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Lutein Cysts in Association with Vesicular Mole and Chorio-Epithelioma ;

A CONTRIBUTION TO THE STUDY OF THE NORMAL AND ABNORMAL PROCESSES SEEN IN THE DEVELOPMENT AND RETROGRESSION OF THE CORPUS LUTEUM.

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I. CORPUS LUTEUM CYSTS.

IN working out the development of these cysts it is necessary to follow as closely as we can the stages of the maturation of the Graäfian follicles and of their retrogression after the rupture of the yellow body. Inasmuch as the latter is the simpler task of the two, I will consider it first. After the ripe follicle has discharged its liquor folliculi, together with the discus proligerus which invests the ovum, the vascular tunic upon which the lutein cells lie suffers considerably. The delicate vessels, already upon the point of rupture, and in frequent instances already ruptured, undergo a further laceration caused by the rise in local blood-pressure which occurs simultaneously with, and seems to explain, the actual bursting of the follicle itself. The increased blood-pressure finds its release by escape of blood from the open vessels in the tunica interna into the interior of the corpus luteum, and some of the lutein cells are swept away into the interior of the blood-stream and can be seen lying in blood-clot. What now immediately follows is a simple illustration of healing by means of blood-clot, such as we meet with after osteotomy for sclerosis of bone. The blood-clot shrinks and divides up into sections, whilst in and around the channels so formed there is a rapid fibroblastic invasion (see Fig. 1). The lutein layer which immediately surrounds the contained clot succumbs before the

invading hordes of leucocytes and fibroblasts, the lutein cells gradually disappear, their place being taken by young granulation tissue. Simultaneously with the formation of this peripheral granulation tissue, the invested clot becomes decolourised and is seen studded all over with branching fibroblasts (see Figs. 2, 3, and 4). A striking difference is now apparent in the fate of the fibrous tissue formed by the organisation of the blood-clot and of that seen at the periphery, whose work it was completely to destroy the lutein cell layer. The latter is true, genuine, highly vascularised tissue, and is essentially reproductive, for by its means the true ovarian stroma is being constantly generated afresh. The former is unworthy of the term "fibrous tissue," and I only call it so for want of a better name; it is not vascularised, it takes no share in regeneration, and is gradually eaten up by such cells as are seen in the peripheral fibrous tissue layer. But this passive termination is not submitted to without some show of resistance; indeed, this inert tissue appears to possess at first a negative chemiotaxis capable of keeping in abeyance at certain points the inroads made upon it by the aggressive circumferential granulations. Tongues of the latter soon however, find their way across it to join up with others, and in this way the hitherto intact corpus albicans is divided up into separate segments. These in their turn allow themselves to be pushed far and wide in the ovarian stroma by the new tissue which is gradually being regenerated within the gland. The islands of passive tissue which are all that now remain to represent a corpus albicans assume striking features. They are to be seen as tortuous snake-like bodies, studded throughout the tissue of the ovary, abundant in the cortex and parenchyma, scanty or non-existent among the vessels of the hilum. They possess a wonderful affinity for eosin dye, which property renders them more easily distinguishable than any other structure of their own size throughout the stroma. They are very hyaline in appearance, and sometimes almost refractile. In Fig. 5 I have represented one of these residual fragments undergoing destruction by fibroblasts derived from the neighbouring young cellular stroma. Of all degenerate tissues with which I am familiar this "*reste*" is the most resistant. In its final stage, without any blood-vessels of its own, and whilst having to subsist like a parasite upon such nutrition as it can pick up from the tissues around, it will exist for years, and its presence is not infrequently capable of demonstration in ovaries which have long lost their normal functions.

As far as I have learned at present, this short description includes all the main facts which are concerned in the healthy natural retro-

gression of a corpus luteum. If the changes proceed in the manner and order in which they are described above, there is no need to say anything upon the subject of the formation of lutein cysts. But the fact is, there are breaks and irregularities in this straightforward process, and these constitute the opportunity for the development—one mode of development—of the cysts in question. A possible error in devolution occurs in the initial stage of the retrogression of a corpus luteum. It happens sometimes that the lutein cells are not completely destroyed by the peripheral layer of granulations (see Fig. 3). Just as in rickets the calcification which precedes ossification proceeds irregularly and allows of islands of cartilage being left unossified, so in the granulations of the lutein layer which precede fibrosis, the process may be irregular, allowing the escape of islands of lutein cells from destruction by phagocytes. The islands of cartilage left after rickets may form a chondroma; the islands of lutein cells may form lutein cysts (see Fig. 6). As there is practically no intercellular substance in an island of compact lutein tissue, the cystic change must occur by cystic degeneration of the cells themselves; and such a process I have been enabled to verify *ab initio*. A lutein cell will lose its nucleus, its protoplasm except at the periphery, will refuse to stain, and it becomes a hollow vesicle. Several will fuse together, by the destruction of their apposed walls, and so a cyst is formed; the inner lining will be lutein cells, uncovered by fibrin and of course devoid of epithelium. It would be difficult, if not impossible, to prove this origin for any non-epithelial lutein cyst which has attained any considerable size; but it is only fair to infer from such microscopical evidence as I have given that such is the origin of some of these cysts. A second way in which cysts develop in the corpus luteum after rupture, is by changes occurring in the central blood-clot, by which it becomes teased out into a coarser and coarser fibrinous network, which breaks down in the centre and a cyst is formed. Another point of interest in the devolution of the corpus luteum concerns the question of the displacement of lutein tissue, but this I intend to refer to under a special heading. For further consideration of the development of lutein cysts, I must now pass on to the more difficult task of investigating the evolution of the corpus luteum, and the origin of the lutein cell.

From the fact that the layers of lutein cells occupy in a corpus luteum the same position which the stratum granulosum occupies in a primordial follicle, I accepted, to start with, the view that the former presented a highly developed type of the latter.

This idea seems supported by the fact that in a ripe corpus luteum, even before rupture, no stratum granulosum can be found as such. In one fortunate section I succeeded in finding an ovum surrounded by its discus proligerus lying free in the fluid contents of the central space, ready, as I suppose, to be extruded; but there was nothing else to be found characteristic of a stratum granulosum. Hence it seemed natural to suppose that this layer had been converted into the lutein layer. Further research has made me alter my opinion. External to the basement-membrane of the stratum granulosum, and lying among the typical oval, rod, and spindle-shaped, young fibrous-tissue cells of the theca interna, and especially in the neighbourhood of free hæmorrhage, we see springing as it were into existence a faintly staining intercellular substance which shows lines of cleavage in the protoplasm. Between these lines a ghost-like oval nucleus makes its appearance, and then the surrounding protoplasm becomes faintly granular and gradually more distinct, and the cell-outlines more definable. If we accept this as histological evidence for the origin of the lutein cell, the explanation of the epithelial lutein cyst becomes a very easy matter, as we shall see later. The question as to when or at what stage we first meet with lutein cells in the normal maturing process of a Graäfian follicle, is difficult. It involves the critical distinction between a small pathological epithelial lutein cystoma and a healthy ripening follicle. If the presence or absence of an ovum in a series of microscopic sections were made the determining factor, the answer would be easy. Unfortunately, the absence of the ovum and its protecting discus proligerus is so common in every series of sections that we are obliged to regard it as due to an accident in section-cutting; for if we could exclude this possibility most ovaries, such as fall into the hands of pathologists, would contain a number of small lutein cysts. There is no reason why they should not; but *prima facie* there is certainly no reason why they should. The argument makes us raise at the same time the question whether we are always correct in our decision as to what constitutes hydrops folliculorum. How are we to say, when adjudging a microscopical cyst, where hydrops begins and where the normal development of the fluid of a maturing follicle ends? The absence of an ovum may be a mechanical accident, even in serial sections, as I have just said. Hence my difficulty with regard to deciding when it is that a healthy follicle puts on its coat of yellow cells. When dealing with a cyst whose size would correspond equally well with that of a follicle midway in its development, or with a small lutein cyst in the absence of an ovum, I know no means of determining which

it may be. But this difficulty does not extend through the whole investigation; for later on a fully ripe follicle is a sufficiently marked structure to be distinguished by the naked eye, and microscopically it is invested by such an abundance of lutein tissue prior to rupture, and with such a comparatively small cyst cavity, that its true nature cannot be doubted. It is in the stage between the commencement of ripening and full maturation that we meet with the development of the majority of lutein cysts. For the want of a better chronological point, we may assume that, at the time certain follicles develop into simple cysts, others acquire, in addition to an excess of liquor folliculi, an early coat of lutein tissue. Now synchronous with the appearance of lutein cells—whether they are to form the investment of a maturing follicle or whether they are to encase a hollow, useless cyst-cavity—some very marked and constant changes occur in the theca interna of the follicle. So constant are these phenomena that I believe the evolution of the lutein cells is entirely dependent upon them; without them the lutein cell could never come into existence. I refer to the enormous increase in vascularity assumed at this time by the theca interna. Not only does this tissue become highly vascularised, but hæmorrhages occur very freely into it; and amongst these free hæmorrhages is seen what I take to be the evolution of the lutein cells. We know how blood-effusions will alter the character of the cells around them, and young newly-formed cells are especially liable to become succulent and swollen. The vascularity of the placenta may account for this feature, as instanced in the decidual cell and the cells of Langhans' layer in the chorionic villi. In the same way I would explain the appearance of the lutein cell: it is a decidua-like cell born in a bath of blood. To pass to the consideration of abnormalities occasioned by this hæmorrhage, I find that it is not uniform in amount around the periphery of a follicle, but may be so excessive at one spot as to invert the stratum granulosum before it, rendering the lumen of the follicle horse-shoe-shaped. At other times the granulosa gives way; and before the ovum is shed, the cavity of the follicle fills with blood, and the ovum if it can be found, then appears as a hollow vesicle surrounded by the cells of the discus proligerus. But in spite of their protection, it will be seen to have lost both nucleus and nucleolus. Another very striking feature is a change in character in the tunica fibrosa which occurs as the follicle approaches maturation. This coat of the follicle secondarily to its increased vascularity, becomes extremely cellular. Young fibrous-tissue cells develop in connection with the delicate capillary loops which everywhere invade this tunic;

and once more, it is amidst these cells, which are their primogenitors, and are surrounded by effused blood, that the lutein cell is evolved. *These lutein cells can be seen to increase in number outside the basement-membrane of the stratum granulosum.* They ultimately form a complete band of large mononuclear cells, densely packed together into segments, and the latter are divided by capillary loops which grow in from the surrounding vessels of the theca interna.

Corpus Luteum Hæmatoma. From the excessive outpouring of blood in the theca interna, a corpus luteum hæmatoma may arise. I regard this phenomenon as always starting prior to rupture of a Graäfian follicle, whilst its blood-supply is at its zenith. After rupture, the cavity fills with blood, it is true; but this is a rapid and temporary effusion, followed very quickly by the organisation of the fibrous tissue layer which replaces the lutein cells. The stimulus of a presiding ovum is gone, and with it subsides the intense vascularity and the risk of hæmorrhage. The local excess of blood is dried up after the final avalanche, and the latter if excessive, would find its vent through the same channel which was provided for the escape of the liquor folliculi, ovum, and discus proligerus. It is during the congestive stage, then, of a maturing corpus luteum that we must expect to find the source of lutein hæmatoma; and this source is amply provided by the phenomena described above, namely, the effusion of blood from the vessels of the tunica interna pushing before it the stratum granulosum, and after rupturing this layer, filling up and distending the cavity of the follicle. This same hæmorrhage may divide the lutein lamina concentrically, so that the latter may appear as two rings at the periphery of a hæmatoma. This was what Rokitansky termed "doubling of the yellow body." When the blood-clot which exists between the now divided layers of lutein cells becomes organised into fibrous tissue, the latter will displace any lutein cells which still remain, so that their association with the hæmatoma, by the time the latter has assumed a considerable size, may be hard if not impossible, to demonstrate. Another structure which disappears even before the lutein cells is the stratum granulosum: this is broken up by the in-rush of blood and is seen, first in small fragments in the blood-clot, and then finally disappears. It is my belief that most true ovarian hæmatomata arise in connection with developing corpora lutea or in the course of formation of lutein cysts. My reason for this conviction is that no other part of the ovary shows such a wealth of young newly-formed, but congested, capillaries, as the fibro-cellular theca immediately investing these hollow bodies. The internal blood-pressure of the ovary, especially

when unduly raised by the stimulus of menstruation, or by the more persistent effects of inflammatory conditions, can more easily cause rupture of these newly-formed vessels than of those which are older and better developed. It seems clear, by the way, that this constant formation of vascular fibrous tissue around developing follicles is continually regenerating and laying down new ovarian stroma. In the development of this fibrous tissue we see a continuous centrifugal new formation of stroma taking place. In the case of a hæmatoma or of a lutein cyst, this process aids in the displacement of lutein tissue, just as during the involution of a normal corpus luteum it caused the dispersal of the fragments of the corpus albicans.

With regard to the clinical association of ovarian hæmatomata, I have never found a hæmatoma of any considerable size apart from tubal disease of some kind or other. In one specimen now in my possession the tube is infected with tubercle, in another it is the seat of a molar pregnancy. In both these instances the ovaries were invested by dense adhesions, but in another specimen—the largest of the three—the somewhat thickened tube is quite free from adhesions and is associated with a fibroid uterus of some size. In this third case there was a closed fissure of the tunica albuginea about an inch long at its thinnest part, showing that rupture had taken place and that the linear rent had closed again. The blood in this instance was the colour of anchovy paste and contained a large amount of cholesterin crystals. In a fourth instance, where I removed the tubes and ovaries for chronic salpingo-oöphoritis during an operation for fixed *retroflexio uteri*, I found within one of the ovaries (which was densely matted to the corresponding tube and parts around) a corpus luteum cyst, the size of a small walnut. This cyst was filled with a glistening, yellow, semi-fluid substance, which on microscopical examination proved to be altered blood containing cholesterin. The cyst therefore represented a type of degenerating lutein hæmatoma. It contained no pus, but its contents afforded a proof that these collections of blood undergo retrograde changes which predispose to pus-formation, so that a lutein hæmatoma may legitimately be regarded as a precursor to a lutein abscess. A good many corpus luteum cysts arise precisely in the same way as a hæmatoma originates from a developing yellow body, so that when small, they appear full of fibrinous clot; but for some unknown reason the hæmorrhage is checked, and a central cystic space forms, whilst the peripheral clot becomes organised and forms a fibrous tunic internal to the lutein layer. This organisation varies greatly in degree, so that in the case of some of the largest cysts we find an

internal lining consisting of nothing but the most delicate fibrin, in which no true fibrous tissue is evident (Fig. 8, Malcolm's case), whilst in comparatively small microscopic cysts there will be found a fairly thick layer of young fibrous tissue (Fig. 9, Oldfield's case).

Other lutein cysts are invested with a layer of cubical or spherical epithelium (Figs. 10, 11, 12, and 13). These cysts arise from the maturing follicle before it loses its epithelial coat. There is much variation in the character of the epithelium, and this is due to the great tendency to metaplasia in this type of cell, a feature which may, or may not be indicative of a pathological condition. In Fig. 8 is shown the transition in shape which these cells are undergoing in a much distended follicle: it is certainly here associated with, if not part of, a pathological change. Again, we see ova surrounded by columnar epithelium instead of the usual spherical cells within primordial follicles, whilst in large pathological cysts lutein cells may be seen covered with typical granulosa cells (Fig. 13, Williamson's case). Why in one instance this metaplasia occurs and in another it does not, I cannot say; but it is more usual to find that the granulosa layer which covers the lutein cells in an epithelial lutein cyst is composed of well-developed columnar epithelium. In my opinion the assumption of a coat of columnar epithelium is a sign of retrogression in a Graäfian follicle.

To sum up, as far as I have gone, the various modes of origin of lutein cysts, we find that they may be tabulated thus:—

Retrograde stages of corpus luteum, give
1. Cysts arising in the central clot.
2. ,, ,, from displaced lutein tissue.

Maturation stages of Graäfian follicle, give
1. Epithelial-lined cysts due to persistence of the granulosa.
2. Non-epithelial cysts due to absence of granulosa.
3. Hæmatomata.
4. (To be referred to later). Lymphangiectases.
5. (To be referred to later). Complication cysts.

Fortunately the majority of these cysts have no clinical significance whatever, but under certain conditions not yet determined, they develop very rapidly by a process of multiple cyst-formation rather than by any enormous distension of a single cyst, the result being a tumour generally not less in size than a fœtal head, composed of a central core of œdematous ovarian stroma and a peripheral zone of cysts. Among these last strands of the central stroma proceed forming the septa, which are often extremely thin,

the cysts being set so closely together. I have reason to believe that these cysts may be multiple from their beginning, as I have found a small bi-locular cyst in process of development from a maturing follicle (Fig. 10). None of the loculi are septate in these large cysts, the structure of walls varying according to size of the loculus. Even in the thinnest there may be a thin lining of fibrous tissue between the lutein cells and the cavity of the cyst, but the lutein cells may themselves form the innermost lining. A fibrinous coating is not uncommon even in cysts of considerable size, and perfect columnar and spherical epithelium may remain in some of the loculi of quite extensive multilocular cysts. The largest cysts generally contain a clear, highly albuminous, pale, straw-coloured fluid, which coagulates spontaneously and which hardens to a firm jelly in Kaiserling-Pick's solution (Fig. 14). Externally these cysts present in the aggregate a very irregular appearance, and have not inaptly been described as resembling "bubbles about to burst." No other type of ovarian cystoma resembles them in the least. In the four pairs which I have studied, there was no sign of their becoming adherent; the tubes were quite free and unaltered in relation to the cystic ovaries. The right-sided cyst in Mr. Malcolm's case was strangulated, and the clear contents were consequently mixed with blood. These cysts are large enough to be of clinical importance. Their presence is an obstruction to delivery, and even to the escape of a molar pregnancy, and they can, as just mentioned, give rise to severe and acute symptoms from twisting of their pedicles. The full description of the naked eye appearances of the eight cysts which I have examined are added in an appendix to this paper. For the above material I am indebted to Mrs. Scharlieb, Drs. Williamson and Andrewes, of St. Bartholomew's Hospital; Dr. Carlton Oldfield, of Leeds, and my colleague, Mr. Malcolm.

A pair of ovaries was kindly lent me by Mrs. Scharlieb (see appendix); Figs. 1, 14, and 15 were taken from sections prepared from these cysts. Fig. 1 represents the structure of a recently-ruptured corpus luteum, and was taken from the cortex of the smaller left ovary. Figs. 14 and 15 show sections taken from the walls of two of the cysts seen in the periphery of the same ovary. These sections were prepared after the cysts had been hardened entire in formalin solution, and they show the solidified albuminous contents with a series of linear cracks due to preparation in the paraffin bath. Fig. 14 represents a septum common to two large cysts; the lutein layers on each side are well represented. The cells have been flattened out by pressure, so that they now appear as

a compact nucleated lamina, not unlike syncytium in general features. The lutein lamina forms the innermost lining to the cysts, no fibrin, fibrous tissue, nor epithelium existing between it and the albuminous contents. Fig. 15 shows a similar cyst-wall, but in this instance the lutein-layer has in part undergone displacement, so that in the lower end of the drawing there are no cells present; here they are relegated to the periphery of the cyst-wall, only a thin strand of fibrous tissue intervening between them and the peritoneal surface. Sections through three of the largest cysts in the right ovary show the lutein tissue reduced to a minimum and in places entirely absent. In one of these, however, a short strand of cubical epithelium is left, showing that this cyst at least did not arise from a ripe corpus luteum. The true ovarian stroma is very œdematous and contains displaced lutein cells.

Dr. Williamson's specimens which can be seen in the Museum of St. Bartholomew's Hospital, are interesting from the fact that the tissues stain well, and the nuclei of the cells show distinctly, in spite of the fact that the specimens have lain in spirit since 1872. Figs. 12, 13, 15a, 16, and 17 were prepared from these cysts. The epithelial type of cyst and the non-epithelial are well represented. Of the epithelial there are two varieties, one lined by several layers of round cells, in shape and size resembling the cells of the stratum granulosum; the other with well-formed columnar epithelium as an internal layer (see Figs. 12 and 13). The fibrinous cysts show thick wavy folds and tufts of partly organised fibrin on a base of fairly dense fibrous tissue, whilst the lutein cells are removed to a distance and lie in ovarian stroma in the neighbourhood of primordial follicles. The most noticeable feature of these ovaries is the uniform distribution of the lutein cells throughout the very œdematous stroma (see Fig. 17); in nearly every field of the microscope they are seen lying in the clefts caused by the separation of the strands of fibrous tissue by the œdematous fluid. Syncytium-like masses of lutein tissue exist also in abundance amongst the yellow granular *débris* which fills the lumina of many of the cysts (see appendix); this is depicted in Fig. 15a. The ovarian stroma contains a great number of primordial follicles; this is explained by the fact that the patient's age was only 23 years.

From Dr. Oldfield's case of double ovarian cystoma were prepared Figs. 9, 18, and 20. No lining of epithelium was found in any of the sections examined, and in the majority of the cysts the lutein tissue was uncovered internally. Some of the thicker walls show the lutein layer split up by fibrin and fibrous tissue alternately, so that

as many as three layers become apparent (see Fig. 18). In Fig. 9 there is a strong well-formed fibrous layer on either side of the lutein lamina. In Fig. 20, on the other hand, the lutein tissue is bare.

In Mr. Malcolm's case the ovarian stroma shows very little displaced lutein tissue. It was œdematous and vascular, but was so encroached upon by the cysts as to be small in amount. Fig. 21 shows the characters of the wall of one of the larger cysts. It consists of an internal layer of fibrin, a second layer of dense lamellar lutein tissue, a third of blood-clot, and a fourth of theca interna shading off into less vascular ovarian stroma. At B is seen an island of displaced lutein tissue. The right-sided tumour, where the pedicle was twisted, shows the result of stasis in all the vessels, and it is noteworthy that the theca interna around the cyst walls has here suffered the most; the fibrous tissue and the lutein lamina are both infiltrated with blood, and the latter has escaped into and filled up many of the cyst cavities. In some of the cysts there are remains of an epithelial lining, the cells in some instances being spherical, in others low-lying cubical epithelium with basal nuclei. In the ovarian stroma are seen some follicles in a state of hydrops, with no lutein investment, a condition which I have not observed in any of the preceding specimens.

So much, then, for the study of lutein cysts, with which I have purposely included hæmatomata, for, as already pointed out, the origins of hæmatomata and of those cysts which arise during the evolution of a corpus luteum, are in so many respects similar. Three pathological conditions remain to be described: (1) the displacement and "excess" of lutein tissue; (2) the lutein abscess; (3) calcification of the corpus luteum, and lutein hæmatoma.

1. It is not always easy to determine an "excess" of lutein tissue, as it is difficult to adopt any standard of measurement for the amount of this substance existing in a normal ovary. This difficulty becomes more and more impressed upon the observer after he has learnt to recognise lutein tissue in the various stages of its evolution and devolution. A casual glance will reveal to the superficial observer the relative amount of healthy ripe lutein cells around cystic spaces, but more careful investigation brings to light the same cellular tissue in process of formation and degeneration around dropsical follicles, and in process of devolution within the meshes of newly-formed ovarian stroma. If we take note of the aggregate of normal lutein cells in process of formation, maturity, and retrogression, we find that in many ovaries—at any rate, many of such as

come to the pathologist,—there is a great amount of this tissue present in cases where it seems to have no pathological significance. Nor is this tissue solely characteristic of the body usually understood by the term "corpus luteum"; it is seen around follicles which have never ruptured and which contain no ova; around follicles, that is, in a state of hydrops, and which will therefore never undergo physiological rupture, there being no ovum present to be extruded. Such cysts as these are present in the majority of the ovaries which I have examined, and I cannot bring myself to believe that amongst something like fifty ovaries I should have found excessive lutein tissue in the majority. When, however, the stroma of the ovary contains large lutein islands or lutein cells profusely distributed in a discrete manner throughout its substance, then we are face to face with an unusual and abnormal phenomenon, and we need have no hesitation in regarding this condition as true excess. I have met with one notable example of this undoubted excess, in the ovaries of the case of chorio-epithelioma which I showed at The Obstetrical Society at the June meeting on the subject of chorio-epithelioma (see *Trans. Obstet. Soc.*, London, Vol. xlv., pp. 245–313, 1903, and for a complete description of the case see *Practitioner*, December, 1904). Both ovaries appeared normal and were described as such by Dr. Hobhouse, of Brighton, who made the autopsy, but on examination I found they contained, in addition to a large number of epithelial-lined lutein cysts, a vast amount of discrete and compact lutein cells throughout the stroma. Figs. 3, 6, 6a, 10, 11 and 26 are drawings taken from sections made of these ovaries. In Fig. 6 is seen a wide belt of lutein tissue situated at the periphery of the ovary, almost flush with the peritoneum. In 6a the ovarian stroma is almost universally studded with lutein cells, and in one island a large well-formed cyst is seen. Again, in Dr. Williamson's case of chorio-epithelioma, where there were polycystic tumours of both ovaries, the solid ovarian stroma was studded throughout with lutein cells (see Fig. 17), as was also the *débris* forming the contents of the cysts (see Fig. 15). Even if in this case there had been no lutein cysts, there was sufficient lutein tissue disseminated in the stroma of the ovary to constitute an excess. Never have I met with anything like this amount of lutein tissue, except in glands such as the above which were associated with vesicular mole or chorio-epithelioma. Inasmuch as all the loculi of the polycystic tumours above described were lined by lutein tissue, the amount of the latter must of course, have far exceeded the normal, even had there been none in the solid stroma, but as a matter of fact, the œdematous stroma forming the core of these tumours was,

without exception, the seat of small lutein cysts surrounded by enormous bands of solid lutein tissue. In Kelly and Teacher's case of chorio-epithelioma—Dr. Teacher kindly sent me segments of both ovaries to examine—the smaller ovary contained many minute lutein cysts, the larger one not so many; but taking the two together, the amount of lutein tissue is striking. There is, however, no general dissemination, such as I found in the case of chorio-epithelioma with "normal" ovaries, published in the *Practitioner*. The question arises, how do these cells become so universally distributed? Have they any malignant propensity, giving them the inherent faculty of invasion? I can find no evidence to show that they have. They are not disseminated by the blood-stream or by the lymphatics; they never find their way even into ruptured lymph-channels or blood-vessels; they show none of the features of invading malignant cells. In my opinion, their distribution is due to a passive displacement. They are only formed in the deeper layers of the theca interna folliculorum, whence they get dislodged as I have already pointed out, firstly by cleavage of the lutein layer by effusion of blood, and secondly by the invasion of the lutein layer by fibroblasts and the subsequent laying-down of fibrous tissue. The centrifugal regeneration of ovarian stroma which has its origin around each retrograde corpus luteum scatters these cells radially towards the periphery of the gland, where they often aggregate in large numbers, or where they may be seen as a narrow band lying just beneath the tunica albuginea. Once again I would repeat that I have never found this process demonstrated except in apparently normal ovaries associated with vesicular mole and chorio-epithelioma.

II. Corpus Luteum Abscess.

During the past eighteen months I have met with two cases of large corpus luteum abscesses—one in my own hospital practice and one from the private practice of a London gynæcologist. In my own case the tumour was the size of a fœtal skull, and was densely embedded in the left side of the pelvis, displacing the uterus to the right. The right ovary in this case contained a calcified corpus luteum. This specimen being almost unique, I am recording the case in the appendix. Upon searching the literature, I find that Orthmann describes a case of double "sacto-salpinx purulenta" (pyosalpinx), in which there was a right-sided corpus luteum abscess, and also two concretions in the left ovary, in size between that of a pea and that of a hazel-nut. These concretions contained a folded hyaline layer like a lutein lamina, and after decalcification the latter

tissue was proved to be present. The description of my own case of calcified corpus luteum will be given below. The main feature of the abscesses derived from the corpus luteum is that their inner wall is tuberculated, appearing as if studded with small papillomata, whilst the entire surface presents, when first opened, a yellow ochre colour. There is nothing distinctive in the appearance of the pus. This in my own case contained flocculent particles of necrotic tissue. It was not examined for micro-organisms, the clinical history did not bespeak the presence of pus, as there had not been a rise of temperature whilst the patient was under observation, and again from the fact that the investing adhesions were densely thick and of cartilaginous hardness, it is to be inferred that the abscess was of very chronic formation. It has been suggested by German observers that corpora lutea become infected after rupture by gonococci, which enter at the point of rupture and find in the blood-clot a suitable nidus for development. I have no proof to offer in support of this statement, but in the two cases I have examined there was purulent salpingitis; whether this was of gonorrhœal origin or not I cannot say. (For a description of the abscess-wall in each of the above cases see Figs. 22, 23, and 24.)

III. Corpus Luteum Calcification.

I have only once met with an example of this condition. The case has been referred to under "abscess of the corpus luteum." The right ovary was reduced to a thin fibrous capsule, from which a corrugated calcareous body was easily shelled out. It was oval in shape, and the size of a large walnut. Its external surface presented irregular rugæ, yellow in colour. On naked-eye section it was found to consist of a thin shell of calcified tissue, within which lay a shrunken dark-red blood-clot. Although very thin, the calcified lamina of lutein tissue was very hard, and it took some six weeks to de-calcify in dilute hydrochloric acid. The microscopical features are shown in Fig. 25; this represents a drawing of the calcareous wall of the cyst. Internally is seen a loose membrane containing lutein cells; then comes a broad band of decalcified tissue, which opens out to include a space filled with a loose reticulum and lutein cells. Several such spaces exist in the calcareous tissue, and in many of them lutein cells still persist, thus showing that the yellow layer is the seat of the deposit. But the calcified bars are not confined to the lutein zone; they spread wide of it into the theca interna. Now this is the situation where new vessels are found, and free hæmorrhage takes place during the final

stages of maturation and also at the time of rupture of a ripe corpus luteum; the calcareous deposit is therefore laid down precisely where extravasation of blood is so frequently detected. This leads to the conclusion that there has been calcification of the peripheral blood-clot around a ripe ruptured or unruptured follicle, or around a corpus luteum hæmatoma. In Orthmann's case of double sacto-salpinx purulenta already referred to, there were two concretions in the left ovary of much smaller size than the calcified lutein body which I am describing. This author mentions that Rokitansky, Bland-Sutton, and Hector Mackenzie have each recorded a case of calcareous corpus luteum. Slavianski mentions a case of a woman aged 71 years, in whom the right ovary, covered with a pseudo-membrane, contained a concretion of the size of a hazel-nut; this easily shelled out, and after decalcification gave the impression of being a degenerated corpus luteum. Orthmann found that his calcareous bodies contained a folded hyaline layer "like the lutein layer."

This completes the only records of these bodies which I have found. Although Orthmann gives Bland-Sutton the credit of recording a case of his own, I cannot find any record of this in Bland-Sutton's book on surgical diseases of the ovary; but under the heading "Ovarian Concretions" in this work the author says, "the only instance of concretions occurring in the ovary is recorded by Dr. H. W. G. Mackenzie (*Trans. Path. Soc.*, London, Vol. xl., p. 198). The patient was forty-one years of age, and suffered for two years from menorrhagia; she had a large myoma of the uterus. The ovaries were enlarged and contained a number of black, hard, flat bodies. The cavities containing them were smooth-walled. The concretions were of various sizes from a coriander seed to a small bean, and of irregular shape, but their surfaces were smooth and flattened where they had come in contact with one another. They were firm and hard, but light, and could be cut with a knife very like hard wax. Under the microscope, sections prepared from the concretions exhibited no structure, but there were *indications* that the mass consisted of spheroidal bodies. Dr. Copeman attempted to determine their chemical constitution. They were insoluble in acid and alkaline solutions, and in ether and chloroform. Prolonged digestion with artificial gastric juice in an incubator at the body temperature dissolved them. The coloured solution thus obtained gave the spectrum of acid hæmatin and the guaiacum reaction for blood. The concretions probably consisted of coagulated proteids derived from blood-clot, akin to lardacein, and of the same family as the concretions of the prostate and the amyloid bodies

sometimes found in old hæmorrhages. It is probable that the cavities which contained the concretions were ovarian follicles, and that blood had been effused into them and undergone a rare colloid change. It is not unusual to find hard clots of blood in ovarian follicles, but concretions of the density exhibited in this specimen are excessively rare." It is clear from this description that the bodies described in no way resemble the definitely calcareous lutein body of which a drawing will be found in Plate I. My specimen is a hollow shell formed by calcareous incrustation of the lutein layer and the theca interna, and containing a shrunken blood-clot of the size of a walnut. Such a structure has hitherto never been described; I have therefore given a short summary of the clinical history of the case in the appendix to this paper. With this account ends my personal investigations on the development and retrogression of the corpus luteum.

(To be Continued.)

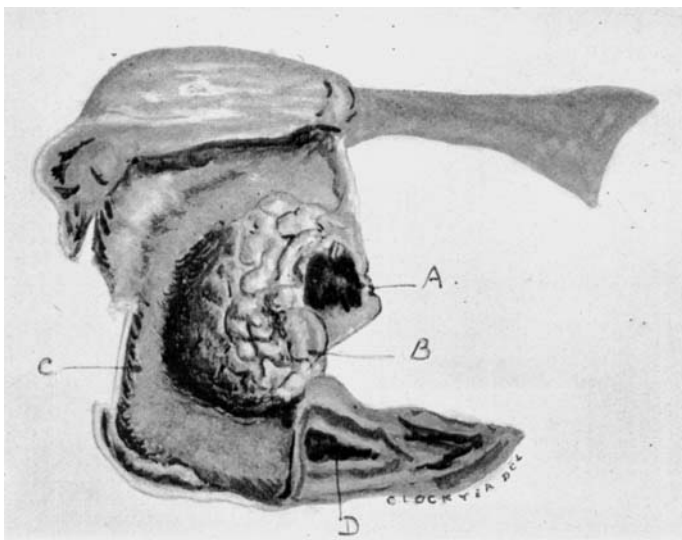

PLATE I.—Calcified Corpus Luteum Hæmatoma. (*a*) Blood-clot, within. (*b*) Thin shell of calcareous yellow tissue. (*c*) Capsule of ovarian tissue. (*d*) Small lutein hæmatoma.

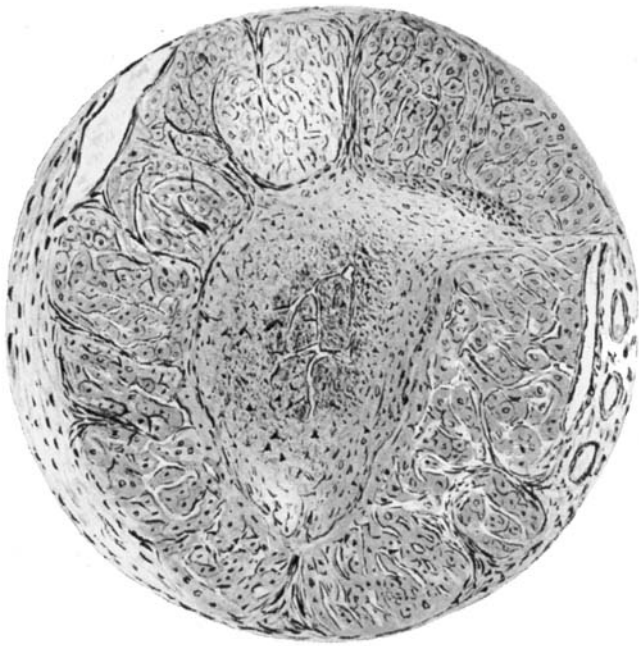

FIG. I. Illustrating corpus luteum filled with blood-clot.

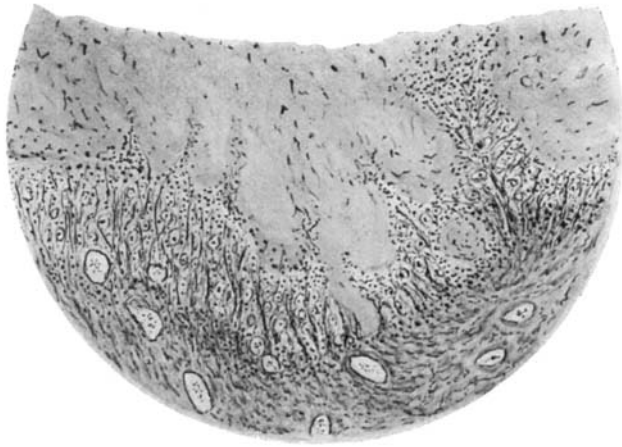

FIG. II. Illustrating fibroblastic invasion of the lutein cell layer after rupture of a corpus luteum, some of the lutein cells still remain undestroyed. The fibroblasts are preceded by a round-celled infiltration which can be seen advancing in cristate form into the already semi-organised fibrinous decolorised clot.

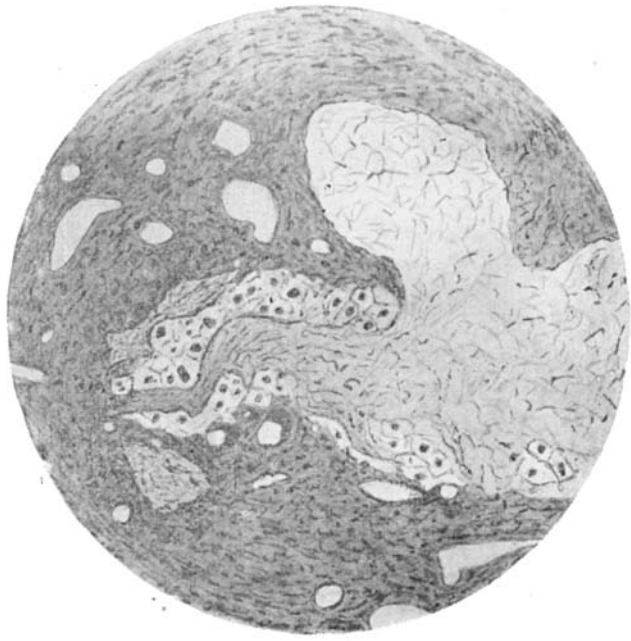

FIG. III. Shows an advanced stage of Fig. ii. There are a few lutein cells left around one process of the corpus albicans which have not yet been replaced by granulation tissue. This must have been purely accidental, as all around is seen fully formed fibrous tissue indistinguishable from ordinary ovarian stroma.

FIG. IV. Illustrating the total displacement of lutein cells by young granulation tissue, which is throwing out centripetal processes into the interior of the corpus albicans preparatory to severing it into tortuous fragments. See Fig. V.

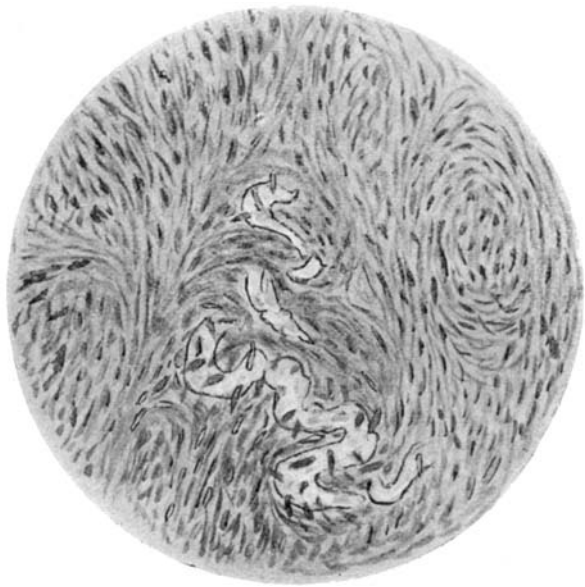

FIG. V. Shows the final stage in the retrogression of a corpus luteum. The corpus albicans now consists of hyaline highly staining, tortuous strands of degenerate tissue, quite devoid of cells. Its destruction by phagocytes is proceeding. It forms no part in the permanent ovarian stroma but may last for years, even after the menopause.

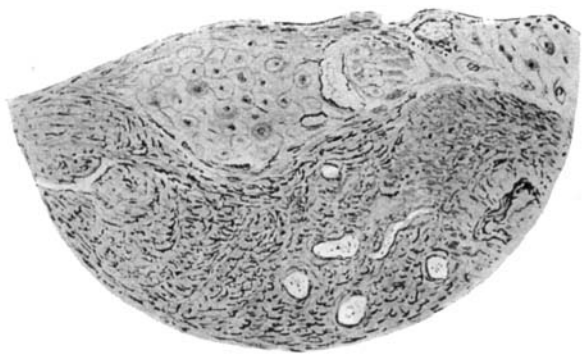

FIG. VI. Showing a displaced island of lutein cells containing a cystic space. The lutein tissue lies under the tunica albuginea which is thinned out over it.

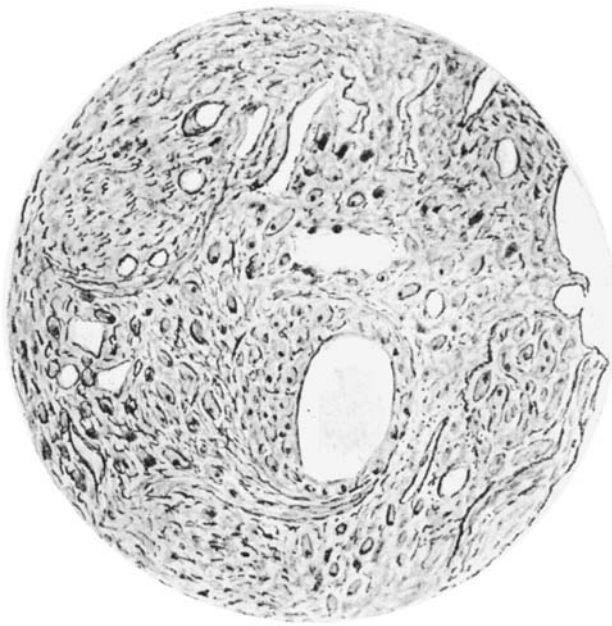

FIG. VI. (*a*). Free lutein cells showing cystic formation.

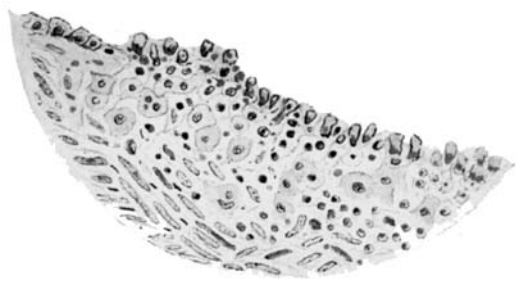

FIG. VII. Suggesting the origin of the lutein cell from inter-cellular substance thrown out by fibroblasts of the theca interna external to the stratum granulosum. The lutein cell, as the decidua cell which it resembles, would be therefore of connective tissue origin.

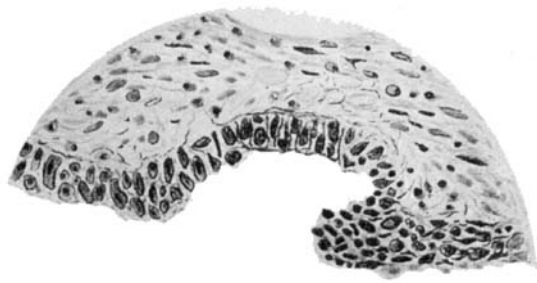

FIG. VIII. Wall of a distended Graäfian follicle, showing the transition from spherical epithelium to columnar, and the early formation of lutein cells.

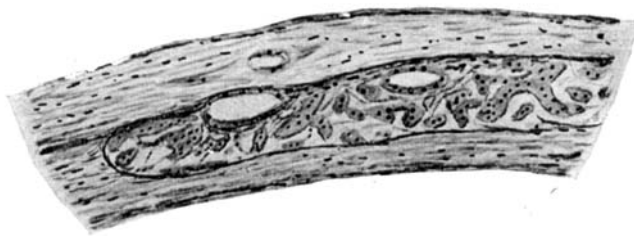

FIG. IX. Showing fibrous lining internal to lutein layer

FIG. XI. Showing lutein cyst lined by the columnar epithelium of the stratum granulosum.

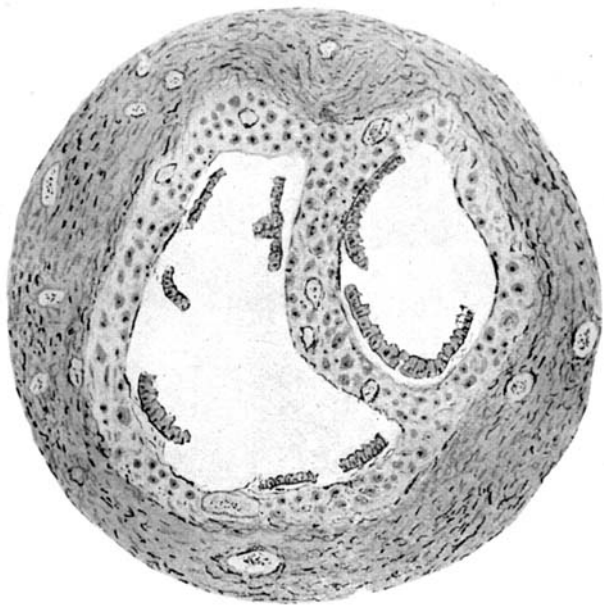

FIG. X. Showing a lutein cyst, bilocular in origin.

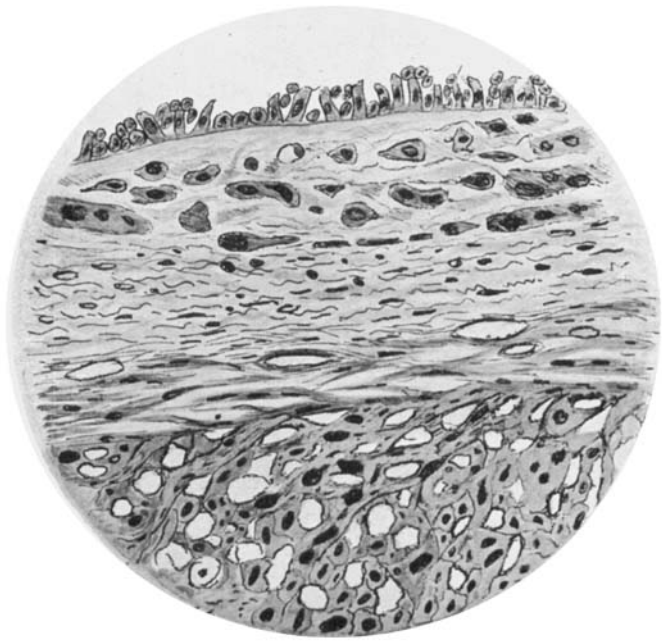

FIG. XII. Lutein Cyst. Showing a lining of columnar epithelium.

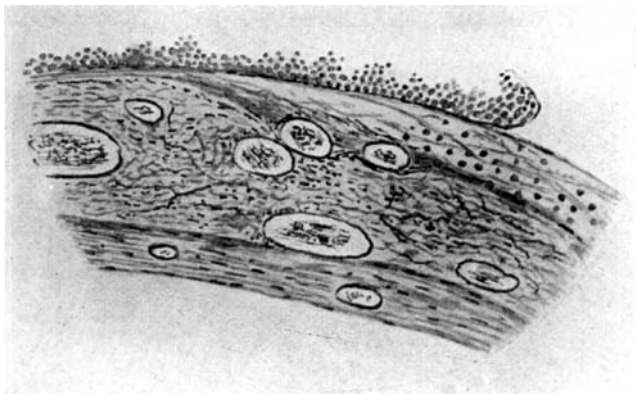

FIG. XIII. Lutein Cyst lined by spherical cells of stratum granulosum.

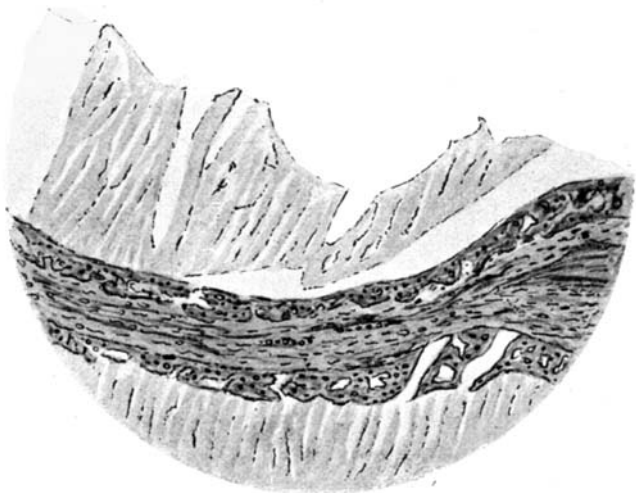

FIG. XIV. Showing septa common to two cysts, each containing albuminous fluid hardened by formalin.

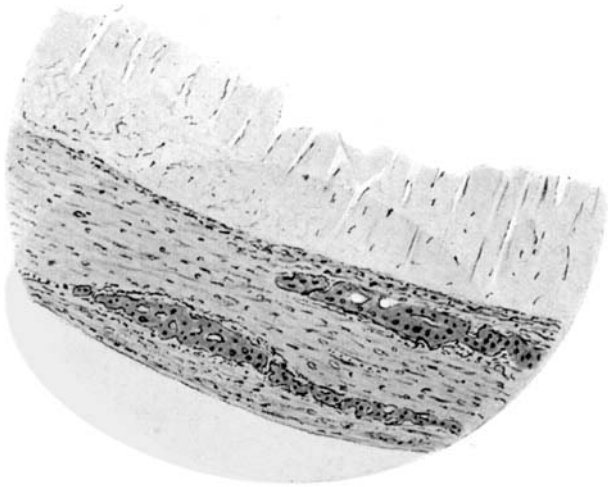

FIG. XV. Showing the albuminous fluid hardened by formalin. Displacement of lutein cells has taken place.

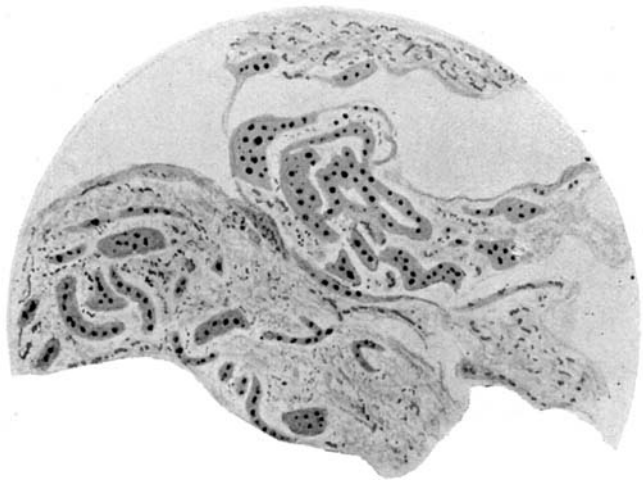

FIG. XV. (*a*). Syncytium-like masses of lutein cells lying in the yellow débris which completely filled a lutein cyst.

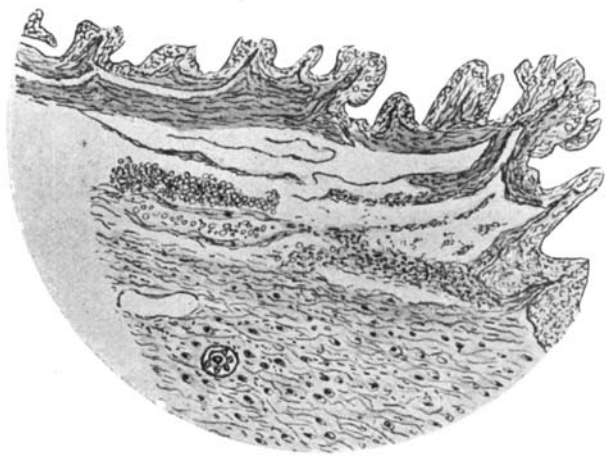

FIG. XVI. Fibrinous wavy lining to cyst wall. Lutein cells distributed in stroma beneath.

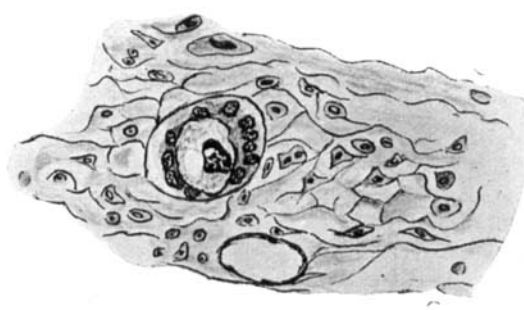

FIG. XVII. Lutein cells distributed in ovarian stroma

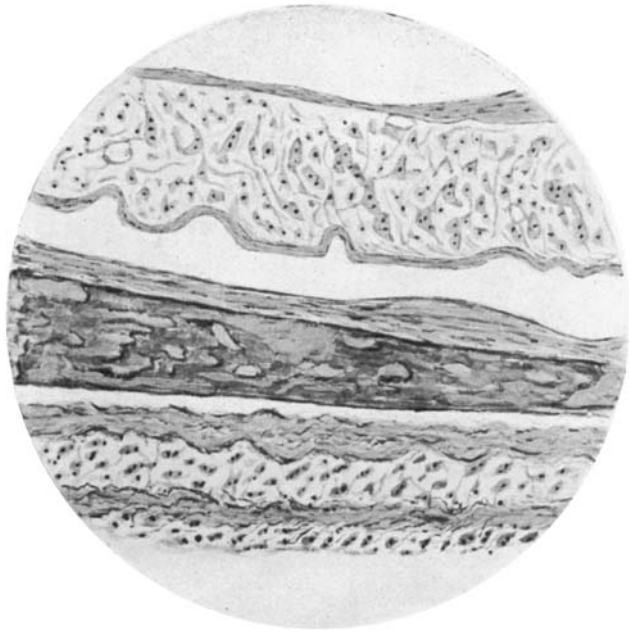

FIG. XVIII. Showing "doubling" of lutein layers by intervention of blood-clot and fibrous tissue.

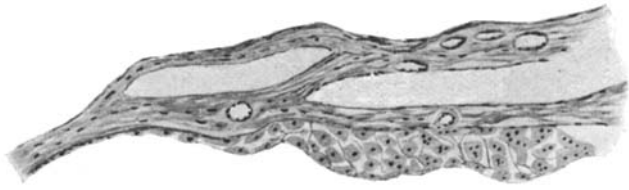

FIG. XX. Lutein Cyst. Taken from the thinnest part of a large loculus.

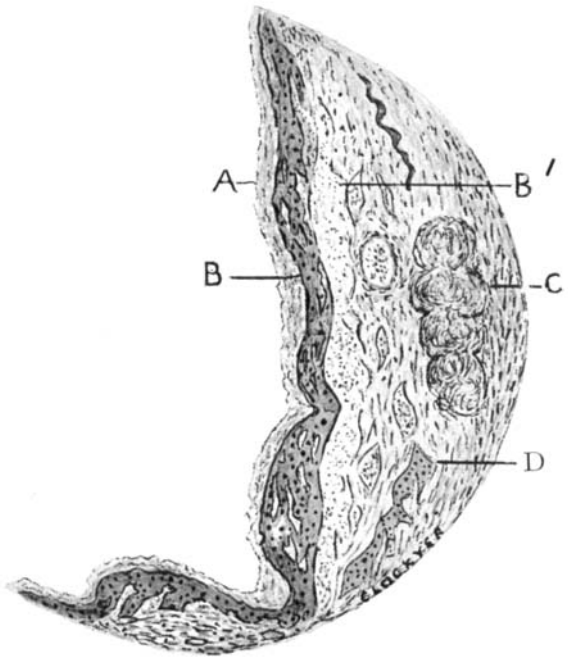

FIG. XXI. Showing (*a*) Internal lining of fibrin. (*b*) Lamellar arrangement of compressed lutein cells. (*b*') Layer of blood-clot within theca interna. (*c*) Corpus albicans. (*d*) Displaced lutein tissue lying in ovarian stroma.

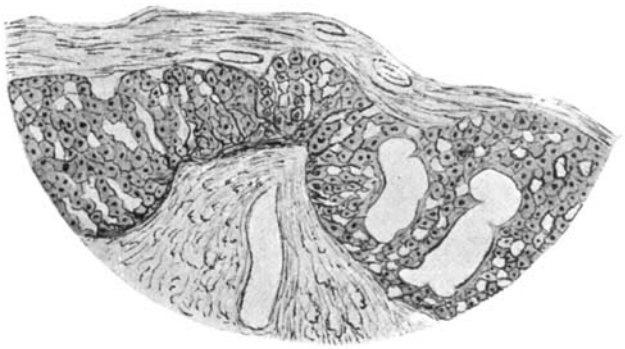

FIG. XXII. Corpus Luteum Abscess. Showing a lining of fibrous tissue internal to lutein cells.

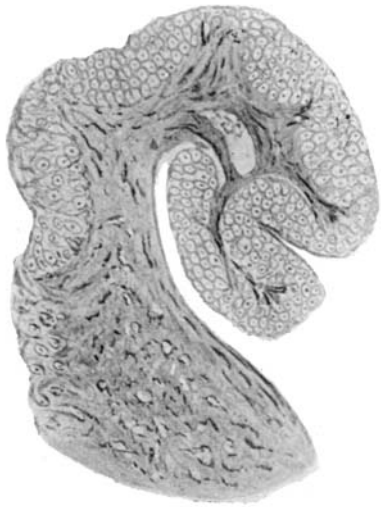

FIG. XXIII. Lutein Abscess. Showing one of the tufts which give the papilliferous or "frog-spawn" appearance to the yellow abscess wall.

FIG. XXIV. Corpus Luteum Abscess. Showing (1) A lining of degenerate lutein tissue devoid of nuclei. (2) Hyaline degeneration of the fibrous tissue contained in the abscess wall.

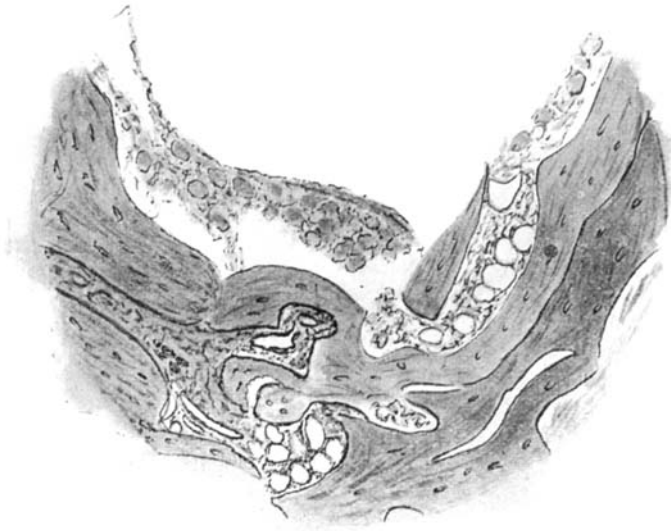

FIG. XXV. Calcareous Corpus Luteum or calcified lutein hæmatoma. Showing (1) Lining of degenerate lutein cells. (2) Calcification of lutein layer and of theca interna.

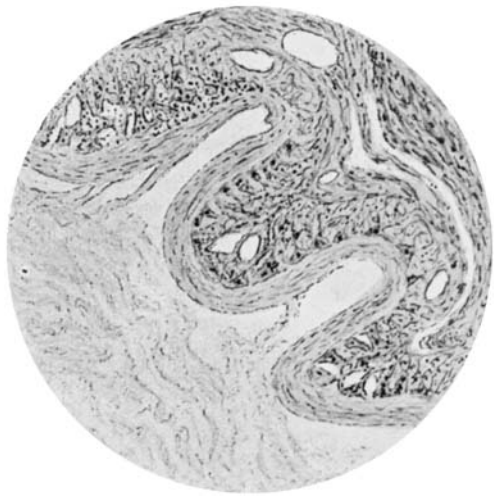

FIG. XXVI. Section shows the convoluted arrangement of the lutein cyst wall.

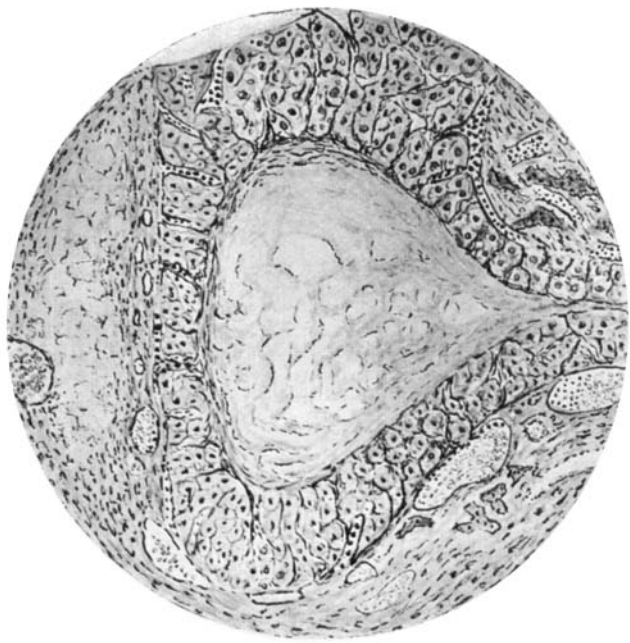

FIG. XXVII. Showing early cystic formation by breaking up of fibrin in centre of a ripe follicle.

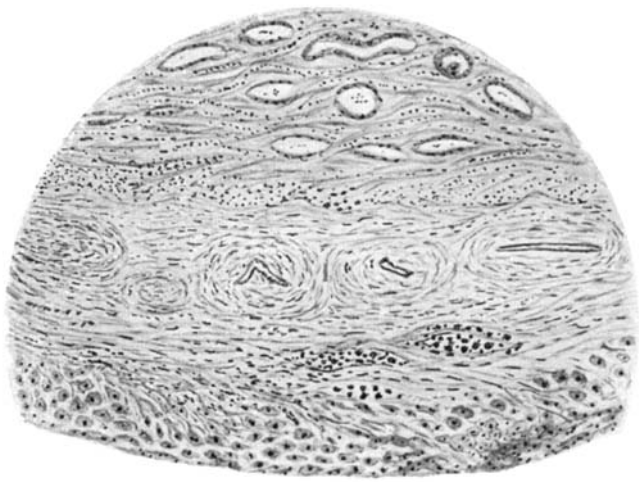

FIG. XXVIII. Lutein Cyst Wall from a case of chronic salpingo-oöphoritis.

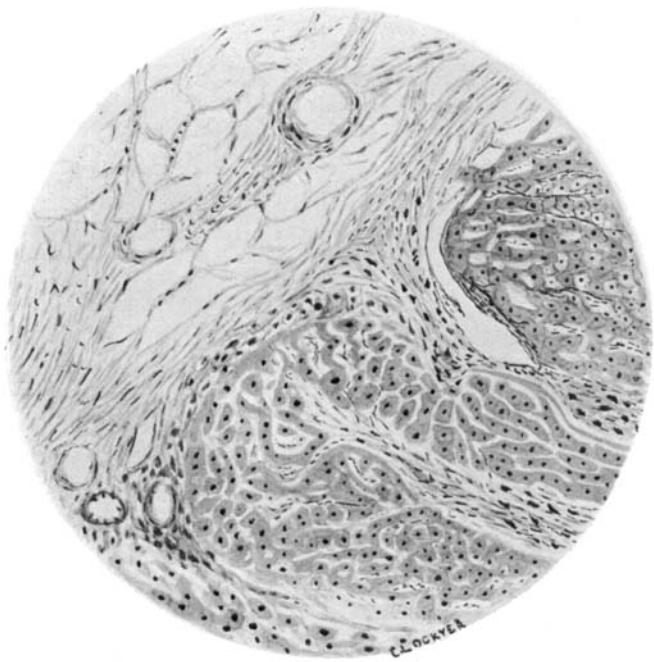

FIG. XXIX. Normal corpus luteum showing festoons of lutein cells.