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Endometriomata.

AN INVESTIGATION OF THE ABNORMAL DEVELOPMENT OF ENDOMETRIAL TISSUE WITHIN THE FEMALE PELVIS.*

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INTRODUCTION.

MUCH work has been done and many interesting facts have come to light during the last few years relating to the ætiology, pathology, and clinical importance of certain glandular tumours arising within the pelvis, and more especially in the uterus and ovaries.

* This paper contains the substance of a Thesis submitted for the degree of M.D. Liverpool.

It would seem, however, that many points, particularly those relating to the ætiology, have not yet been definitely settled; and it was with a view to eliciting new facts that this work was undertaken.

The main object has been, therefore, to endeavour to find, in every specimen examined some indication likely to assist in the solution of this interesting question.

HISTORICAL NOTE.

Only when an examination of the literature bearing upon the subject under discussion is made, is it possible to realize how many cases have been recorded, and how much work has been done since the condition was first described.

It is impossible, however, to attempt to discuss or even mention many of the excellent descriptions given of cases of so-called "adenoma," or "adenomyoma," occurring in connection with the uterus, ovaries, Fallopian* tubes, ligaments of the uterus, and even with other parts of the lower abdomen such as the intestines, umbilicus and various hernial sacs.

It will be sufficient here to recount the various views and theories held at different times regarding this lesion :—

(a) *Origin by direct extension of endometrial tissue from the actual lining of the uterine cavity.*

This is a well-recognized mode of origin of endometrial tumours—especially of those in the uterine wall, or in relation to the uterosacral ligaments. Cullen,⁷ in 1917, described many cases affording proof of this explanation. In nine cases operated upon by him in which "adenomyomata" of the uterosacral ligaments were found to be present, there was no sign of involvement of the appendages by a similar pathological condition, but rather there seemed to be a direct connexion in all with the uterine endometrium.

Again, in 1921,⁶ he described three cases in which he found subperitoneal pedunculated "adenomyomata" of the uterus. In these specimens the tumours contained patches of endometrium, some of which, being immediately under the peritoneal coat, projected as small bluish-black cysts, closely resembling the "implantations" described by Sampson and others, and to be considered later. The endometrium was, in these cases, as in those previously reported, continuous with that lining the uterine cavity.

Lockyer,¹³ in a very full description of "adenomyomata," distinguished between uterine and extra-uterine tumours of this type. He further divided the uterine tumours into central and peripheral (or circumscribed) forms, and stated that in all cases of the central,

* The above spelling of the word "Fallopian" is strictly correct and so has been adopted here, although contrary to common usage.

and in many cases of the peripheral type, the origin is by direct extension from the endometrium.

On the other hand, he holds totally different views regarding the origin of certain uterine and extra-uterine tumours of a similar nature, to which reference will be made later.

Casler,⁵ in 1920, described a case in which there was a diffuse "adenomyoma" of the uterus characterized by the presence of a relatively large amount of stroma with few glands, and he showed that this tissue could be traced directly from the uterine mucosa almost to the serous coat of the uterus—an observation which supports Cullen's mucosal theory. From this patient, however, four years later, Casler removed an ovarian cyst of the left ovary, which had attained to the same size as that of a grape-fruit, and which was densely adherent to the sigmoid flexure of the colon, and had, in fact, actually extended round the colon and caused constriction thereof by pressure from without. On cutting sections of the cyst wall and of tissue in the adhesions to the bowel he found that the cyst was, as he described it, "made up of uterine tissue"—that is, typical endometrial glands and stroma and involuntary muscle were present. The point of special interest as regards the ætiology in this case is the fact that the left ovary was carefully examined at the first operation, and found to be normal in appearance and size. In spite of repeated and careful clinical examinations, the tumour was only detected three and a half years later.

It would seem to be most unlikely that the endometrial tissue in the ovary in this case could have been derived from that of the uterus either by direct extension along the ovarian ligament, or by implantation, for, had either of these conditions been present it is probable that there would have been some sign of this at the first operation. Rather is it more probable that the ovarian tumour arose from aberrant Müllerian tissue, or by metaplasia from some other tissue, either Wolffian tubules or germinal epithelium.

In addition to direct extension of Müllerian tissue from the uterine endometrium, a similar process may occur in connexion with the lining membrane of the Fallopian tubes, as shown by Marchand,¹⁴ who clearly demonstrated the fact that extension of epithelium from the tube may give rise to adenomatous structures in the ovary.

(b) *Origin from mesonephric or Wolffian relics.* This mode of origin of uterine or, most commonly, extra-uterine tumours of adenomatous nature formed the basis of Von Recklinghausen's theory which he advanced in the year 1896.¹⁷ The same observer was one of the first to recognize the fact that endometrium-like tissue might be found in extra-uterine situations.

Martin¹⁵ described a cystic tumour of the round ligament in

which he found that the structure of the walls and the contents of the cysts in parts corresponded with those of tumours arising from the parovarium. Yet many of the cysts contained chocolate material and the tumour was histologically an "adenoma."

The claims of his theory have not been advocated so persistently of late years, and there seems to be a tendency to relegate it to oblivion. Lockyer, however, in 1920 admitted the possibility of the Wolffian origin of some tumours, especially those of the round ligament.

(c) *Origin from the serous (peritoneal) endothelium.* About the time when Von Recklinghausen's work was first published, Ivanoff suggested that extra-uterine "adenomyomata," especially those in the region of the uterosacral ligaments, might be due to alteration of the overlying peritoneal endothelium, following infection. Many cases have been described in support of this theory, most of them being recorded by continental authors, of whose work that of Meyer¹⁶ may be taken as an example. Meyer laid stress on the frequent presence of inflammation as a primary condition, and more recently Gough⁹ has described a case in which the uterus, Fallopian tube and sigmoid were involved, and which was characterized by the presence of chronic infection involving the appendages. Gough quotes Spencer and Cullen, both of whom laid special emphasis on the frequent presence of infection, and he refers to the fact that in several reported cases chronic tuberculous conditions of the tubes were associated with "adenomyoma" of the uterus.

(d) *Origin from the Graafian follicle.* This theory, which implies metaplasia of the cells of the membrana granulosa, lacks confirmation, and was abandoned many years ago.

(e) *Origin from the germinal epithelium.* Waldeyer²² held the view that adenomatous tumours of the ovary were derived from the surface epithelium of the ovary. In confirmation of this Whitridge Williams²³ proved conclusively that the germinal epithelium of the ovary in adult females may be represented by a single layer of high columnar ciliated epithelium, and that from this layer both adenomatous and papillomatous tumours may take origin.

(f) *Origin from relics or "rests" of Müllerian tissue in abnormal situations.* Among the early supporters of this theory Russell¹⁸ takes a prominent place. In a paper written in 1899 he refers to the belief held by Waldeyer and Nagel that the epithelial elements of the Müllerian duct are derived from the germinal epithelium. He therefore concludes, and demonstrates in a specimen described, that certain portions of Müllerian tissue may come to lie in the germinal epithelium.

In 1922, Blair Bell,² in investigating a case of bilateral appendage swellings, found to be due to the presence of chocolate cysts in both ovaries, observed, for the first time in this country, endometrium-like tissue with hyperplasia of involuntary muscle in both ovaries. Neither ovarian ligament contained any glandular tissue, and the tumours were held to be due to the growth and functional activity of aberrant Müllerian tissue. He considered this to be true endometrium, and, therefore, gave to this condition the name of "endometrioma," or "endometriomyoma" should involuntary muscle be present in the tumour in addition to endometrium,—a name he had previously adopted for so-called "adenomyoma" of the uterus.³ Blair Bell mentioned as a probable explanation the fact that the developing Müllerian duct lies in close proximity to the germinal epithelium during the early stages of growth of the embryo.

Janney¹¹ and Blair⁴ have arrived at a similar ætiological conclusion. They also attempt to answer the question why this endometrium, if of developmental origin, does not become functional at puberty instead of showing no signs of activity until the age of 30 or even 40 years, as in some cases. They say that, in the first place, the ovarian endometrium is retarded by unusual surroundings, and, secondly, that some stimulus is necessary before the endometrium actually becomes perforative. They give possible sources of this stimulus, such as infection in the pelvis, neoplasms, conditions causing congestion, and general diseases, especially those affecting the blood in any way.

(g) *Origin by "cellular spill" and implantation.* The implantation theory was elaborated by Sampson¹⁹ in 1921, and his descriptions and proofs are so clear and definite that it is impossible to dispute that in some cases, at any rate, the whole of the lesions found may be due to a process of retrograde menstruation, with implantation of fragments of endometrial tissue on the surface of the ovary, which subsequently invade the ovarian stroma. He considered that the ovary acted as a "hot-bed" or "incubator," favourable to the growth of endometrial fragments. Later, the chocolate cyst which had formed perforated its wall and, Sampson believed, gave rise to secondary dissemination of the endometrial tissue in any part of the pelvic cavity, but especially in the pouch of Douglas. He stated that the implantation of either uterine or tubal mucosa might occur, and that in many cases the source of origin could not be discovered by an examination of the lesion produced.

He supported his theory in a convincing manner, both from pathological and experimental points of view; and stated that he had found the condition present in 37 out of 170 operations upon

women between the ages of 30 and 50 years, and in six cases in which the patients were under 30 or over 50 years of age.

The main arguments in favour of his theory are:—

(1) The histological appearance of superficial "adenomyomata" suggests implantation.

(2) The site of development of "adenomyoma" of the ovary is near the abdominal ostium of the tube.

(3) Retrograde menstruation has been seen to occur at operation.

(4) The lesion may occur in the abdominal scar after Cæsarean section and other operations.

Working with Sampson, Jacobsen,¹⁰ in a series of experiments on rabbits, proved that when endometrial tissue is artificially implanted in the pelvis small "adenomatous" tumours develop.

These tumours on the surface of ovary, tube and broad ligament were infiltrative, but did not involve the intestines; and although some blood was present, no hæmorrhagic cysts were formed. It is interesting to note that in some cases in which tissue containing muscle was transplanted, a structure resembling a rudimentary uterine horn was found.

Blair Bell supports this view, and considers that it is the commonest method of origin of endometrioma of the ovary.

Bailey,¹ adopting *en bloc* Sampson's views and classification, has described a series of cases, in all of which he considers that the essential lesion is an implantation of tubal or uterine mucosa, either at the site of election—the ovary—or the peritoneal surface of other pelvic structures, notably the Falloppian tube, posterior wall of the uterus and the pouch of Douglas. He also enters into the question of retrograde menstruation, and, like Sampson, obtained microscopical evidence that this does occur, and that portions of uterine endometrium may be seen actually passing down the Falloppian tube towards the abdominal ostium.*

Such then are the main views that have been brought forward in the past, or are actually held at the present time. I have considered it advisable to enter rather fully into an account of them, as many of the points raised have a direct bearing on the present investigation.

NOMENCLATURE.

Several names have been given to tumours in various parts of the pelvis, characterized by the presence of glandular tissue resembling endometrium. Those used by Sampson, namely,

* In a later communication, Sampson, while affirming the truth of the implantation theory, also suggests the possibility of metastasis via lymph vessels or veins resulting in tumours in the pelvis, and especially in the inguinal region. (*Amer. Journ. Obstet. and Gynecol.*, 1925, iv, 462.)

“adenomyoma,” and later “adenoma,” have been widely adopted. These terms, however, do not indicate in any way that a specialized form of glandular tissue is present, that is, true endometrium, and for this reason they appear unsuitable.†

Bailey, following a hint thrown out by Sampson, has suggested the name “Ectopic Müllerianoma.”

There can, however, be no doubt that the tissue concerned is really endometrium, as has been emphasized by many observers; but if any further proof is required I hope to furnish it, for this tissue shows menstrual reaction, corresponding exactly with that of uterine endometrium, atrophy at or about the menopause, and, in association with pregnancy, evidence of true decidual reaction. Further, in the series of cases investigated I have, in every instance, found that the presence of true endometrium of uterine type is essential for the production of a definite lesion. I, therefore, consider that the term ENDOMETRIOMA (or endometriomyoma in some cases), as first used by Blair Bell,^{2,3} fulfils all possible requirements.

By adopting this title at this early stage in the work, rather than doing so later, I hope to make the descriptions which are to follow both clearer and briefer than would otherwise be possible.

PATHOLOGICAL INVESTIGATION OF SPECIMENS.

I have been fortunate in having at my disposal over 200 specimens of pelvic organs and tissues, the great majority of which were removed by Professor Blair Bell in the Royal Infirmary, Liverpool, or at private operations performed by him.

Collection and preparation of sections for histological examinations.

(a) In those specimens in which there was any microscopical appearance suggesting, however remotely, the presence of endometrium, multiple sections were cut at all important situations, that is, the posterior uterine wall, the ovarian and uterosacral ligaments, Fallopian tubes, and, of course, the ovary, special attention being paid to hæmatomata and adhesions. Should the presence of endometrial tissue be thereby demonstrated, further sections—serial in many cases—were cut, in an endeavour to trace this tissue to its origin.

(b) Sections of the organs removed were carefully examined in all specimens, even those presenting no macroscopical signs of abnormal growth of endometrial tissue, and if any tubules or glandular tissue were found, further sections were cut.

† Sampson has now apparently discarded these terms, and has adopted that of “endometriosis.” This name, while more descriptive of the true pathology of the condition, suggests that a diffuse endometriomatous state is invariably present—which is not always true. Single and localized lesions may be found, and for these “endometriosis” is hardly suitable.

(c) Sections were stained by the hæmatoxylin-eosin method, Van Gieson's stain being used in certain cases for confirmation.

General description of specimens.

It soon became apparent as the work progressed that all the specimens of interest might be divided into two groups, according to the microscopical appearance presented, namely :—

- (1) Specimens containing true, but aberrant, endometrial tissue. This group comprises a series of 25 cases, in all of which endometrial tissue was shown to be present in abnormal situations.
- (2) Specimens, usually of the ovary, showing the presence of abnormal glandular or other epithelial structures not resembling uterine endometrium. These specimens have been included, although of no great clinical or pathological importance in many instances, in the hope that by this investigation some light may be thrown upon the question of the ætiology of endometrial inclusions that are present in the cases belonging to the first group.

Group 1.

I propose to consider the cases in this group according to the result of the combined macroscopical and microscopical findings.

The most important lesion, or lesions, may be situated in the uterus alone, the uterus and also in one or both ovaries, the ovary alone, either superficially or deeply invaded, and in other situations in or about the pelvis.

A. *Uterus.* Endometrioma of the uterus associated with other lesions.

Case 1. *Gyn. Path.*, No. 3674. Diffuse endometriomatous invasion of the wall, together with fibromyomata of uterus.

Case 2. *Gyn. Path.*, No. 4081. Diffuse endometriomatous invasion of wall, associated with an cedematous polyp of cervix.

Case 3. *Gyn. Path.*, No. 4289. Diffuse endometriomatous invasion of the wall. Follicular retention cysts of the right ovary.

B. *Uterus with one or both ovaries involved.* In case 4 the ovarian hæmatomata are *superficial*, and were found only on microscopical examination. In cases 5, 6, 7 and 8 the ovarian hæmatomata are *deep*.

Case 4. *Gyn. Path.*, No. 3771. Endometrioma of uterus, ovaries and the left ovarian ligament. There are large ill-defined tumours of the posterior wall and a small nodule near the attachment of the left round ligament—endometriofibromyoma in both cases. There are also small areas of endometriomatous tissue in both ovaries, and tubules and stroma in the left ovarian ligament.

Case 5. *Gyn. Path.*, No. 3736. Endometrioma of uterus

and ovaries. There is diffuse invasion of the uterine wall by endometrium, but no macroscopical evidence of abnormality. Tarry cysts with endometrium in the walls thereof are present in both ovaries, and endometrium is present in adhesions between the left gonad and the tubal fimbriæ.

Case 6. Gyn. Path., No. 3599. Endometrioma of uterus, ovaries and uterosacral ligaments. There is a diffuse tumour of the posterior wall of the uterus containing endometrium. Tarry cysts with endometrium in the walls are present in both ovaries, and the right ovarian and uterosacral ligaments are invaded by endometrial tissue.

Case 7. Gyn. Path., No. 4160. Endometrioma of uterus and both ovaries. Multiple endometrio-fibromatous tumours of the uterus are present, and there are tarry cysts of the left ovary. Endometrium is present in both ovaries.

Case 8. Gyn. Path., No. 4129. Endometrioma of uterus, ovaries and tubes. There is diffuse deep invasion of the uterine muscle by endometrium. Tarry cysts are present in both ovaries, and there is a small tumour near the abdominal ostium of the tube containing endometrium.

C. Ovary alone, superficially or deeply invaded. In cases 9, 10, 11, 12 and 13 the ovarian hæmatomata were superficial, while in cases 14 to 24 inclusive they were deeply placed, the uterus being apparently normal, and so not always removed at operation.

<i>No. of case.</i>	<i>Ovary.</i>	<i>Other situations.</i>
9. <i>Gyn. Path.</i> No. 3884.	Superficial hæmatomata in the right ovary.	None.
10. <i>Gyn. Path.</i> No. 4025.	Ovaries contained hæmorrhagic cysts, and both were adherent to large intestine. Endometrium present superficially in ovaries.	Endometrium in adhesions between the tubes and fundus uteri and the bladder.
11. <i>Gyn. Path.</i> No. 4051a.	Endometrium in the right ovary, which was apparently the only part to be involved.	None.
12. <i>Gyn. Path.</i> No. 4241.	Endometrium in the free borders of both ovaries, superficially placed.	None.
13. <i>Gyn. Path.</i> No. 4273.	Piece removed from the free border of the right ovary—containing superficial endometriomata.	None.
14. <i>Gyn. Path.</i> No. 3415.	Both ovaries adherent to the uterus and containing large tarry cysts.	None.

<i>No. of case.</i>	<i>Ovary.</i>	<i>Other situations.</i>
15. <i>Gyn. Path.</i> No. 3881.	The right ovary and tube embedded in adhesions and old blood clot. A tarry cyst in the right ovary, and also endometrium in the left ovary.	None.
16. <i>Gyn. Path.</i> No. 2646.	A very large tarry cyst of endometriomatous nature in the right ovary.	None.
17. <i>Gyn. Path.</i> , No. 3774.	Tarry cysts of the right ovary containing typical glands and stroma.	None.
18. <i>Gyn. Path.</i> No. 4325a.	Large tumours of both ovaries consisting of both tarry endometrial, and of hæmorrhagic follicular cysts.	None.
19. <i>Gyn. Path.</i> No. 4326a.	Right ovary containing small tarry cysts—endometrium in the walls.	Endometrial tissue in the right ovarian ligament.
20. <i>Gyn. Path.</i> No. 3983.	Follicular cyst of the right ovary which contained a few endometrial tarry cysts.	None.
21. <i>Gyn. Path.</i> No. 4254.	Left ovary containing deep endometrium. (Removed with a fibromyomatous uterus).	None.
22. <i>Gyn. Path.</i> No. 1871.	Hæmorrhagic cysts of the right ovary (case of uterus bicornis) in some of which endometrial tissue was found.	Blood cysts in omentum.
23. <i>Gyn. Path.</i> No. 3757.	Old endometrioma of the right ovary.	None.
24. <i>Gyn. Path.</i> No. 4367.	Follicular cyst of right ovary which, as well as a piece of the left ovary, contained endometrial tissue.	Endometrium in the right ovarian ligament.

D. Endometrial tissue in other situations in the pelvis.

25. <i>Gyn. Path.</i> No. 4315a.	A small tumour removed from the wall of an inguinal hernial sac. An endometriomyoma, probably of the round ligament.	None.
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MACROSCOPICAL AND MICROSCOPICAL APPEARANCES OF
ENDOMETRIOMATA.

I propose at this stage to describe what appear to be the typical findings in the various stages of development and situations of this lesion, and at the same time to indicate which of the cases coincide with the different types.

THE UTERUS.

The macroscopical appearance of endometrioma of the uterine wall varies more than in any other situation.

1. There may be a generalized thickening of the walls of the uterus; but this thickening, when present, is usually irregular, and most frequently affects the posterior wall. (Cases 4, 5, 6 and 7. Fig. 1.)

2. The endometrioma may be localized to one part of the uterine wall, and there form a miniature cavity containing menstrual blood. (Case 2.)

3. Encapsulated tumours resembling fibromyomata, but containing a large amount of typical endometrium in addition to fibrous and muscular tissue, are sometimes present. (Cases 1 and 7. Fig. 3.)

In addition it must be borne in mind that abnormal deposits of endometrium may occur, yet not be visible macroscopically.

4. On inspection of the serous aspect adhesions are frequently observed. They vary greatly in character, but are usually dense in old-established cases. The adhesions, although present on the anterior serous surface of the uterus in one of my specimens (Case 10) usually involve the posterior surface and fix the uterus backwards. Associated with the adhesions bluish-black cysts may project on the surface of the uterus, most commonly involving the posterior wall.

Microscopically, the uterine endometrium proper has shown very little of any importance in my specimens. When polypi were present they consisted of typical adenomatous, or in some cases, of endometriomatous tissue, and in these, as in several other specimens in which the endometrium appeared quite normal to the naked eye, varying degrees of glandular hypertrophy and hyperplasia were observed. This adenomatous condition of the endometrium does not appear to bear any direct relation to endometrioma; but, when fibromyomata or endometrio-fibromyomata are present, there may, of course, be thickening of the endometrium itself. The important phenomenon that I have observed in several specimens has consisted of an abnormally deep invasion of the uterine muscle by the endometrium—as though in the particular patient the endometrium was unusually invasive. Careful examination of sections

of the wall of the uterus in 140 specimens revealed the fact that endometrium was found deep in the wall—that is in the outer half—in 10, and of these in seven there was endometrium in extra-uterine situations. It seems, therefore, that a state may exist in which endometrium, wherever situated, possesses unusual powers of invasion and growth. The aberrant tissue consists of glands and stroma, but some variation exists in different cases. The glands differ in size and shape, and may present an appearance similar to that shown by those lining the cavity of the uterus, or become distended with secretion or blood, and so form cystic spaces (Fig. 4). The epithelium likewise varies, its appearance depending on the particular stage of the menstrual cycle, with which it exactly corresponds, and upon the size of the gland space of which it forms the lining. Thus the usual type of epithelium is a high columnar variety, in which the deep parts of many cells may be distended by secretion (intermenstrual phase), but this epithelium may show all the gradations to a low cubical form as the gland lumen becomes enlarged.

The stroma is usually plentiful and forms a complete investment for the glandular tissue, except when a few of the deeper tubules have occasionally outpaced the developing stroma, and lie in direct contact with bundles of muscular tissue. There is often a small amount of extravasated blood, both in the lumina of the glands and in the stroma, but this is not a marked feature in most of the specimens.

I have been able to trace the endometrial tissue outwards from the true endometrium in six cases (Cases 1, 4, 5, 6, 7 and 8), sometimes to within close proximity to the serous surface of the uterus, and in one specimen (Case 7) distended gland spaces containing blood were to be seen actually projecting from the serous surface of the uterus. When the endometrial tissue is traced outwards there seems a tendency for degeneration to take place in those parts of the invasions lying near the cavity, while the deeper and later formed tissue is still active. I believe that such degeneration, which may even lead to disappearance of the glandular tissue, makes it difficult at times to trace endometriomata in the uterosacral ligaments, and in other situations, to their true source, and that this may be responsible for misconceptions that have arisen.

With regard to the localized form of endometrioma of the uterus little need be said. On section the tumours show the regular arrangement of fibrous and muscular tissue in bundles, with scattered chains of glands extending between them (Fig. 5). The connexion between the uterine endometrium and that of the tumour is often difficult, if not impossible, to trace. This may indicate that no such connection has ever existed, or if

such did at any time exist, the intervening glandular tissue had subsequently disappeared in the way described, or that it only persisted as ill-defined degenerated tubules.

THE OVARY.

Whatever the relationship between endometrioma in the ovary and the same lesion in the other parts of the pelvis may be, there can be no doubt that the ovary is implicated in a large number of cases, and that the condition is usually visible to the naked eye. As proof of this I found endometrioma of the ovary in 21 cases out of 25, and in 17 of the specimens there was macroscopical evidence of the lesion.

On external examination of the ovary the following conditions may be noticed :—

Superficial endometriomata. The appearances in this type conform with the classical description given by Sampson. I have observed the minute blue or purple cysts projecting from the surface of the ovary, usually in the region of the unattached border, in several specimens (Cases 5, 7, 12 and 13), and also small puckerings or scars, often with a fine adhesion or a minute red area in the centre. These scars have been described as the sites of implantation of endometrium, but many of them closely resemble the condition present after rupture of a Graafian follicle, and on cutting the ovary open I have often found the remains of a corpus luteum in close proximity.

Erosion or invasion of the ovary. In other specimens, possibly at a later stage, I have observed that the surface of the ovary may become eroded, and a series of irregular depressions form. These were described by Sampson as arising by rupture of superficial hæmatomata, but doubt concerning this has since been expressed. In the specimens examined all the evidence seems to point to Sampson's view being correct, for one small area of ovarian surface may show the two conditions side by side, with clear indications that the hæmatomata have given rise to the crypts or depressions.

Adhesions. Further comment must be made on the presence of adhesions to the surface of the ovary. These may be light and filmy or very dense in character, and it is interesting to note that both Sampson and Bailey, in describing this fact, consider the presence of fine adhesions to be associated with implantations of Fallopian epithelium, and the dense adhesions with implantations of uterine endometrium. In my series fine adhesions were present on the surface of the ovary in seven cases, and I have noticed that the endometrioma was rarely well advanced. This

fact bears out the views already mentioned, but I consider it equally possible that as the ovary becomes more involved the adhesions and consequent fixation may become more marked. Further, it is impossible to decide in any particular case whether the presence of adhesions is definitely due to endometrioma, or whether it is due to associated infective conditions, which are so often present. Dense adhesions, sometimes noted, appear to be more definitely associated with deep endometriomata of the ovaries—chocolate or tarry cysts. In 11 cases in which the ovary was extensively involved tough adhesions were present. The ovaries were fixed to the uterus or broad ligament only in six cases (Nos. 5, 6, 7, 14, 16 and 19), in three cases to the intestine or rectum only (Nos. 10, 15 and 20), in one case to the uterosacral ligament (Case 14), and in one other case dense adhesions fixed both ovaries to the uterus, rectum, bladder, sigmoid colon, and omentum (Case 18). There is nothing special about the appearance of the adhesions except that old blood clot is usually noticed in the vicinity, and in one of my cases the first impression gained upon the abdomen being opened was that an ectopic gestation was present. I believe that when the adhesions are not due to an associated infective condition their presence is simply due to free blood in the peritoneal cavity. Whatever view may be held regarding the pathology of endometriomata there can be no doubt that in the case of the ovary leakage of menstrual fluid into the peritoneal cavity from a ruptured or leaking “chocolate cyst” does occur. I have found in four such specimens an aperture in the wall of the cyst, with old blood and adhesions collected round that point (Cases 5, 7, 14 and 19).

To recapitulate, it may be said that the following description is typical of endometrioma of the ovary: One or both ovaries are enlarged and have old blood on the surface, and they are densely adherent to the uterus and rectum, and possibly to other structures in the neighbourhood.

Appearance on incision of the ovary. In the first place, small subcapsular hæmatomata and erosions or excavations on the surface may be visible, as already described. A further stage has been described, namely, the “chocolate streak,” which is, as the name suggests, an extension of the superficial erosion into the deeper parts of the ovary.

I shall now describe the most characteristic lesions produced by ovarian endometriomata, namely, the “chocolate” or “tarry” cysts. These cysts vary greatly in size, their greatest diameter in some of my cases being only a few millimetres, while in other specimens the cysts were of the same size as that of a tangerine orange (Fig. 7).

In all specimens examined the cyst contained chocolate material exactly similar to that found in cases of hæmatocolpos or hæmatometra associated with vaginal atresia or a rudimentary horn of a bicornute uterus. This material is quite distinct from that contained in the so-called ovarian apoplexy or hæmorrhagic follicular cyst, the appearance in the latter case being simply that of a cyst, usually thin-walled, containing ordinary blood-clot.

With regard to the situation of the cysts in the ovary, I have found that the smaller ones occur superficially and deeply with almost equal frequency, but there appears to be some relationship between the size of the cyst and the depth of the surface. When small endometriomata are deeply placed, there are signs of invasion from the surface in some cases; in others, however, there has been absolutely no macroscopical evidence of any connexion between the cyst and the surface of the ovary.

The earliest evidence I can discover microscopically of endometrial invasion of the ovary lies in the presence of fragments of glandular tissue, usually with enveloping blood-infiltrated stroma, on the surface of the ovary (Figs. 8 and 9). Some adhesions are frequently present at these points, and I believe these fragments to be derived from the uterus *via* the Fallopian tubes, as described by Sampson.^{19, 20} This appearance of endometrial implantation, of which I found definite evidence in four specimens (Cases 9, 10, 12 and 19), gives the clue as to the origin of the ovarian endometrioma in these cases.

In Case 12 (Fig. 8), the implantation is merely lying on the surface of the ovary, but in Case 9 (Fig. 9) a further stage is visible, namely, the invasion of the ovarian substance.

In all implantations of glandular tissue upon the surface of the ovary, I have observed that the structure of the glands closely resembles that of uterine endometrium, and not of Fallopian epithelium, as others have described, and also that signs of reaction to menstruation, that is, hæmorrhages into the lumen or the stroma, have been present in every specimen.

A totally different appearance may be produced in other specimens by the presence of superficial endometriomata. This is characterized by the occurrence of small, often minute, subcapsular hæmatomata (Figs. 10 and 11). These often project from the surface of the ovary and are visible to the naked eye, as already described. No adhesions are present, and the hæmatomata are usually multiple, several being visible in one low power field. A typical hæmatoma has a definite structure: there is a space, often containing blood, lined by epithelium varying between the high columnar (often ciliated), and low cubical, types, and both varieties may be present in different parts of the same cyst. There is also a

distinctly specific loose stroma surrounding the gland spaces, and this often contains a considerable amount of extravasated blood

Very little evidence of penetrative power can be found, but deep to the hæmatomata there are occasionally similar spaces extending for a short distance into the ovarian substance, and probably constituting an invasion. More frequently a few atypical tubules are present immediately deep to the hæmatomata, and these are lined by low cubical epithelium, possess no differentiated stroma, but resemble crypts or invasions of capsular epithelium cut transversely.

In the ovarian stroma proper, I have observed an increase in the amount of involuntary muscle present in relation to the endometrium. This muscular tissue appears to arise by a process of simple hypertrophy of that already present, and not as part of the endometrial development.

Before describing the more advanced stages of the lesion, it is necessary to refer to certain abnormalities of the capsular epithelium. In all the cases in which superficial hæmatomata were present, there have been signs of unusual activity of the capsular epithelium, and I believe this to be important. Crypts are present, and some of these resemble cellular invasions. Moreover, in the deeper parts of these crypts the capsular epithelium may become high columnar in type, and even ciliated (Fig. 12). Although this appearance has been described as being due to implantation of epithelium derived from the Fallopian tubes, it is possible to trace the gradual change in the character of the epithelium, from typical cubical to high columnar (Fig. 13). Further, careful examination of those sections in which the small hæmatomata on the surface of the ovary are visible reveals the fact that, in certain capsular invasions, the epithelial cells, in addition to changing in shape, are lying upon a stroma which is infiltrated with blood; consequently, had the section been cut in another direction, an appearance exactly resembling that of the superficial hæmatoma might have been observed (Fig. 14). Another observation made with regard to these capsular invasions is that fine adhesions to the ovarian surface are often associated with persistence, and deepening, of the cells of the capsular epithelium.

It is important, therefore, to emphasize the fact that the capsular epithelium is columnar in some ovaries. I have taken special care to confirm this fact.

Before dealing with the appearances of deeper lesions of the ovary, there is another abnormality of the capsular epithelium: namely, deep invasions of the ovary not uncommonly occur. I have been able to trace the invasion of the ovary by the capsular epithelium in Case 12 for a distance of over 2mm, and the

importance of this lies in the fact that although lined in all but the deep parts by simple capsular epithelium, there are definite signs that in the deepest part the tissue has become altered in type, for a series of tubules are present lined by columnar epithelium, and lying in a very loose stroma in which is a small amount of blood (Figs. 15 and 16).

It will now be evident, on studying the microphotographs and on comparing figures 15 and 16 with figures 17 and 18, which were taken from an ovary containing a definite endometrioma (Case 3), that there is a marked similarity between the two conditions. The appearances seen in figures 15 and 16 are those of an early stage of the development of endometrioma of the ovary.

Up to this point I have described the microscopical appearances of superficial endometriomata and the early invasions of deeper parts of the ovary. In the specimens examined there has appeared to be a distinct gap between superficial and deep endometriomata; that is, I have only found an intermediate stage in a very small number of cases. There can be no doubt that an intermediate stage does exist, as is well shown in the right ovary in Case 5 (Figs. 17 and 18). In this chains of tubules lying in a special stroma are to be seen extending from the surface into the deep parts of the organ. It is to be noted that some of the gland tubules have become cystic, and this may represent an early stage in the actual formation of some tarry or chocolate cysts.

Upon microscopical examination of the deep endometrioma it is to be observed that a great variety of appearances may be presented, and I will attempt to describe the condition of the wall surrounding the collections of menstrual blood known as tarry cysts, according to the stage of development reached.

Stage 1. The epithelium lining the cyst in those specimens in which the cyst is only of moderate dimensions usually consists of a complete layer of columnar epithelium. This epithelium, occasionally ciliated in parts, is exactly similar to that of uterine endometrium. The nuclei are for the most part centrally situated, but may be displaced by the presence of secretion, and the free surface of the cells, as Bailey has pointed out, is rough in appearance owing to the adherence of red blood corpuscles. In addition to a lining layer of epithelium the wall of the cyst may contain collections of endometrial tissue with glands and stroma of very definite character (Fig. 19). The epithelium of the glands is similar to that lining the large cyst, but the cells are deeper.

The stroma in a small or recently formed and active endometriomatous cyst is very distinctive, and forms supporting tissue for the glands. It is usually dense, contains varying amounts

of extravasated blood, and shows a distinct line of demarcation from the surrounding ovarian tissue. In this and the other stages the presence of excess of involuntary muscle may be noted, but this is not usually sufficient to justify the term endometriomyoma.

Stage 2. Signs of atrophy of the epithelium indicate diminution in the activity of the endometrium. The epithelium tends to become flattened, and the stroma less distinct. It is interesting to note that the atrophic change, which appears to be due to pressure caused by retained blood, only affects parts of the wall at first, and that the stroma always tends to disappear as the epithelium atrophies; that is, stroma and epithelium bear a direct relationship to one another.

Stage 3. The final condition in an endometriomatous cyst is one of complete inactivity. The typical chocolate material, in addition to containing red and white cells, often contains broken off and degenerated epithelial cells. The true lining of the cyst cavity is only present in parts of the wall, where it may reveal itself as an irregular line of cubical cells. Although this lining is sometimes incomplete, I believe that endometrioma forms true cysts in the ovary; that is, the menstrual blood is not scattered in the ovarian tissue but is contained in cysts possessing—in the active stage at least—an epithelial lining.

Deep to the epithelium there may be the remains of a differentiated layer of stroma, and when this is present large cells containing pigment—probably blood pigment—are visible in parts.

In the walls of the old endometriomatous cavities the surrounding ovarian tissue is converted into a layer of hyaline tissue. This was observed by Sampson, and I have found it to be of frequent occurrence.

It is necessary to describe the appearances of the ovary apart from the lesions already referred to. In many specimens the rest of the ovary appears quite normal, others show an excess of involuntary muscle, as already described; and a third condition often noticed is the presence of varying degrees of cystic development originating in the Graafian follicles. This last lesion is only likely to be mistaken for endometrioma in its final stage when the stroma is disappearing and the epithelium flattened. Nevertheless, the absence of evidence of menstrual hæmorrhage, of glands or of a columnar-celled lining, should render the recognition of follicular cysts easy.

A recent corpus luteum may also simulate a tarry cyst, but the absence of epithelium, and the presence of the closely packed lutein cells should obviate any difficulty in distinguishing between the two conditions.

These are the typical appearances I have found in the ovary in cases of endometrioma. It will now be necessary to refer briefly to certain specimens in which a further description is necessary.

Description of microscopical findings in certain specimens of endometrioma of the ovary in which the tumour had some relation to surrounding structures.

Case 4. The right ovary was densely adherent to the side wall of the uterus. Sections of the wall of the uterus at this point show endometrial tubules extending throughout the thickness of the wall, and further, in one section, including uterine wall, ovary and adhesion, the tubules can actually be seen invading the substance of the ovary (Figs. 21 and 22). In this case the ovarian endometrium has been derived from that of the uterus by direct extension.

Case 5. The endometrial tubules in this specimen may be traced through the uterine wall and were seen to invade the ovarian ligament on the right side. At the point of attachment of the ovarian ligament to the inner pole of the right ovary similar endometrial tubules are present. Although serial sections were not cut of the ovarian ligament in this case, it is highly probable that this was the route by which endometrium reached the ovary. Further proof of this is afforded by the fact that no tubules are present in either the left ovarian ligament or the left ovary.

Case 15. This specimen, in which endometrioma of the right ovary is present, together with a recent tubal gestation, is interesting because there is a relation between the two conditions. Microscopical examination of the contents of the tube reveals the presence of blood clot and a few villi, but sections of the ovary show active endometrial invasion of the ovary, and in the stroma surrounding some of the tubules true decidual reaction is present (Figs. 23 and 24).

Case 11. In this specimen it has been possible to trace the tubal epithelium along the ovarian fimbria and into the ovary. At one point the structure changes from epithelium of Fallopian to that of uterine type with gland-formation and stroma, although there is no break in the continuity. This condition is clearly shown in figure 26, and indicates that the epithelium of the tube can undergo metaplasia and form endometrium.

From the point at which the endometrium is first observed a chain of tubules with stroma may be traced into the substance of the ovary.

Case 24. In this specimen it was noticed at the time of operation that there was hæmorrhagic infiltration of the left ovarian ligament, in addition to tarry cysts of the ovary, at a

point close to the attachment of the ligament. Serial sections were, therefore, cut, and it was possible to trace endometrial tissue through the whole length of the ligament and into the substance of the ovary (Fig. 27).

Case 8. As a small semi-solid tumour was observed to lie between the abdominal ostium of the tube and the left ovary, apparently arising from the ovarian fimbria, careful sections were cut, and it was shown that the tumour consisted almost entirely of endometrium, lying in a small amount of fibrous tissue and involuntary muscle (Fig. 28). Further, the epithelium of the fimbriæ could be traced into the tumour, thus again suggesting a metaplasia of Falloppian epithelium. When an attempt was made to trace a connection with the ovary a few tubules were observed invading that organ, but no typical endometrium was present.

ENDOMETRIOMA IN OTHER SITUATIONS IN THE PELVIS.

Macroscopically, the Falloppian tube has not been deeply involved in many cases. In some specimens there is marked thickening of the tube, which may also be kinked; but these changes are due to associated infection. The only lesions of the tube that I have observed have been adhesions, and the presence of minute cysts suggesting superficial hæmatomata similar to those observed on the surface of the ovary. In the ovarian fimbriæ in Case 8 there was a solid tumour, 1 cm. in diameter, of mixed cystic and solid character, which was closely associated with the abdominal ostium of the tube and with the ovary, the latter showing signs of endometrial invasion at the point of contact (Fig. 29). In Case 11 the abdominal ostium of the tube was again closely attached to the ovary, and there appeared to be an area of blood-infiltrated tissue extending from the tubal fimbriæ into the deeper parts of the ovary.

The ovarian ligaments. In addition to involvement of these structures in adhesions, I have found tarry or hæmorrhagic filtration to be present in two cases (Cases 4 and 24). (Figs. 30 and 27.)

The uterosacral ligaments. Adhesions, either light or dense, are present in association with these structures with great frequency. In Case 6, hæmorrhagic cysts are present, and in several cases the ligaments were buried in adhesions and old blood, so that it was difficult to identify them.

On microscopical examination of the uterosacral ligaments, small clusters of tubules may be found (Fig. 31). It is to be observed that signs of reaction to menstruation—though present—are not well marked. In one specimen it was possible to trace the direct connexion between uterine endometrium and that of the uterosacral ligament (Case 6).

The round ligaments. Macroscopically, the endometrium in Case 25 presented the appearance of a mixed solid and cystic tumour, 1.5 × 2 cms. in diameter, lying in close relation to an inguinal hernial sac.

Microscopically, sections of the tumour show very typical glands with plentiful stroma but no hæmorrhage. Figure 32 is a photomicrograph of the condition found, which appears to have been due to developmental displacement of Müllerian epithelium.

Other situations. In Case 22 there were omental adhesions to the ovary and small tarry cysts in the omentum. I have found the small and large intestine and the rectum to be frequently attached to the internal genital organs by adhesions, but in no specimen is there any macroscopical evidence of actual invasion of the wall of the bowel by endometrium.

Microscopically, small masses of stroma with doubtful glands lying on the serous surface of the tube, broad ligament and other structures, have been seen, but it has not been possible to confirm the suggestion that these are implantations.

A description of the microscopical appearances of the ovary would not be complete without mention of another abnormal condition.

I have found evidence of excessive activity of the capsular epithelium in three cases. In these specimens the mere presence of invaginations was not regarded as important, but the essential point lay in the fact that in the deep part of the cysts, cell proliferation and invasion of the ovarian tissue were taking place.

Group 2.

A brief reference may be made to non-endometrial tubules in the ovary. After studying closely many sections, I have come to the conclusion that Wolffian tubules are rare except in the hilum or deepest parts of the ovary, and that all superficial tubules are of capsular origin. This conclusion has only been reached after examination of sections of Wolffian tissue in the hilum of the ovary, and comparison of these with sections of tubules in the superficial parts of the ovary. There are slight but evident differences in the appearances of the two types of epithelium.

Non-endometriomatous lesions. In certain cases abnormalities other than endometrioma were present. Some of these show features having a bearing on the question of the ætiology of endometrioma.

Case 26. The patient had a large fixed tumour of the right ovary diagnosed as primary carcinoma. No glandular tissue was found in this ovary apart from the malignant growth, and there was no appearance to suggest the way in which the neoplasm had

arisen. In the left ovary, however, all sections show tubular and cystic spaces extending into the ovary from the surface and lined by deep columnar epithelium frequently ciliated, and in places forming intracystic projections. On the surface of the ovary clumps of degenerated glands of Falloppian type are present. It seems quite likely that this condition was due to implantation of tubal epithelium. There is no "cell mantle" of stroma, and, as the ovary appears normal to the naked eye, the case has not been included among the endometriomata. It is conceivable that the condition of the left ovary might be the preliminary stage to primary carcinoma (as was present in the right ovary) or to some form of innocent cystic neoplasm.

Case 27. This patient suffered from bilateral salpingo-öphoritis, and at operation, in addition to this condition, a nodule at the uterine extremity of the right tube was discovered. Histologically, this was found to consist of muscle with scattered endometrial tubules and stroma. The fundus of the uterus was also removed, and in this there was evidence of deep endometrial invasion of the muscle. It appears highly probable from a study of this and other cases, that local infective conditions may have some effect upon the endometrium as regards activity and penetrative power.

Case 28. The specimen consists of a uterus with fibromyomata, and of bilateral salpingo-öphoritis. Here again, as if in response to some stimulus, the endometrium of the uterus is invading the muscle coat and is forming cystic spaces in the deeper parts. Further, sections of the Falloppian tube undoubtedly show epithelial penetration of the deeper parts of the tube wall.

CLINICAL FEATURES OF ENDOMETRIOMATA.

Before relating the points of clinical importance in the cases recorded here, brief reference to the findings in some of the cases recently published, may be made.

Sampson²¹ states that in many of his 64 cases the lesions were small and therefore symptomless, but that in about 30 per cent. thereof very definite symptoms were produced. He lays stress on the onset of severe dysmenorrhœa, especially if arising in a woman who is over the age of 35, as important, and notes that when a large hæmatoma perforates, the resulting symptoms may simulate peritonitis.

Donald⁸, in reporting ten cases of ovarian endometriomata, agrees with Sampson in regarding acute dysmenorrhœa arising after middle age as being of considerable diagnostic significance, for this symptom was present in all of his cases. All the patients were between the ages of 26 and 47 years, while seven were between

41 and 47 years of age. Other symptoms found to be frequently present were menorrhagia or irregular hæmorrhage, leucorrhœa, and dyspareunia.

It was noted that in seven out of the ten cases of tarry cysts of the ovaries, associated endometriomatous lesions were found in other sites, chiefly in the uterus and uterosacral ligaments.

Again King,²¹ in a paper read before the annual meeting of the British Medical Association in 1924, gives a detailed account of the clinical features of 122 cases of endometrioma. He finds that in 16 per cent. of all cases there is no symptom. The commonest complaint is pain, especially that associated with menstruation, the onset being acute. Other symptoms described are sterility, nausea or vomiting, menorrhagia, and dyspareunia. King draws attention to the frequency with which the tumours are complicated by the presence of other conditions, especially infections and neoplasms, namely, 40 and 30 per cent. respectively. He thus confirms Sampson's view that the presence of tumours, displacements, and infections, appear to favour the occurrence of abnormal endometrial developments.

In agreement with the reports of Sampson, King, and others, fibromyomata and inflammatory conditions were frequently present in the cases I have investigated. Typical fibromyomata of the uterus were present in five cases out of a series of 22, and this number would have been greater had several cases in which the fibromyomata also contained endometriomatous tissue, been included.

In two cases the history of recent tubal gestation was given, and two other patients who had become pregnant during the previous two years aborted at an early stage in the gestation.

There was definite evidence of the occurrence of infection within the pelvis in 10 out of 23 cases.

In 22 of my established cases of this lesion, either intrauterine or extrauterine, or both, in disposition, a full clinical history was available. There seemed to be a direct relationship between the symptoms and the presence of endometriomatous tissue in abnormal situations in 15 of these cases. It was, however, extremely difficult to decide in some cases whether the symptoms were due to an endometrioma or to some associated condition, such as fibromyoma, inflammatory lesions or displacements of the uterus.

Symptomatology.

1. There can be no doubt of the fact, already described by Sampson, Donald, King and others, that severe dysmenorrhœa, usually occurring on the first and second days of the period, is a common symptom. In nine of the cases out of 15 here recorded—that is, in 60 per cent.—it was definitely present, the usual history

given being that of a fairly sudden onset in a patient whose menses had previously been painless. This symptom is due to actual menstrual hæmorrhage, either into the musculature of the uterine wall or into the tissues of the ovary.

2. Sterility probably constitutes the next most prominent symptom, for it was present in 10 cases out of 17—58 per cent. Here, again, we must exclude three cases, in which sterility was probably due to other conditions, namely, multiple fibromyomata of the uterus, bilateral salpingo-oöphoritis of long standing, and conical cervix with pinhole os externum. This leaves seven uncomplicated cases—41 per cent. of all the women who were married—characterized by the presence of sterility.

3. Of the other leading symptoms menorrhagia and attacks of intermenstrual hæmorrhage were fairly frequent, occurring in 12 cases out of 21 in which full details were available. Before ascribing the symptom to any endometriomatous lesion, however, it is necessary to exclude other causes of menorrhagia. A careful investigation of these 12 cases reveals the fact that other lesions were present in eight cases, namely :—

Fibromyomata of uterus (interstitial or submucous) ...	= 3
Chronic infection of uterus or appendages, or both ...	= 3
Primary carcinoma of the ovary	= 1
Mitral stenosis	= 1

Thus it will be seen that in only four of the 21 cases—18 per cent.—can the symptom be positively declared to be due to abnormal endometrial development.

4. Attacks of acute pain of a stabbing nature were recorded in seven of the 22 cases—31 per cent. This symptom was probably caused by the ovarian endometriomata which were present in every case. Pain of this nature appears to be frequently associated with the condition of acute dysmenorrhœa already mentioned.

5. Dyspareunia does not appear to be a common symptom, it was present only in three cases, and in one of these the presence of an associated inflammatory condition may have been the cause. It is possible, however, that a more careful interrogation of the patient would elicit evidence of this symptom in a greater proportion of cases.

6. In three cases in which adhesions involving the bladder were found frequency of micturition or dysuria was present.

Analysis of the main symptoms.

In my series of 22 cases, in which a history was available, 15 presented symptoms directly attributable to endometriomatous lesions.

(a) *Dysmenorrhœa* in nine (60 per cent.).

Intramenstrual in seven cases.

1. Tarry cysts of ovaries and endometrioma of uterus.
2. Tarry cysts of ovaries and multiple adhesions in pelvis.
3. Endometrioma of uterus.
4. Tarry cysts of ovaries and large fibromyomatous submucous polyp.
5. Tarry cysts of ovaries and endometrio-fibromyoma of uterus.
6. Tarry cysts of ovaries.
7. Tarry cysts of ovaries and small submucous fibromyoma.

Premenstrual and intramenstrual in two cases.

1. Tarry cysts of ovaries and chronic pelvic infection.
2. Tarry cysts of ovaries, multiple fibromyomata of uterus, and chronic infection of the appendages.

(b) *Sterility*. Ten cases out of a possible 17 (58 per cent.).

1. Tarry cysts of ovaries. Endometrio-fibromyoma of uterus.
2. Tarry and follicular cysts of ovaries, and multiple fibromyomata of uterus.
3. Tarry cysts, chronic infection of appendages, tubes not patent.
4. Tarry cysts, endometrioma of uterus.
5. Tarry and follicular cysts of ovaries, and endometrioma of uterus.
6. Tarry and follicular cysts of ovaries, and endometrioma of uterus.
7. Tarry cysts with dense adhesions, and endometrioma of uterus.
8. Tarry cysts of ovaries, conical cervix, and pinhole os externum.
9. Tarry cysts of ovaries, adhesions to bladder and sigmoid flexure of colon.
10. Endometrioma present in ovaries, old blood clot and adhesions in the pouch of Douglas.

After excluding cases 2, 3 and 8 of the above list, the number of cases in which sterility was present is seven (41 per cent.).

(c) *Menorrhagia, epimenorrhagia, or irregular hæmorrhage*.

Twelve out of 22 cases (54 per cent.).

1. Endometrioma of uterus.
2. Tarry cysts of ovaries, and submucous fibromyomatous polyp.
3. Tarry and follicular cysts of ovaries, and endometrioma of uterus.

4. Tarry and follicular cysts of ovaries, and fibromyomata of uterus.
5. Endometrium present in left ovary, and primary carcinoma of right ovary.
6. Tarry and follicular cysts of ovaries, and fibromyomata of uterus.
7. Endometriofibromyoma of uterus, and mitral stenosis.
8. Tarry cysts of ovaries, and endometrioma of uterus.
9. Tarry and follicular cysts of ovaries, and endometrioma of uterus.
10. Tarry cysts of ovaries, and endometrioma of uterus.
11. Endometrium in right ovary, and chronic infection of appendages.
12. Endometrium in right follicular cystic ovary.

Excluding cases 2, 3, 4, 5, 6, 7, 9, and 11, it appears that in four cases, or 18 per cent., menorrhagia was due solely to the presence of endometrioma.

Age of the patient.

It is an interesting fact that, with but two exceptions, all the patients were between the ages of 30 and 50 years, and in 12 out of a total of 24 patients, the age was 40 to 50 years. Of the other two patients, one aged 52 suffered from multiple fibromyomatous lesions causing a delayed menopause, and in the other, who was 67 years of age, senile atrophy was present in the ovarian endometrial tissue, as it was in that of the uterus.

Physical signs.

The physical findings, both before and at the time of operation, may vary considerably, but certain signs, when taken in conjunction with the typical symptoms already described, are of assistance in arriving at a diagnosis.

In many cases the presence of other tumours or of infective conditions in the pelvis may mask the condition and make the diagnosis difficult or impossible. The presence of fixed backward displacement of the uterus with or without fixed appendage swellings and tenderness, and the absence of a history of salpingitis is very suggestive. A certain diagnosis can only be made without operation in the presence of a further sign which was not found in any of the cases I have examined, namely, the appearance of a tumour in the posterior vaginal fornix by direct extension from the region of the uterosacral ligaments.

SUMMARY AND CONCLUSIONS.

General.

(1) It is not unusual to find endometrium in abnormal situations in and about the pelvis, but in many cases—over 25 per cent. in my series—this gave rise to no definite symptoms and no macroscopical feature. There is no reason to doubt that the “adenomatous” tissue described is endometrium. In addition to its appearance the facts that it corresponds accurately to the uterine endometrium in all phases of menstruation, and undergoes the other physiological changes in connexion with the uterine endometrium—that is, atrophy at the menopause and decidual reaction in pregnancy—are conclusive.

(2) When either macroscopical changes or symptoms are present, true endometrium is always to be found, and, therefore, the most appropriate and simple name to adopt is “endometrioma.”

(3) In a small proportion of cases involuntary muscle or fibrous tissue may combine with endometrium to form a tumour, usually in the uterus. In these circumstances the most descriptive terms are “endometriomyoma” and “endometrio-fibromyoma.” Involuntary muscle, when present in excess, is usually in close relation with, but not an intrinsic part of, the endometrioma. This is especially the case in regard to the ovary.

(4) The most important situations in which endometriomata may develop are the uterine wall and the ovary, occurring in the latter in 80 per cent. of my cases. When present in the ovary endometrioma eventually results in the production of a tarry or chocolate cyst. I believe the word “cyst” to be quite correct in this connexion, as the tarry material is usually lying in a greatly distended glandular lumen, and is not free in the ovarian stroma.

(5) When well-marked evidence of involvement of the ovaries is present the clinical signs are those of a fixed, enlarged ovary, or ovaries, usually lying in the pouch of Douglas, with fixed backward displacement of the uterus—a state of affairs difficult to distinguish from that produced in chronic inflammatory lesions.

(6) Endometrioma is somewhat difficult to diagnose clinically, but patients may complain of a recent onset of acute intramenstrual dysmenorrhœa, attacks of sharp, acute pain in the lower abdomen, menorrhagia, and sterility. The age of the patient is usually between 40 and 50 years.

(7) It is rare for endometrioma to be present in other parts of the pelvis independently of the ovaries, but such may be the case, the round and uterosacral ligaments being most often involved.

(8) When invasion of the ovaries is extensive it is usually found that endometrium is present in adhesions thereto, and also in

the ligaments of the uterus, peritoneum of the pouch of Douglas, and even on the wall of the sigmoid colon or rectum.

(9) Although it is quite probable that the implantation of Fallopian epithelium may occur upon the surface of the ovary, there is no evidence to suggest that any lesion of clinical or pathological importance results from this.

Ætiological.

The uterus. There can be no doubt that in the majority of these tumours of the uterus the endometrial tissue present is derived directly from the endometrium, as I was able to prove in all cases. Possibly implantation and invasion from without may occur, but it is improbable that any but the most minute lesions could be produced in this way.

The ovary. There appear to be five distinct ways in which endometrial tissue reaches the ovary, and of these I have observed the first four, namely :—

(1) Implantation of uterine endometrium on the surface of the ovary by way of the Fallopian tubes (Cases 9, 10, 16 and 19). See figure 33.

(2) From the uterus by direct extension along the ovarian ligament (Cases 4, 6, 21 and 24).

(3) By changes taking place in the epithelium at the abdominal ostium of the tube, whereby it is converted into endometrium which invades the ovary (Cases 8 and 11).

(4) By alteration of capsular epithelium (Cases 12 and 13).

(5) By developmental errors. This theory, as suggested by Russell and Blair Bell, and amplified by the latter, is worthy of close attention, for it is extremely suggestive on theoretical grounds, and in the pathological investigation one is impressed by the number of specimens in which this theory is applicable in every aspect of the case.

In the case of ovarian endometriomata part of the anlage of the Müllerian duct may be included in the ovarian anlage in the earliest stages of development of the intermediate cell mass.

Other situations. Endometriomata may arise in other situations in one of four ways :—

(1) Implantations of endometrium by way of the Fallopian tubes.

(2) Extension, either directly from, or following rupture of, an endometriomatous, tarry cyst of the ovary.

(3) By developmental errors during the formation of the uterine ligaments. This is illustrated by Case 25, in which a tumour of

endometrial type arose primarily in relation to an inguinal hernial sac from the round ligament. There was no evidence of abnormality in the pelvis in this case.

Blair Bell believes that in the case of "ligamentary" endometriomata part of the embryonic endometrial lining of the uterus may be displaced during the fusion of the Müllerian ducts and be drawn out by the round and uterosacral ligaments which are derived from the external muscular coats of the Müllerian ducts (uterus).

(4) By direct extension from the uterus, as in Case 6. Here tubules can be traced from the uterus directly into the uterosacral ligaments.

With reference to the implantation theory, I believe that passage of endometrial fragments along the Fallopian tubes is most likely to occur when tumours of the uterus cause a partial obstruction to the normal outflow of menstrual blood. Even when retrograde menstruation is present and implants are lodged on the surface of the ovary, or when endometrioma arises in other ways, I believe that some further factor is present, and that this activates the endometrium and endows it with special powers of penetration and proliferation. One of these factors is no doubt the effect of the internal secretion of the ovary. It is, of course, well known that the ovarian secretion influences the state of the endometrium and affects menstruation.

Other factors which play some part in the activation of endometrial tissue are local inflammatory conditions of the uterus and appendages and tumours of the pelvic organs. Also it is highly probable that certain other conditions, both local and general, may act in the same way, among the latter group abnormalities of the hormonopoeitic system, resulting in derangement of the internal secretions, being worthy of attention.

It will be clear from what has gone before, that there are many different ways in which extrauterine endometriomata may arise.

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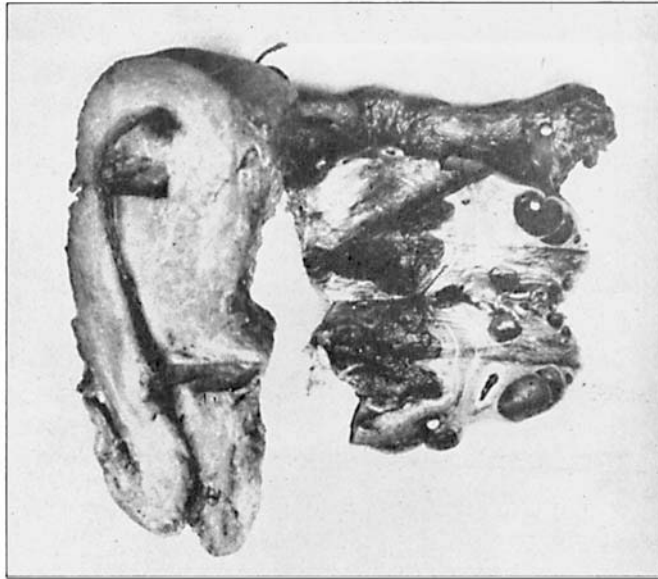


Fig. 1. The uterus and the right tube and ovary (Case 6). In the posterior wall of the uterus there is a diffuse thickening causing distortion of the cavity. This wall proved to be muscle infiltrated with endometrial tissue in all parts. The ovary shows "tarry" and follicular cysts, and corpora lutea.

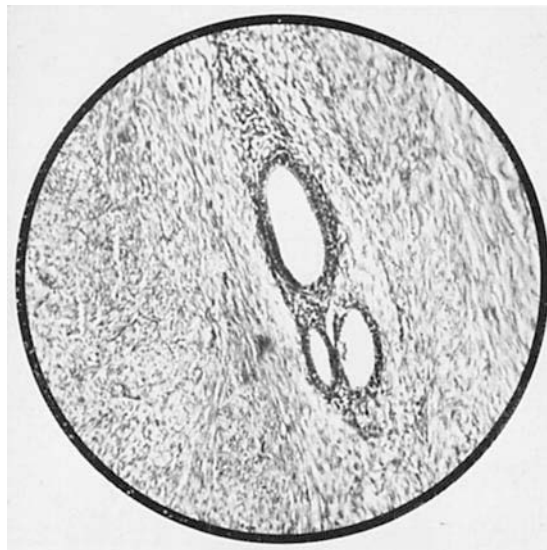


Fig. 4. Section of the deep part of the uterine wall. $\times 75$. (Case 4.) Endometrial tubules with stroma lying between the muscle bundles, are present.



Fig. 3. The uterus and the left tube and ovary (Case 7). The photograph shows a diffuse endometriomyomatous tumour of the posterior wall and fundus of the uterus. The left ovary, which has been cut open, contains a large tarry cyst of endometrial origin—for microscopical appearances see Fig. 4.



Fig. 5. Endometriomyoma of the uterus. $\times 75$. (Case 7.) A section taken from one of the localized tumours in the uterine wall.



Fig. 8. Implantation on the surface of the ovary (Case 12). An early stage of invasion.

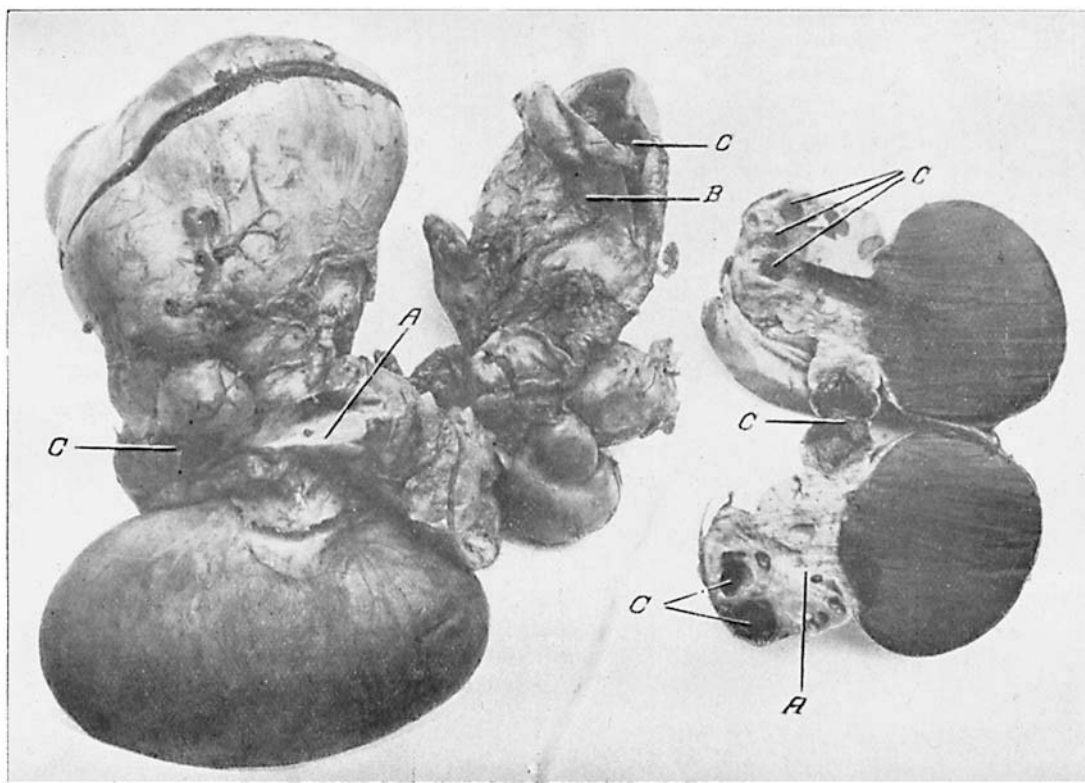


Fig. 7. The appendages from Case 18. Ovarian tissue is visible at points (a, a) and adherent omentum at (b). The remainder of the tumour consists of hæmorrhagic cysts, some follicular, but the majority of endometrial origin (c, c, c).

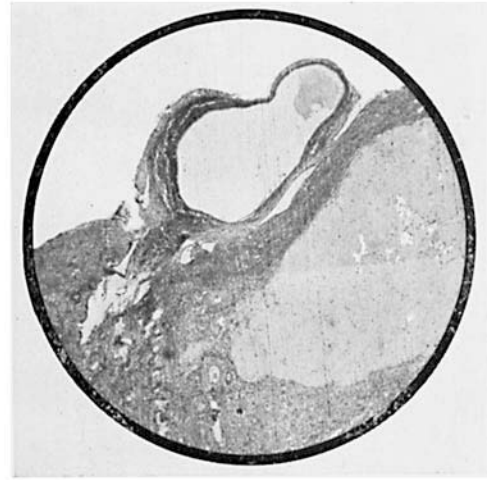
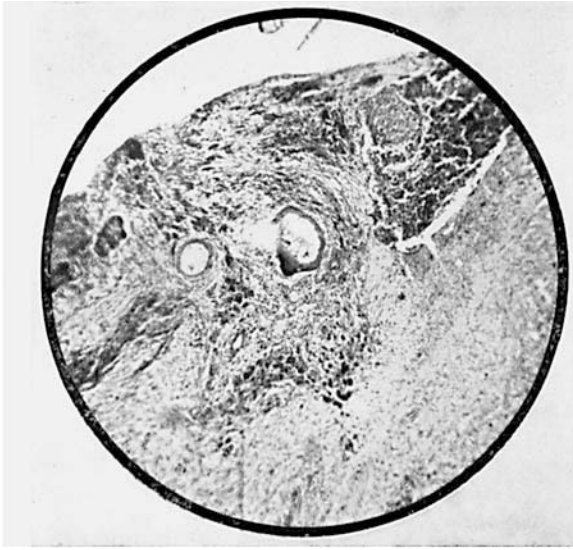
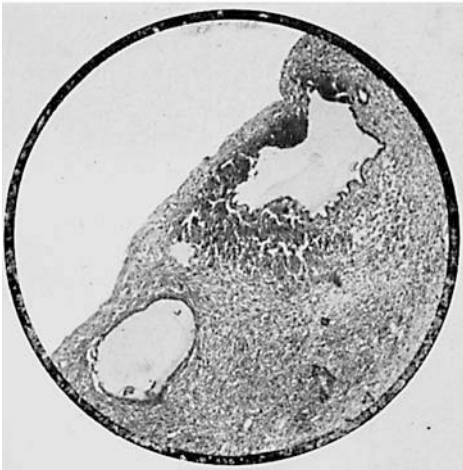


Fig. 9. Implantation on the surface of the ovary (Case 9). Here a later stage of invasion is shown.

Fig. 11. Minute hæmatoma projecting from the surface of the ovary. (Case 12.)



Figs. 10 & 10a. Superficial hæmatomata of the ovary (Case 13). The columnar epithelium, ciliated in parts, is shown, and also encircling stroma with hæmorrhage.



Fig. 12. An invagination from the surface of the ovary in Case 18 in which the gradual deepening of the epithelium could be traced. $\times 25$.

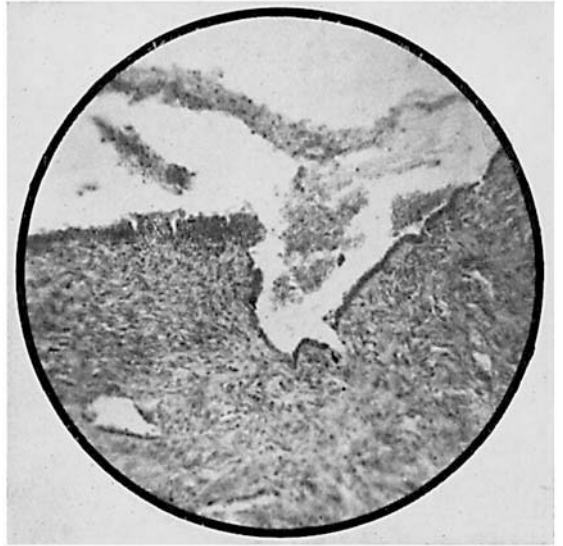


Fig. 13. A higher power photo of Figure 12 showing the character of the epithelium described. $\times 150$.

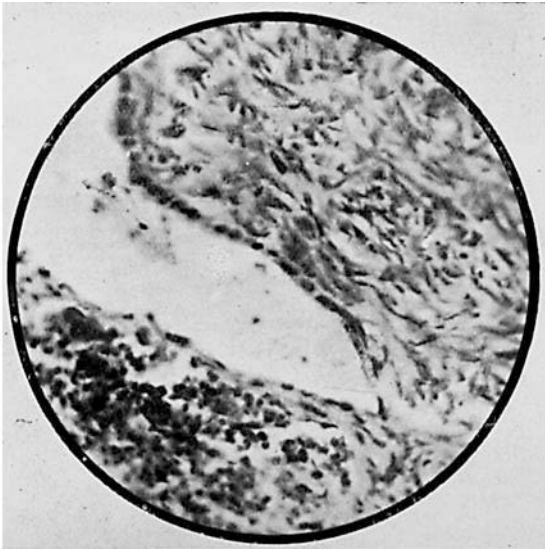
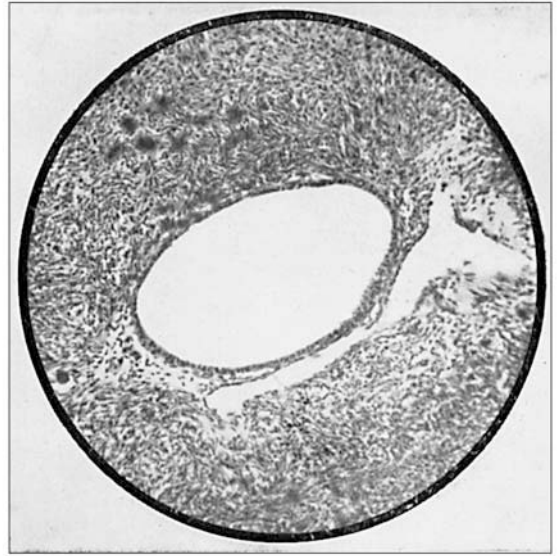
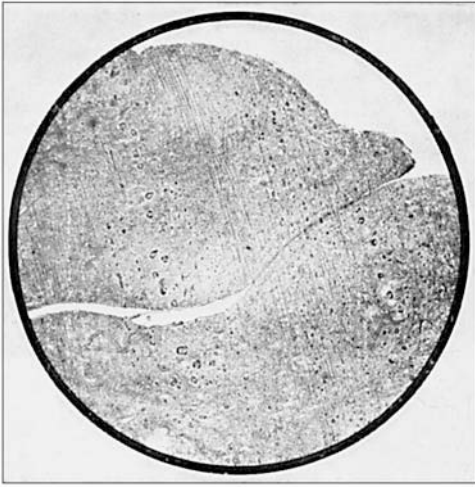


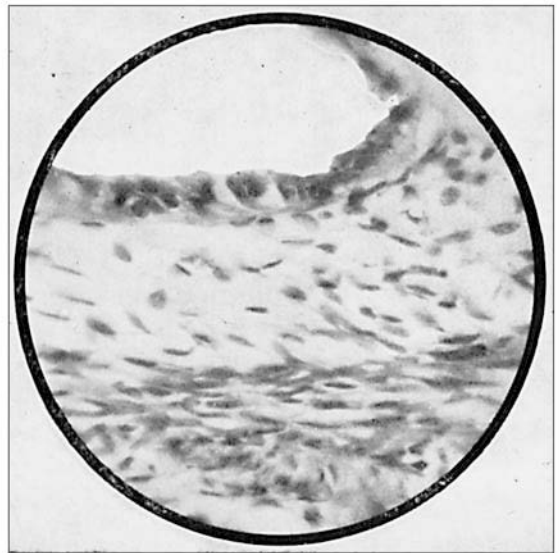
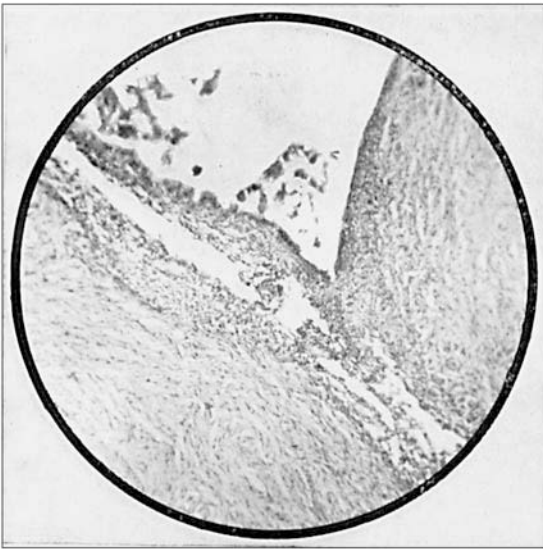
Fig. 14. A crypt lined by capsular epithelium which is undergoing metaplasia, and with sub-epithelial haemorrhage. This illustrates one of the ways in which superficial haematomata may arise. $\times 300$. (Case 13.)



Fig. 19. Section of the wall of a tarry cyst (Case 16). The actual lining epithelium of the cyst is shown, and, in addition an area containing glandular tissue and stroma. ($\times 50$.)



Figs. 15 and 16. High and low power photographs are shown of a capsular invagination (Case 12). Fig. 16 shows a tubule lined by epithelium which is becoming deeper in character. There is, too, evidence of the formation of a mantle of stroma around the tubule.



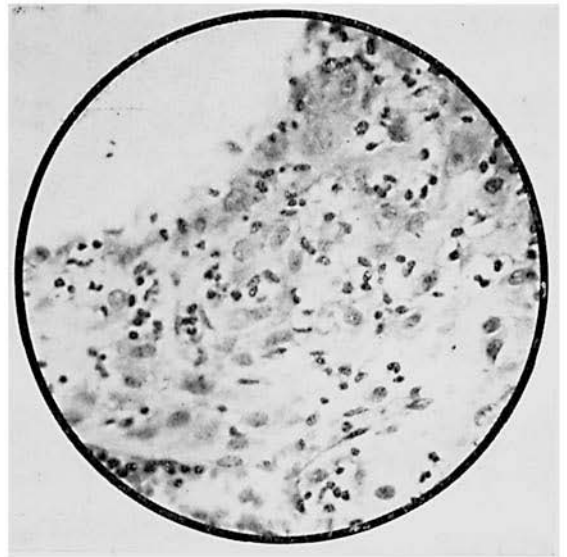
Figs. 17 and 18. Photos of sections showing the early stage of ovarian invasion. Gland and cyst spaces are present with typical stroma. The appearance in Figure 16 is very similar to this but illustrates a still earlier stage.



Fig. 21. The uterine wall contains endometrial tubules in its outermost part.



Fig. 22. A photograph of an adjoining part of the same section showing similar tubules in process of invading the ovary.



Figs. 23 and 24. Low and high power photomicrographs showing decidual reaction in the stroma in relation to an endometriomatous cyst. (Case 15.)



Fig. 26. Showing the development of endometrioma in relation to the fimbriated end of the Fallopian tube . (Case 11.)

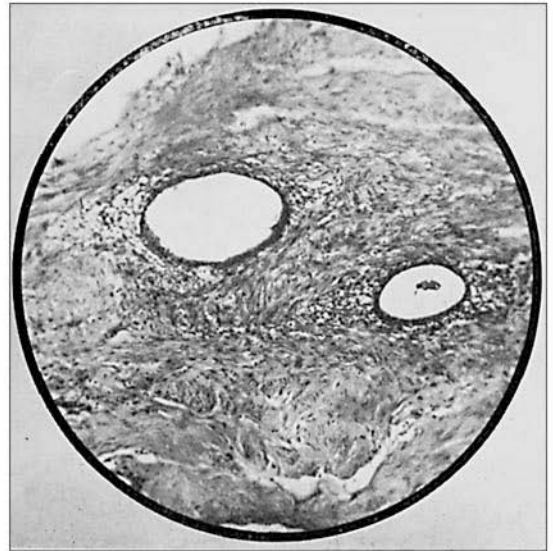


Fig. 27. Endometrium in right ovarian ligament (Case 24). $\times 75$.



Fig. 28. Endometriomatous tumour attached to the ovarian fimbria (Case 8). $\times 100$.

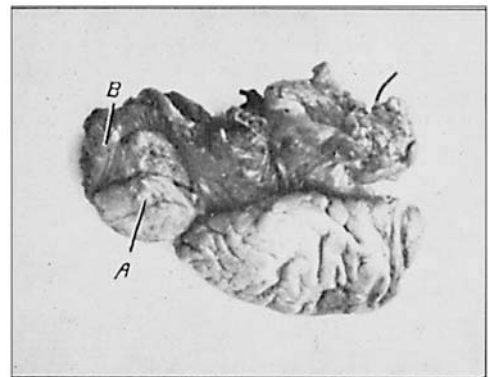


Fig. 29. The left tube and ovary (Case 8). The ovary appears normal, but a mixed solid and cystic tumour (a) is shown lying between the abdominal ostium of the tube and the outer pole of the ovary—this contained endometrium. The abdominal ostium and the ovarian fimbria are shown (b).



Fig. 30. The right ovary and ovarian ligament (Case 24). The ovary contains both endometrial and follicular cysts. The photograph also shows hæmorrhagic infiltration of the ovarian ligament.



Fig. 31. Endometrioma of the utero-sacral ligaments (Case 6). $\times 75$.

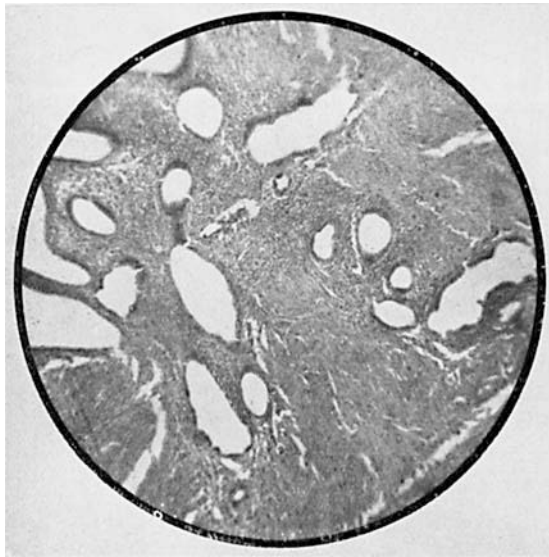


Fig. 32. Endometriomyoma of the round ligament in the groin (Case 25). $\times 50$.



Fig. 33. Tumour from peritoneal cavity of rabbit. $\times 100$.

This specimen affords conclusive evidence of the fact that endometrial implantation on the peritoneum is possible. The left horn of the uterus of a non-pregnant rabbit was removed in the course of some experimental work, and it was noticed that the pelvis and broad ligaments were absolutely normal. Sixty-five days later the abdomen was again opened, and a small solid nodule was observed on the left broad ligament situated 2 cms. from the stump of the horn. As this nodule was unconnected with the cut end, and consisted of endometrium resembling that of the uterus of the rabbit, the specimen confirms the work of Sampson and Petersen, to which reference has already been made.