in the centre of the field .

Fig. 122. Section taken from the uterine wall towards the peritoneal surface in the case of chorio-epithelioma shewn in Figs. 95 and 96 stained by Weigert's elastic tissue method. It shews a large syncytial element (below and to the left of the lumen) in the process of leaving the lumen of a large vein and burrowing its way through its wall into the surrounding tissue. It had travelled to its present site as an embolus, become fixed, and in a degenerated condition is leaving the vessel again.



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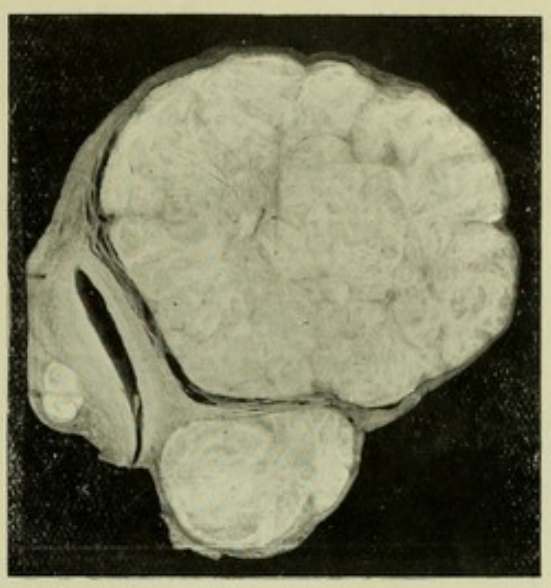

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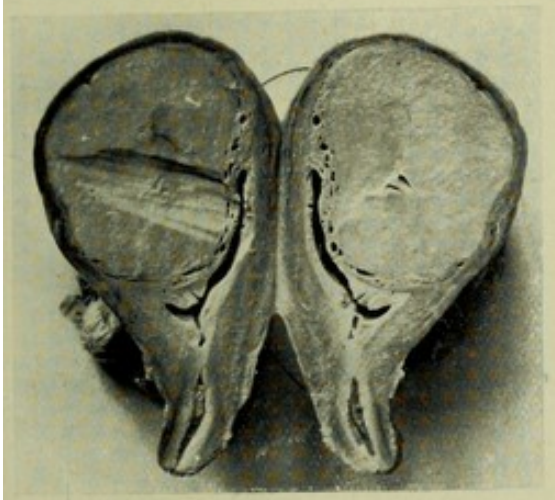
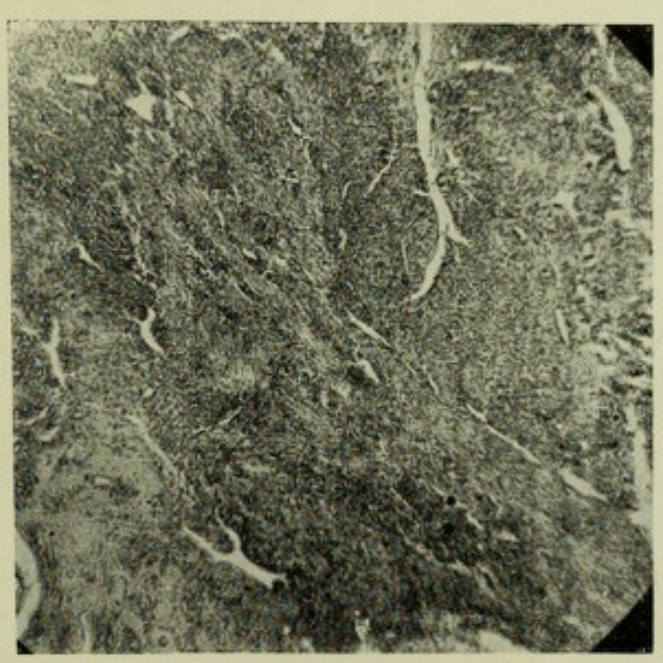


Fig. 3



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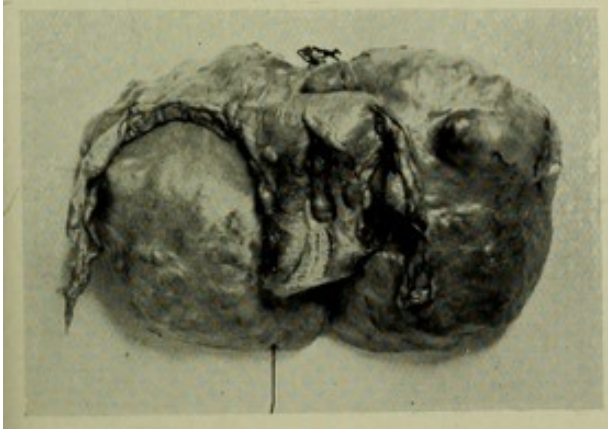

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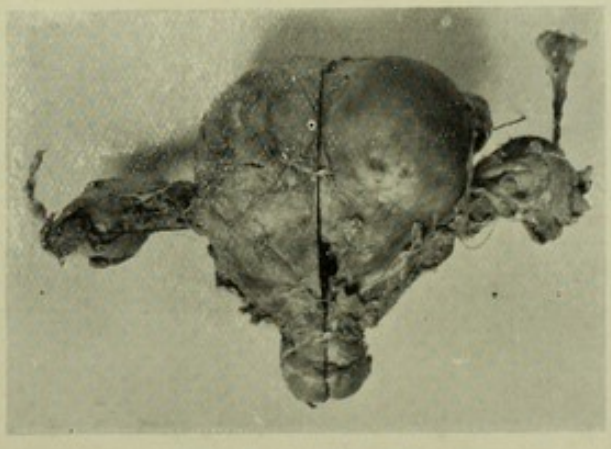


Fig. 6.

Fig. 7.

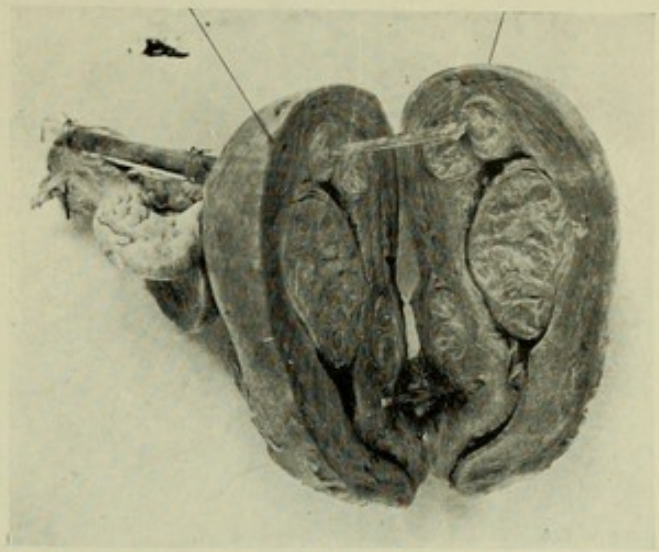


Fig. 8.

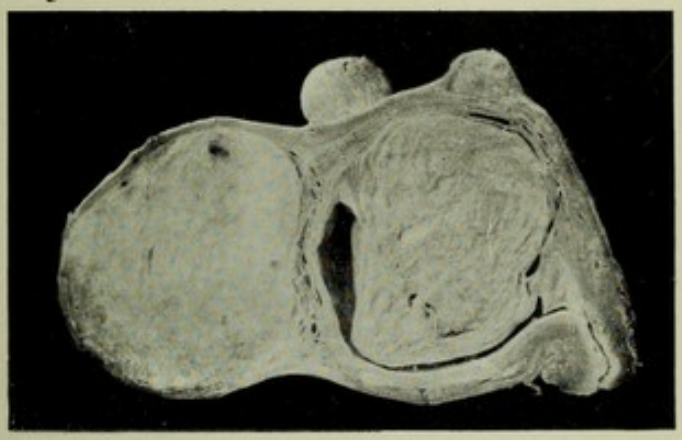


Fig. 9.

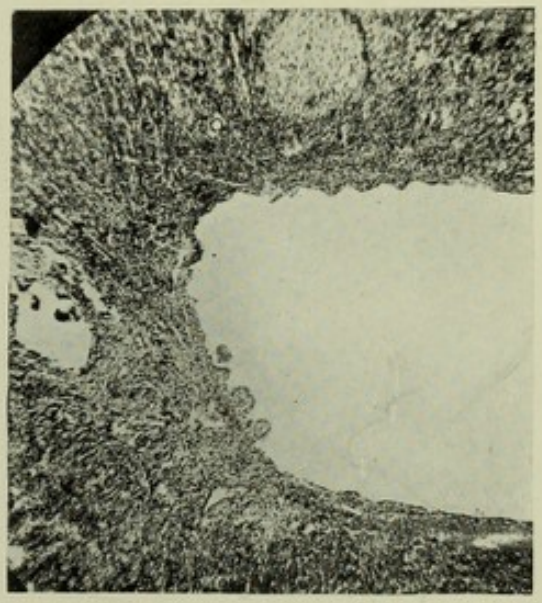
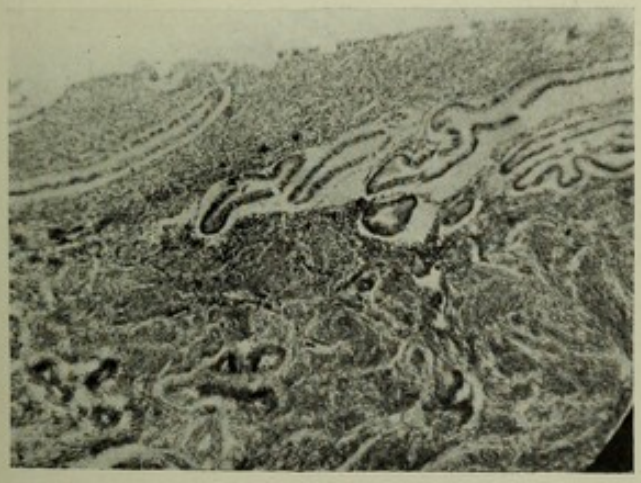


Fig. 10.



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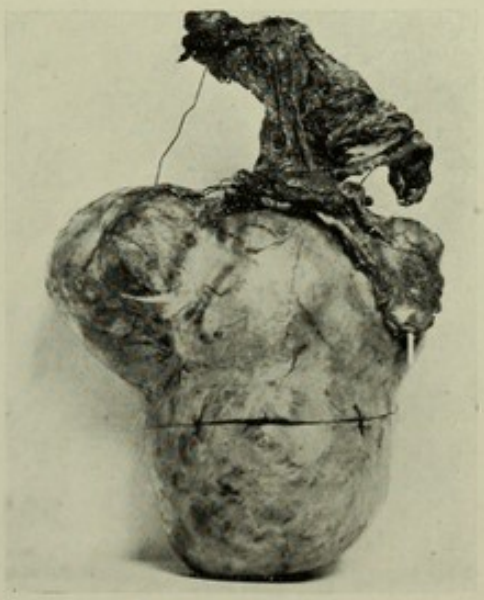
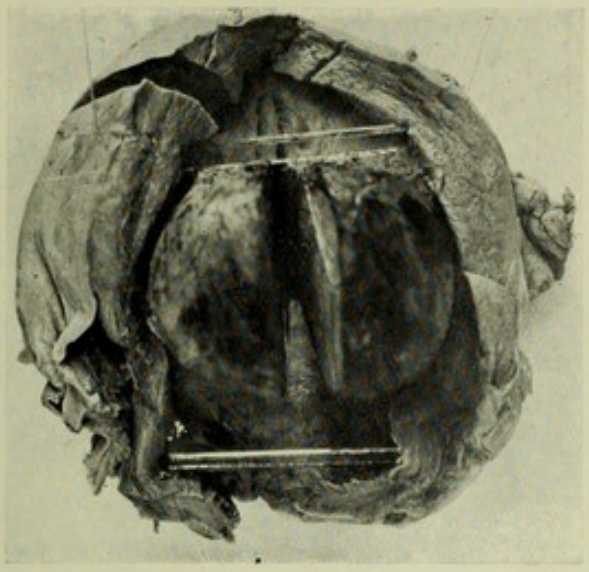


Fig. 12.



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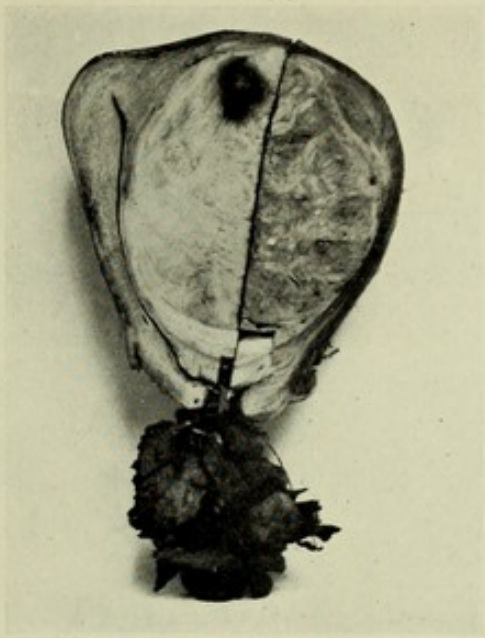
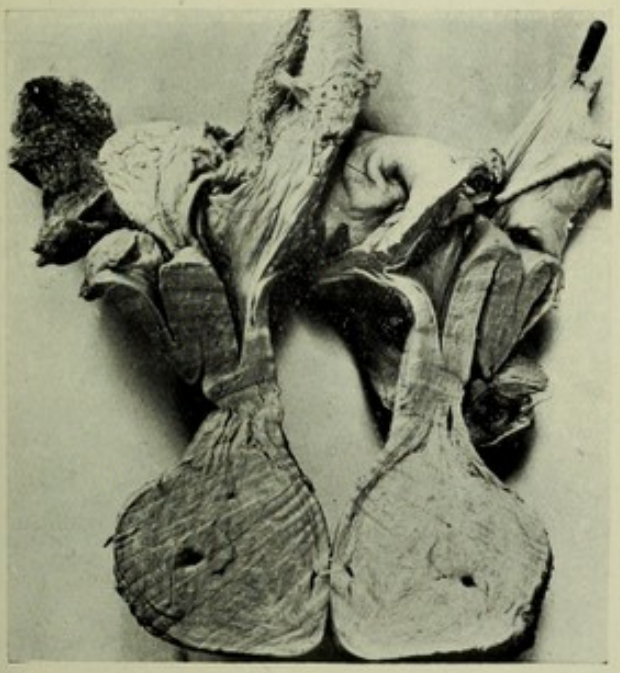


Fig. 14.



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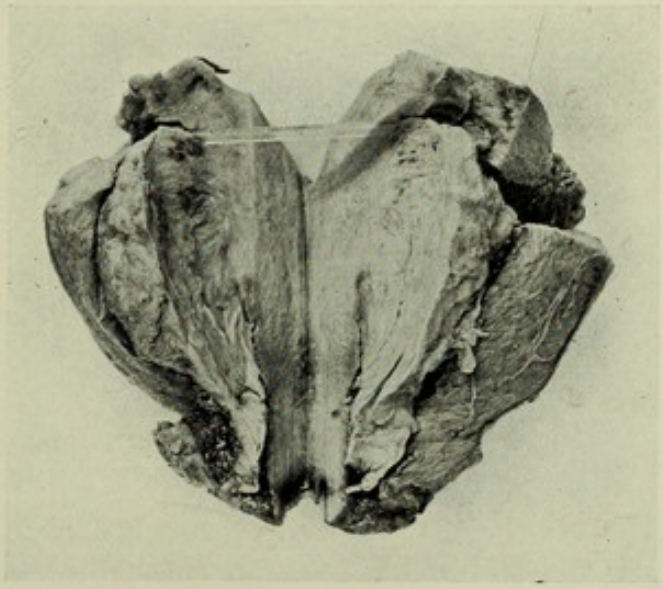


Fig. 16.

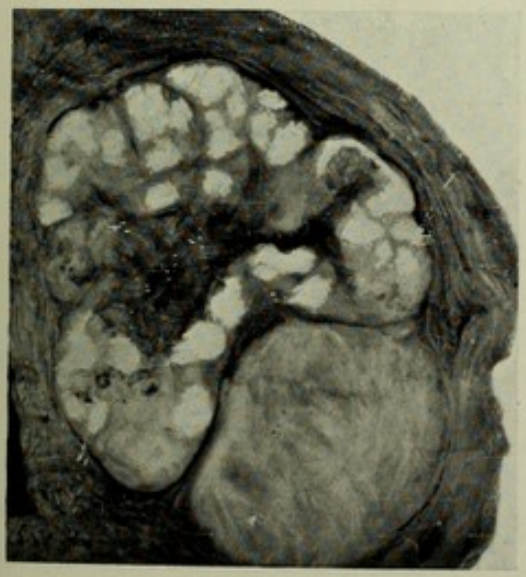


Fig. 17.

Fig. 18.

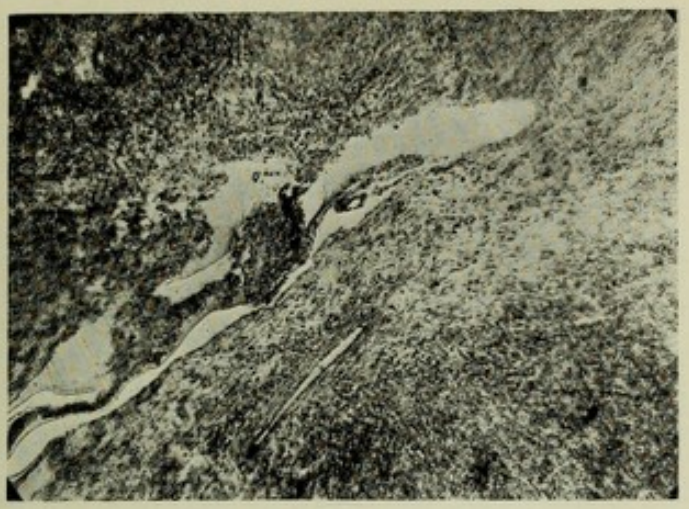
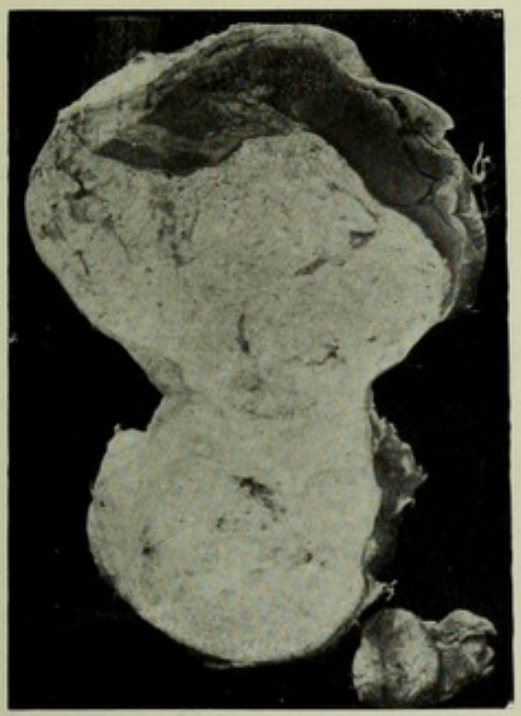


Fig. 19.

Fig. 20.



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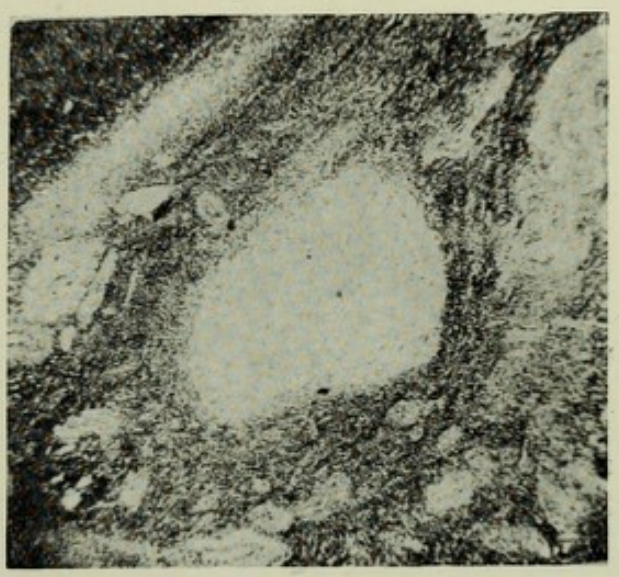

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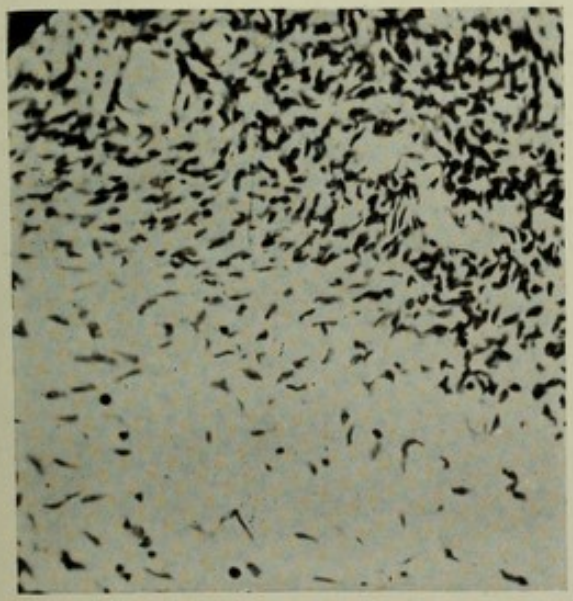

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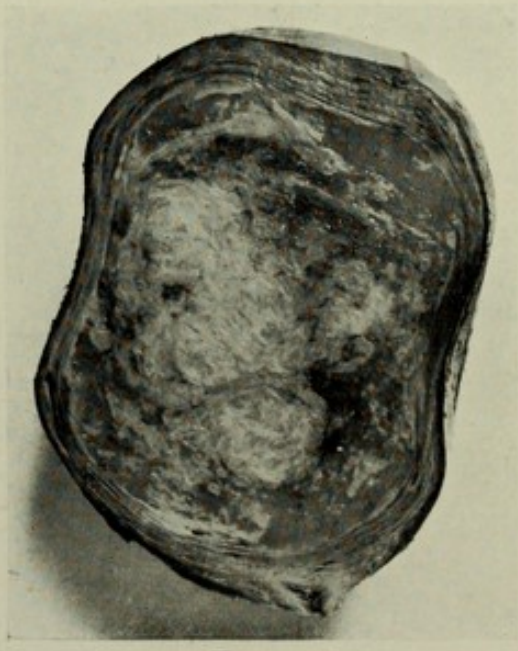

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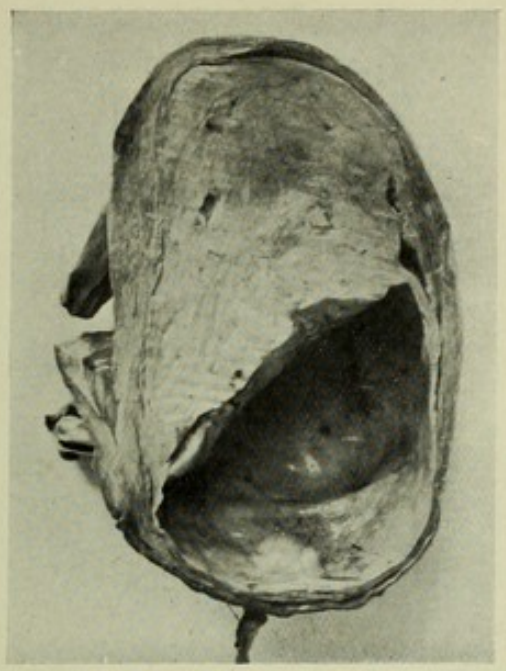

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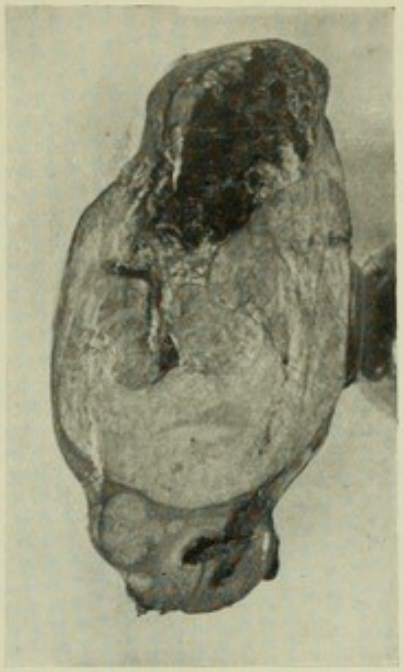

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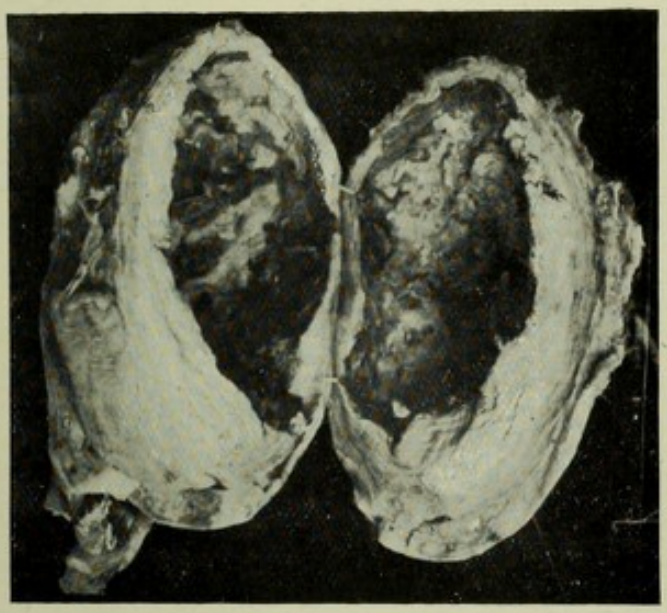

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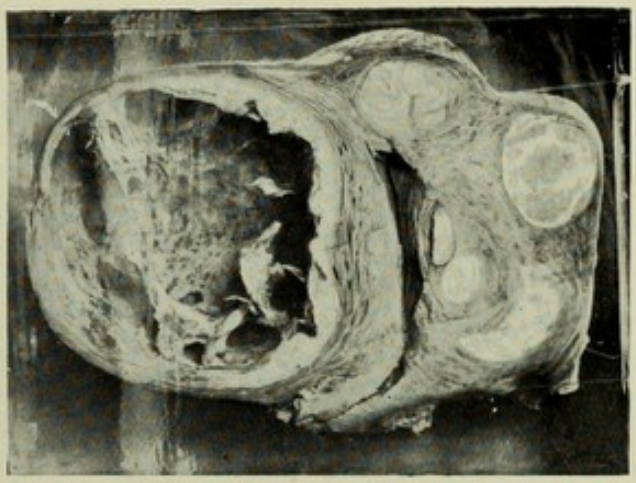

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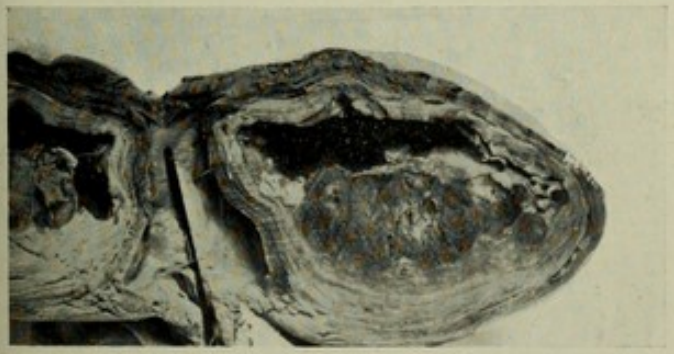

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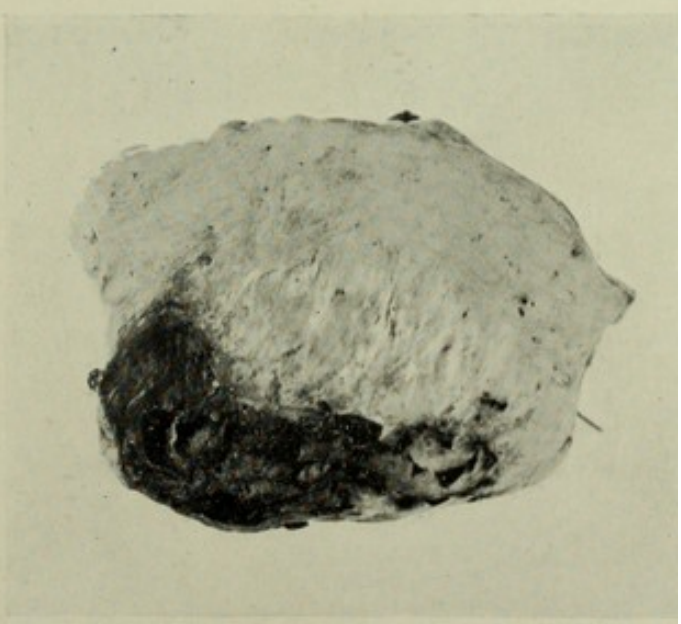

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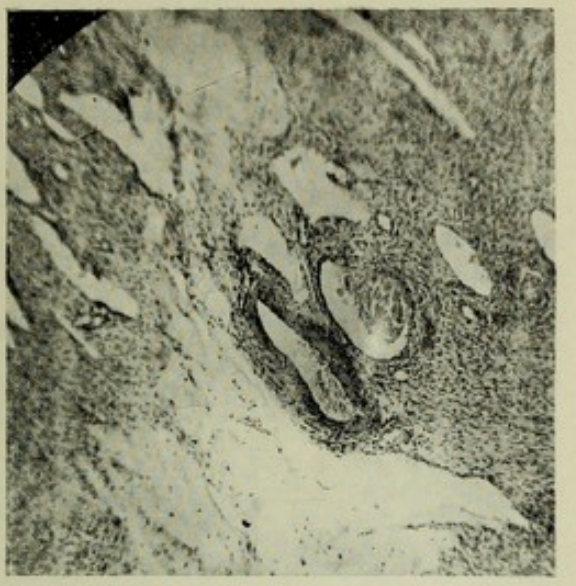

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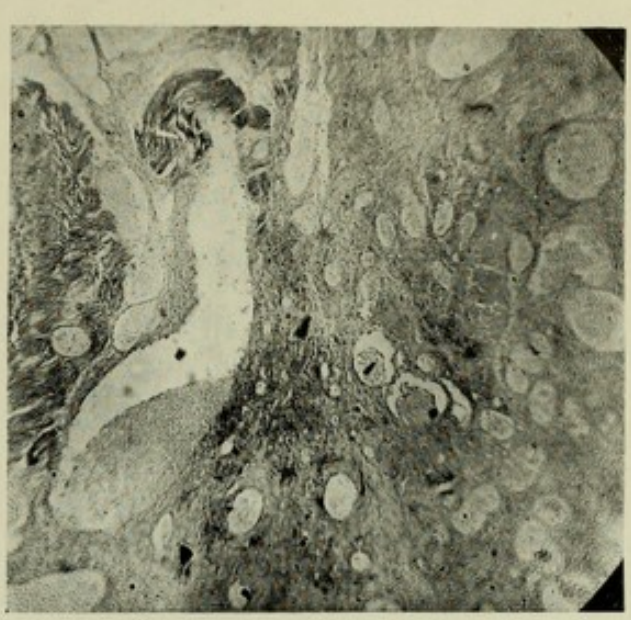

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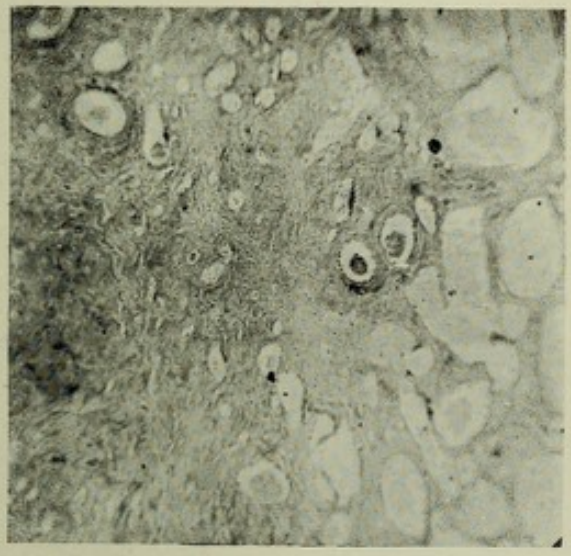

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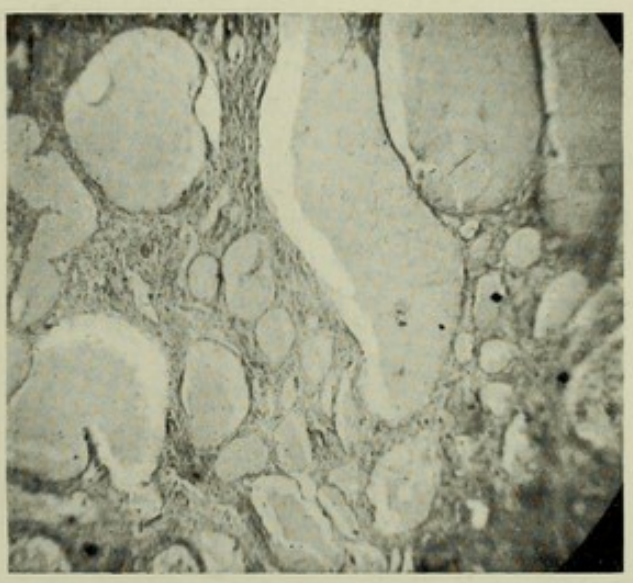

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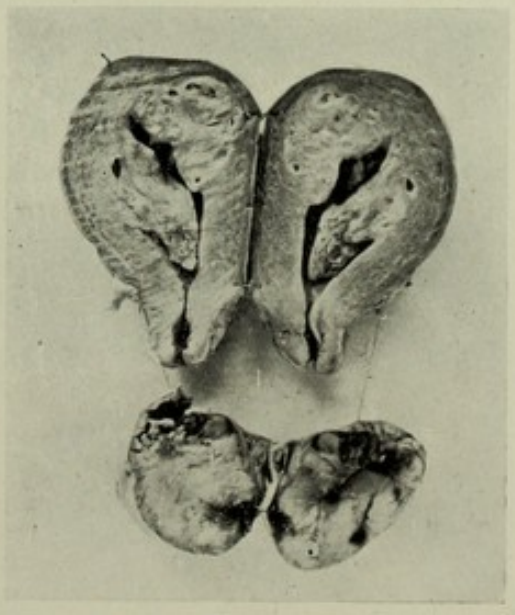

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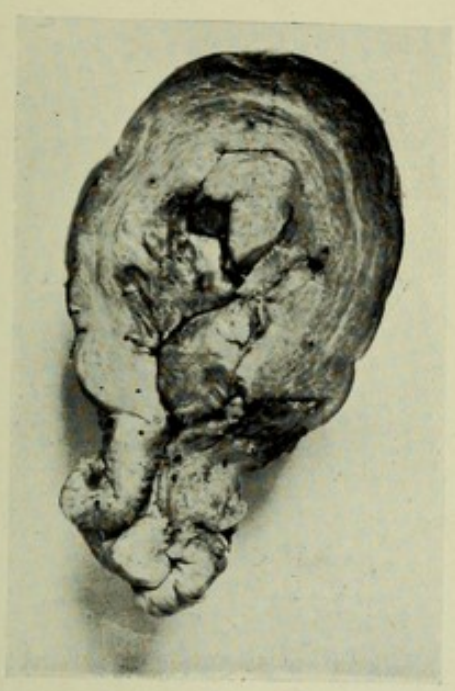

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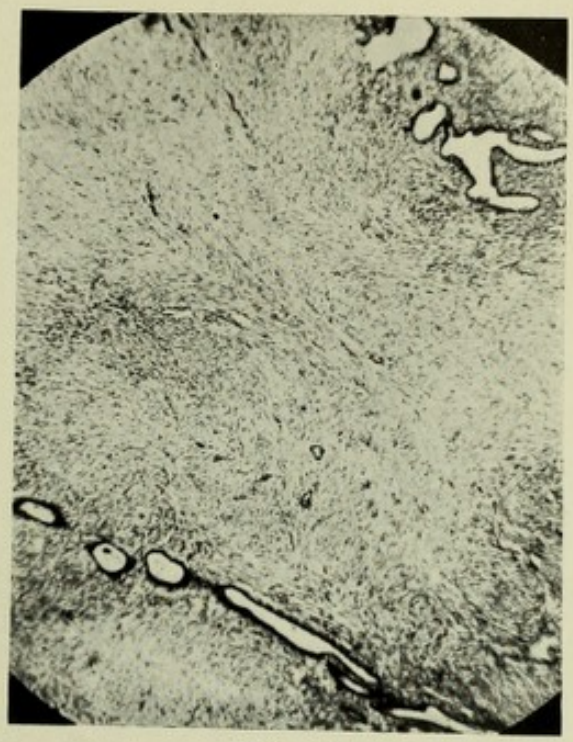

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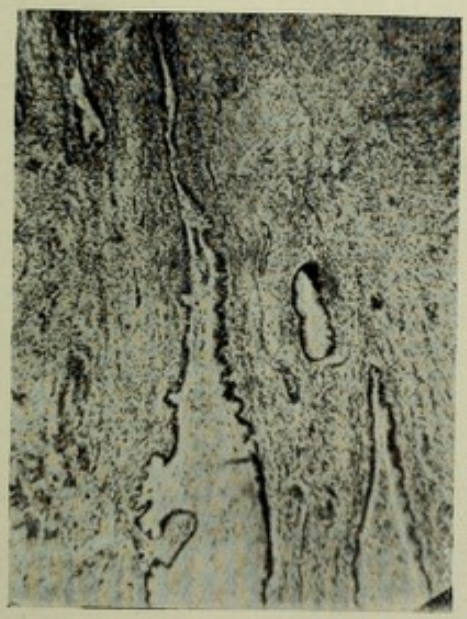

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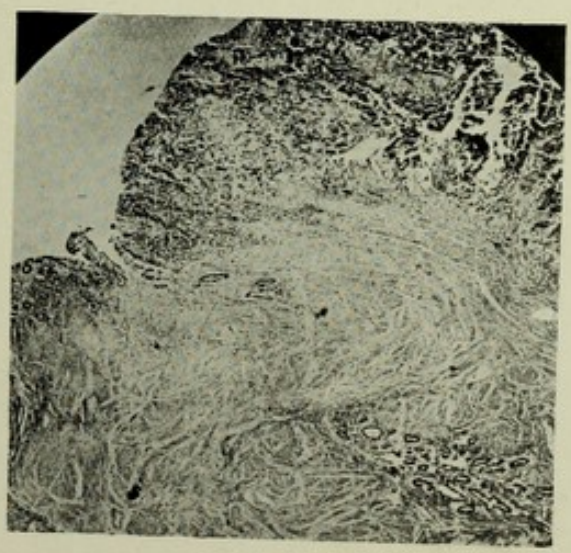

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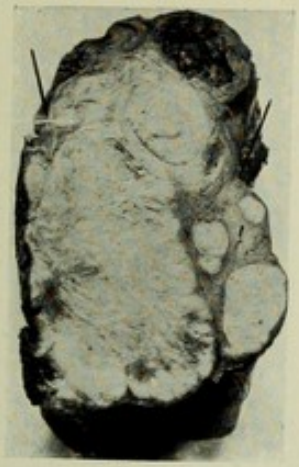

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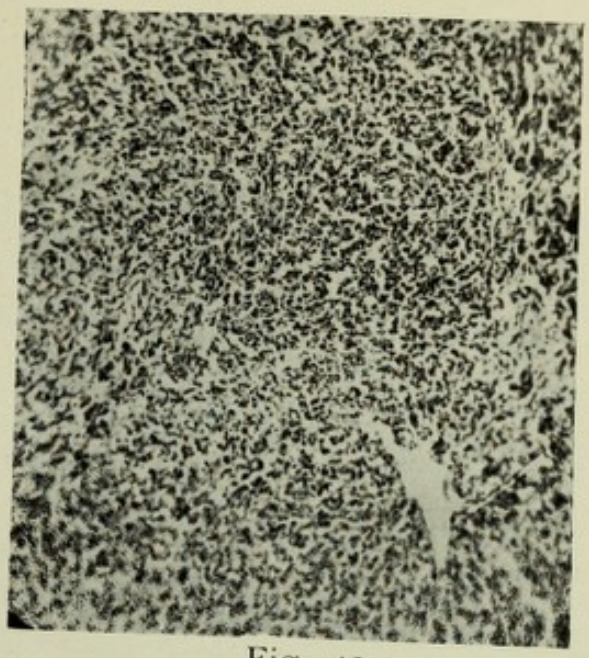

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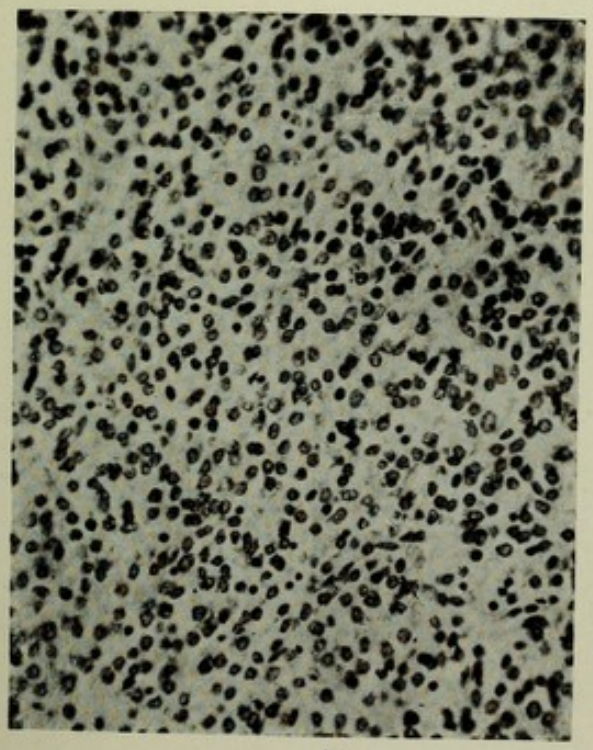

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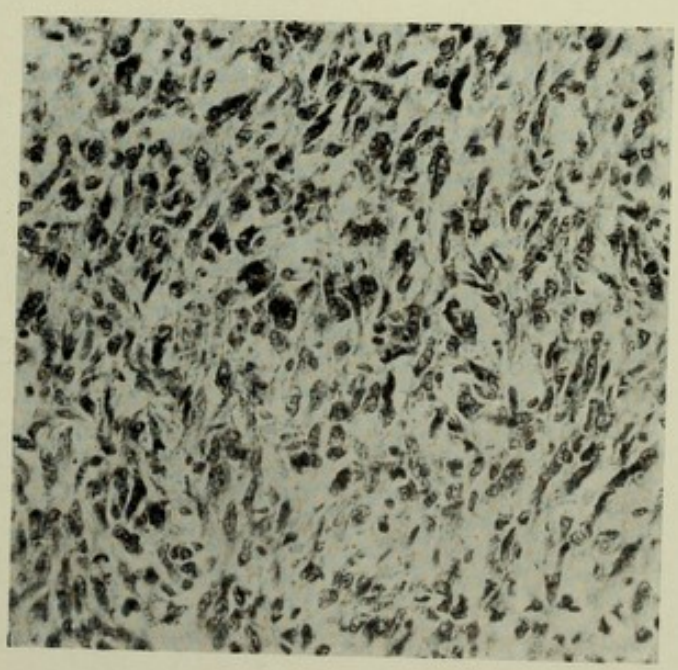

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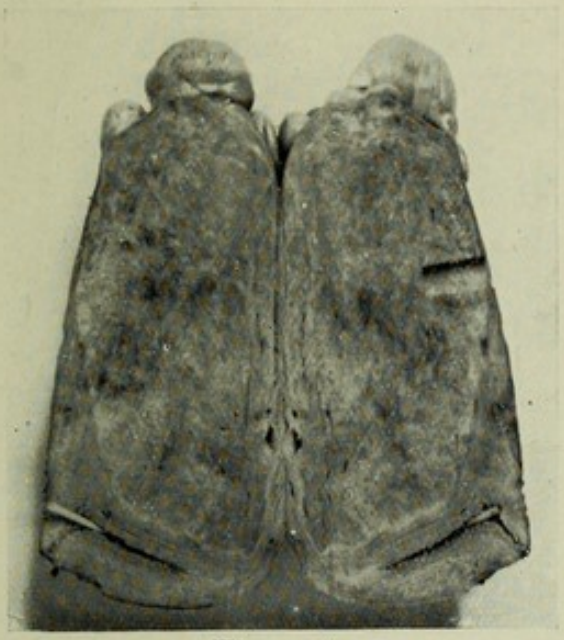

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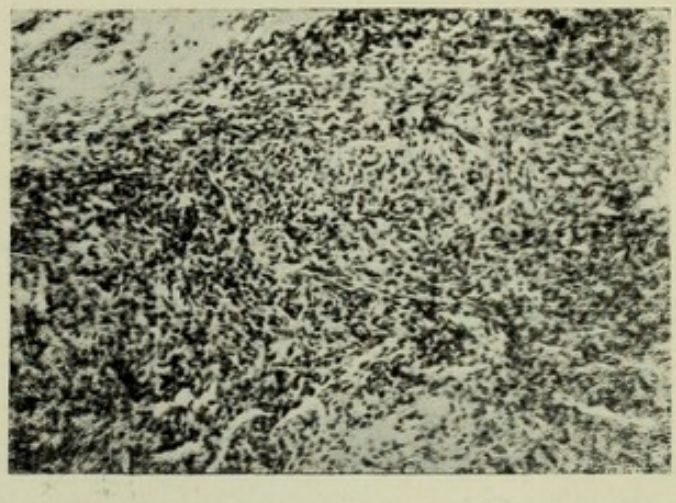

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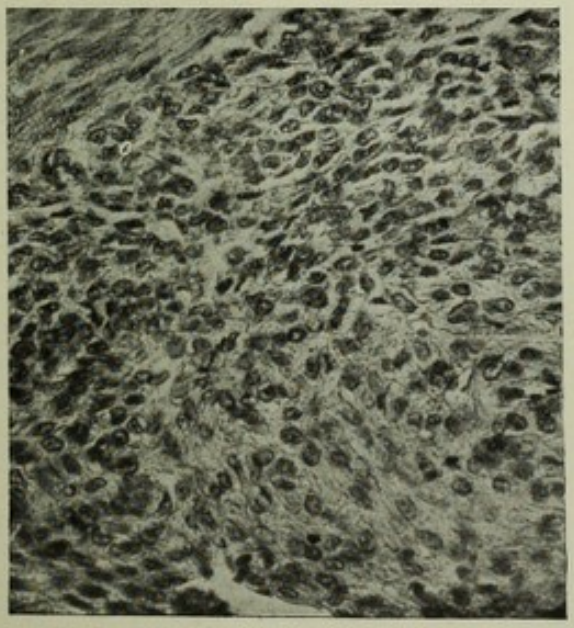

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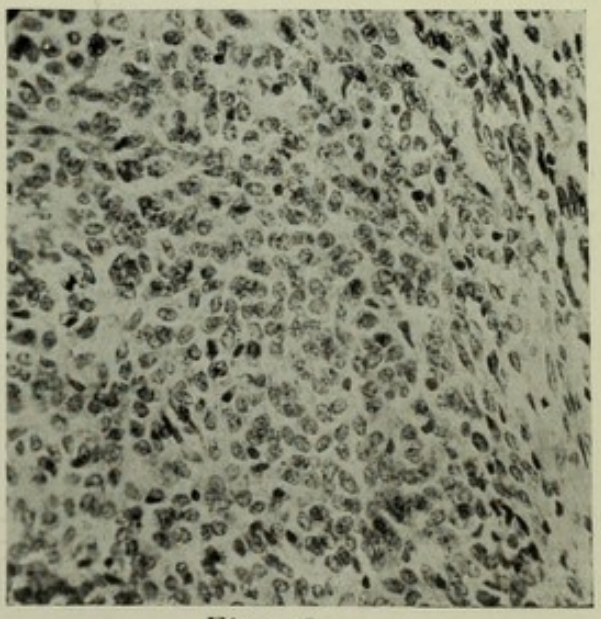

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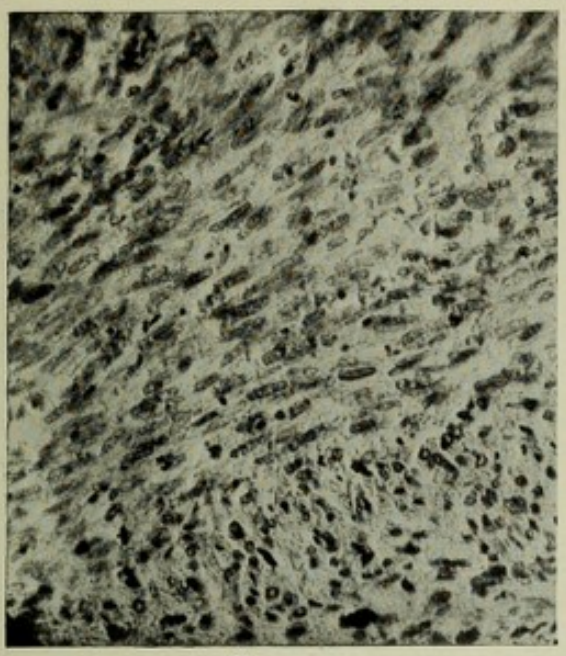

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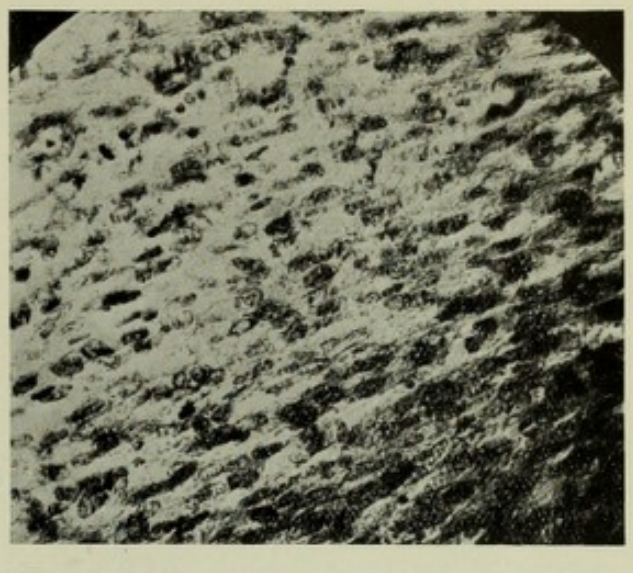

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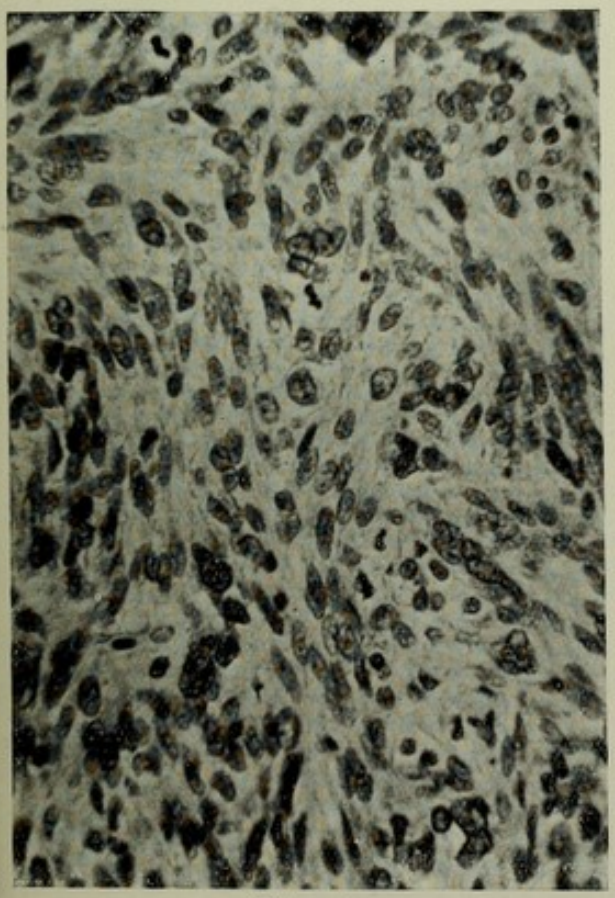

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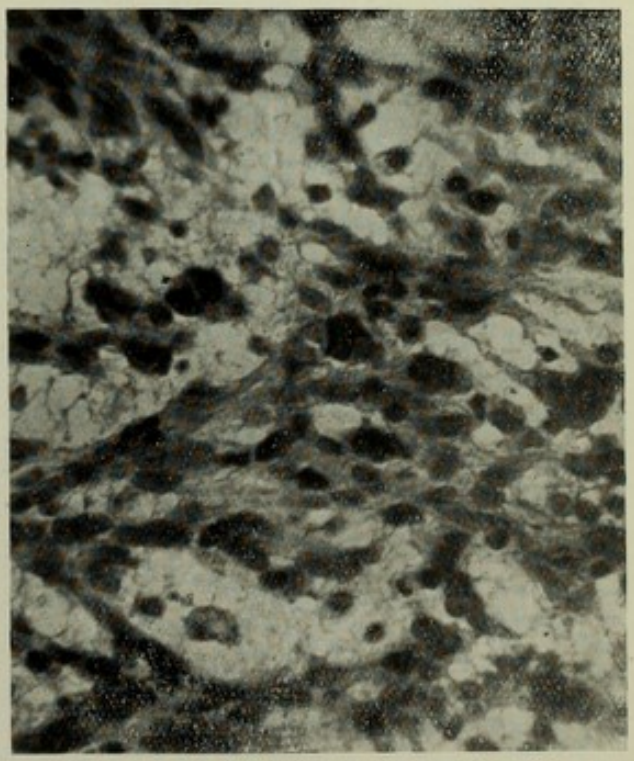

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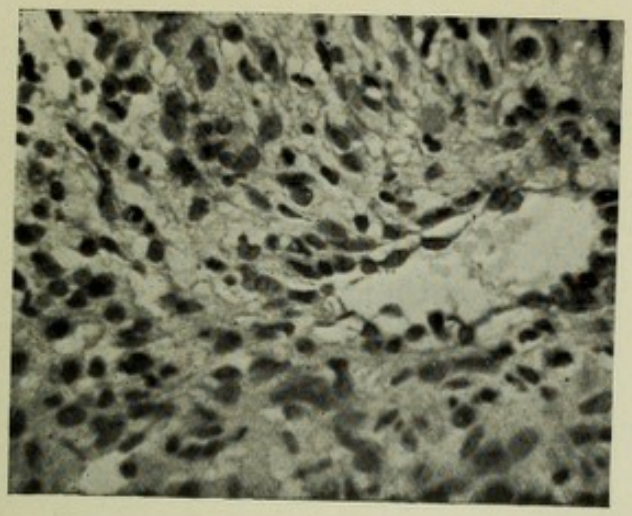

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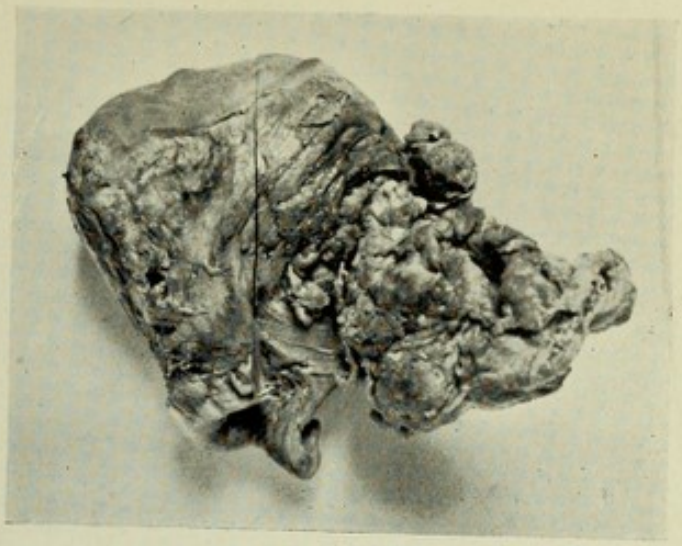

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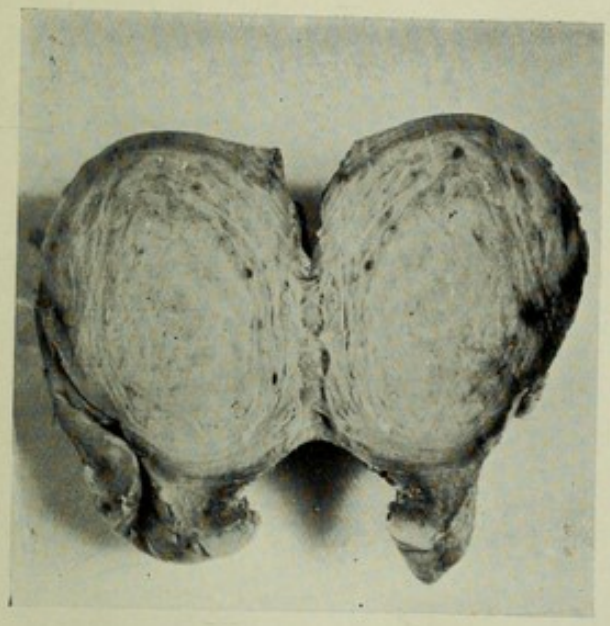

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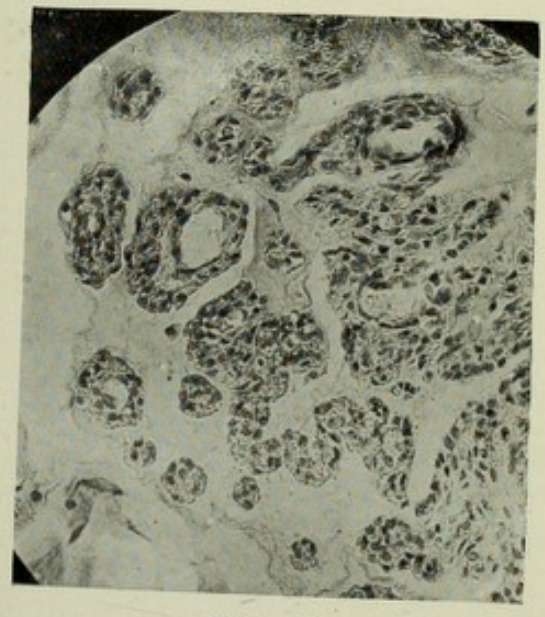

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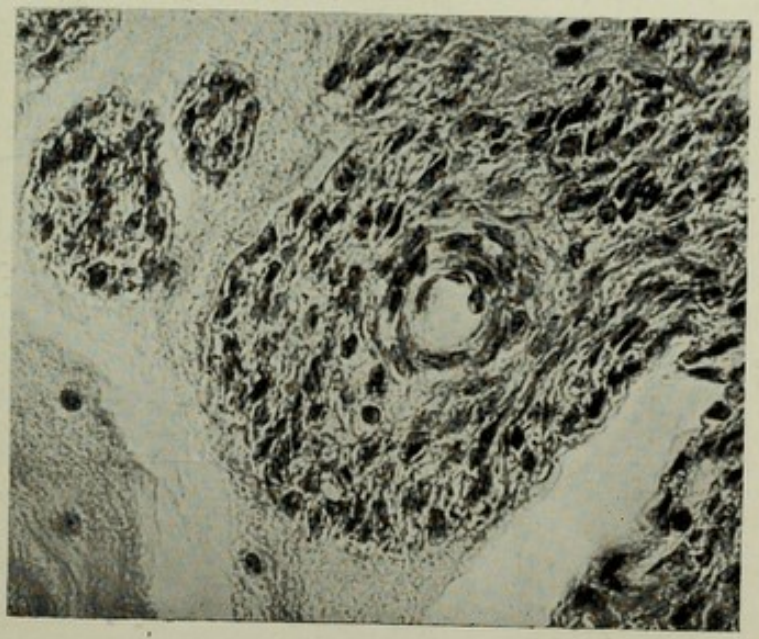
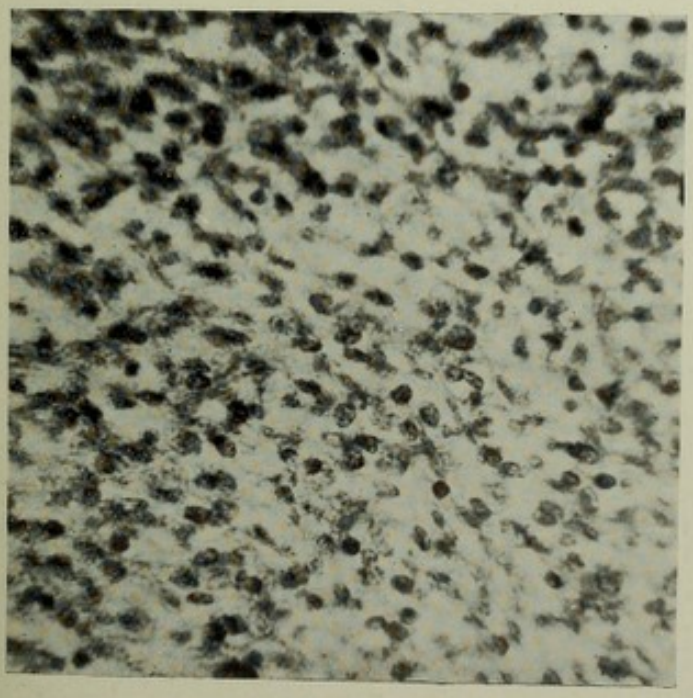


Fig. 57.

Fig. 58.



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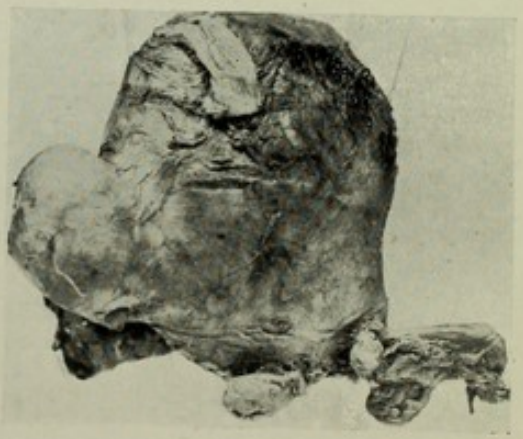

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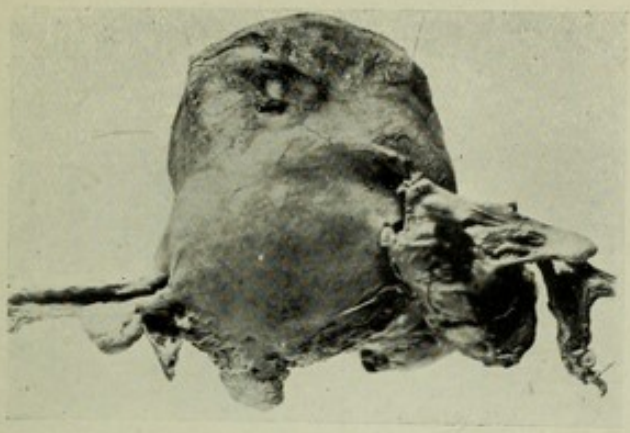

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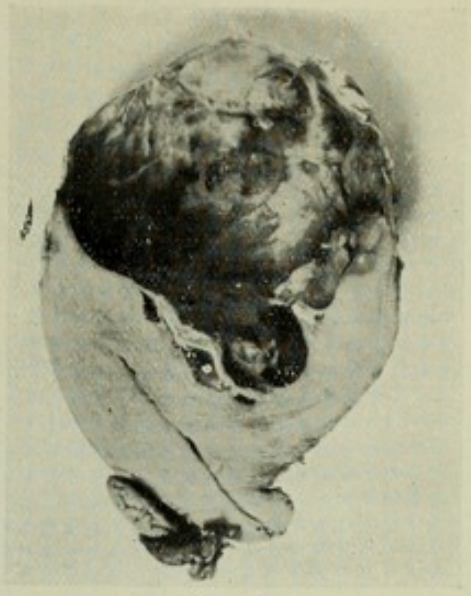

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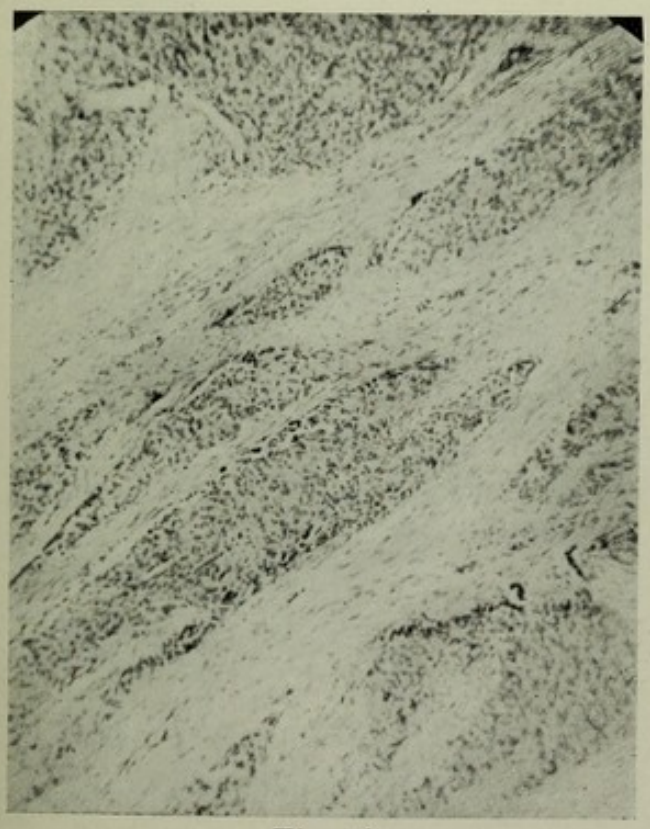

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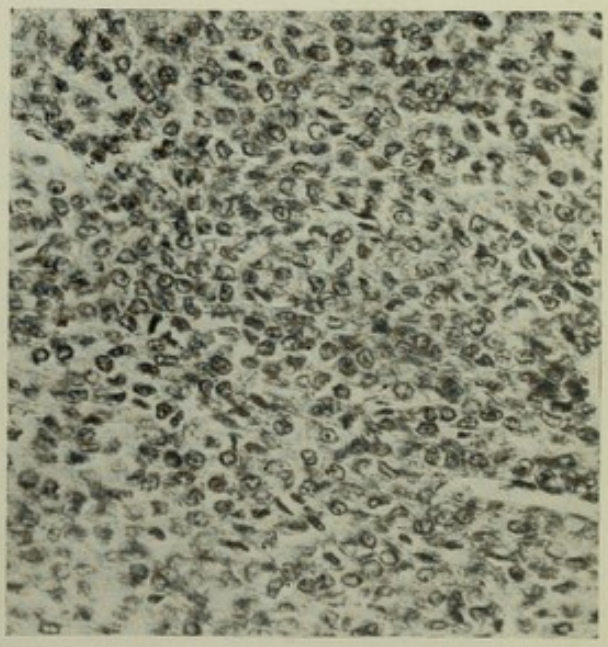

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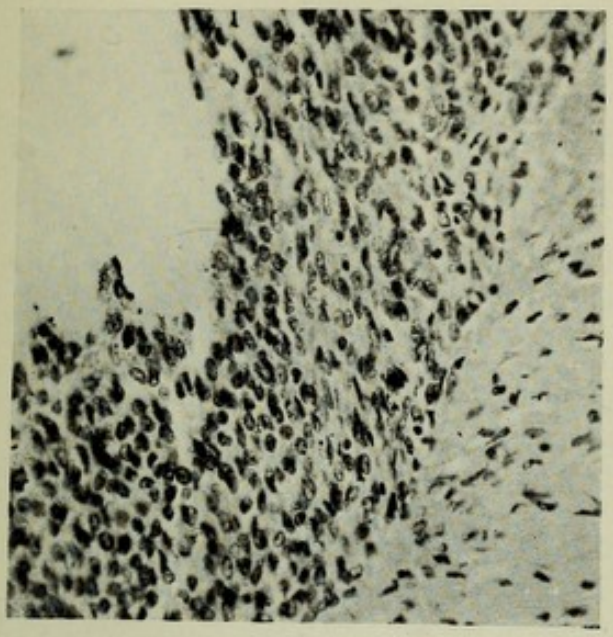

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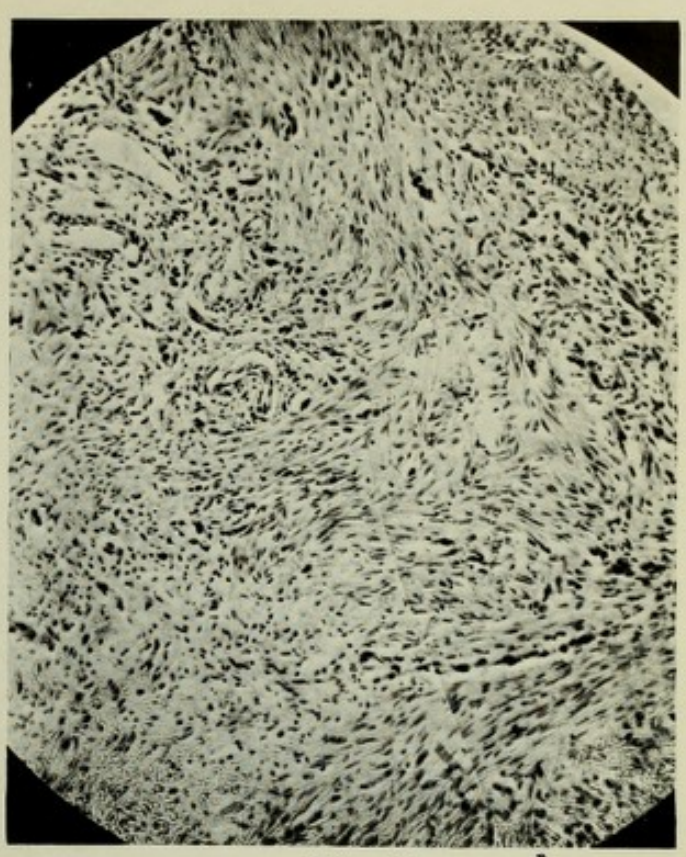

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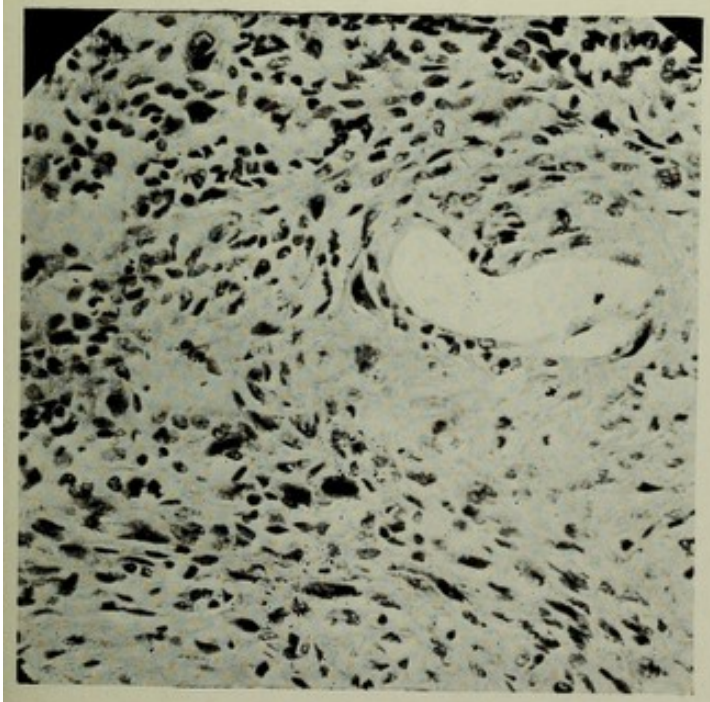
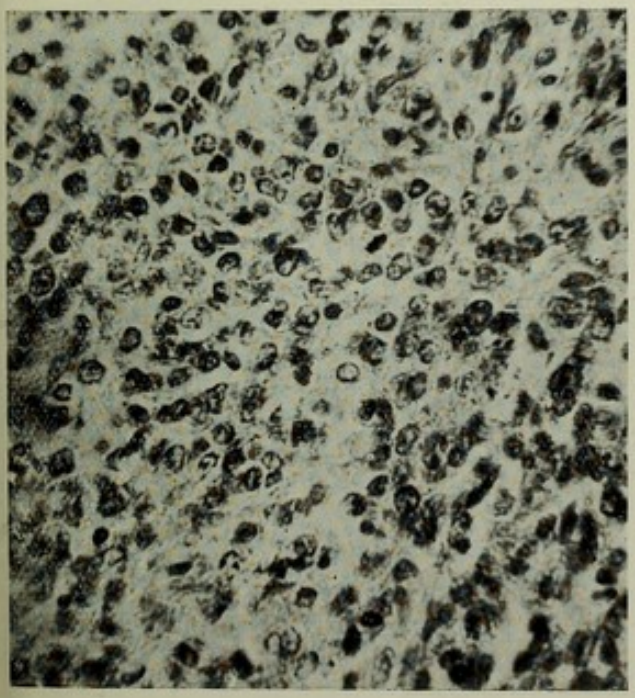


Fig. 67.

Fig. 68.

Fig. 69.

Fig. 70.



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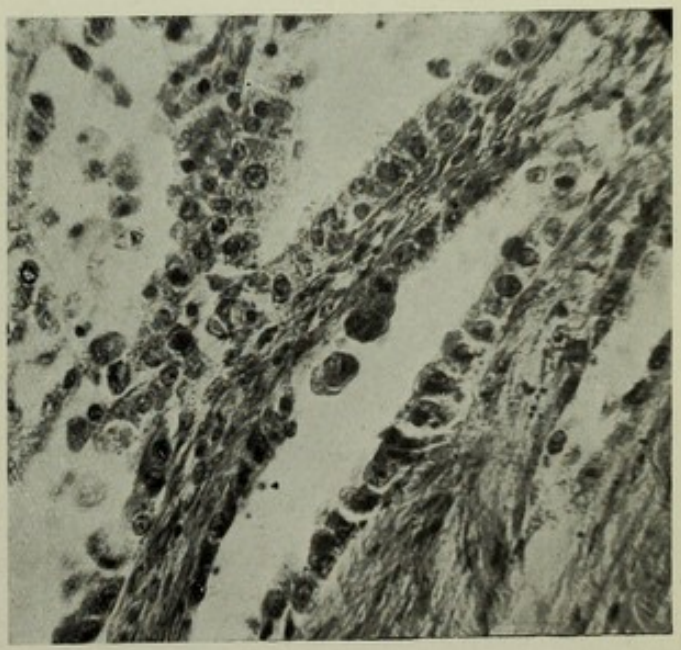

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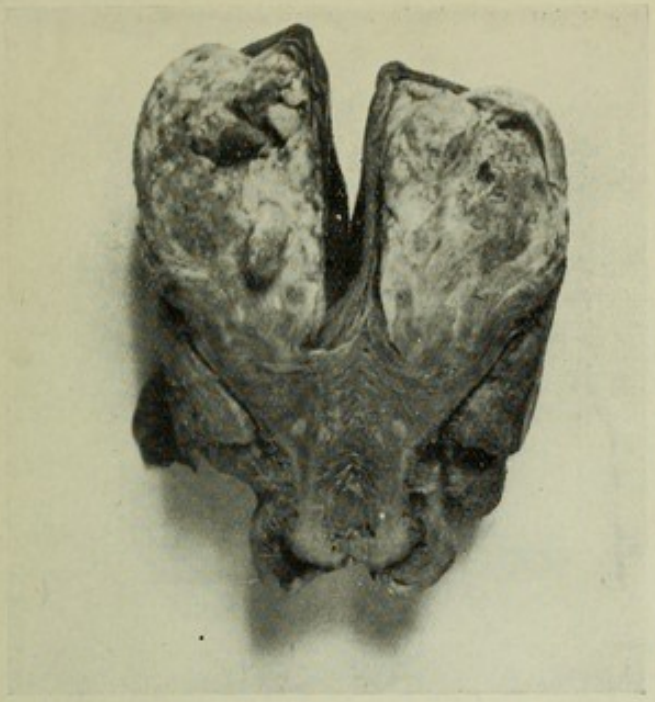

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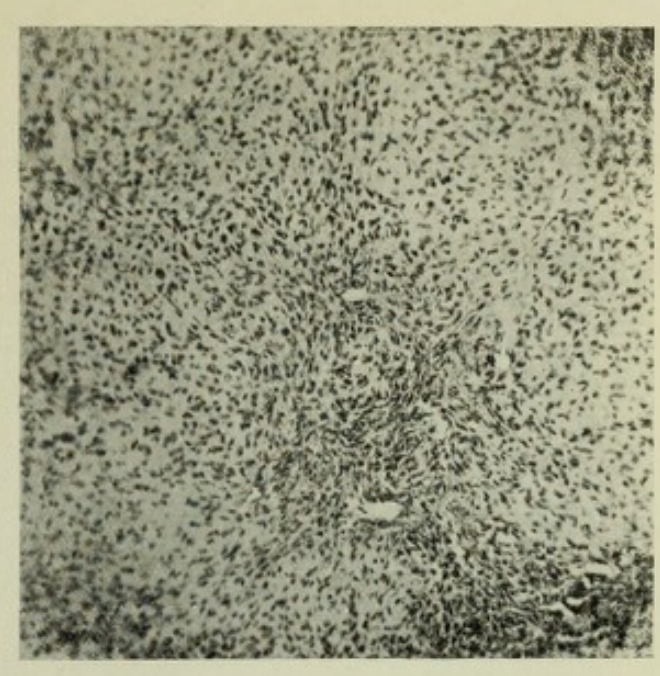

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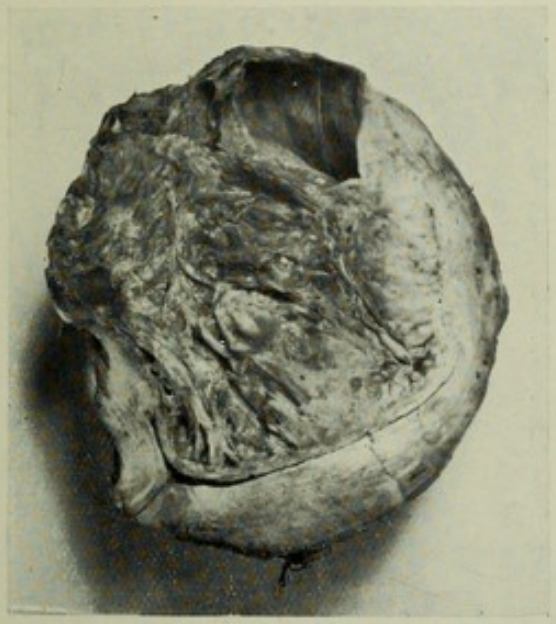

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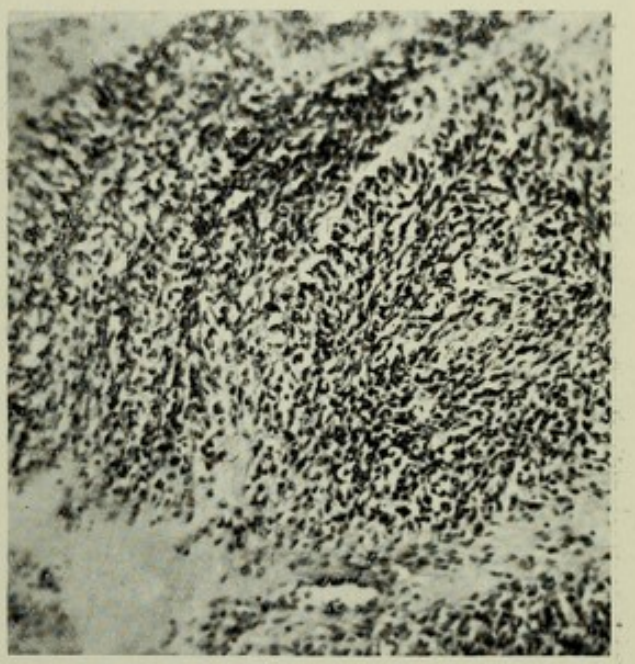

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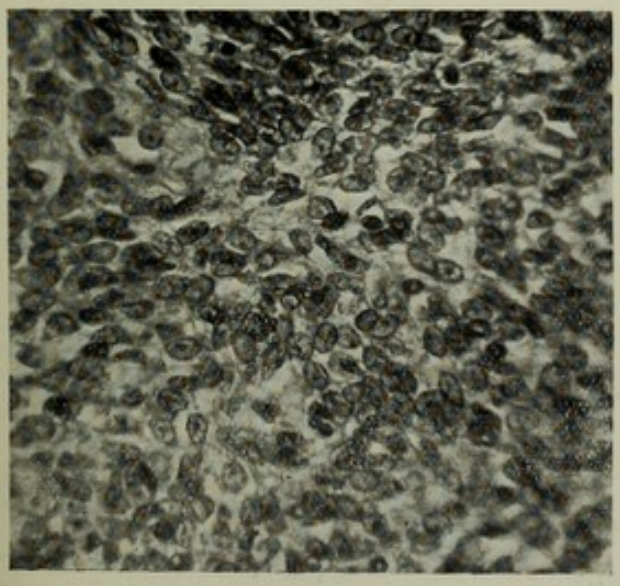

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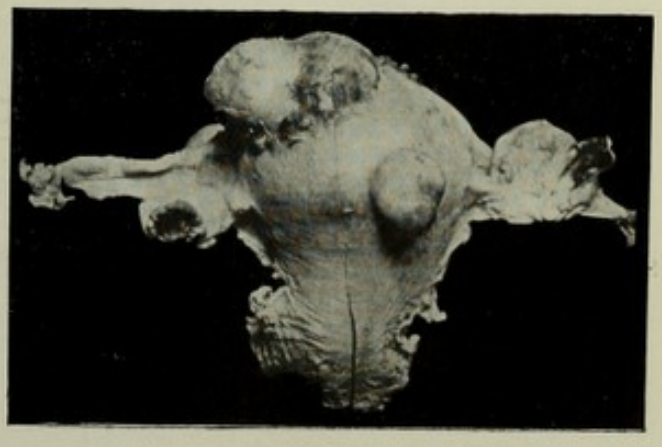

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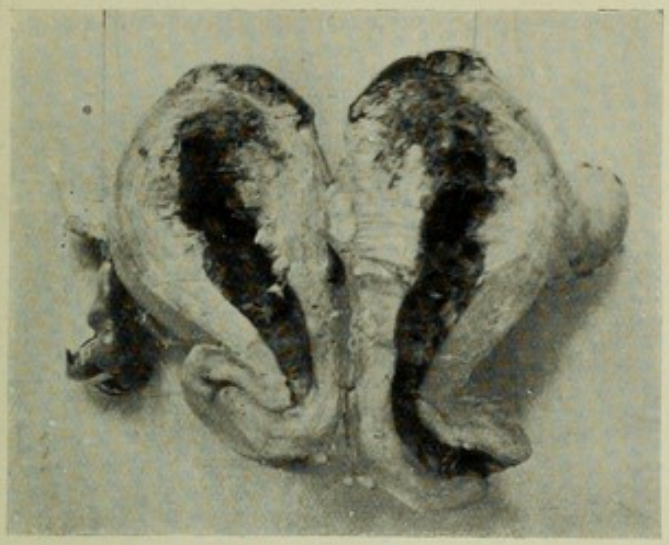
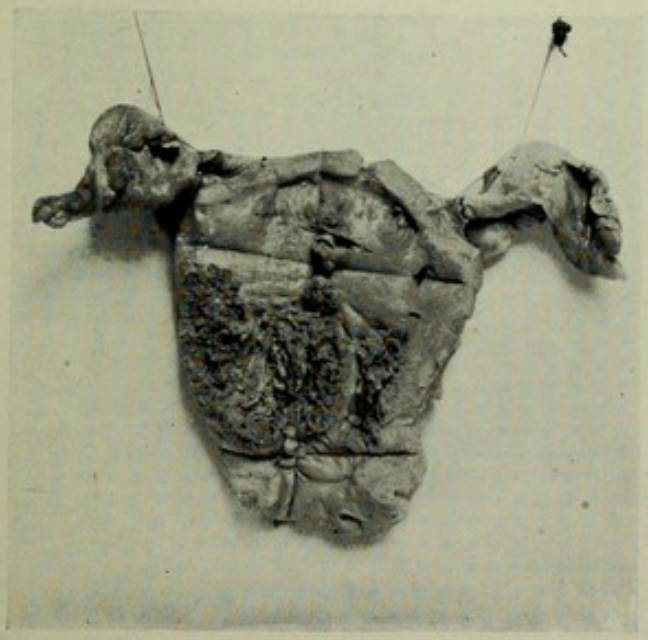


Fig. 79.

Fig. 80.



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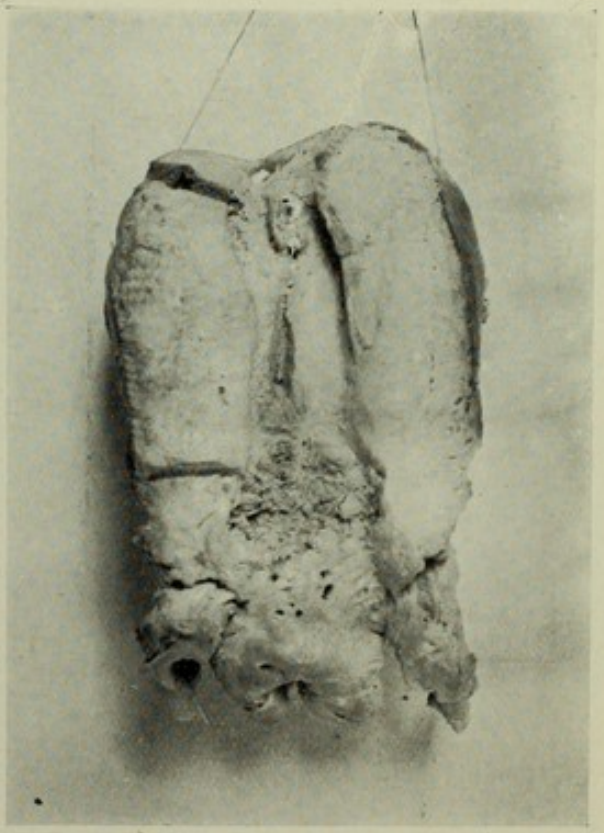

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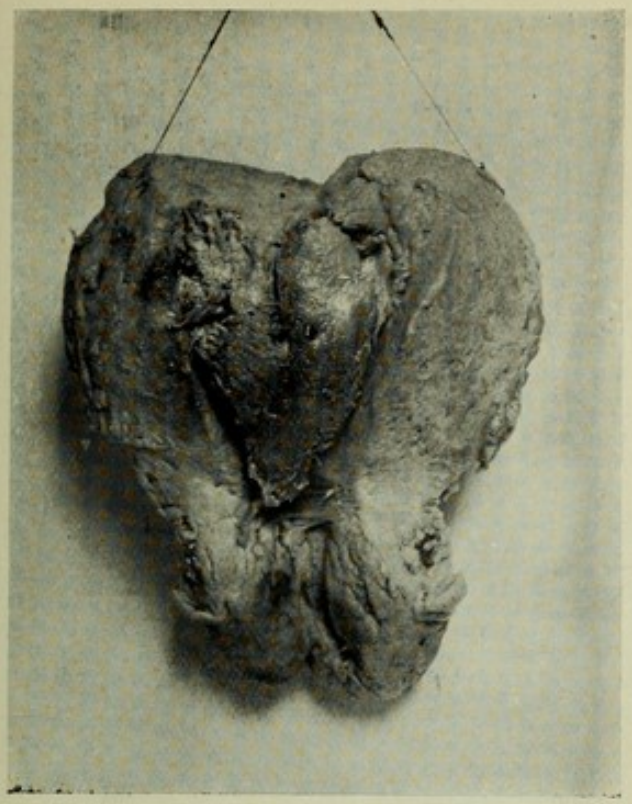

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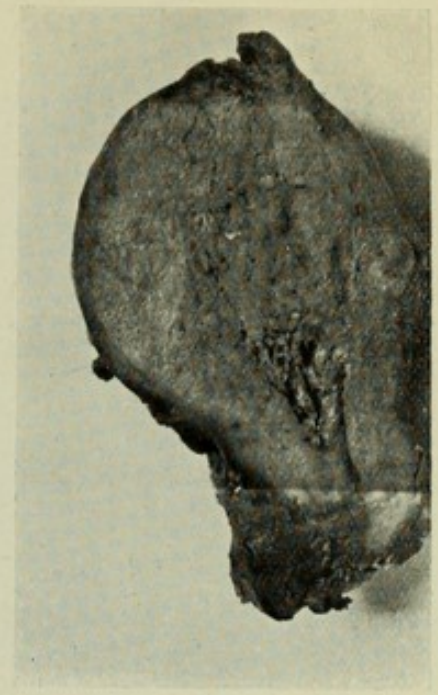
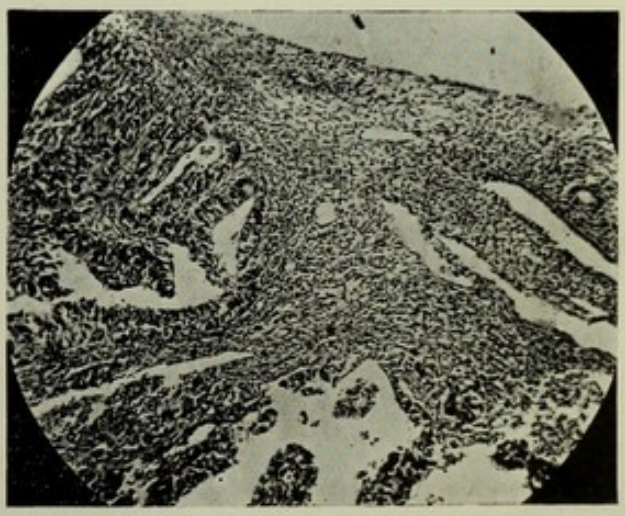


Fig. 84.

Fig. 85.



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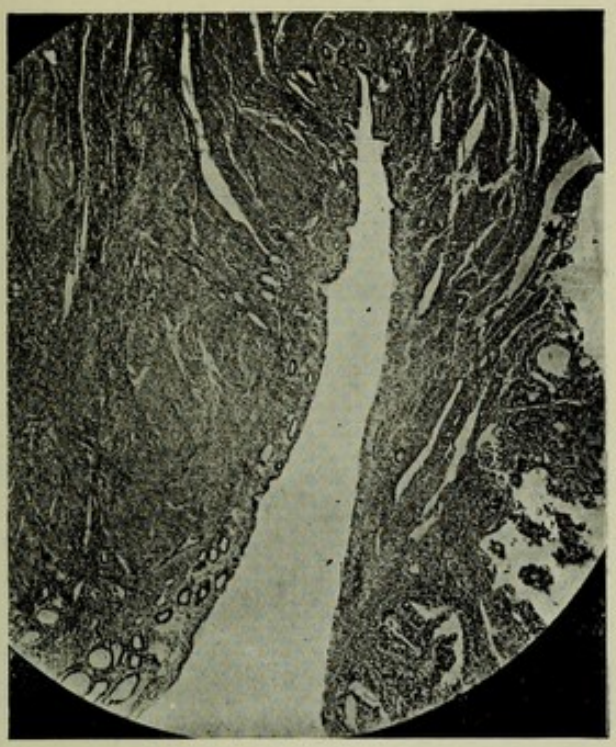

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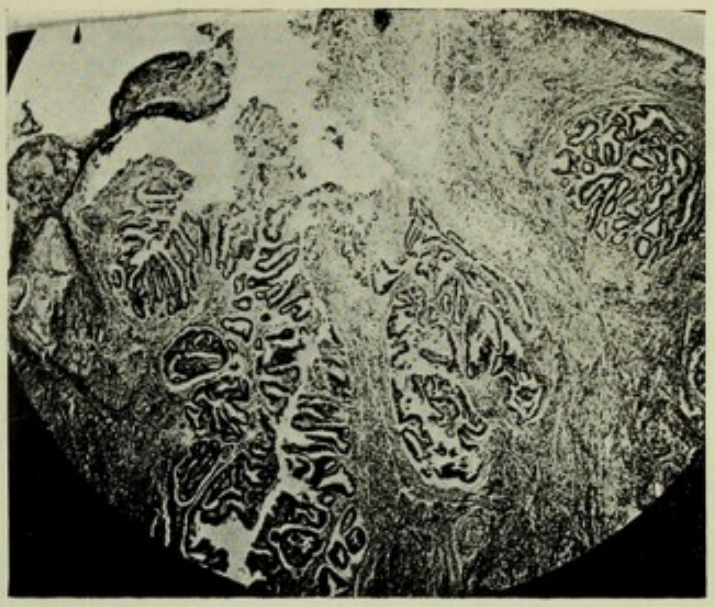

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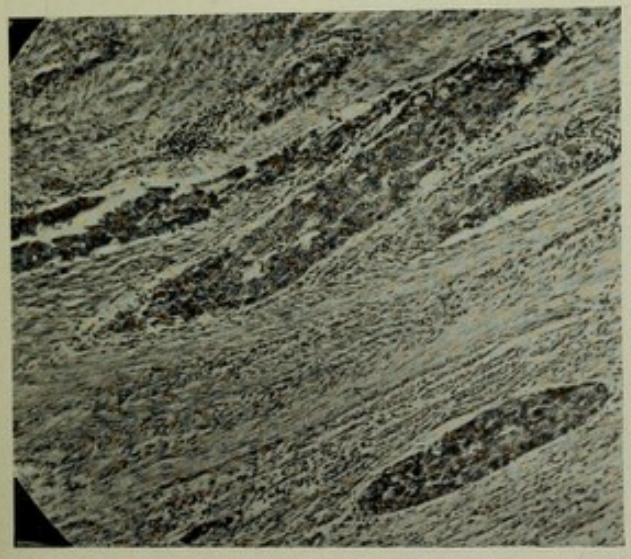

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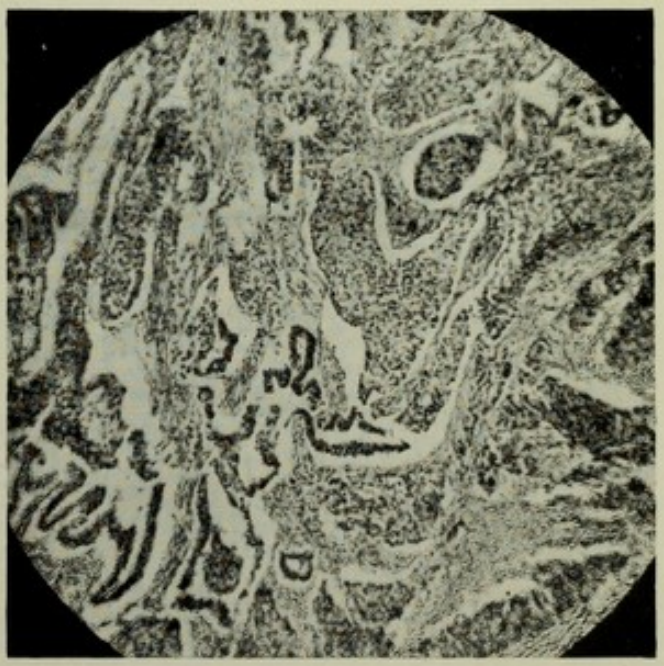

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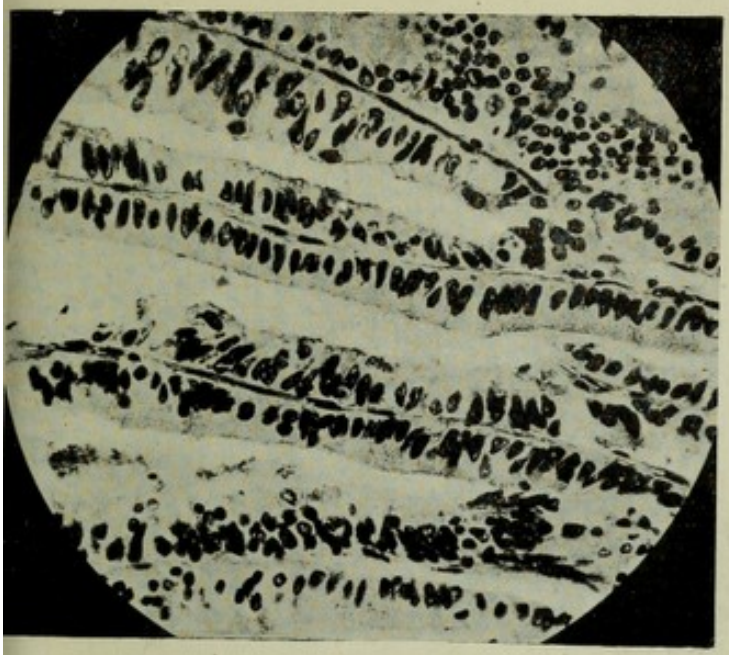

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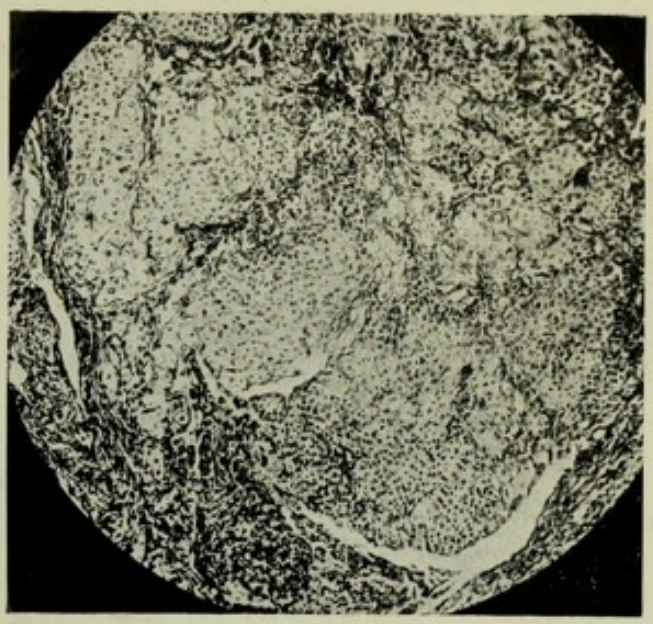

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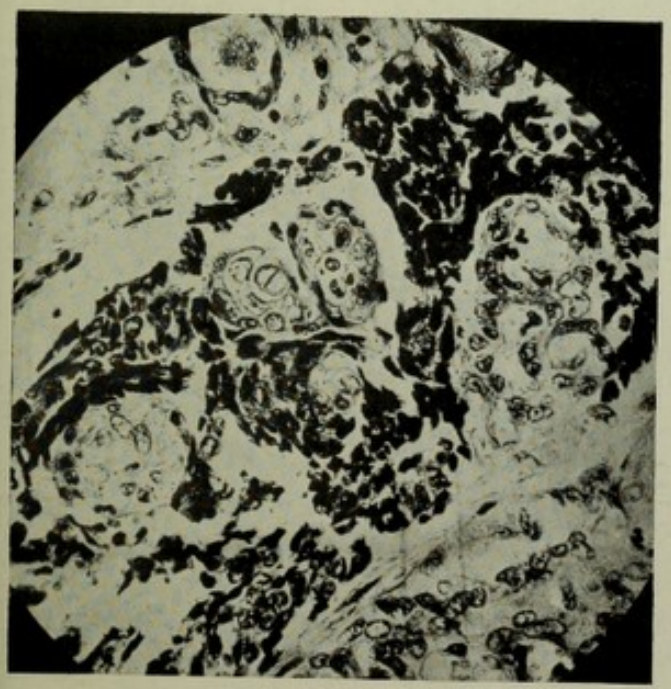

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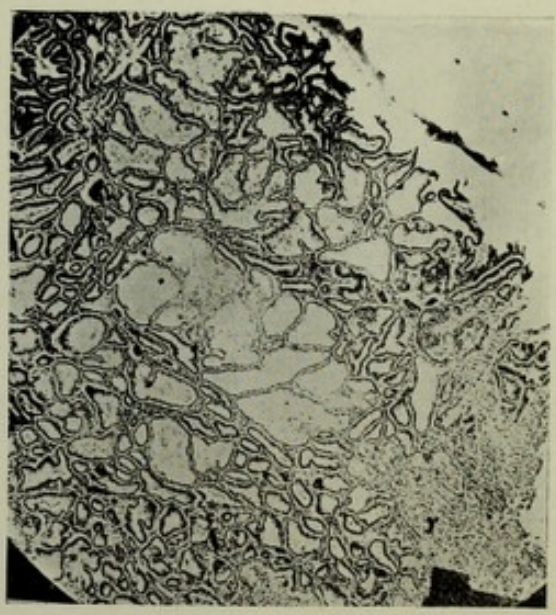

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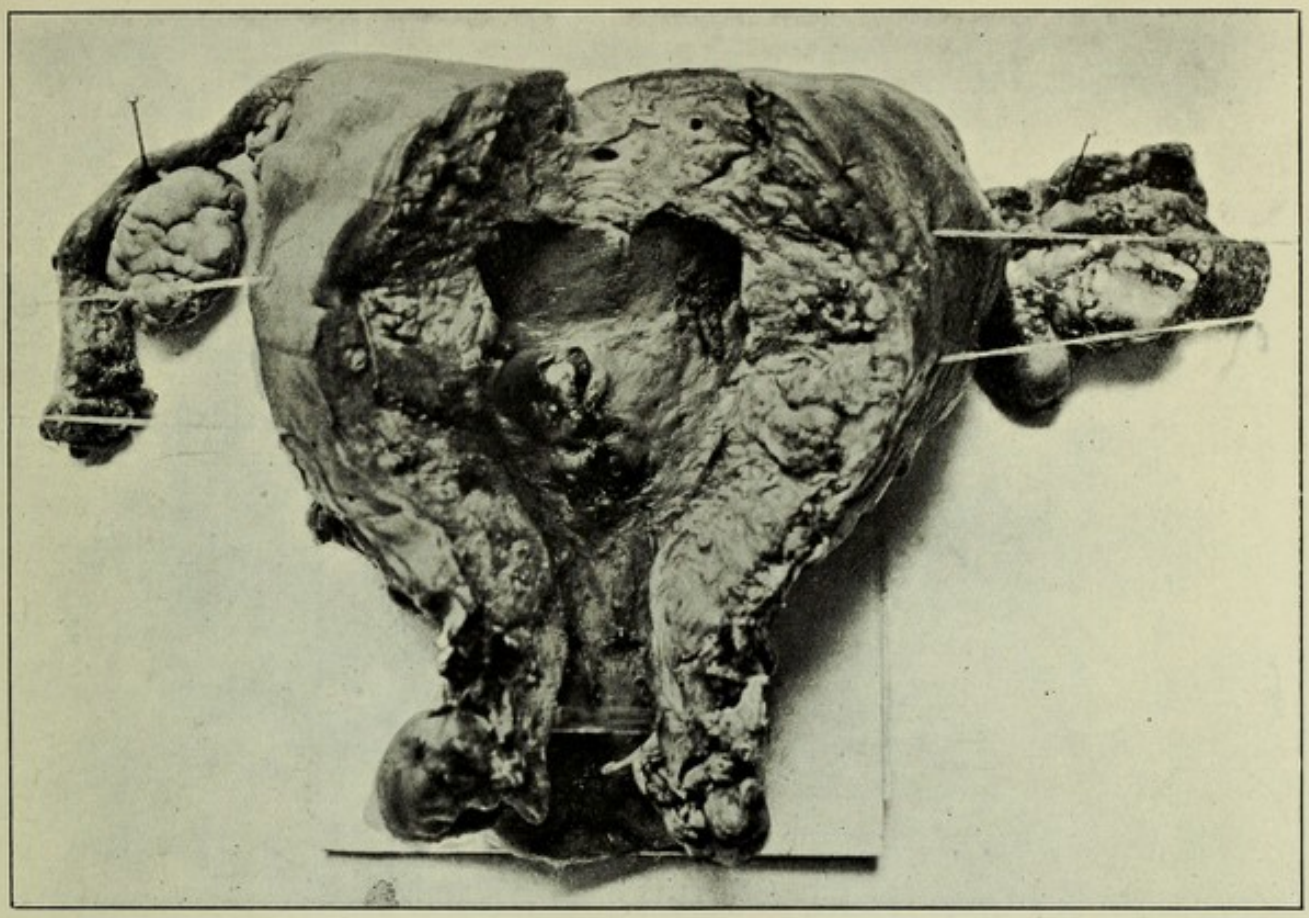

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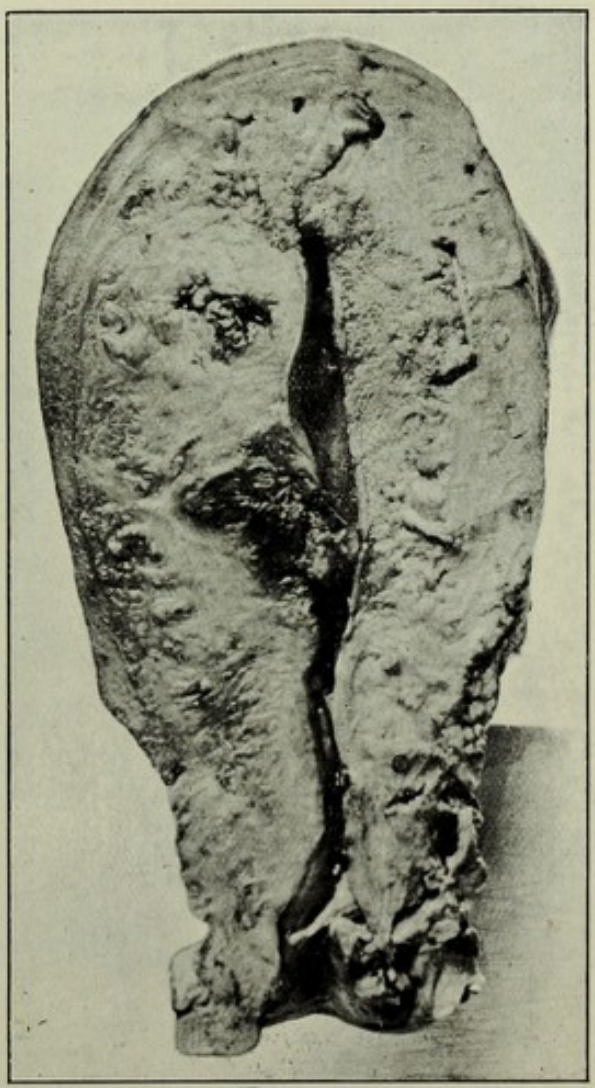

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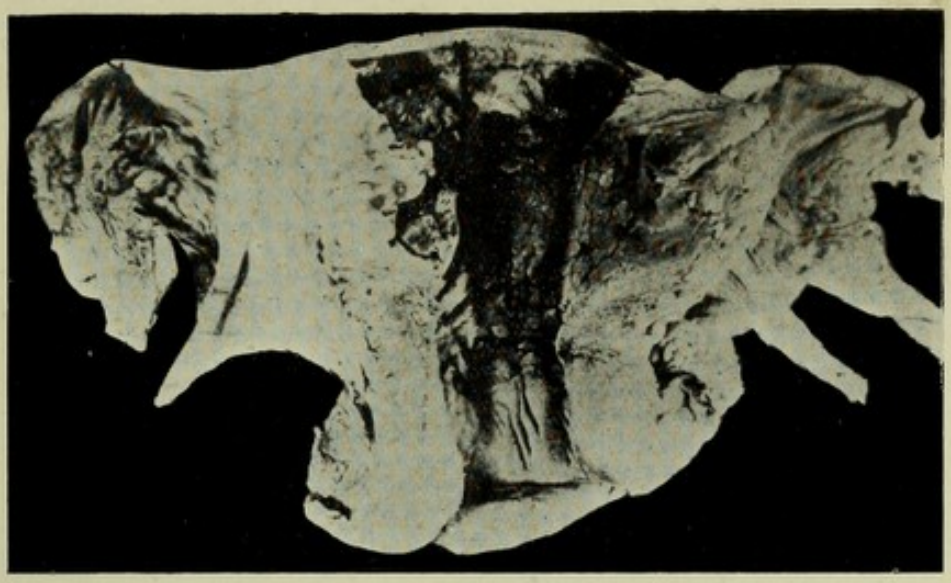

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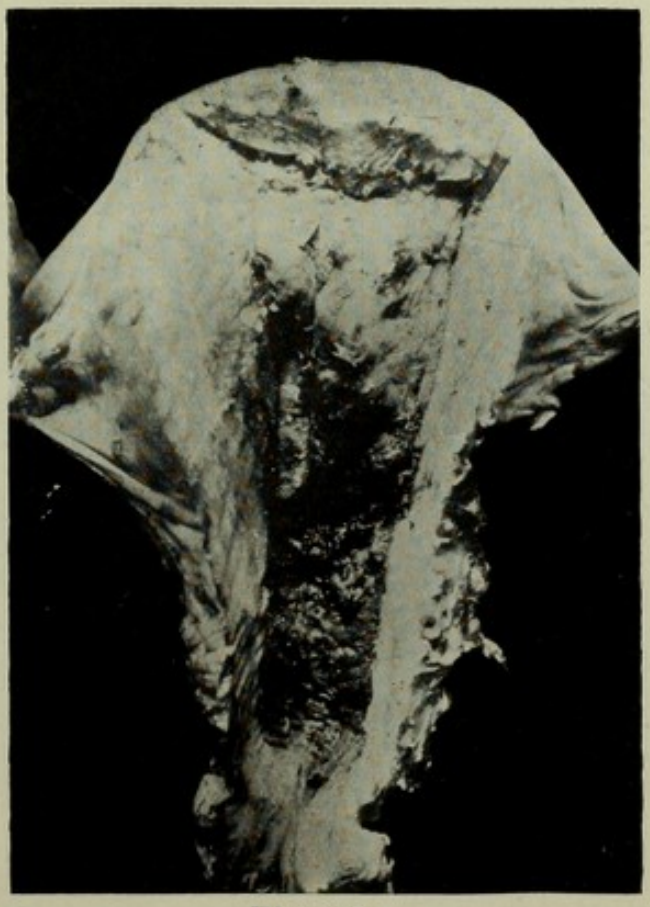
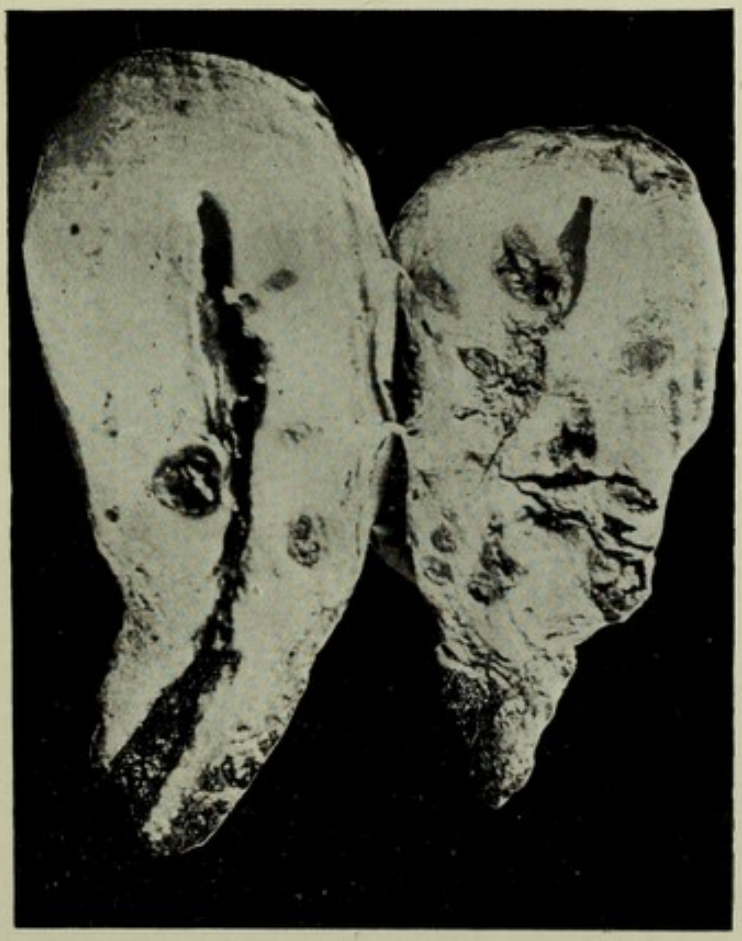


Fig. 98.

Fig. 99.



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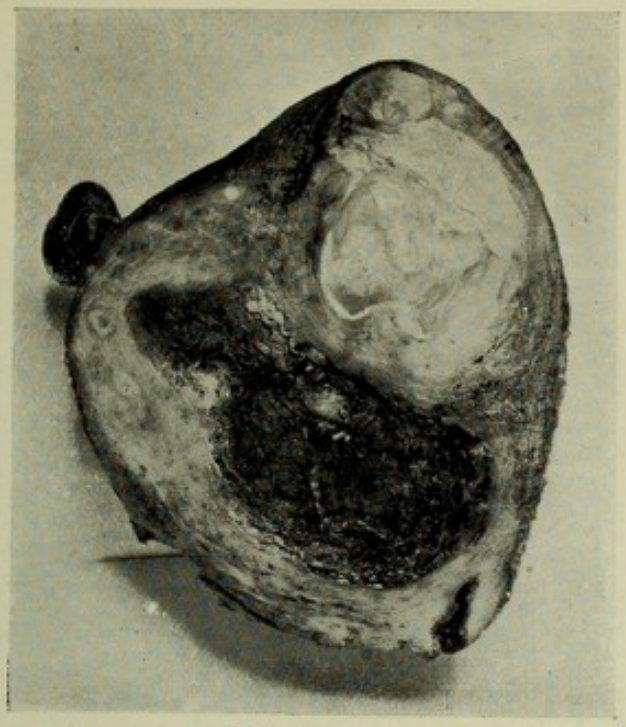

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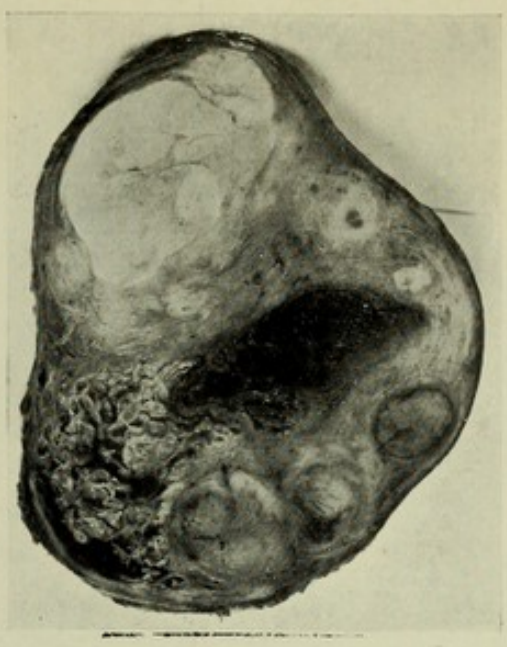

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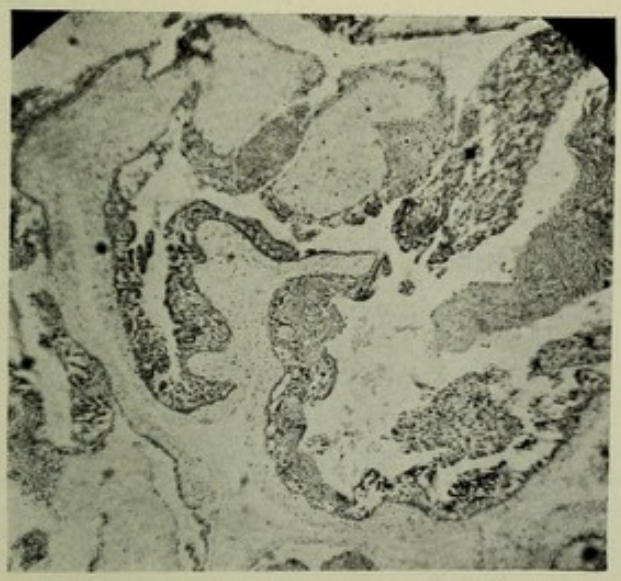

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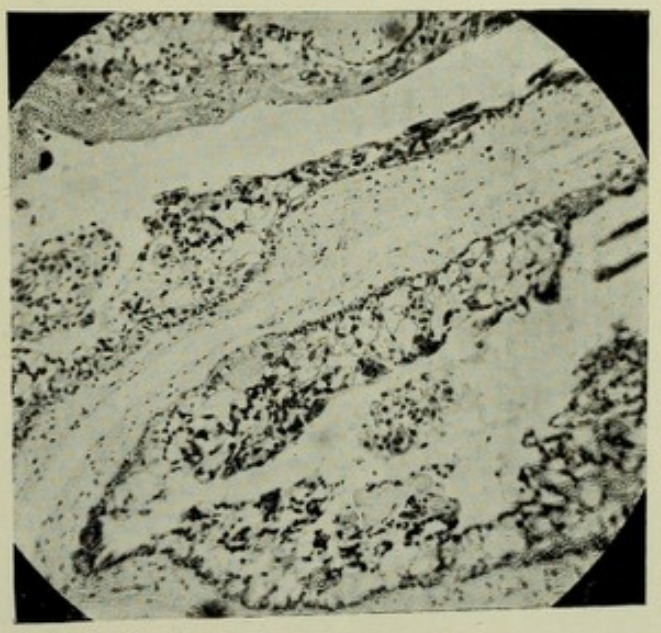

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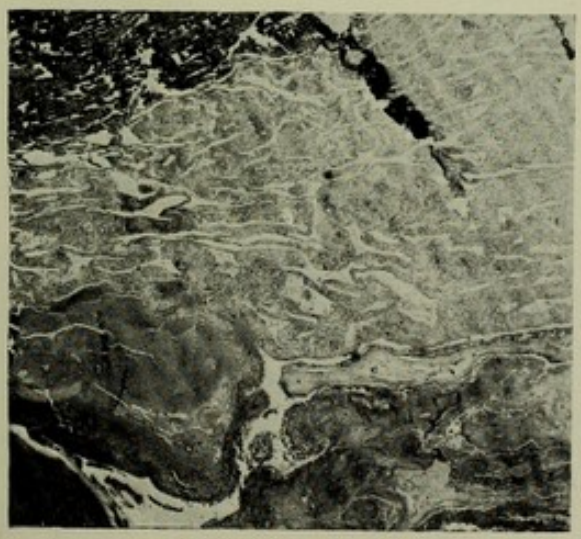

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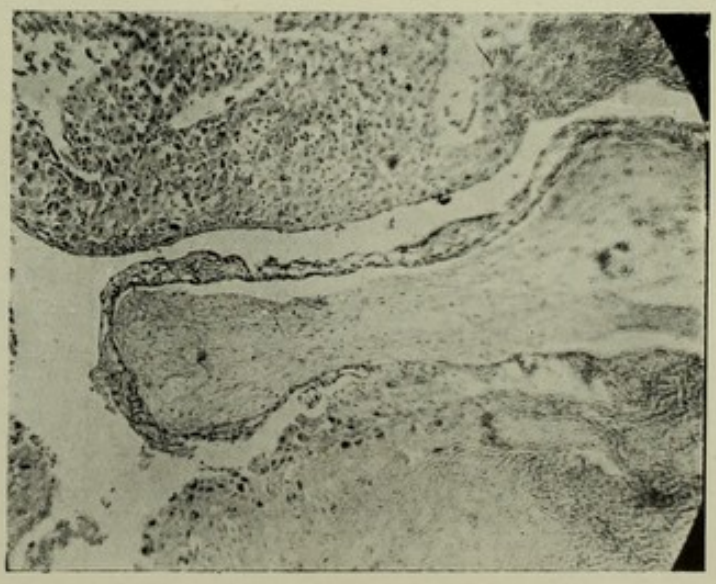

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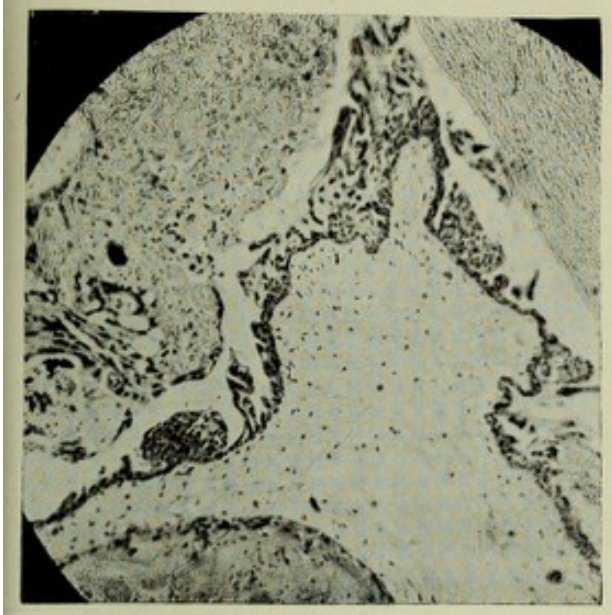

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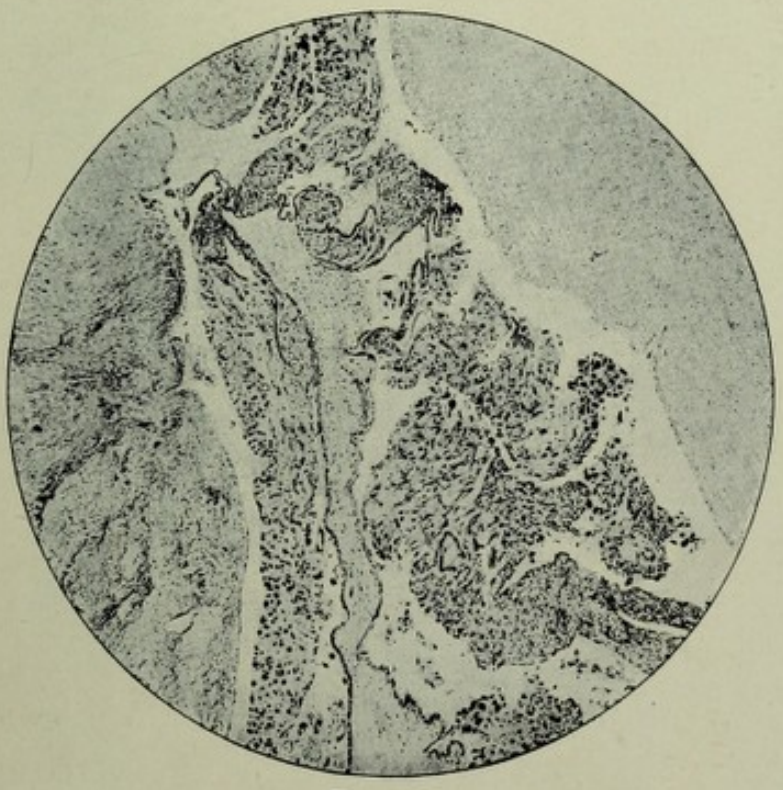

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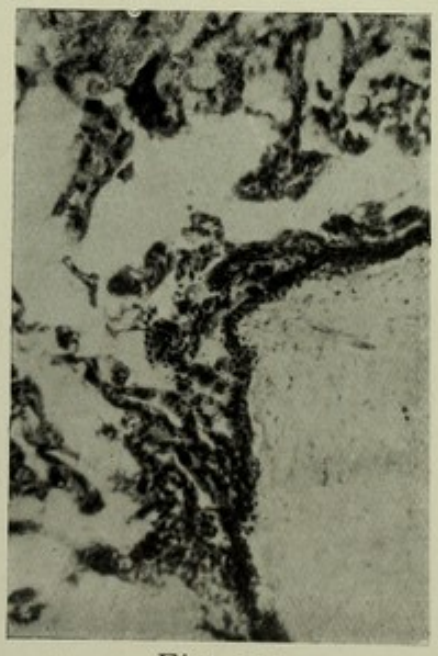

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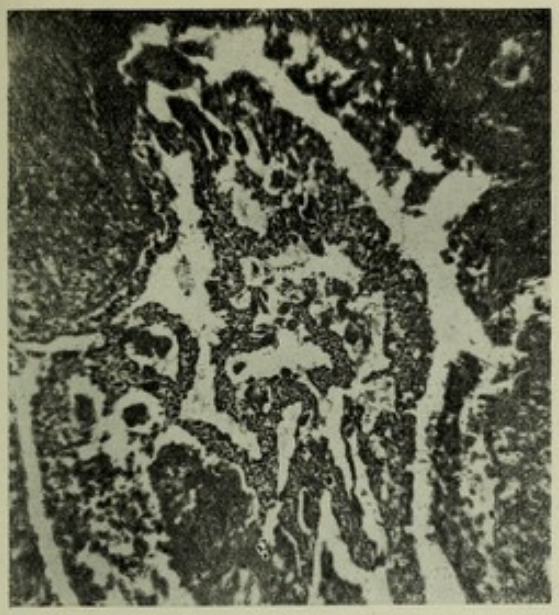

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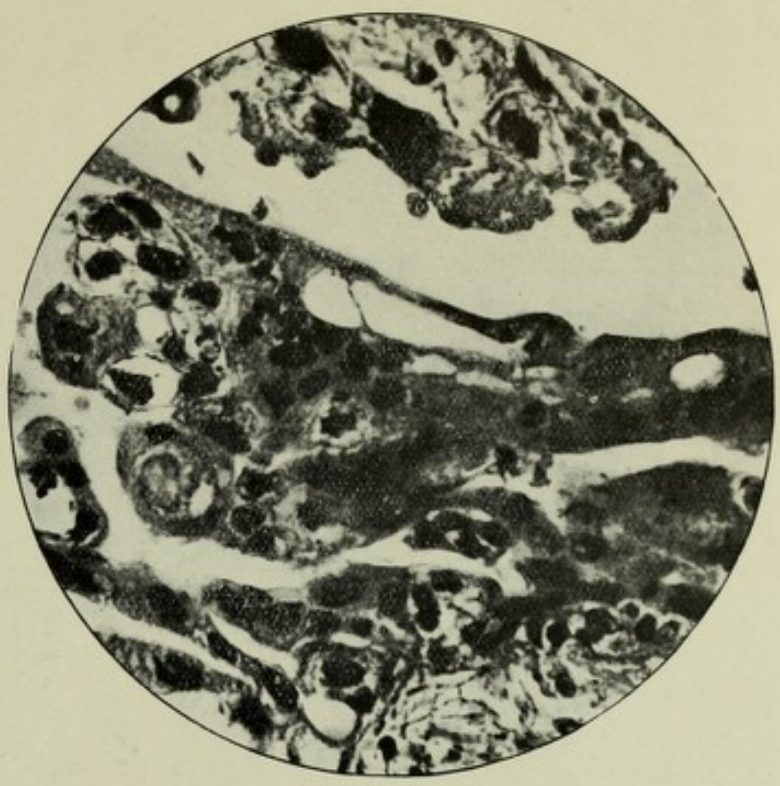

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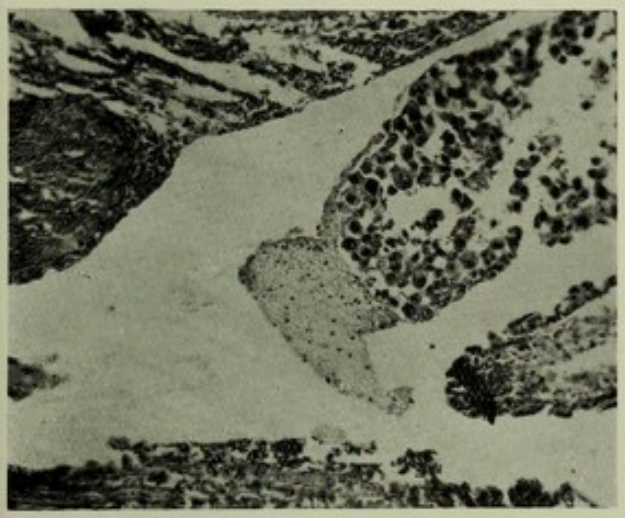

Fig. 113.

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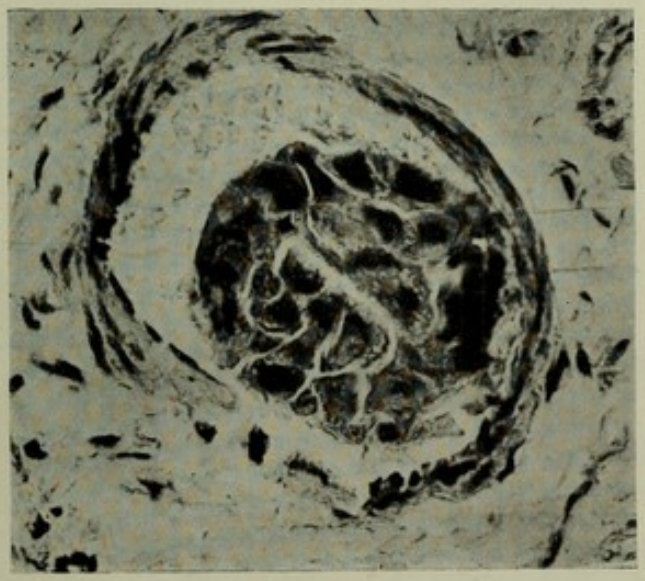

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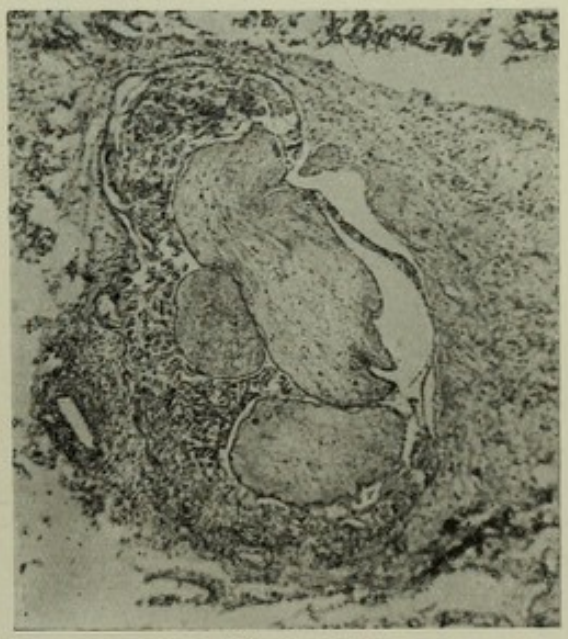

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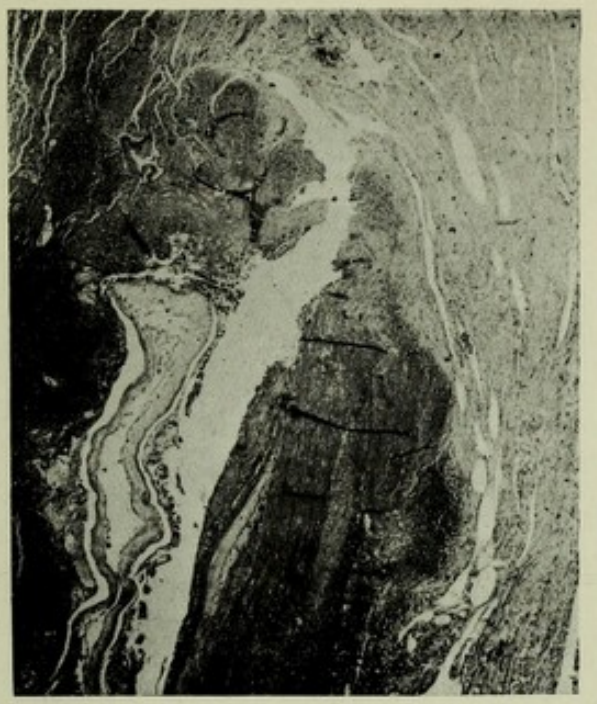
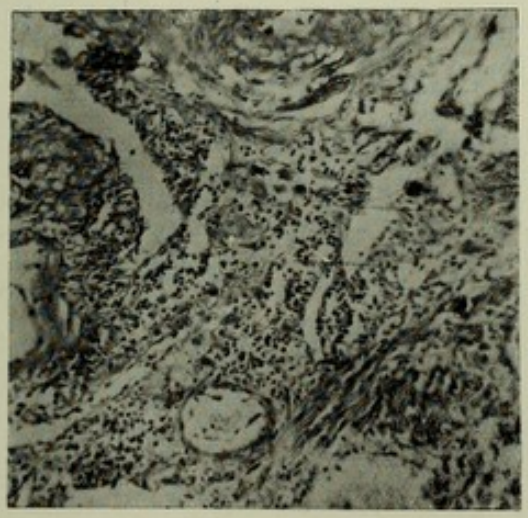


Fig. 117.

Fig. 118.



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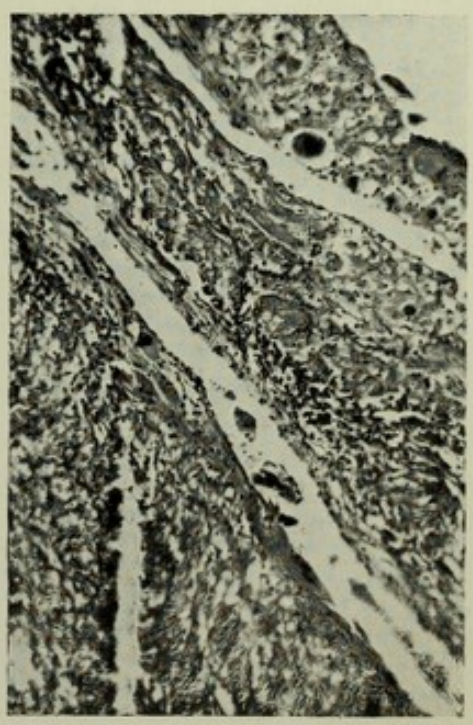

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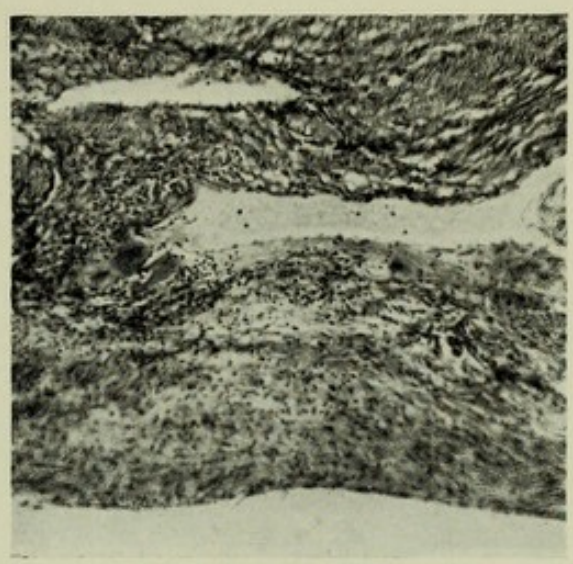

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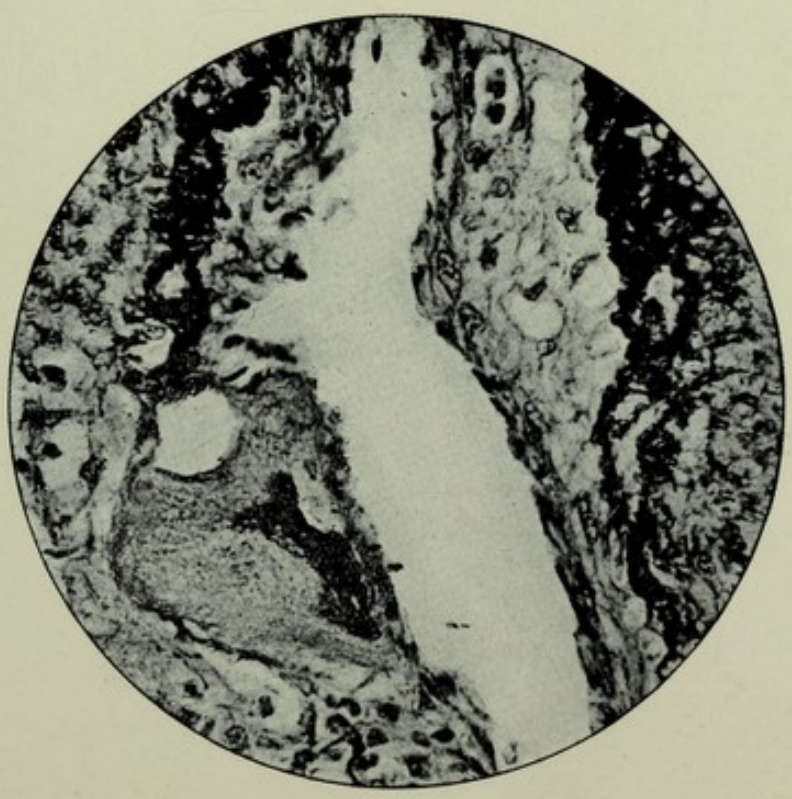

Fig. 122.