

Contributions to the morbid anatomy of chronic inflammation of the mucous membrane of the uterus (endometritis corporis chronica) / by Leopold Meyer.

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CONTRIBUTIONS TO THE MORBID ANATOMY OF CHRONIC
INFLAMMATION OF THE MUCOUS MEMBRANE OF THE
UTERUS (*ENDOMETRITIS CORPORIS CHRONICA*).

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Read before the Gynecological Section of the Ninth International Medical Congress.

I. THE INTERGLANDULAR TISSUE.

DURING the last half-score of years, since investigators have begun to take a more lively interest in the pathological anatomy of Chronic Endometritis, they have especially endeavored to draw up different forms of this disease. They formerly distinguished between a glandular, an interstitial, a mixed, and a vascular form; but it very soon became apparent that it was only possible in very few cases to classify the disease under one or other of these forms; nay, we often found in the mucous membrane of the self-same patient some parts that must belong to one of these forms, and others that belonged to another. In these investigations the inquirers chiefly took heed of the relations of glands, blood-vessels, and lymphatics, whilst but slight attention was bestowed on the more intricate construction of the interglandular tissue. Some, especially *Wyder*,¹ denied that Decidua-cells could be found in the mucous membrane of the uterus, except during pregnancy; others, chiefly *C. Ruge*,² assert that we can find them during the course of an Endometritis, especially that Endometritis which accompanies myomata uteri. *Schröder*³ lays down a form of Endometritis (*E. dysmenorrhoeica*) distinguished by peculiar symptoms, where there are strong bands of fibrillous connective tissue in the interglandular tissue. But, generally, the interglandular tissue is dismissed with such remarks as, that it, as usual, consisted of closely-packed cells with small, round, or spindle-shaped nuclei, that almost filled up the cell, — or some such expressions. *Heinricius*⁴ alone gives the following description, accompanied by a drawing, of the construction of the interglandular tissue in Chronic Hyperplastic Endometritis (*E. fungosa*): The stroma consists of a net of meshes formed by cells, with thin, star-shaped processes communicating with each other. The nuclei of these cells are irregular or triangular, 5–12 micromillimetre (μ) long, 2.5–5 μ broad. In the meshes there are two species of nuclei: large, oval, slightly stained ones,

¹ Arch. f. Gyn. Bd. II. Pag. 1–55.

² Ctrbl. f. Gyn. 1881. No. 12.

³ Zeitschr. f. Geburtsh. u. Gynækol. Bd. X. Pag. 441.

⁴ Arch. f. Gyn. Bd. 28. Pag. 203.

often provided with a nucleolus, 7-15 μ long, 5-10 μ broad, and small, highly-stained ones, oval or spindle-shaped, the oval ones' diameter being 3.7-6 μ , that of the spindle-shaped 7-8 μ long, 3-4 μ broad.

The investigations, the results of which are given in this paper, have been made by me on parts of the uterine mucous membrane, scraped off by aid of Sims' Curette, and then laid as quickly as possible in absolute alcohol. They are then imbedded in Celloidin, the sections stained with Hæmatoxylin, with Hæmatoxylin and Eosin, with Lithion-picro-carmin, and Bismark brown, and they were then examined, either in glycerine or Canada-balsam-xylol. The patients on whom the curettings of the mucous membrane were performed suffered from severe metrorrhagia or menorrhagia. In one patient only was there a chronic catarrh, with considerable discharge, but no hemorrhage,

The interglandular tissue is generally seen formed by closely packed cells, so that the basal substance properly so-called, the stroma, is not visible, not even in very thin sections. Where the stroma is distinctly visible, it appears almost always structureless, with an irregular, delicate delineation, perhaps produced by the influence of the alcohol. But *I never saw anything resembling that described by Heinrichius*: a net of meshes formed by star-formed cells with thin processes that anastomose among each other. It seems evident from *H.'s* description that it is his opinion that this net of meshes is not a morbid inflammatory product, but that it is present in the normal uterine mucous membrane. But neither here have I been able to find anything corresponding to this reticular tissue. Of course it is much more difficult to get fresh *normal* uterine mucous membrane for investigation than pathological, and I have only had two normal specimens at my disposal, both of which were procured 6-8 hours after death. The one patient had given birth to five children, the last time one-half year ago, and was still suckling. She died very suddenly of Uræmia. The other patient, a girl fifteen years old, died of acute miliary tuberculosis during a catamenial period. The specimen from this patient was first treated with Müller's fluid and then with alcohol; the other specimen was immediately laid in absolute alcohol. The sections were stained and examined as above described. Notwithstanding a very careful examination, — also by aid of immersion, as *H.* recommends, — I did not, however, succeed in finding the net of meshes in these two specimens, nor do any other investigators mention it. In the not-menstruated patient the body of the mucous membrane is formed of cells so close together that no basal substance is to be seen, nor can the borders of the single cells be distinctly observed, notwithstanding several different methods of preparation, *nuclei only*, side by side, are visible. Most of

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these are oval or spindle shaped (perhaps rather formed like bacilli, as they are nearly equally thick all along), the latter, as a rule arranged in strong bands. Perhaps many of the smallest oval nuclei are sections of the bacillus-shaped ones; these nuclei are stained rather deeply by all the different staining media. The diameter of the oval nuclei ranges from $3.7-5.9 \mu^1$ one way, $1.5-2.9 \mu$ the other way (generally $4.4-3.17 \mu$); of the bacillus-like ones from $5.9-10.3 \mu$: $1.5-2.9 \mu$. Among these nuclei we see a few little larger oval ones, that very much resemble endothelium cells. They are granular, become but slightly stained, have one or two distinct nucleoli, their diameter is $7.3-8.8 \mu$: 4.4μ . This find agrees in all essential points with the common description of the normal mucous membrane of the uterus. *Heinricius*² is not quite justified in asserting that the results of his investigations agree with those of *Leopold*. It strikes me that if one lays such a new and important discovery as *Heinricius*' before the medical profession, then one really ought to use better and safer methods than simple staining with Bismark brown and microscopic examination in balsam.

Whilst I therefore cannot agree with *Heinricius* in his statement, that the ground substance in the normal and inflamed uterine mucous membrane forms a net of meshes, I, on the other hand, perfectly agree with him that in Endometritis we nearly always find *the chief mass of the interglandular tissue composed of two different kinds of nuclei, or rather of cells*,—a discovery which former investigators, to be sure, have remarked, but without paying further attention to it.

In most cases of chronic endometritis we see in the interglandular tissue, (1) round or polygonal nuclei, slightly larger than a red blood corpuscle; they are brightly and generally evenly stained with carmine, Hæmatoxylin and aniline colors; seldom they are slightly granular. In those cases where we can see the corresponding cell protoplasm, it is homogeneous, and forms a narrow border round the nucleus, the diameter of the cell usually being only twice as large as that of the nucleus. I shall later on notice the modifications which these cells suffer. (2) Larger oval nuclei of granular nature, usually provided with one or two distinct nucleoli.

These nuclei are but slightly stained by the above-named staining media, so that the tissue, where these nuclei are in the majority, looks lighter, whereas it is darker there, where there are many of the cells

¹ I am well aware that the decimal fractions of a micromillimetre, given in my measurements, are not and cannot be exact. But I have preferred to give them just as I have found them, and leave it to the reader to throw them off.

² L. cit. Pag. 204.

spoken of under (1). If the corresponding cell-protoplasm be visible, it is slightly granular, and the quantity of it is always much greater in proportion than around the first-named cells. These cells, which, let us say so at once, in their most exquisite form, have the greatest likeness to the so-called decidua cells, can, like the latter, have many different forms. I shall later on remark that we can also find other sorts of cells besides these two.

As stated above, *Heinricius* has also found these two kinds of nuclei, and he explains what he finds thus: That the large nuclei are the nuclei of the fixed cells of the connective tissue (endothelial cells); the small nuclei belong to immigrated lymph-cells. But I cannot agree with him in this explanation, for the following reasons: We found the tissue of the normal mucous membrane of the uterus composed of just those small cells with small, deeply-tinged nucleus, whilst the light nuclei were only present in small numbers, and did not by far reach the size they have in endometritis, or during the catamenial period. But even in the inflamed mucous membrane what he finds is not constant; it is possible, to be sure, although rare, to find an inflamed mucous membrane in which the interglandular tissue is formed almost exclusively of one kind of cells: small cells with a minute deeply-stained nucleus, whilst the light nuclei, which are also here, are proportionately few and small. Besides, we find in some patients distinct gradations between the two kinds of cells; nay, in some, the chief mass of the tissue consists of such cells, which we only with great difficulty can classify under one of the two sorts named. But during the catamenial period we find numerous large cells with large granular nuclei in the mucous membrane. I shall now review these points singly, and shall therefore, at the same time, endeavor to give reasons for the explanation which I, after my researches, think ought to be given to the above-named find, viz.: 1. *The round cells with dark nucleus are those cells which, in the healthy state, form the chief mass of the interglandular tissue.* 2. *The large cells, that resemble decidua cells, are formed from the former ones by irritative processes (endometritis, menstruation, pregnancy).* 3. *The cells named in 1 can also become more spindle-shaped.* They are constantly so in the closest neighborhood of the glands, but not seldom we find them spread and scattered about in the tissue, just like connective tissue-cells.

Those cells whose nuclei are small, roundish, and deeply stained may be seen in Fig. 1. Whilst red blood-corpuscles in the different preparations have a diameter of from $3.7-5.9 \mu$, mostly 4.4μ , most of these nuclei measure $5.5:4.4 \mu$ (from $2.9-5.9 \mu$), while the cell itself measures $10.0:8.8 \mu$ (from $6-11.8 \mu$). The nucleus itself is thus about

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the same size as those we found in the normal mucous membrane, or a little larger, whilst I, in this case, was unable to measure the cell itself. As aforesaid, these cells are always found in great numbers in the interglandular tissue; but still their number varies highly. In some cases they make up quite half of the interglandular tissue; but, as before stated, we may also meet cases in which they form almost the whole of it, whilst there are but extremely few of the large, light nuclei. Among the twenty cases which I have investigated very thoroughly, I found this to be the case three times, viz., in the following patients:—

I. Forty-four years old; seven births, the last eleven years ago, and four miscarriages, the last one nine years ago; considerable secretion; no menorrhagia. The mucous membrane resembled greatly a normal one.

II. Twenty-seven years old; four births, the last one three months since; severe hæmorrhage. The mucous membrane was distinguished by an enormous wealth of glands; in many spots the glands were two-thirds of the whole tissue, and the interglandular septa were only 20–30 μ broad. Besides, solid epithelial cones projected from the glands out into the surrounding tissue. The mucous membrane, very much thickened, over 3.5 millimeters thick. Numerous vessels, chiefly arteries, with very thick walls. The interglandular tissue was composed of closely-packed nuclei, without distinct limits of the cells. Most of these nuclei were round or polygonal, slightly larger than a red blood-corpuscle; some of them were spindle-shaped. This was chiefly the case around the glands. But very few large (5.0 : 8.8 μ) oval, slightly-stained nuclei.

III. Twenty-seven years of age; three births, with intervals of only one year, last one two years ago. Three months ago she miscarried in the second month of her fourth pregnancy, and since then almost continual hæmorrhage. The pieces of the mucous membrane that were scraped out were more than two millimeters thick, with many vessels; but besides, there is an enormous quantity of very much twisted glands. The interglandular tissue is composed of roundish cells (5.9–8.8 μ : 5.9–10.3 μ) with deeply-stained nucleus half the size of the cell (4.4 : 5.9 μ), among which are a few rather larger cells (9 μ : 10.3 μ , the nucleus 6.0 μ : 6.0 μ), but likewise with dark, not granular, nuclei.

We find in the interglandular tissue, formed of the two oft-named kinds of cells, some cells and nuclei which it is difficult to classify under either sort; are we to reckon them to one or the other? Thus they can resemble the small nuclei in size and form, but are granular and but slightly stained. And if we examine them more closely we are often able to discover gradations from one species to the other. But these cells, which

we neither dare bring under the one kind nor the other, form often the chief mass of the interglandular tissue. This is the case in both of the following patients:—

IV. Twenty-nine years old, single, one birth six years ago. Severe metrorrhagia during the last months, especially during the last six weeks. The mucous membrane, in part, in adenomatous degeneration. In other parts of it many vessels, chiefly small arteries. The interglandular tissue is composed of closely-packed nuclei (protoplasm not distinctly visible); they were spindle-shaped, $7.3-14.7 \mu$ long (mostly 8.8), $1.5-2.9 \mu$ broad (mostly 2.2). They were but slightly stained, were somewhat granular. However, there were also smaller nuclei, both round and spindle-shaped, which were deeply stained, but there was a decisive majority of the former ones.

V. Forty-six years of age; nine births and four miscarriages; her last child was born nine months ago, and since frequent hæmorrhages. The glands somewhat more numerous, expanded, and twisted than in normal state. Enormous quantity of vessels, chiefly arteries of middle size. The borders of the cells indistinct. There were dark small nuclei ($4.4 \mu: 3.7 \mu$) and larger oval, slightly-stained nuclei ($7.3 \mu: 6.0 \mu$); but most of the nuclei are between these two with respect to their size, form, and appearance.

I have mentioned that we often find spindle-shaped cells, — cells resembling those of connective tissue, and that they are chiefly found surrounding the glands. They can, however, also appear elsewhere in the tissue. We sometimes even find them in broad bands, although I never saw this so exquisitely developed as it seems to have been in the cases which *Schröder*¹ describes by the name of Endometritis dysmenorrhœica. We find in some patients gradual transitions from the common cells with the round nuclei to the spindle-shaped cells; in others, transitions from the small spindle-shaped cells with dark nuclei to large spindle-shaped cells with granular protoplasm and oval, slightly granular, light nucleus. Such gradatory cells may be seen in Fig. 2. We often find in the interglandular tissue cells whose nuclei are dividing or have already divided. I am unable to decide whether these cells are immigrated lymphoid cells (pus cells), or whether they are the cells originally present in the mucous membrane. But we often see the tissue infiltrated with quantities of small, round, very deeply-stained nuclei whose diameter is $3-4 \mu$. Without any doubt these are immigrated lymphoid cells, and in one case I saw them gather in small, round heaps immediately under the epithelium, *i.e.*, forming small abscesses, about 0.2 mm. in diameter.

¹ L. cit.

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If we now turn our attention to *those cells which have a large, oval, granular nucleus*, which are but slightly stained by those staining media we generally use, we have already seen that they may be more or less completely wanting. But in the great majority of cases of chronic endometritis we find them there, and they are, as a rule, quite as numerous as the first-named sort of cells. As these cells can highly resemble the so-called decidua cells, not only by those peculiarities which we already have noticed, but also — as we soon shall see — by the form and size of nuclei and cells, it might really seem proper to suppose that this was their real origin, that they originated in a pregnancy; and this supposition is by so much the more probable, as we, for instance, from *Küstner's*¹ researches, are well aware of the fact that decidua can be retained in the uterus after parturition or miscarriage; it can be altered in its structure, and prevent the regeneration of the normal mucous membrane. In some patients, where the malady, *i.e.*, the hæmorrhage, was developed in direct connection with a birth or a miscarriage, we may also find parts of the curetted tissue that are almost solely composed of genuine decidua cells, as may be seen, for instance, in Fig. 3. The case in point is a peculiar one.

VI. The woman was 27 years of age; had given birth twice in due time, last time two and one half years ago; then she had miscarried twice in the sixth week of pregnancy; she is unable to say when it happened, but it was, at all events, long ago. Her menses were normal until a fortnight ago, when a severe hæmorrhage set in at the time she expected the catamenials. A polypus, as large as the last phalanx of a finger, was found in the uterine cavity, and, besides, the mucous membrane was velvety and thickened. The polypus proved a genuine placenta-polypus, formed by villi chorii and decidual tissue, besides coagulated blood. Several parts of the mucous membrane were chiefly composed of cells like those in the drawing; the tissue was infiltrated with blood, and there were many pus cells; in several places villi chorii were also found. But other parts resembled a mucous membrane in a common Chronic Endometritis, with the two kinds of nuclei among each other. The diameter of the cells in the drawing was $17.6-23.5 \mu$; $8.8-17.6 \mu$; the size of the nuclei, 11.8μ ; $8.8-11.8 \mu$. Genuine decidua-cells appeared in the following case in a rare way:—

VII. The patient, 32 years old, had given birth to five children, last time three years ago, and had since then suffered from hæmorrhage. Two months ago a miscarriage in the third month. The parts scraped out showed a very varied structure. Part of the tissue was evidently in adenomatous degeneration, and here the interglandular tissue consisted of

¹ Beiträge zur Lehre von der Endometritis. Jena, 1883.

the first-named small cells, with dark, round, or spindle-shaped nuclei. In other parts the glands were, to be sure, numerous and greatly distended, but no adenoma-formation; numerous vessels; the interglandular tissue was composed of small cells with roundish, dark nuclei, and, besides, of larger spindle-shaped cells with light granular nuclei (the nuclei measured $8.5-14.5\mu$: $8.5-4.5\mu$; most of them, 9μ : 6.5μ); the latter cells were, however, not to be found in the deeper layers. In this tissue was seen at one single spot what I have endeavored to reproduce in Fig. 4. Close to the surface, and probably reaching it, lies a piece of tissue 130μ broad and $24-65\mu$ high, formed by very large decidua cells (some of these are shown in Fig. 5), and scattered about here and there are few pus cells. The diameter of the large decidua cells was $26.5-32.3\mu$: $20.6-17.6\mu$, that of the nuclei 11.8 : $8.8-11.8\mu$.

If we were now tempted to draw the conclusion that the decidua-like cells in endometritis have their origin in a previous pregnancy, we should, however, be just as much mistaken as if we believed that these cells were always to be found when the commencement of the disease might be dated from a birth or a miscarriage. With respect to this point I need only refer to the cases Nos. II., III., and V., mentioned before; in all three the decidua-like cells were entirely wanting, although the disease, without the slightest doubt, originated in a birth or miscarriage. And as to the former point, that the cells that resembled decidua-like cells really should be descended from genuine decidua cells, we can very easily prove that this is by no means the case. For not only do we find them (or the nuclei, in those cells in which the confines of the cells are not distinct) in patients whose last pregnancy is far away, whilst they are wanting in others (see Cases I. and IV.), but the decisive point is, *that we can find them in nulliparæ, nay, in doubtless virgines intactæ*. To be sure, it is a very difficult matter to be *certain* that a woman is a virgin; but when the genital organs in every respect bear signs of virginity, and when (as is the case in the first-named of the following cases) the family physician, who has known her intimately a very long time, is perfectly convinced of her virginity, then it would be unreasonable to doubt it.

VIII. The patient, twenty-eight years of age, has, during six to seven years, suffered from frequent and lasting attacks of menorrhagia; the uterus is slightly enlarged; no tumors; by aid of the curette great quantities of very thick mucous membrane were removed; it is above 6^{mm} . in thickness; the surface smooth, covered with a low, ciliated columnar epithelium ($17.6\mu-7.4\mu$); the glands, numerous and very much distended, form the chief mass of the tissue; there are many vessels, chiefly arteries.

The interglandular tissue is formed by two kinds of cells, some large ones, resembling decidua cells, others smaller, with dark nuclei; spindle-shaped cells around the glands. Fig. 6 shows partly a group of these different cells, partly some few decidua-like cells and nuclei. If we compare these with genuine decidua cells, the similarity will be striking. Fig. 7 shows a piece of the decidua from a miscarriage in the second month. The cells with dark nuclei are probably pus cells (foul abortion-*débris*). The decidua-like cells in our virgin were of the following size: One of the largest, $20.6\mu : 17.7\mu$; the nucleus, $10.3\mu : 10.3\mu$. The others were $13.16\mu : 12-16\mu$; the nucleus, $7.5\mu-9\mu : 6-9\mu$. One more spindle-shaped cell measured $26.5\mu-5.9\mu$; the nucleus, $11.0\mu : 5.5\mu$.

The second case of endometritis hyperplastica chronica in a virgin is the following:—

IX. The patient is twenty-three years old; very chloro-anæmic. The catamenia regular, but profuse; last time, twenty-three days ago; a week afterwards a severe hæmorrhage commenced, which has continued since. The genital organs exquisitely virginal. The considerable mass of mucous membrane that was removed proves to consist of numerous twisted glands and many vessels, that suffer from evident endarteritis. The interglandular tissue consists of common cells with round, dark nuclei (some of them are seen in Fig. 1, *c*), and, besides, of cells resembling those of decidua (Fig. 1, *e*, and 8). These latter were somewhat smaller than in the preceding patient; they measured $11.8-16.2\mu : 8.8-10.3\mu$; the nuclei, $6.6-9.5\mu : 5.5-7.3\mu$. *Leopold*¹ also states a case in which he, in a woman with “virginal genitals,” found cells resembling decidua cells in the uterine mucous membrane; this was during the catamenial period. But I shall later on return to this case.

With respect to those patients who, to be sure, have given birth or miscarried, but where this was a long time previously, and where we cannot regard the endometritis as having any connection at all with pregnancy, in these cases we also find these decidua-like cells. For instance, I may state that I have found this to be the case in a woman seventy-four years old:—

X. She had given birth seven times; the menopause was in her forty-fifth year. She had suffered from hæmorrhage during four months. I found a small mucous polypus, and, besides, the mucous membrane was much thickened. The smooth surface was covered by a tall, ciliated, columnar epithelium ($23.5-26.5\mu : 3.7-4.4\mu$); the glands enormously distended; the interglandular tissue consisted of a homogeneous or delicately fibrillated stroma, in which were small, round, deeply-stained

¹ Arch. f. Gyn. Bd. II., pp. 119-120.

nuclei, and others larger, oval, granular, and faintly tinged, lying close to one another. The limits of the cells indistinct. Whilst most of the dark nuclei measured $3.9:3.7\ \mu$, most of the light ones measured $10.3-5.9\ \mu$. In most of the other patients they were larger; the nuclei especially were larger in proportion than they are wont to be in decidua cells. As examples, the following measurements from three patients may be given: $14.0\ \mu:14.0\ \mu$; nucleus, $10.3\ \mu:8.8\ \mu$. — $11.8-15.0\ \mu:11.0-15.0\ \mu$; the nucleus, $7.4-12.0\ \mu:7.4:8.8\ \mu$. — $18.0\ \mu-15.0\ \mu$; the nucleus, $11.5\ \mu:6.0\ \mu$. These decidua-like cells can also, as stated above, become perfectly spindle-shaped (see Fig. 2). Such a cell measured $35.3\ \mu:5.5\ \mu$; the nucleus, $11.8\ \mu:5.9\ \mu$. I must here remark that *I have found such cells quite similar to decidua-like cells in the mucous membrane during menstruation*, and I stated above that *Leopold* had made a similar discovery in a virgin, and by chance the menstruating uterus which I examined was likewise that of a virgin. Also, here were found closely-packed nuclei, but it was, however, also possible, in many cases, to see the limits of the cells themselves. There were small cells with small, round, or long-drawn, deeply-stained nuclei, and innumerable transitions from these to large decidua-like cells, with oval or round, granular, slightly-stained nuclei. But most of the dark nuclei were larger than in the healthy mucous membrane I described first, — many of them were $6\ \mu$ every way (red blood-corpuscles were but $5\ \mu$). One of the largest of these decidua-like cells measured $26.6\ \mu:16.2\ \mu$; its nucleus, $8.8\ \mu:10.3\ \mu$; many measured $14.7\ \mu:11.8\ \mu$, with nucleus measuring $9.0\ \mu:8.5\ \mu$. Some few nuclei were still larger, $11.8\ \mu:8.1\ \mu$.

However, it seems that these decidua-like cells are not always present in the menstruating (nor in the inflamed) mucous membrane, and this is shown by the fact that *Leopold*,¹ in the mucous membrane that he described, which was in the stage immediately preceding menstruation, only found small cells with nuclei that almost filled the whole cell.

As *Leopold*² has found *giant-cells* in the mucous membrane during the catamenial period, and as they are also to be found in the decidua of pregnancy, it seemed reasonable to me to endeavor to find them in my preparations. I was not able to observe any in the deep layers near the muscularis, where *Leopold* chiefly found them, and they were altogether wanting in most of my preparations. I found them in the following two patients only:—

XI. A woman forty years old; three births, the last of which was

¹ Arch. f. Gyn. Bd. II., page 132.

² *Ibid.*, page 116.

four and a half years ago; no miscarriage; menorrhagia during the last years' time; the uterus was enlarged; a considerable quantity of mucous membrane was removed; it showed the following structure: The glands were somewhat less numerous than in the normal state, and they were even perfectly wanting in large tracts; the surface was papillomatous and uneven. I shall speak of the superficial epithelium in a subsequent part of my paper. Besides the two common kinds of cells that here, as elsewhere, formed the greater part of the body of the tissue, there were many cells with divided nuclei. This was principally the case close to the surface, where you may see figures resembling the one in Fig. 9. There are large giant cells, formed by fusion of many smaller ones, with divided nuclei. The largest of these giant cells measured $32.4 \mu : 23.4 \mu$; another one, $32.1 : 17.7 \mu$. In one of the patients I mentioned above — No. IV. — there were likewise, close under the surface, numerous cells in division (pus cells?), besides giant cells.

What I have described here must be sufficient to confirm the ideas put forward in the above, which I might also express thus: *The interglandular tissue of the uterine mucous membrane is composed of cells that mostly resemble embryonal cells. Like these latter, they are able to suffer many transformations, become spindle-shaped, and so on. But, above all, they seem to be liable, under the influence of irritative processes, normal (menstruation, pregnancy) or pathological (inflammation), to undergo a change, the final stage of which is the decidual cell in its most exquisite form.*

Thus these inquiries lead to results in direct opposition to Wyder's¹ opinion, that the formation of decidual cells is a phenomenon proper to pregnancy. And they are just as positively in favor of the opinion that the decidua cells descend from the cells of interglandular tissue. As to the latter question, it would lead us too far were I to discuss all that has been written concerning the origin of the decidua cells. I shall, therefore, limit myself to stating that at present most investigators agree with the opinion put forth, for instance, by Friedländer² and Leopold,³ which is in harmony with the conclusions at which I have arrived in my investigations. I made them a couple of years ago, although they are only published now; and in the interval two papers have appeared which are devoted particularly to the origin of the decidual cells, which I therefore shall mention shortly. One is by Overlach: "Die pseudo-

¹ L. cit.

² Physiologische anatomische Untersuchungen über den Uterus. Leipzig, 1870. p. 8.

³ Arch. f. Gyn. Bd. II. p. 450 and pp. 461-462.

menstruierende mucosa uteri nach akuter Phosphorvergiftung."¹ On examining the uterine mucous membrane of a woman who died of acute phosphorus poisoning, he found it in a state which he thinks proper to call pseudo-menstruation (better, perhaps, acute inflammation), and he found numerous cells very similar to decidua cells in the interglandular tissue. With respect to the origin of these cells, he arrives at the conclusion that *they are of epithelial origin*, and he believes that they chiefly descend from the tall, narrow epithelium of the cervix, and wander hence into the mucous membrane of the corpus. I have not a single time in my researches met with anything that could support such an opinion, although I have very often examined the mucous membrane of the upper part of the cervical canal. Nor have I found any other investigator who has confirmed *Overlach's* startling discovery (although, indeed, it is said that decidua can be developed from the mucous membrane of the cervix; thus, in the second of *R. Maier's*² well-known cases, the "Deciduom" originated in the mucous membrane of the cervix). So we must as yet suppose that acute phosphorus poisoning provokes a specific morbid alteration of the uterine mucous membrane, and the results of this cannot, without further ado, be brought to bear on other matters.

The other paper is by *Walker*, and treats of the anatomy of the membranes of the ovum in extra-uterine pregnancy.³ He here arrives at conclusions that essentially agree with mine, viz., that decidua cells descend from connective tissue cells, and that we find gradual gradations between these two kinds of cells, whilst the endothelium of the vessels has nothing whatever to do with the origin of the decidua cells.

II. THE LINING EPITHELIUM.

Still less attention than to the interglandular tissue has, with a single exception (*Zeller*, v. i.), been given to the changes which *the lining epithelium* may undergo during chronic endometritis. The only statement usually found about the epithelium lining the healthy mucous membrane of the corpus uteri is, that it is a ciliated columnar epithelium. *Hennig*⁴ gives its length from 10-30 μ ; *Moericke*,⁵ from 16-28 μ . The last-named author adds that the shape may be altered by the mutual pressure of the cells.⁶ About the mucous membrane during *menstruation*, *Wyder*⁷

¹ Arch. f. mikroskop. Anatomie. Bd. 25. pp. 191-235.

² Virchow's Arch. f. pathol. Anat. Bd. 67. pp. 55-71.

³ Ibid. Bd. 107. Hft. 1. pp. 72-99.

⁴ Katarrh der inneren weibl. Geschlechtsorgane. Leipzig, 1862. p. ii.

⁵ Zeitschr. f. Geburtsh. u. Gynäk. Bd. vii. Hft. 1. p. 107 cfr. p. 99.

⁶ Ibid.

⁷ L. cit. p. 21.

states that its surface is partly villous, and here and there is lined by a columnar epithelium.¹ In cases of membranous dysmenorrhœa he has found the epithelium tessellated $12\ \mu$ high.² *Olshausen*³ mentions that in cases of endometritis fungosa the epithelium does not present changes from the normal state. *Ruge*⁴ states that the surface is lined with columnar epithelium, is smooth or slightly papillary, warty. A more detailed account of the changes which the epithelium may undergo in cases of endometritis is only given by *Zeller*,⁵ and this author has mainly given attention to the appearance of *squamous epithelium* in the womb. However, he states⁶ (like *Moericke*) that the cells rarely are *strictly cylindrical*; as a rule they are conical or pyramidal. He further mentions the frequency with which are found excrescences and villi on the surface. With regard to the squamous epithelium, he has very often found it; the cells even often changed into horny scales (wherefore he speaks of an *ichthyosis uterina*). In the same case he now finds columnar and now squamous epithelium, and also both forms beside each other. He has examined four cases of *E. fungosa*, and in each case he found squamous epithelium.

Though it is now three years since these researches were published, at about the same time that *Küstner*⁷ had found squamous epithelium lining a mucous polypus springing from the cervical canal, I have not found one single author who has published similar results. *Heinricius*⁸ states expressly that he never has found squamous epithelium. It was mainly *Zeller's* paper which made me enter into these researches; but *not in a single case have I been able to find squamous epithelium lining the mucous membrane* curetted from the corpus uteri.

Before going on to describe the character of the epithelium in the cases of chronic hyperplastic endometritis which I have examined, I shall mention the character of the epithelium in the above-mentioned mucous membrane from the patient who died from uræmia (six months post partum; lactation). The surface was rather smooth. It was lined with a single layer of columnar epithelium; the cells were narrow, not very high. The measurements were $11.7-17.7\ \mu: 3.7-4.7\ \mu$ (most of them $14.7: 3.7\ \mu$). The nuclei measured $6.0-8.8\ \mu: 2.8\ \mu.-4.4\ \mu$. In this place we may perhaps also mention the above-described case (No. I.⁹) in which the patient did

¹ I shall not here enter further into the dispute, whether the epithelium is lost during menstruation, or whether it remains wholly intact.

² L. cit. p. 26.

³ L. cit. p. 104.

⁴ Zeitschr. f. Geburtsh. u. Gynäk. Bd. v. p. 320.

⁵ Ibid. Bd. XL. pp. 56-88.

⁶ Ibid. p. 60.

⁷ Ctrbl. f. Gyn. 1884. No. 21. p. 320.

⁸ L. cit. p. 206.

⁹ These numbers refer to the cases mentioned in the first part of this paper.

not suffer from hæmorrhages, and in which the mucous membrane did not differ visibly from the normal one. The ciliated cylindrical cells showed the following measurements: 17.5μ : 5.9μ ; the nuclei, $6.0-8.8 \mu$: $3.7-4.4 \mu$.

Only in a few of the cases of chronic inflammation examined was the epithelium found so small, or even smaller. In case No. V. the cells measured but $13.7-14.7 \mu$: $5.2-5.6 \mu$; the nuclei, $7.4-8.8 \mu$: 2.9μ . In case No. II. the measurements were 17.7μ : $4.4-7.4 \mu$; the nuclei, $8.8-12.0 \mu$: $4.2-5.9 \mu$. In case No. VIII., where the surface also was quite smooth, the epithelial cells were proportionally broad, measuring $17.7-19.1 \mu$: 11.8μ ; the nuclei, $5.9-11.8 \mu$: $4.4-6.0 \mu$ (most of the nuclei, 5.9μ : 5.9μ). In other cases the cells are alike longer and broader than those which we found lining the normal mucous membrane. But sometimes we also find very long and narrow cells. In one case, for instance, the measurements were $22.1-23.5 \mu$: $2.2-3.7 \mu$; the nuclei, $7.4-8.8 \mu$: $1.7-3.7 \mu$; in another case (No. X.), $23.5-26.5 \mu$: $3.7-4.4 \mu$; the nuclei, $10.3-11.8 \mu$: 3.1μ . In this case, where the patient was seventy-four years of age, the ciliated character of the cells was plainly visible, which is at variance with the statement of *Moericke*,¹ that the epithelium loses the cilia at an advanced age.

Nevertheless, in all these cases the epithelium had still preserved the normal main type. The cells usually stained rather brightly, as did the oblong, frequently granulated nuclei, which were seated near the basis of the cells. In other cases, however, *the epithelium changed character altogether*, the cells took a club-like or fan-like shape, or the epithelium grew villous, etc., as I am now going to describe. The *surface*, too, instead of being rather smooth, frequently had an uneven, papillomatous aspect, which changes could assume a very high degree.

In the following case the epithelium presented a kind of transition to these abnormal shapes:—

XII. Thirty-six years of age; has borne two children, fourteen and nine years ago, and miscarried twice, the last time before last child. Suffered for years from severe menorrhagia. The surface is uneven, with broad prominences. The shape of the epithelium is seen in Fig. 10. The measurements are $32.4-36.8 \mu$: $4.4-5.9 \mu$; the nuclei, $11.2-14.7 \mu$: $4.4-5.1 \mu$.

In the following case the epithelium resembled the last one, but the cells had a more fan-like shape:—

XIII. Fifty-three years of age, four deliveries and four miscarriages, the last one ten years ago. One year ago she was treated for menorrhagia

¹ L. cit. pp. 114 and 119.

ENDOMETRITIS CORPORIS CHRONICA.

by curetting the mucous membrane, but three months ago the hæmorrhage recommenced. The surface is rather smooth. The epithelial cells are long, narrow, partly fan-shaped, with the nucleus near the free, thick end, as seen in Fig. 11. The measurements are $29.4-38.2 \mu : 3.1-8.8 \mu$ (most of them 4.4μ broad); the nuclei, $7.4-16.2 \mu : 2.3-5.9 \mu$.

In Case IV. it was mentioned that there were found giant cells, and many cells with the nucleus becoming divided just below the epithelium lining the adenomatous parts of the mucous membrane (I was not able to find the lining epithelium of the non-adenomatous parts). The shape of the epithelial cells was polymorphous; most of them still presented the cylindrical type, but had the free end a little swollen, and from these were found transitions to the club-shaped cells seen in Fig. 12. The measurements of these four cells varies from $22.0-35.3 \mu : 3.7-8.8 \mu$; the nuclei, $10.3-14.7 \mu : 2.9-5.5 \mu$.

In the following cases the character of the surface and the epithelium is still more different from the normal state:—

Case VII. is mentioned in the first part of this paper. The surface is partly rather smooth, partly it offers smaller and larger prominences, and this, combined with the circumstance that the openings of the glands are dilated into a funnel-shape, may produce such an appearance as the one seen in Fig. 13, where one of the prominences is narrowed at the basis like a little polypus. The lining epithelium is polymorphous to such a degree that we may find cells of very different types in the same section. A large part of the surface is lined with a low, proportionally broad columnar epithelium. The measurements are $11.8-14.7 \mu : 4.4-7.4 \mu$; the nuclei, $5.5-7.4 \mu : 3.7-5.1 \mu$. Near up to these cells long and very narrow cells may be found measuring $23.5 \mu : 1.5 \mu$; the nuclei, $11.8 : 1.5 \mu$. Further on we find fan-shaped or pyramidal cells (Fig. 14), with a long process at the basis, and transitions from these to long, narrow, fan-shaped cells, and from these again to the long, narrow, cylindrical cells already mentioned. The cells with processes are (the process included) $20.6-26.5 \mu$ long (whereof the process, $5.9-11.7 \mu$), $3.7-8.5 \mu$ broad; the nuclei, $5.9-8.8 \mu : 3.7 \mu$. The long fan-shaped cells are $23.5-26.5 \mu$ long, 2.2μ broad near the basis, 5.9μ at the broad end; their nuclei measure $8.8-10.3 \mu : 1.5-4.4 \mu$. In the adenomatous parts from this patient I have not been able to discover the lining epithelium.

Case XI. is also mentioned in the first part of this paper, and the giant cells found direct under the surface were described and figured (Fig. 9). The surface itself is rarely smooth, most frequently uneven, with broad papillæ, but never to such a degree as in the case last mentioned. The character of the lining epithelium varies very much, but most fre-

quently its character is like that seen in Figs. 15, 16, and 17. The shape of the single cells resembles mostly a club, but they appear like separated bushes, and frequently seem to spring radially from an edge, which runs vertically through the middle of such a bush (like a Christmas-tree), through which the surface of the membrane receives a villous aspect. Such epithelial bushes may reach a height of $121\ \mu$; the ones seen in Fig. 15 are 88.2 and $85.3\ \mu$ high. The measurements of the single cells are $32.4-41.2:8.8\ \mu$. In other parts we find a nearly true columnar epithelium; the measurements are $14.7-20.6\ \mu:6.0-8.8\ \mu$; the nuclei, $7.5-9.0\ \mu:4.5-7.4\ \mu$. From these cells transitions are again found to very long and narrow cylindrical cells ($29.5-47.0\ \mu:3.0-4.4\ \mu$; the nuclei, $9.0:29\ \mu$); and from these again to long, club-shaped cells, $32.4-44.1\ \mu$ long. The part of the mucous membrane poor in glands is lined with a stratified epithelium of pear-shaped cells. The epithelial layer is $29.4-41.2\ \mu$ high; the height of the single cells is difficult to measure, but they are $8.8-9.0\ \mu$ broad; the nuclei measure $9.0-10.3\ \mu:6.0-8.5\ \mu$.

In Case VI., where we find a placental polypus, parts of the mucous membrane were lined with a bushy, villous epithelium similar to that described in the foregoing case. The cells were club-shaped, with the nucleus at the dilated end. The measurements of these cells are $14.7-20.6\ \mu:4.4-5.9\ \mu$; of their nuclei, $5.9\ \mu:2.9-3.7\ \mu$. Other parts of the surface of the mucous membrane present broad, flat papillæ, lined with columnar epithelium, whose cells measure $14.7-17.7\ \mu:5.9-7.4\ \mu$; their nuclei, $8.8\ \mu:3.0-5.5\ \mu$.

As was to be expected, these researches prove that *the lining epithelium takes a great part in the morbid changes going on in the mucous membrane during chronic inflammation*. Not only that the surface can become uneven, papillous, nearly polypous,—not only that a lively throwing off and regeneration of epithelium takes place, but the epithelium may change character altogether: its cells may become long and thin, or narrow, short, and broad; may take a pear, a club, a fan shape, etc.; and, lastly, it may present a bushy, villous character.

ENDOMETRITIS CORPORIS CHRONICA.

EXPLANATION TO THE PLATES

ILLUSTRATING DR. LEOPOLD MEYER'S PAPER ON THE MORBID ANATOMY OF
CHRONIC ENDOMETRITIS.

FIGURE 1. Small round cells with brightly-staining nucleus. Magnified 550 times.

a. From Case XII.

b. From Case XI.

c. From Case IX.

e. Decidua-like cells.

FIG. 2. Gradual transition from round to spindle-shaped cells (Case XII.), and transition from spindle-shaped to decidua-like cells. Magnified 550 times.

FIG. 3. True decidua cells (Case VI.). Magnified 550 times.

FIG. 4. Piece of decidua in the mucous membrane (Case VII.). Magnified 30 times.

a. Decidua.

b. Lining epithelium.

c. Section of gland.

d. Large blood-vessel.

FIG. 5. Decidua cells, from *a*, Fig. 4. Magnified 550 times.

FIG. 6. Different kind of cells from Case VIII. Magnified 550 times.

FIG. 7. True decidua (inflamed). Magnified 550 times.

FIG. 8. Decidua-like cells, from Case IX. (compare Fig. 1, *c* β). Magnified, 550 times.

FIG. 9. Giant cells, etc., from Case XI. Magnified 550 times.

FIG. 10. Lining epithelium, from Case XII. Magnified 550 times.

FIG. 11. Lining epithelium, from Case XIII. Magnified 550 times.

FIG. 12. Lining epithelium, from Case IV. Magnified 550 times.

FIG. 13. Surface of the mucous membrane (Case VII.). Magnified 110 times.

FIG. 14. Epithelial cells, from Case VII. Magnified 550 times.

FIGS. 15, 16, and 17. Lining epithelium, from Case XI. Magnified 550 times.

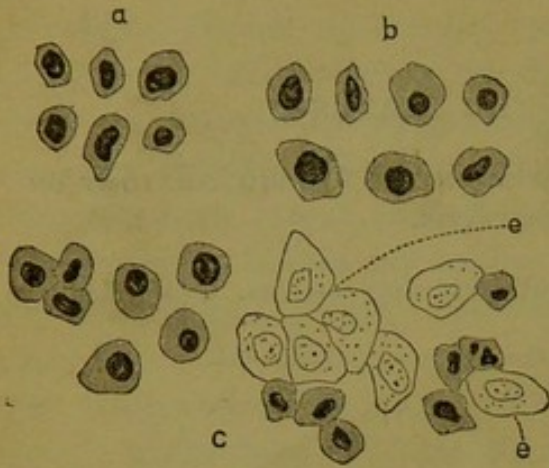


Fig. 1.

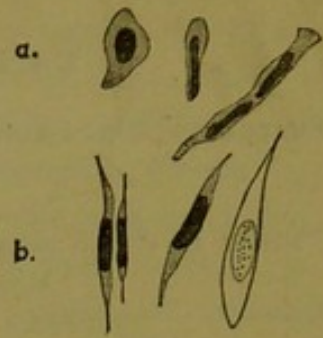


Fig. 2.



Fig. 3.

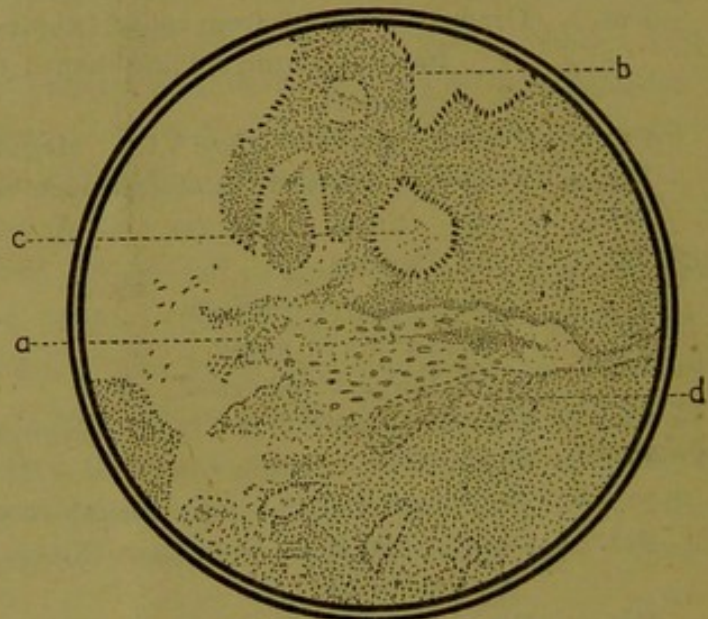


Fig. 4.

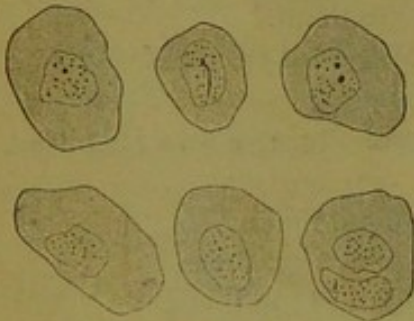


Fig. 5.

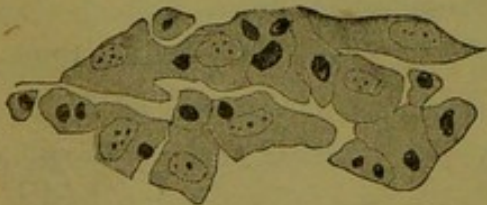


Fig. 7.

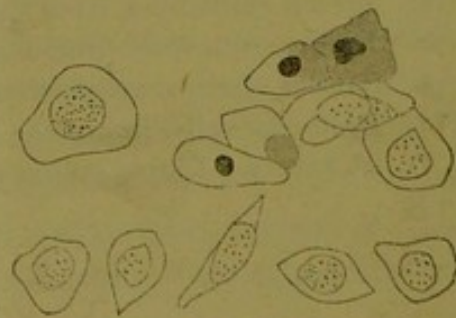


Fig. 6.



Fig. 8.



Fig. 9.

ENDOMETRITIS CORPORIS CHRONICA.

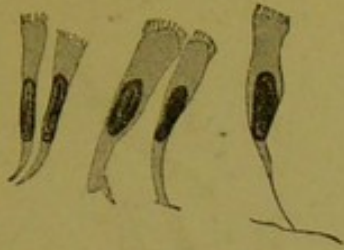


Fig. 10.

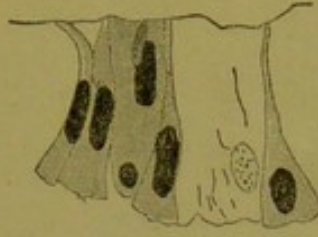


Fig. 11.

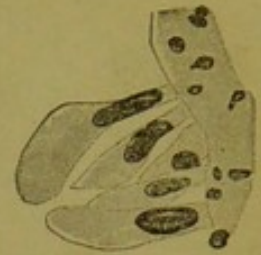


Fig. 12.

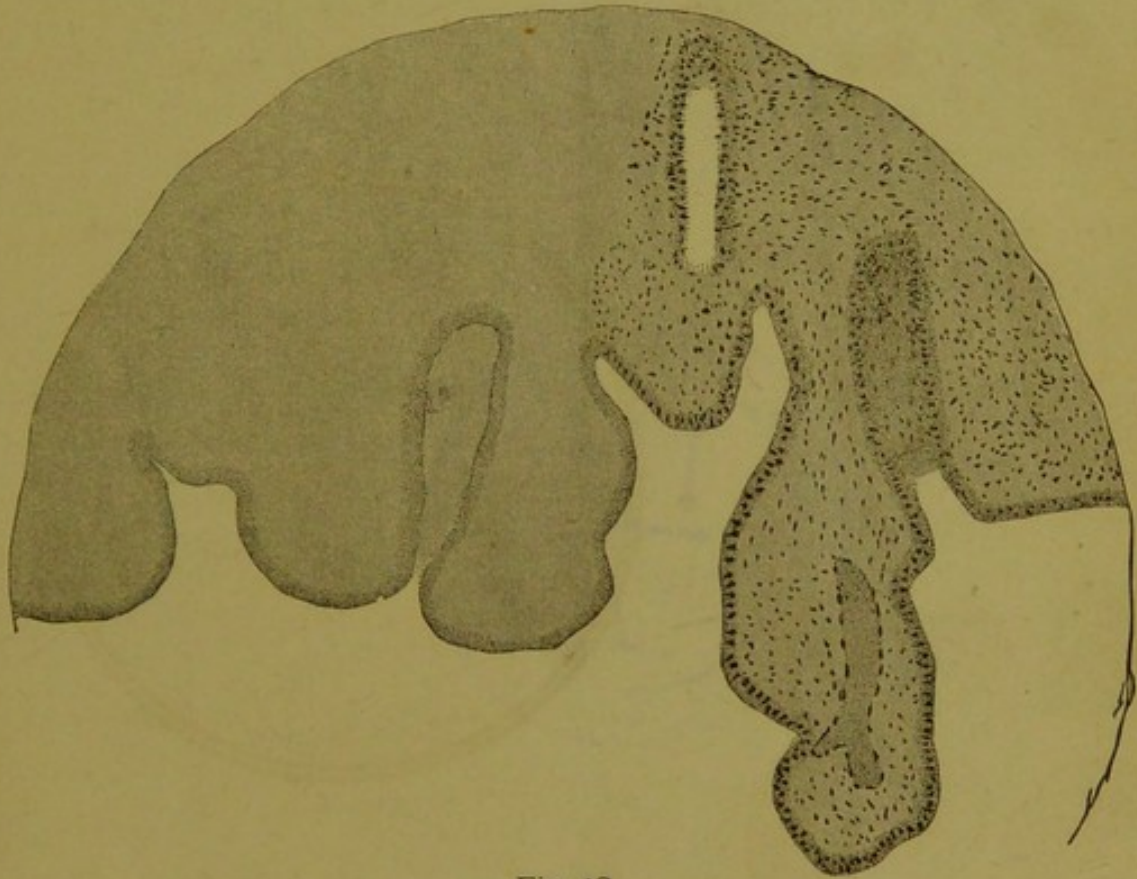


Fig. 13.



Fig. 16.



Fig. 14.

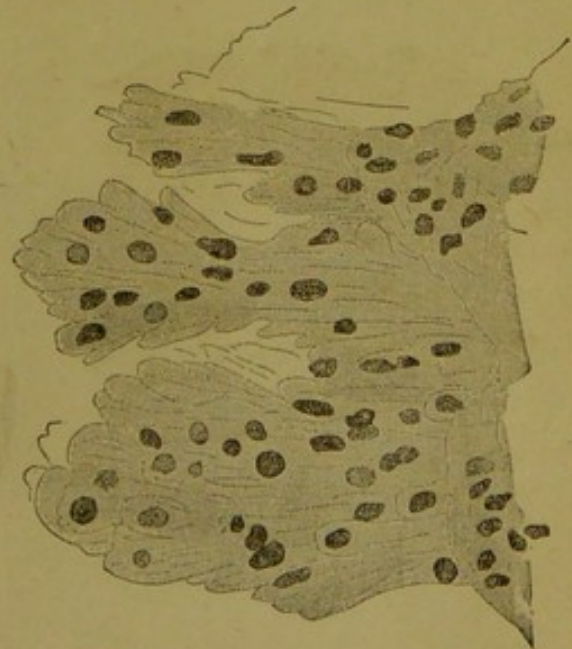


Fig. 15.



Fig. 17.

