XI. *The Menstruation of* Semnopithecus entellus.

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Communicated by Professor Michael Foster, *Sec. R.S.*

Received May 16,—Read June 15, 1893.

[Plates 35–41.]

Contents.

Introduction.

During a visit to India in 1888–89 I passed through Calcutta, and made inquiries from the Superintendent of the Zoological Gardens there, Mr. Sányál, as to the breeding time of *Macacus rhesus*.

I was informed they bred freely in the gardens all the year round, and that full-grown specimens were readily obtainable in the bazaars.

In consequence of my representations to this effect, the Managers of the Balfour Memorial Fund handed over to me the sum of £100, for the purpose of investigating in this country the embryology of Monkeys.

Through the kindness of Mr. SÁNYÁL, forty female *Macacus rhesus* were purchased and shipped in Calcutta, and arrived in England in March, 1890; and it was with great disappointment I found they were too young for my purpose.

I was then informed that adult *M. rhesus* are so savage it was found impossible to send them so long a journey without providing a separate cage for each, and I therefore determined to go to Calcutta to carry on researches there.

The Committee of the Royal Society appointed to administer the Government Grant for the endowment of research gave me, in October, 1890, the sum of £100, for "an investigation of the phenomena of menstruation and ovulation, and of the early stages of development of the Monkey." I was elected Balfour Student in the November following, left England the same month, and arrived in Calcutta in the middle of December.

My object in visiting Calcutta was placed before the Committee of Management of the Zoological Gardens by Professor D. D. CUNNINGHAM, the Secretary, and these gentlemen most kindly placed at my disposal a small building within the gardens, which was converted into a temporary laboratory.

I should like to take this opportunity of expressing to these gentlemen my thanks for their courtesy, and to thank especially Professor CUNNINGHAM for his never-failing willingness to put at my disposal all the accurate and varied knowledge he possesses, and for very many acts of kindness which were of the greatest service to me. The varied religious beliefs of the natives, the fanaticism of some of them, and the special reverence accorded to Monkeys by many, rendered secrecy and some considerable caution necessary; it was in this direction, and in overcoming the difficulties which presented themselves of obtaining a sufficient number of satisfactory animals to work upon, that Professor CUNNINGHAM's advice and help was of especial, and indeed essential, importance.

Finding that none but very young Monkeys were obtainable in the bazaars, collectors were dispatched to the jungle to secure as many specimens as possible of adult female *Semnopithecus entellus* and *Macacus rhesus*.

The latter were not obtainable near Calcutta in this way, and in spite of daily promises from the dealers, it was not until the middle of January that *S. entellus* arrived in numbers from the jungles on the south bank of the Hugli. Subsequently, large numbers of *M. rhesus* were sent to me from the North-West Provinces, where the protection afforded by numerous Monkey temples and worshippers had favoured their increase to such an extent that some of the inhabitants were very willing to assist in capturing and sending away as many as possible.

Of the one hundred and eight specimens of *S. entellus* examined, a considerable number had already borne young, and were suckling them; six were found to have very lately borne young, and one to be undergoing the process of aborting an advanced embryo; the rest were not breeding, and about fifty of these, adult females, were killed, and the uteri preserved, in order to study the phenomena attending menstruation.

I was informed by the dealer—a Eurasian—who supplied me with these animals, that *S. entellus* breeds twice a year, in April and October, and that, when breeding, they retire into the thickest parts of the jungle, and cannot then be caught. This information was doubtless obtained from native collectors, and all evidence supplied by natives was found to be so untrustworthy that little reliance can be placed upon this report.

Bearing in mind the fact that the animals examined were either not breeding, or else had recently borne young, it would seem fair to assume there are one or more limited breeding seasons for *S. entellus*, but my information warrants no further assumption.

I made attempts, during February and March, to induce these animals to copulate while in captivity. Two large cages were put at my disposal in one of the Monkey houses at the gardens, and an adult male with several females put in one cage, while in the other a pair of adult Monkeys were kept.

Many of the females seemed quite prepared for copulation and tried to induce the male to fertilize them, but without success.

I do not consider these observations at all conclusive towards establishing the fact that the animals in a wild state do not breed during these months; *S. entellus* is a very shy animal, and the circumstances of captivity may well account for their non-breeding in the cages; at the same time, if the breeding season had begun before I left, it is highly probable I should have seen some evidence of the fact in one or more of the numerous specimens I examined.

With *Macacus rhesus* I was even less successful in obtaining material for work.

Of several hundreds of these animals sent to me from the North-West Provinces during February and March, a very large proportion, probably not less than four-fifths, bore advanced embryos in utero, or had lately borne young, or had recently aborted the embryo.

In two specimens I found embryos of a stage probably similar to a six-weeks-old human embryo, and these were the only specimens of breeding females I saw which bore any but nearly full-grown embryos. The rest of the females were mostly young ones, but about twenty-five were adults, not pregnant, and the uteri of these were preserved for the investigation of menstrual phenomena.

The large majority of breeding females which either bore young of an advanced age *in utero*, or which had recently borne young, is strong evidence in favour of the assumption that *M. rhesus* has one or more definite breeding seasons; Mr. SÁNYÁL,

however, assures me he has had various specimens of this species in the gardens, which gave birth at different times of the year, and I can only assume it is probable the species breed at different times in different parts of the continent.

The term of embryonic life of *M. rhesus* was calculated by FRÉDÉRIC CUVIER (quoted by BRESCHET, No. 5A) to be seven months; the female upon which he carried on his observations giving birth to one young one in the month of October.

Dr. J. E. T. AITCHISON, however, assures me that in Simla *M. rhesus* copulates about October and gives birth during August and September following. The time for copulation, he adds, doubtless extends over two months. This would indicate the term of embryonic life to be nine to ten months, and Dr. AITCHISON's observations are so circumstantial I have no hesitation in accepting them.

It follows that *M. rhesus* of the plains of the North-West Provinces, which give birth during February and March, begin to breed about May. The great difference in the climate of the hills and the plains may be sufficient to account for the different breeding times in the different districts, and, as I have already pointed out, the fact that such different breeding times do exist, is substantiated by the experience of Mr. SÁNYÁL.

My stay in Calcutta was cut short by an attack of rheumatism and fever, and in April I was advised to leave the country as soon as possible. On this account I was compelled to defer my researches on the embryology of Monkeys, and to confine my attention to the menstrual phenomena.

In this paper I propose to describe the histological changes taking place in the uterus of *Semnopithecus entellus* during menstruation, and before long I hope to supplement these researches by an account of the same process in *Macacus rhesus*.

METHODS.

The methods adopted for the preservation of the uteri were—

Fixing:—

1. In PERENYI's fluid, for 4 to 5 hours.
2. In a saturated solution of corrosive sublimate, for 3 to 6 hours, after which careful washing in water intervened before hardening.
3. In FLEMMING's solution, without acetic acid, for half an hour.
4. In FLEMMING's solution, with equal volume of ·5 per cent. osmic acid, from half to 2½ hours.
5. In osmic vapour, for 5 minutes to half an hour, followed by FLEMMING's solution, either with equal volume of ·5 per cent. osmic acid added, or without the acetic acid, from half to 20 hours.

Hardening with spirit followed, attention being paid to a gradual increase in the strength of the spirit, and the specimens were kept in 70 per cent. or 90 per cent. spirit, until required.

The tissue was embedded in paraffin, and cut, by the Cambridge Scientific Instrument Company's rocking microtome, into sections of a thickness varying from ·0025 millim. to ·00625 millim. in different series.

The combination of soft mucosa tissue and thick, hard, muscular tissue caused much trouble by a folding or wrinkling of the sections, as they were cut, and it was not until several methods had been tried to get rid of this fault that I devised a plan of running hot water on to the slide upon which the sections were to be mounted, through a pipette, and placing the sections on the water; the latter is used at a temperature sufficient to soften the wrinkled paraffin and cause it to straighten out, but not quite hot enough to melt it.

The slide is previously coated with a thin layer of MAYER'S albumen, and when the water is run off, by tilting the slide, the sections sink down on to the albumen. The slide is then put on to a water bath, until all trace of water is lost by evaporation, and the sections become fixed in the hardened albumen.

By this method, several rows of consecutive sections can be mounted on one slide, which is then treated with turpentine, spirit, and staining reagents, then back through spirit to xylol, and mounted in Canada balsam in the usual way.

I used various stains with good results, especially dahlia, eosin, methylin blue, hæmatoxylin, EHRLICH'S Biondi gentian violet, borax-carmine, and picro carmine, methylin blue and eosin, hæmatoxylin and eosin, saffranin, or fuchsin. After using picro-carmine, the slides were passed through spirits of various strengths in which a little picric acid had been dissolved, and this stain was perhaps the most successful of all for general work, but for finer histological examination the other stains, especially gentian violet and hæmatoxylin and eosin, were more advantageous.

The sections were cut through the body of the uterus, at right angles to its antero-posterior plane and vertical to the wall of the uterus. It will be observed that in some of the figures the mucosa is not so deep as it is in others, and I should remark that, where it is more shallow, the drawing has been taken from the lateral part of the section, where (*vide* fig. 12) this layer is considerably less thick than it is in the middle of the layer.

SUPERFICIAL MENSTRUAL PHENOMENA.

After histological examination, the uteri were grouped into the following four menstrual periods, which were subdivided into eight stages, and, as it will be convenient to describe the superficial phenomena in relation to these periods and stages, I will mention them now.

A. Period of rest.

Stage I.—The resting stage.

B. Period of growth.

Stage II.—The growth of the stroma.

Stage III.—The increase of vessels.

C. Period of degeneration.
  Stage IV.—The breaking down of vessels.
  Stage V.—The formation of lacunæ.
  Stage VI.—The rupture of lacunæ.
  Stage VII.—The formation of the menstrual clot.
D. Period of recuperation.
  Stage VIII.—The recuperation stage.

The external phenomena attending menstruation in *S. entellus* is marked by the discharge which flows from the vagina during about four days each month.

Unlike *M. rhesus*, there is no vivid colouring of the buttocks, stomach, thighs, or tail, and the only other external sign of menstruation is a slight swelling of the vulva, and, sometimes, of the nipples of the mammæ.

The dark colour of the labia and of the nipples prevents any external sign of flushing being seen, but just within the labia the skin is seen to be flushed during the menstrual period.

I have not examined the discharge from the vagina of *S. entellus* further than to determine the presence of a slimy white matter—probably mucus, of cells resembling pus cells, of red blood corpuscles, and of débris of cells both epithelial and belonging to the stroma layer of the uterus and squamous epithelial cells from the vagina.

The climate of Calcutta, and the fact that the discharge occupies some time in travelling down the vagina, made it difficult, if not impossible, to obtain material in a condition to repay study. I have, however, several menstruating *M. rhesus* now in my possession, and hope before long to publish the results of examination of the menstrual discharge in these animals.

As soon as the Monkeys were killed, the uterus, with part of the vagina, the tubes, and ovaries were cut out altogether. The uterus was then opened from the external os uteri along the left and anterior borders, and the ventral wall was turned back.

The vagina is a wide sac with very thick muscular walls, much folded on their inner side and lined with a thick layer of squamous epithelium. Projecting into the vagina at the further end of the sac is a small papilla, in the centre of which is a small hole leading into the cervix of the uterus. The lips surrounding this hole are soft, and, as the papilla is more closely attached to the ventral wall of the vagina than it is to the dorsal wall, the dorsal lip is longer and looser than the ventral lip.

The cervix is a narrow, straight canal, the walls are very thick and muscular, and its inner surface is longitudinally folded; it opens into the cavity of the body of the uterus by a gradually widening aperture.

The cavity of the body of the uterus is triangular in shape, all the sides of which are concave, the apex is at the cervix end, and the concave base is formed by the anterior wall of the fundus; it is lined by a mucous membrane, which I have called

the mucosa. The Fallopian tubes open by small pores on either side at the widest part of the triangle.

A superficial examination of the mucosa during Stages I. and II. shows the surface to be of a more or less opaque white colour, either smooth, slightly ridged, or divided into polygonal areas by pits connected by narrow depressions.

The opacity is more marked in some than it is in other specimens, and is regulated by the density of the stroma layer below the epithelium layer of the mucosa (fig. 12).

The smooth ridged or reticulate appearance is likewise due to the growth of the stroma. The reticulate appearance is brought about by the growth of the stroma between the glands; it rises like a number of small hillocks having valleys or depressions connecting the widely open mouths of the glands one with the other. In those uteri in which the mucosa is ridged, the epithelium has also grown and allowed the swelling stroma below it more room to expand; and where the mucosa is smooth the mouths of the glands are very small, and the interglandular tissue is evenly swollen all round them.

Throughout the process of menstruation, whenever an epithelium is present, the surface of the mucosa presents one or other of these three appearances; generally it is ridged or folded, but it may be smooth, or more rarely reticulated.

As shown above, these appearances are due to the growth of the stroma, restrained, as it were, by the epithelial covering. Where most restraint is exercised, hillocks or ridges are formed; where free growth is allowed the mucosa is smooth.

The soft mucosa is dry, and there is no trace of discharge from the glands within the cavity of the uterus during Stages I. and II. During Stages III. and IV. the mucosa is more or less flushed, the flush occurring uniformly over the surface when the mucosa is smooth, but more concentrated at the top of the ridges when the mucosa is folded.

At the end of Stage IV., at which stage, as will be seen later, the superficial capillaries of the mucosa break down and the blood contained therein is scattered among the meshes of the stroma, this flushing becomes exaggerated into congestion; and at Stage V. dark red spots are to be seen scattered about all over the surface of the mucosa: they are contained within the epithelium, and are caused by the formation of lacunæ.

It is to be noted that when only few specks of blood are seen they are confined to the dorsal wall of the uterus, or are more numerous there, and it is only when they are plentiful that they occupy both walls in equal proportions. This circumstance indicates that the increased supply of blood, which is a marked feature during menstruation, affects the dorsal before it affects the ventral walls, a supposition which is confirmed by histological examination.

The fact that during pregnancy the dorsal disc of the bilobed placenta is developed faster than the ventral disc is in harmony with this statement.

In the cavity of the uterus there is no discharge from the glands during Stage III.;

during Stages IV. and V., however, a colourless viscid material is sometimes seen therein; the labia, also, have a viscid discharge adhering to them, and I am inclined to think much of this is derived from the glands of the cervix.

The discharge in the uterus appears under the microscope as a stringy non-cellular substance; that taken from the labia contains, besides, many squamous epithelial cells derived from the vagina.

Stage VI. presents a further development; although no rupture of the surface can be discerned by a superficial examination, the cavity of the uterus contains free blood, which evidently proceeds from the mucosa, and, as will be seen, is expelled into the uterus by the breaking down of the epithelium covering the lacunæ, thus setting free the blood contained therein.

The lacunæ do not all rupture at the same time; free blood is found in the uterus, while specks of blood, *i.e.*, lacunæ, are still to be seen in the walls.

The blood is thin and mixed with viscid material; it contains, also, epithelial cells. The os uteri is generally softened.

Stage VII. shows the formation of the menstrual clot; and now the surface of the mucosa presents a ragged and torn appearance, due, as will be seen, to the casting off of the superficial part of the mucosa. The clot itself is found to consist of great quantities of red-blood corpuscles, leucocytes, epithelial cells both from the epithelium covering the surface of the mucosa and from the epithelium of the glands, and great masses of stroma.

The size and consistency of the clot varies in different specimens. In some specimens it is small, stringy, and soft, in others it is large enough to distend the narrow cavity of the uterus, and to swell out the walls, in which case it is much harder, and approaches the consistency of putty when ready for use. The labia now are soft and flabby.

Stage VIII.—After the clot is naturally expelled, a process which takes place during this stage, the mucosa appears less ragged than during the formation of the clot owing to the re-formation of epithelium over the surface.

Free blood is still found in the uterine cavity for some time after the blood clot has been expelled, but only in small quantities, and a few epithelial and other cells are still found in the blood.

Gradually the ragged appearance of the mucosa gives places to a smooth surface, which is at first much flushed, but which becomes later a semi-transparent and then a more opaque white colour. At this latter stage the mucosa has returned to its resting state, only to be again disturbed after a brief interval by renewed growth, congestion, and rupture, as before.

Sections show the transparency observed at this stage to be due to the sparsely scattered nuclei of the stroma underlying the newly-formed thin and flattened epithelium (fig. 10).

The os uteri remains flaccid, and the labia are still swollen until towards the close of this stage.

Histology.

General Description of the Body of the Uterus.

The whole of the cavity of the body and fundus of the uterus is lined with mucous membrane, called henceforth the mucosa. The mucosa consists of a single layer of cubical epithelium, below which is a tissue of a very primitive nature, which I have called the stroma, and about which a few words are here necessary.

The stroma is formed of a network of protoplasm in which nuclei are embedded; no definite cell boundaries are to be seen, the internuclear protoplasm is continuous. being drawn out into very fine processes; no intercellular substance is distinguishable and, with the exception of a few long radially arranged fibres which are present in the deeper part of the stroma during the resting stage only, there is no sign of connective tissue fibres or other skeletal structures.

At certain times the stroma grows rapidly, the nuclei increasing in number by division; the material which is cast off during menstruation is chiefly composed of stroma, and it is from stroma that the new blood vessels and some of the new epithelial cells, which are formed during the recuperation stage, are derived. It is, in fact, more like embryonic mesoderm than any tissue with which I am acquainted.

This stroma then is essentially primitive tissue capable of extensive and rapid growth, capable also of transformation into other and more specialized tissues, and may be entirely devoid of skeletal structures.

That portion of a mucous membrane which lies below the epithelium is usually called the corium, and, according to Quain (56), consists of connective tissue, either areolar or retiform.

Johnstone (29) describes the corium of the human uterus as adenoid tissue, and considers it is a highly specialized form of connective tissue. Chrobak (7) on the other hand finds no definite connective tissue framework in the mucosa of the human uterus, and I find practically none in the mucosa of *S. entellus*.

The nature of the so-called corium may be, and indeed is, different in different animals, in some it is denser than it is in others, while in others again a more or less definite connective tissue framework appears to exist.

In *S. entellus*, however, at any rate it does not consist of either areolar or retiform connective tissue, and the entire absence of fibres, except at one particular time, in my opinion, prevents it from being considered as definite connective tissue at all.

The mucosa then consists of a cubical epithelium below which is the stroma, the stroma contains blood vessels, a few radially disposed muscles in connection with the internal muscular coat, and long or short, generally straight and simple glands, the columnar epithelium of which merges into and is continuous with the epithelium lining the cavity of the uterus (see figs. 1 and 2, &c.). During Stage I. a few long fibres are present (fig. 1), but these are not present at any other stage.

The mucosa is thickest along the middle line of the dorsal and ventral aspects, and gradually becomes thinner laterally, leaving the cavity of the uterus as a triangular shallow slit the sides of which are concave.

The cavity itself is shallowest laterally, and widest at a point where the Fallopian tubes are inserted. The base of the triangle is formed by the curved wall of the fundus, the apex is at the entrance of the cervix into the body of the uterus.

Bounding the mucosa on its outer side is an inner layer of muscles mostly consisting of bundles disposed in an irregular circular direction, they run more or less obliquely round the mucosa, but at so small an angle that I have called them circular muscles; besides these, and enclosed between the bundles of circular muscles, are bundles of longitudinal muscles; but these are not so numerous as the circular bundles in this inner layer.

From the circular muscle bundles scattered fibres run radially inwards a short distance into the mucosa, they are not numerous and are irregularly placed, their existence, however, prevents the mucosa being sharply marked off from the muscle layer as MINOT (47) describes for the uterus of the human female.

Outside the inner layer is an external layer of muscles, chiefly composed of bundles of longitudinal fibres, but between them are smaller bundles disposed in a circular direction.

Outside the longitudinal layer of muscles is a thin layer, represented by a dark line in fig. 12, which is only superficially different from the external layer of muscles by reason of the fact that it does not stain so deeply.

It is composed of scattered fibres of longitudinal and circular muscles, with a few connective tissue cells, the whole embedded in a gelatinous material, and covered outside with a layer of flattened epithelium. I have called this layer the sheath.

All the muscles are non-striated muscles.

The cervix.—At the cervix end or posterior end of the body of the uterus, the stroma layer becomes thinner and gradually merges into a tissue in which the nuclei are more scattered and an intercellular substance is present. This tissue is much more dense than the stroma of the body of the uterus. The glands are short and the epithelium lining the cavity of the cervix is cubical.

I may here mention that neither the epithelium nor any portion of the underlying layer of the cervix is cast off during menstruation. During Stages II. and III., however, there is a slight increase in the density of the tissue at the anterior end of the cervix, but this is slight, and there is also a slight increase in the blood supply during these stages, but it is not at any time considerable.

The glands of the cervix secrete during menstruation, and I am inclined to think it is probable more secretion comes from them than from the glands of the body of the uterus.

The Fallopian tubes.—At the junction of the Fallopian tubes with the uterus the muscle layers of the latter are continued over the tubes, and a thin layer of stroma

underlies the layer of columnar epithelium, which lines the cavity of the tubes. Both these latter layers are continuous with the same layers of the mucosa.

I can detect no change in the structure of the Fallopian tubes during menstruation.

I will now give a description of the histological changes which take place from Stages I. to VIII. of menstruation.

A. Period of Rest.

Stage I.—The resting stage. Figs. 1, 13, 14.

During the resting stage the mucosa appears in section as of remarkably even consistency throughout.

The epithelial cells, either cubical or columnar, have large rounded nuclei in which a nuclear network is plainly visible with a high power. The epithelium is formed of a single row of such cells, their superficial edge is sharply delineated, but the inner edge is not so; there the protoplasm of the epithelial cells is continuous with the protoplasmic processes of the stroma which lies beneath, and indeed the similarity of the nuclei in these two layers and the continuity of their protoplasm point to the conclusion that the epithelium is merely a specialized layer of the stroma. The phenomena, which will be described later, of the re-formation of the epithelium after the mucosa menstrualis is cast off, although not absolutely conclusive evidence of this relationship, nevertheless renders it more than probable.

The uterine epithelium is directly continuous with the epithelium of the so-called uterine glands (fig. 1). These glands consist solely of columnar epithelium, which may be one or two rows deep, the cells are much elongated and their nuclei large, exhibiting a nuclear network. The superficial edge of the cells is usually beset in my preparations with ragged processes which may be cilia, but I have not been able to prove this to my satisfaction. The inner edge of the cells is very evenly disposed and attached to a non-nucleated basement membrane, which becomes thinner near the mouth of the gland and disappears altogether where the uterine epithelium joins the epithelium of the gland at its mouth.

There is a difference of opinion on this point with regard to the glands of the human uterus; ENGELMANN (11) says the glands of the fully developed human uterus have no basement membrane, MINOT (47) and LEOPOLD (38), however, state that a basement membrane is present.

No definite sheath invests the glands of *S. entellus;* close round the glands the nuclei of the stroma are more flattened than they are elsewhere during this stage. There may be one or more rows of such flattened nuclei, but the protoplasmic processes of the stroma do not combine to form a definite sheath, and they are continuous with the protoplasm of the surrounding stroma.

The protoplasm of the stroma does not appear to be continuous with that of the cells of the glands, as it obviously is with the uterine epithelial cells.

The glands secrete a clear viscid material, but at Stage I. this is rarely evident. During this stage the glands are generally short and their lumen narrow.

The nuclei of the stroma are regularly disposed for one-third of the depth of the mucosa; they are not closely packed, and the delicate protoplasmic processes of the stroma, in which granules are distinctly seen, form a network of open tissue, within which no intercellular substance was observed.

The nuclei are rounded or oval, and of very regular size; a nuclear network is always seen in them.

For one-third of the depth of the mucosa this arrangement is very uniform, but deeper down a few long fibrils run through the tissue, spreading out fanwise in the interglandular regions, and more closely concentrated at the base of the layer.

These fibrils stain darker than the neighbouring branching protoplasmic processes of the stroma, with which, however, they are in very close relation, a series of nuclei being disposed alongside each fibril.

The fibrils have not the structure of muscles, and are not continuous with the muscles lying below the mucosa; I judge them to be formed from united protoplasmic processes of the stroma, and to be similar to connective tissue fibrils; they were only seen in specimens of this stage of menstruation. Subsequently they entirely disappear, and it is remarkable that it is only that portion of the stroma situated superficially to these fibrils which undergoes in the next stage active growth, and becomes in the later stages cast off as the mucosa menstrualis.

The temporary presence of these fibrils is striking evidence in favour of the view, that we have here tissue of a very primitive character. It would appear that it is capable of developing into connective tissue, and, as I will show below, into blood vessels and epithelial cells; it is then not definite connective tissue, but primitive tissue, from which connective tissue and other structures may be derived.

There is no sign of the multiplication of epithelial cells or of the nuclei of the stroma at this stage.

The blood vessels in the mucosa are small. A few arteries are seen in the deeper parts of the layer, but only thin-walled capillaries in the superficial part.

The capillaries are fairly numerous, and contain plenty of blood corpuscles, while, now and then, but only rarely, a leucocyte is seen in a vessel.

It is noticeable that the blood vessels do not closely invest the glands in *S. entellus* as they do in the mucosa of many animals; on the contrary, they are specially noticeable in the interglandular tissue.

Of the muscle layers I need not say more than I have said already, since they do not concern the phenomena of menstruation as described below.

B. Period of Growth.

Stage II.—The growth of the stroma. Figs. 2, 15, 16.

Three changes are now seen in the mucosa. The first of these is a gradual increase in the density of the stroma in the superficial third of the mucosa; the second, an increase in the size of the blood vessels, and the third, an interglandular swelling of the mucosa into the lumen of the uterus in the form of ridges or hillocks.

1. *The growth of the stroma.*—The increase in density of the stroma comes about gradually. It is due to the increase in number of the nuclei of that layer by means of division, and to the fact that they are packed closely together. That is to say, hyperplasia occurs.

As I have before remarked, no definite division of this tissue into separate cells is possible, and the protoplasmic network is always continuous. When nuclei divide and separate, they carry with them a portion of the protoplasm which originally surrounded the parent nucleus, but this protoplasm is never thus entirely separated, it is merely extended, and no actual division of a cell is seen. In speaking of the finer histology of the stroma, however, I have sometimes referred to the individual nuclei with the protoplasm immediately surrounding them as cells.

The multiplication takes place by simple division of a nucleus into two, and probably also by fragmentation of a nucleus. Owing to want of space and consequent pressure, a very large proportion of the nuclei become elongated and spindle-shaped, while the protoplasmic processes of the cells are still branched, but in a longitudinal direction (fig. 15). These nuclei divide by simple amitotic division.

c_1 to c_5, fig. 16, are figures of five nuclei undergoing division into two; it is noticeable that the characteristic phenomena of mitosis are not discernible.

The cell marked c_2 is very commonly seen, but in no case have I been able to see polar stars or other details of karyokinesis. The same phenomena is shown in fig. 15, where also stages in the growth of the newly-formed nuclei are shown (d_2). The series d_1 to d_4, in fig. 16, shows stages in the fragmentation of the nuclei of the stroma; d_1 is a typical nucleus with its surrounding branched protoplasm, of Stage I.

The cells of this series are markedly different from those of the c series, owing to the division of their nuclei into three or more parts, and in the appearance of the protoplasm.

d_4 shows the fragments of a nucleus somewhat separated, but I have never seen the fragments draw away and carry with them the protoplasm which surrounded the mother nucleus, as is done when nuclei divide into two; at the same time, as will be seen later, such separation is probable.

The d series of cells is rarely seen, and then only on the edge of the denser layer of the stroma.

The cell indicated by f_1 is commonly seen in the midst of the dense layer. Its

three nuclei are not like those seen in d_3, nor are they quite like the two nuclei seen in the *c* series; at the same time, its protoplasm is much more like the *c* series than the *d* series, and I am disposed to think it should be classed with the former.

I at one time thought that these cells might be leucocytes, but have convinced myself this is not so. They have an entirely different appearance to leucocytes, their protoplasm stains much darker and their nuclei much lighter than do these parts in a leucocyte, and it is noticeable that no cells with four nuclei, which is the most usual condition of leucocytes at this and at other stages, are present in the stroma layer (compare *leu.*, fig. 16).

The same remarks apply to d_4 in the same figure; the appearance of the protoplasm itself and of the five nuclei therein is quite different from the appearance of those parts of a leucocyte.

The cells marked h_1 to h_5 are also very commonly seen in the dense part of the layer. They are very small cells and have very small nuclei; those represented in the figure were drawn with the same lens as the rest of the cells in fig. 16 (REICHERT'S $\frac{1}{15}$ immersion and occ. 4). Their nuclei, also, are commonly seen to be undergoing division into two by simple amitotic division.

The origin of these cells I have been unable to determine, they may be either the product of the larger fusiform cells or they may be derived from those cells in which the fragmentation of the nucleus was observed; their size and the appearance of their nucleus strongly inclines me to the latter view, but there is so much difference of opinion as to the possible formation of cells in this manner that I must leave their origin an open question, merely insisting upon the fact that they are a new formation, and that they were not present during Stage I.

The occurrence of amitotic division or of fragmentation, and the entire absence of mitosis in the cells of the stroma, is remarkable. According to the researches of FLEMMING (14), and ZIEGLER (84), fragmentation does not lead to the reproduction of cells, but to degeneration, while, on the other hand, METCHNIKOFF'S researches (45), throw grave doubts upon the destruction of polynuclear cells, and HICKSON (22, 23) shows that the nucleus of the ovum of *Millepora plicata* and of *Allopora* fragments, and that the cells of the blastoderm are formed of cells whose nuclei consist of the fragments of the nucleus of the ovum.

These researches are extended in a paper by the same author (24), and Dr. HICKSON informs me that in a forthcoming paper he will refer to some forty instances recorded by other writers, showing or implying the same thing.

Should this account be true, the origin of the *h* series of cells (fig. 16) from cells in which fragmentation of the nucleus is observed (the *d* series), is by no means improbable.

With regard to the occurrence of amitotic division, ZIEGLER (84) states that those nuclei which divide without mitosis are always distinguishable by their excessive size, and he connects the large size with increased functional activity.

My observations are not in accord with ZIEGLER'S; the stroma cells of the non-pregnant mucosa of *S. entellus* are at no time possessed of large nuclei, while during the period of activity just described, many of the nuclei exhibiting amitotic division are excessively small (series *h*, fig. 16), their size varies from ·005 to ·0075 millim.

It is not uncommonly remarked where no karyokinetic figures are observed that the failure to see them is due to faulty preservation or unsatisfactory staining; that is, of course, possibly the case with my own preparations, but I venture to think it is an improbable explanation in this instance. Possibly the relative size of the nucleus and the cell protoplasm may affect the method of division (figs. 16 and 17); in the examples before us there would seem to be no room for the formation of polar stars or nuclear spindle.

In the deeper two-thirds of the mucosa the stroma remains in the same condition as it was in Stage I., except that no fibrils are present; division of the nuclei is not seen, they are not crowded together, and hyperplasia does not occur.

Alongside the glands also the tissue is more open than in the interglandular regions (fig. 2).

I find no giant cells such as LEOPOLD (38) describes in the human menstruating uterus, and like WYDER (83) and MINOT (47), I do not find any decidual cells.

2. *The growth of vessels.*—The blood vessels in the deeper part of the mucosa are bigger in Stage II. than they were in Stage I., and the enlargement follows the first sign of growth in the stroma. The enlargement is not confined to vessels of the mucosa, those of the muscle layer are also enlarged, and further the vessels in the lower part of the mucosa begin to enlarge before the more superficial vessels are similarly affected, the increase in size gradually extending from below upwards.

In the densest part of the mucosa the vessels are still very small; pieces of capillaries from this region are shown in figs. 16, *a* and *b*, but a detailed description of the vessels will be given later, and I will not say more of them here.

3. *The swelling of the mucosa.*—The mucosa of the uterus from which fig. 2 was taken was swollen and thrown into folds; in that figure the swelling is seen to concern the interglandular substance and not to concern the gland itself.

The epithelium is very little, if at all, altered from what it was in Stage I.; the glands are firmly fixed deep down in a part of the stroma which undergoes no change at this time, and the growth of the stroma is greatest between the glands; in consequence of these facts the epithelium is held tightly down at the gland mouths and the swelling occurs where least resistance is offered by the epithelium, namely, midway between the glands.

The glands themselves remain short, but their lumen is wider than in Stage I.

Stage III.—The Increase of Vessels. Figs. 3–22.

A uterus at this stage of menstruation is readily distinguished in superficial examination by its flushed and swollen surface.

In section the cause of the flush is seen to be an increase in the size and number of the vessels directly below the epithelium, and to their congestion.

The epithelium itself is considerably thinner than before, the cells being somewhat flattened out though they are still cubical; this thinning is due to stretching, and there are now signs of cell division in this layer.

The nuclei of the stroma which were very densely packed in the preceding stage are now somewhat less dense, not on account of any decrease in their number, but in consequence of the increased room made for them by the stretching of the epithelium and its growth.

A reference to fig. 3 shows that advantage has been taken of this increased room, especially by those stroma cells lying directly beneath the epithelium; they have extended themselves and, in consequence, a layer of more scattered nuclei now intervenes between the epithelium and the denser layer below.

The thickness of the mucosa is thus increased in Stage III.

The blood vessels, which in Stage II. had begun to grow larger, are now larger still and more numerous. They have forced themselves through the dense layer of the stroma, reached the comparatively open tissue underlying the epithelium, and have there become enlarged to form flattened vessels which are gorged with blood.

The growth in size of the vessels is shown in fig. 22 to be due to the division and consequent increase of the cells forming the walls of the vessels. The vessels drawn in this figure lie below the denser layer of the stroma, but a similar increase in the cells of the walls of the more superficial vessels is also seen.

The increase in the number of the vessels, hyperplasia, may be a natural result following, and due to, hyperplasia of the stroma, according to ZIEGLER (85); and the congestion, to an increased flow of blood which is more marked in the next stage.

There is no change in the constitution of the deeper portion of the stroma, and no change in the glands during Stage III.

The number of the leucocytes in the vessels is increasing somewhat.

It is noticeable that many of the nuclei of the stroma in fig. 3 are smaller than they are in fig. 2. I have made a large number of measurements of these nuclei in different regions of the mucosa at the various stages of menstruation, with ZEISS' E. lens and occ. 3, and find there is a variation in size during Stages II. and III., a considerable number of the nuclei in the region of the denser portion of the layer being smaller than the rest. These small nuclei measure ·005 millim., while the usual size of nuclei during Stage I. is ·0075 millim.

The glands are much the same in length as they are in Stage II., but their lumen is still wider, and excretive action is apparent.

So far then, the changes which have taken place are changes due to the growth of the stroma or of the vessels contained therein.

C. *Period of Degeneration.*

Stage IV.—The Breaking down of Vessels. Figs. 4, 17, 18, 19, 23, 24, 25, 37.

This stage, which is perhaps the most important and instructive of all, witnesses remarkable changes in the constitution of the mucosa.

Further swelling of the mucosa takes place, there is a growth of internuclear material of the stroma, and the nuclei which formed the dense layer of the previous stage become consequently more scattered. Simple hypertrophy follows, probably in consequence of the increased blood-pressure described in Stages II. and III. and which exists now to a greater extent (85), and degeneration supervenes in the superficial region of the mucosa.

The walls of the superficial vessels, which are dilated, rupture, and the red blood corpuscles, with which they are densely charged, escape and are scattered about in the network of the stroma. This extravasated blood is present below the whole of the uterine epithelium and causes a deep flush over the whole surface of the mucosa readily recognized with the naked eye.

The histological changes which take place in this stage are as follows :

The cells of the uterine epithelium increase in size and their nuclei become paler, the nuclear network less pronounced and frequently invisible, and the nodal points of the network combine to form a large, darkly staining nucleolus situated at the base of the nucleus (fig. 19).

The protoplasm of the epithelial cells is still continuous with the protoplasmic processes of the stroma.

The nuclei of the glandular epithelium exhibit less change, they become rounder than formerly and stain less deeply than they did during Stage I. ; a nuclear network, however, commonly exists, and there are several nucleoli, as formerly. The cells of the glands are the same as before and the basement membrane is present (fig. 18).

With regard to the stroma and its nuclei. The dense layer is still present in places and nuclei undergoing division, although much more rarely seen, still exist in this stage (fig. 17). As I have already mentioned, the mucosa is now still further swollen ; fig. 4 is taken from a region so much swollen that the dense layer has altogether disappeared, and here the change in the constitution of the protoplasmic material of the stroma can be most clearly seen.

The protoplasmic processes are not so definitely marked, and are more irregular than in Stage I. ; there is an increase in volume of the protoplasm, and a corresponding decrease in density and consistency (compare figs. 14 and 24).

The nuclei have also become larger than they were in Stages II. and III., they are more rounded, stain less deeply, and exhibit a nuclear network and many deeply staining nucleoli (compare figs. 15 and 24); indeed many of them are larger than those in Stage I.

These changes are undoubtedly of the nature of hypertrophy.

The greatest change, however, is noticeable in the cells forming the walls of the vessels, which also undergo hypertrophy. Fig. 23 is a drawing of an early stage of the process in a small vessel near the surface of the mucosa; the nuclei are much swollen and stain but lightly.

Fig. 24 shows a dilated capillary in an advanced stage, in which the nuclei and cells are still further enlarged, and in which the walls of the vessel have broken down, distributing the blood corpuscles amongst the network of the surrounding stroma. Both these drawings are taken from a uterus of Stage IV., from the region close to the uterine epithelium.

The hypertrophy of the vessel's wall is probably consequent upon increased blood-pressure (ZIEGLER, 85), while the rupture of the vessels is due to degeneration, and the decreased resisting power of their walls. A withdrawal of efficient support from the surrounding tissue of the stroma, brought about by the increased swelling of the mucosa, and the extension of the protoplasmic processes of the stroma, combined with their hypertrophy and degeneration, no doubt assist the rupture.

Further, there can be little doubt that similar changes are affecting the other parts of the mucosa, both epithelial and stroma tissue. It is very noticeable, however, that both hypertrophy and degeneration are most active in the superficial region, and that the deeper tissue is less and less affected in proportion to its remoteness from the surface.

The cells of the walls of the vessels in the deeper mucosa are hypertrophied (fig. 25), and strands of protoplasm project across the lumen of the vessels, but the degenerative changes are comparatively slight; these vessels do not break down, and no extravasated blood is found at this or any other stage of menstruation in the deeper regions of the mucosa.

Some authors, FEOKTISTOW, KUNDRAT and ENGELMANN, and WILLIAMS (13, 34, and 78), have ascribed the breaking down of the tissue of the mucosa to fatty degeneration; I have been quite unable to detect any signs of fatty degeneration in any cells of the mucosa at any period of menstruation. This conclusion has been arrived at only after careful examination of specimens preserved and stained in various ways (see Methods), and I have been compelled to reject the theory of fatty degeneration, and to adopt that of simple hypertrophy followed by degeneration, probably of an amyloid or hyaline type, as an explanation of the cause of the phenomena described above.

The size of the hypertrophied nuclei of the stroma may reach, during Stage IV., ·0125 millim., which is a very considerably larger size than the nuclei of the stroma of Stage I. attain to, namely ·0075 millim.

There is a decided increase in the number of leucocytes during this stage. They occur in the deeper vessels in greater numbers than formerly, and appear to be travelling, from some other region of the body, towards the surface of the mucosa by means of the vessels.

In the deeper region of the mucosa, where there is no extravasation of blood, no leucocytes are present outside the walls of the blood vessels, that is to say, migration of leucocytes does not occur there.

Superficially, where the blood vessels have broken down, leucocytes are found, together with red blood corpuscles, distributed within the network of the stroma; but, in my opinion, their presence there is not due so much to voluntary wandering as to their expulsion from the vessels by means of the sweeping action of the rush of blood.

My reason for this view is, that more leucocytes are seen adhering to the remnants of the walls of the broken down vessels than are seen in a free wandering state in the stroma (figs. 24 and 37). Indeed the occurrence of wandering leucocytes is rare, while leucocytes adhering to the remains of ruptured vessels are very frequently seen.

In METCHNIKOFF'S recent work on inflammation (45) he defines that process as a reaction of leucocytes against a dangerous element, and describes a congregation of leucocytes taking place at the required spot, and the absorption by them of the irritating element.

He adds that diapedesis only takes place when the element to be attacked by the leucocyte is outside the walls of the vessels, where that element is inside the vessel no diapedesis occurs.

At this stage of menstruation then, the phenomena exhibited, namely, swelling of the tissue, dilatation and congestion of the vessels and a congregation of leucocytes, indicates the existence of a noxious element in the blood at the surface of the mucosa, which is of an inflammatory nature.

The size of the glands is now somewhat increased, they become longer, apparently on account of the superficial swelling of the mucosa and not by downward growth, their lumen is wide, and active excretion is going on.

Stage V.—The Formation of Lacunæ. Figs. 5, 6.

The extravasated blood collects during this stage into lacunæ. The lacunæ are first formed (fig. 5) in the midst of the loose layer of the stroma, situated between the epithelium and the remnants of the denser portion of the former layer. The dense tissue still persists here and there, although of rare occurrence now.

Between the primitive lacunæ and the epithelium the stroma network is filled with extravasated blood corpuscles, and gradually, as more blood pours out of the broken vessels, the lacunæ increase in size, push aside the stroma tissue and arrive at the boundary wall of the mucosa, namely, the uterine epithelium (fig. 6).

Lacunæ so situated may be recognized, when the mucosa is examined superficially, by the presence of dark red spots scattered all over the surface, and they give to the mucosa its characteristic appearance during this stage.

It is noticeable that the lacunæ are formed in the mucosa of the dorsal wall of the

uterus earlier than in the ventral wall, which shows that the increased supply of blood affects the dorsal before it affects the ventral wall.

At this stage there are still vessels in the superficial part of the mucosa that have not entirely broken down; eventually they do so, but many are seen in figs. 5 and 6 with complete walls.

In the deeper mucosa all the vessels remain intact, and the veins in that region and in the muscle layer contain but little blood.

The only change which takes place in the stroma is the occurrence of certain nuclei, but few in number, which stain differently from the rest. They are generally rounded opaque nuclei which stain deeply, and are highly refractive; they are most frequently seen near the surface, and are never seen deep down in the mucosa.

A similar appearance is assumed by some of the free leucocytes.

I was unable to determine what this change might mean by examination of specimens of this stage only, but the occurrence of similar nuclei in the same region during the following stage, together with large numbers of stroma cells whose protoplasm is barely discernible, and whose nuclei are much shrivelled, leads me to believe they exhibit now the first changes due to degeneration. The nuclei of a few cells of the uterine epithelium are similarly affected, but with that exception the epithelium, whether surface or glandular epithelium, remains the same as in Stage IV.

The condition of the glands is the same as in Stage IV.

Stage VI.—The Rupture of Lacunæ. Figs. 7, 20, 21, and 38.

The stage now to be considered exhibits the primary phases of denudation resulting from the preceding occurrences. The lacunæ now become very much enlarged, the degenerating epithelium which lies above them is greatly stretched and eventually ruptures, allowing the contents of the lacunæ to flow into the cavity of the uterus; but the lacunæ do not all rupture at once, and before a complete breakdown takes place blood escapes from them through small spaces in the epithelial outer wall (fig. 7).

In consequence of this, a superficial examination of the uterus discovers free blood in its cavity, while large spots of blood are still seen dotted about the mucosa.

In conjunction with the existence of these large lacunæ and the consequent stretching of the epithelium, the glands at this stage are widely open, and in some instances their epithelium even is thinned.

The pushing inwards into the cavity of the uterus of the interglandular material, doubtless produces the force which pulls the walls of the glands widely apart, and the fact that the mouths of the glands are wider open than the lower part, confirms this suggestion.

It is very generally noticeable that the largest lacunæ are in the region of a gland, the lacunar space often running downwards alongside the wall of the gland for a considerable distance. In one of the lacunæ drawn in fig. 7, a whole gland is seen to

be included and surrounded by the blood space, and this is not an uncommon occurrence.

The vessels in the deeper mucosa remain intact without exception, and a few, but only very few, dilated capillaries with complete walls are seen close to the epithelium in places where no lacuna is present.

The lacunæ themselves have no regular lower wall, they are bounded on that side by the stroma; in some places the stroma processes appear to combine to form a wall which restricts further inroad of the blood into the tissue, but generally there is no such wall, and irregularly branching diverticula exist continuous with the main lacuna and containing extravasated blood.

Leucocytes are now more numerous both in the deeper situated vessels and in the extravasated blood, but the greatest number by far are found sticking to the broken down walls of ruptured vessels near the surface.

Colonies of leucocytes are not unfrequently seen within the deeper vessels, and nuclear reproduction appears to be vigorously progressing there (fig. 38); leucocytes with a single nucleus, some of them dividing, and with two, three, and four nuclei are indiscriminately seen.

I have never seen the division of the leucocyte cell, and FLEMMING (14) states the division of the cell itself does not usually take place. The occurrence of an increased number of these cells in the deeper vessels would indicate that the increased number in the superficial tissues is brought about by an increased supply from other parts of the body; on the other hand, the occurrence of small leucocytes together with larger ones suggests local increase (fig. 38).

With regard to the proportion of leucocytes to red blood corpuscles, there are 2 per cent. of leucocytes in vessels which are full of blood, while in ruptured vessels out of which blood has escaped there are 18·75 per cent. of leucocytes. This fact shows very clearly that, since they do not migrate in any numbers from the vessels, the business of the leucocytes lies within the vessels and not directly with the degenerating tissues of the mucosa.

The probability of the accuracy of this view is substantially increased by an examination of the percentages in Stage VIII., a record of which will be found in that section.

A further change now takes place in the superficial stroma and in the epithelial cells (figs. 20, 21). Some of the superficial stroma retains the appearance observed in Stage IV. (figs. 18, 24, &c.), but a large proportion now consists of nuclei much shrivelled and surrounded by little or no appreciable protoplasm.

These shrivelled nuclei stain very deeply, and it is with difficulty that any internal structure can be seen. I have, however, been able to determine the existence of the remnants of a nuclear network in many of them, in others it is not possible to do so.

Close beneath the epithelium forming the outer covering of a lacuna, isolated stroma cells are scattered, these are all in the same condition as those described

above, and are undoubtedly undergoing degeneration (fig. 21); below the lacunæ however the tissue contains normal as well as shrivelled tissue, while deeper in the mucosa the stroma has changed but little.

The highly refractile nuclei seen in the previous stage are now recognized to be nuclei undergoing the preliminary stages of degeneration, their identity with the shrivelled nuclei of this stage is demonstrable.

The nuclei of the uterine epithelium, especially where that layer covers a lacuna, are now also distorted in shape and of irregular size, while the protoplasm of the cells has become less dense and has lost entirely those processes which connect the epithelium with the network of the stroma.

The nuclei of some of the glandular cells near the surface are also shrivelled.

There is little doubt that in all cases the cells so affected are destined to be thrown off during Stage VII.

The glands remain the same as they were in the last stage; excretion continues to manifest itself in the contents of the glands.

Stage VII.—The Formation of the Menstrual Clot. Figs. 8, 30.

During Stage VII. the full extent of the act of denudation is reached, the severe action disclosed being almost worthy of the term devastating. All over the body and fundus of the uterus the superficial portion, about one-third, of the mucosa, including uterine and glandular epithelium, stroma and blood-vessels, is cast away, leaving behind a ragged wreck of tissue, torn glands, ruptured vessels, jagged edges of stroma, and masses of blood corpuscles, which it would seem hardly possible could be satisfactorily healed without the aid of surgical treatment.

When it is remembered that this extensive denudation of the mucosa is a periodic function in the adult animal so long as it remains unimpregnated, and when the various and complicated structures to which the mucosa gives rise when a fertilized ovum is present be recollected, it must be owned that we have here to deal with tissue of a most unusual character.

I am not aware of any organ or tissue in the animal kingdom which is subjected periodically to such a completely devastating action as menstruation causes in the mucosa, and none endowed with such powers of recuperation as that tissue manifests.

Fig. 8 is an accurate representation of a portion of a section through a uterus undergoing denudation. The cavity of the uterus contains débris in the shape of pieces of glandular and uterine epithelium, masses of stroma and red blood corpuscles, and leucocytes, both fresh and degenerated; and there a clot is in the act of being formed from this débris.

The blood corpuscles are closely packed together, forming plastic cakes or lumps, and it is noteworthy there are no signs of threads of blood fibrin amongst the débris.

Many of the leucocytes in the uterine cavity are degenerated cells, their nuclei

being shrivelled and opaque, but living leucocytes are also seen, though not in a condition of active reproduction of their nuclei.

The percentage of leucocytes is now much more equal in the vessels and on the surface; in the vessels they exist at the rate of 3 per cent., and on the surface at 2·5 per cent., in comparison with the red blood corpuscles. This equalization is probably due to the fact that the ruptured vessels, to which, in the previous stages, a great number of leucocytes were found adhering, have been themselves cast off, and their contents mingled with the extravasated blood. A continued supply is, however, maintained in the vessels.

The stroma may be thrown off as scattered cells in masses, and the glands may be entirely ejected, though more usually only the superficial part of them is broken away.

The uterine epithelium is practically entirely destroyed over the whole surface of the mucosa; a few small pieces are seen in fig. 8, still retained *in situ*, but from their position and surroundings it is more than probable they will be swept away before the process is completed.

The portion of the mucosa thus cast off I propose to call the mucosa menstrualis, in accordance with WYDER'S (82) suggestion, whose reasons for rejecting the term decidua menstrualis—namely, the absence of decidual cells in the menstrual mucosa—appear to me sound.

In the deeper part of the mucosa the stroma suffers no change, the blood-vessels there are still possessed of complete walls, and are larger and more numerous than before, and there is no sign of extravasated blood in this region.

Many of the stroma nuclei on the surface are shrivelled, and will doubtless be rejected eventually, the remainder appear like those drawn from a specimen of Stage VI., marked st_1 in fig. 20.

Near the surface, vessels with complete walls are very rarely met with in sections; most of the blood in that region, and there is no inconsiderable amount of blood still remaining within the mucosa, is contained in lacuna spaces, some of which are in direct communication with the cavity of the uterus, while others are completely enclosed by, and retained within, the stroma (fig. 8).

Those of the glands which remain deeply embedded are in a condition of considerable activity, if we may judge from the material contained therein, but they, also, usually contain blood and cast-off cells, which have been washed into them through the mouth. The necks of these remaining glands project into the uterine cavity, often unsupported by any other tissue.

Here the period of degeneration comes to a close; beginning with the breaking down of blood-vessels, it passes through the stages of lacuna formation, and culminates in the casting away of the menstrual mucosa.

D. Period of Recuperation.

Stage VIII.—The Recuperation. Figs. 9 to 12, 26 to 29, 31 to 36, 39 and 40.

The history of the recuperation of the mucosa comprises an account of five important processes, namely :—

1. The re-formation of the epithelium.
2. The reduction of the blood supply.
3. The formation of new and recuperation of old blood-vessels.
4. The changes which take place in the stroma.
5. The behaviour of the leucocytes.

1. *The Re-formation of the Epithelium.*—This process begins before the menstrual clot is expelled from the uterus, and prior to the cessation of the flow of blood into the uterine cavity.

In the specimen from which fig. 9 is taken, a clot was present in the uterus, and fresh blood was flowing from the mucosa, but in various places on the uterine wall new epithelium was forming (*ep.ut.*).

Fig. 33 is an enlarged representation of some of that epithelium which is formed of flattened cells; it covers a stroma of scattered nuclei embedded in protoplasm, whose long, irregular protoplasmic processes are disposed more or less parallel to the plane of the epithelium, and the meshes formed by these processes are filled with red blood corpuscles and here and there a leucocyte.

These protoplasmic processes are directly continuous with the protoplasm of the newly-formed epithelial cells; the nuclei of the stroma and of the epithelium are remarkably alike, their structure is similar, they stain similarly, and, as far as I can discern, they are at this stage identical.

I have found it impossible to trace many pieces of such flattened epithelium to a point of origin from uterine and glandular epithelium already existing. As I will show directly, the torn epithelium at the mouths of the glands does give rise to some of the new uterine epithelium, but there is a large proportion of epithelium now formed, which I cannot convince myself is derived from any pre-existing epithelial structures.

In the drawing before us (fig. 33) there is a cell marked y; this cell is undoubtedly included in the same layer with the cells forming the epithelium, and at the same time it is quite impossible to separate it from the stroma cell x, which lies directly below it in the figure. The cell x is, without doubt, a stroma cell in close contact with three other stroma cells lying alongside of it, and its intimate relation with y makes it exceedingly probable the latter has been drawn into its present position from below.

Such instances as this are very numerous where isolated flattened epithelium is in

course of formation; sometimes a cell like x will be found somewhat more completely included in the epithelial layer, sometimes less completely removed from the rest of the stroma.

The transference of elements of the stroma to the epithelial layer is not, however, confined to such places as fig. 33 represents. Fig. 31 is a drawing of the growing point of a piece of epithelium, which is directly connected with the epithelium of a gland at its mouth. That end of the epithelial layer, marked *ep.ut.*, consists of columnar cells, and is directed towards the mouth of the gland, while, at the opposite end, the cells are flattened and the nuclei arranged longitudinally. Below the flattened epithelial cells and beyond them, is stroma tissue, which is so intimately connected with the former that it is quite impossible to determine to which layer it belongs now, or will belong in the future. Instances of this description are always very numerous, and increase the probability that stroma cells take part in the re-formation of the epithelium of the mucosa.

Other specimens, of which fig. 32 is an example, conclusively prove that some of the epithelium is formed by the division of cells already occupying that position. In this figure the nucleus of the terminal cell of a growing point of epithelium is seen in the actual process of simple division, and the relation of the stroma below, while showing connection with the epithelium, gives no indication of participation in the reproduction of that layer in the region from which this specimen was derived.

It is to be noted also in this specimen, that the nuclei of the epithelium, which are not yet columnar in arrangement, are closely packed, and have the appearance of having been produced *in situ* by division.

The further growth of the epithelium is shown in figs. 10, 11, 34, 35, and 36; during which the columnar arrangement is gradually resumed. At first (fig. 34) the nuclei are very irregular in shape, size, and arrangement; gradually, however (fig. 35), their arrangement becomes more uniform, and in fig. 36, which is taken from the same uterus from which fig. 10 is taken, they are but little different from the nuclei of the epithelium of Stage I. (fig. 14).

The cells marked d in figs. 34 and 35 are columnar cells, whose nuclei are undergoing simple division.

The so-called glands of the uterus are specialized portions of that epithelium which lines the cavity of the uterus, and as the deeper portions of the glands are not as a rule cast away with the menstrual mucosa, but remain firmly fixed in the deeper parts of the mucosa, their cells are at hand when the time comes for the re-formation of the uterine epithelium.

There is no doubt that a certain part of the new epithelium has its origin from the torn edges of the glands, but I have been able to assure myself that all the new epithelium has not such origin, and I have shown there are frequent instances of the occurrence of flattened epithelial cells on the surface of the torn mucosa, which are not connected with glandular epithelium, and which are derived from cells of the stroma;

further, I have shown that, at the growing point of epithelium already differentiated, stroma cells are probably drawn into the service, and assume the properties of epithelial cells.

The similarity of the nuclei in these two layers at the close of menstruation and during the recuperation stage, is perhaps further evidence in favour of my view.

I would here draw attention to a circumstance which may be considered to confirm the opinion that the stroma does give rise to epithelial cells.

There are, during Stage VIII., small masses of tissue not quite torn away from the rest of the mucosa, but hanging to it only by the protoplasmic processes of a few cells, and which consist of blood corpuscles and stroma cells. Some of these pieces are enclosed by the new epithelium, but some are not so enclosed. In the latter case the epithelium bores its way through the slender attachment, and so cuts off the dependent piece.

Two pieces of this description are shown in fig. 9 (marked x), and it is noticeable the outer layer of cells in one of these pieces has the appearance of flattened epithelium.

The outer layer of certain pieces is more marked than it is in others, but in all the same tendency is observed, and, in some, the likeness of the flattened outer layer to newly-formed flat epithelium is very remarkable.

Finally, the history of the development of the uterus shows that it is formed from the coalesced Müllerian ducts, and that the epithelium of the embryonic duct, which forms these parts, is at one time of a stratified character, becoming modified later into cylindrical epithelium (6 and 76).

This epithelium is derived from embryonic mesoderm cells in the embryo, from the same layer of cells, in fact, which gives rise to the rest of the mucosa.

It can, then, hardly be a matter of surprise to find, in dealing with a tissue which has so many primitive characteristics, that the new epithelium formed after the menstrual mucosa is cast off, is first of all formed of flat cells, and that its re-formation may be due largely to the specialization of cells from the same layer which, in the embryo, performed the same feat.

I should here draw attention to the absence, on the healing surface of the mucosa, of any pus. The multi-nucleated leucocytes, which give rise to pus, are either washed away with the menstrual flow, or included within the newly-formed vessels of the circulatory system.

2. *The Reduction of the Blood Supply.*—On this matter I have little to say. There is, undoubtedly, an escape of blood, while the menstrual clot is still in the uterus, and it appears that this flow is checked, if it does not altogether stop, when the clot is evacuated.

Helme (21) shows that an involuntary muscle during contraction becomes anæmic, and that the result of the contraction of the muscles of the uterus, which are involuntary muscles, is a diminution of the blood flow. It would thus seem possible that the

contractions of the uterus performed in order to expel the clot would have the effect of checking the flow of blood to the organ.

Again, as we have seen, epithelium grows over the torn mucosa before the clot is expelled. I cannot say it grows over the whole surface, but it undoubtedly encloses a considerable part of the stroma while the clot is in utero, and, in so doing, prevents hæmorrhage.

These two circumstances combined, probably suffice to check the flow of blood, which the completion of the epithelium and the formation of new blood vessels entirely stops.

3. *The Formation of New and the Recuperation of Old Blood Vessels.*—The formation of new capillaries is one of the earliest signs of recuperation. In fig. 9, although there is still much extravasated blood in the mucosa, many new blood vessels have been formed in the superficial region; while in fig. 10 all the extravasated blood has been enclosed within vessels, with the exception of a few isolated red blood corpuscles scattered here and there in the tissue. Newly-formed capillaries are shown in figs. 26 and 28.

As I have already shown in Stage VII., during which hypertrophy of the stroma prevails, extravasation of blood corpuscles takes place. The corpuscles lie within the meshes of the stroma, in spaces which are to some extent filled up by the distended protoplasm during this stage. When the hypertrophied tissue recuperates the distended protoplasm is largely withdrawn, and the resulting processes are fewer, firmer, more dense, and stronger; at the same time this withdrawal of the hypertrophied protoplasm leaves angular spaces in which the corpuscles lie.

Such a condition is attained during the early period of Stage VIII. Subsequently, in those spaces in which the blood corpuscles lie, the angularity gradually disappears, and a regular rounded smooth-walled space is formed, continuous with certain neighbouring spaces similarly constituted.

The protoplasm of the cells bounding these spaces flattens out, the nuclei of the cells becoming also flattened and elongated, and numerous fine capillary vessels are thus formed, continuous in the deeper parts of the mucosa with larger pre-existing capillaries, and so with the circulatory system.

These fine capillaries exist only temporarily; when the blood corpuscles are again drawn into the circulation, and when the mucosa has shrunk again to its resting condition, the fine capillaries are no longer seen; but during the time in which the reclaiming process goes on they exist in very large numbers.

It appears that the only known mode of creation of new vessels in pathological formations is by the development of offshoots from the walls of existing vessels (85); Quain (56) describes the usual method of the formation of vessels in the embryo by canalization of connecting tissue cells, and Balfour (2) describes also larger vessels formed from solid cords of cells, the central cells forming the corpuscles, and the peripheral cells the walls of the vessels.

None of these methods is adopted in the formation of the new capillary vessels of the mucosa. They are undoubedly formed by enclosing intercellular spaces with the protoplasmic processes of the stroma cells; they are developed in countless numbers; wherever a solitary corpuscle is present in the midst of the tissue, there a vessel is formed, they cannot, therefore, be derived from the cells of the walls of vessels already existing.

With regard to canalization there seems no reason at all to suppose that the spaces in the network of the stroma are intracellular. They are undoubtedly intercellular spaces. BALFOUR states that GÖTTE (18) finds that the larger vessels in the Frog are formed as longitudinal spaces, the walls of which are derived from the indifferent cells bounding these spaces, which become flattened and united into a continuous layer. This is the only observation which I have been able to find which is at all in accord with the description given above.

There is no appearance of disintegration in the blood corpuscles which are retained in the tissue of the mucosa; their even contour and general appearance is the same as before the rupture of the vessels.

When the final stage of recuperation is reached (fig. 11) the vessels all over the mucosa are reduced in size (compare figs. 9, 10, 11), the minute branches described above (fig. 26) are but rarely seen, most of them have entirely disappeared, and the extravasated blood has been drawn again into the circulation.

Fig. 28 shows the appearance of a capillary situated near the epithelium, about the close of the recuperation stage.

As to the recuperation of the old vessels, a stage is shown in figs. 27A and 27B. The hypertrophied nuclei become reduced in size, and the swollen protoplasm of the cells is contracted and becomes more dense (compare fig. 25). The inner boundary of the wall of the vessel is now once more sharply delineated, and the vessel itself reduced to its normal size. The vessels in both these figures (figs. 25 and 27) were situated in the deeper part of the mucosa.

4. *The Changes in the Stroma.*—These changes are practically the same as those changes which reduce the cells forming the walls of the hypertrophied vessels to a normal size and consistency. Just as the swollen nuclei and cell processes of the vessels in fig. 25 become reduced to the proportions of those in fig. 27; so the enlarged nuclei and swollen protoplasm of the stroma, seen in fig. 24, give place to the compact, darker staining nuclei and fine thread-like protoplasmic processes seen in fig. 28.

This change is not simultaneous, nor, apparently, very rapid; cells which are still hypertrophied are seen in the midst of other cells which have assumed their normal size, and it is easy to trace the gradual return of the tissue to a resting condition again.

The multiplication of the nuclei of the stroma goes on to a limited extent, especially in the early stages of recuperation and near the surface of the mucosa (such cells are

shown in figs. 31, 33, 34, and 36, and marked *d*), but the amount of tissue so formed is not great. The method employed is either constriction into two by amitotic division or fragmentation (fig. 29).

Here again my observations are at variance with ZIEGLER'S (84) conclusions, inasmuch as although the cells so formed constitute tissue which is probably destined to be cast off as the next menstrual mucosa, still that end will be preceded by a stage of very active reproduction; hence, although the product of these cells may be destined to die, yet amitotic division in their case now, does not indicate the end of the series of division.

The effect of the reduction in size of the hypertrophied mucosa and the effect of the withdrawal of the extravasated blood into the circulatory system, naturally is to reduce the bulk of the tissue enclosed by the new epithelium. In consequence of this reduction of bulk the tissue is at first very open, the stroma is then drawn together and the epithelium follows.

A stage is shown in fig. 10, in which the stroma has become more compact, leaving behind the thin layer of newly-formed epithelium, but retaining connection therewith by means of excessively long and very delicate protoplasmic processes.

The epithelium then follows, its flattened cells becoming converted into columnar cells, and thus increasing the thickness while decreasing the length of the layer.

The cells of the glands in the region of the mouth of the gland are similarly affected, as a comparison of figs. 10 and 11 will show.

A still more efficient means of reducing the length of the epithelium is a process of folding, which takes place in that layer on the surface of the mucosa and in the walls of the glands themselves.

This folding of the epithelium is shown in fig. 11, and it is by this means that new glands are formed, which take the place of those lost in the mucosa menstrualis.

It is worthy of note that these new glands are formed from newly-formed surface epithelium, as well as from epithelium which already functions as glandular epithelium.

5. *The Behaviour of the Leucocytes.*—The leucocytes seen in the earlier periods of Stage VIII. are very numerous, and it is a noteworthy fact they are, almost without exception, found congregated in the newly-formed capillaries, or included amongst the masses of red blood corpuscles which will eventually be enclosed within the circulatory system.

Isolated wandering leucocytes apart from red blood corpuscles, at this period are very rare indeed, and, after the new vessels are completed and all the extravasated blood reclaimed, I have never met with a wandering leucocyte.

The actual proportion of leucocytes to red blood corpuscles within the superficial vessels is much greater now than it ever has been before. Fig. 40 is a drawing of a newly-formed vessel, and the leucocytes therein reach the proportion of 47·115 per cent.

This is not an isolated instance; I have frequently seen such vessels containing more than 50 per cent. of leucocytes.

In this stage, as in the earlier stages, when the leucocytes first became numerous, active division of the nucleus is going on.

The horse-shoe nucleus, the large single round nucleus, or the same dividing, the small nucleus either single or in the act of division, and leucocytes with two, three, or four nuclei, are all commonly seen within the vessels (fig. 39A).

In one specimen I saw a leucocyte whose large single nucleus was in the act of division into four by fragmentation (fig. 39B); this, however, is an exceptional specimen, the commonest are those represented in fig. 39A.

The absence of the phenomena of diapedesis, the absence of wandering leucocytes in either the deep or superficial layers of the mucosa, and the fact that leucocytes take no part in the re-formation of the tissue are points of no little interest, and require further notice.

COHNHEIM asserted that colourless corpuscles of the blood are a source of the new tissue which an inflammatory process may produce, and he is supported by various writers, mention of whom is made in a paper by SHERRINGTON and BALLANCE (65).

Amongst these perhaps the chief supporter of COHNHEIM'S view is ZIEGLER (86, 87). SHERRINGTON and BALLANCE also give a list of writers who deny to the migrating leucocytes any power of further development, and seek to show by their own experiments that COHNHEIM and ZIEGLER are wrong.

Since then METCHNIKOFF (45) has attempted to prove that mononuclear leucocytes are capable of transformation into epithelial cells, and quotes researches to prove that the nuclei present in polynuclear leucocytes may fuse together and form a mononuclear leucocyte.

My researches, hitherto carried on upon preserved tissue only, and studied by means of sections, cannot be utilised with the hope of making important additions to the knowledge which has been gained by the admirable investigations of the writers quoted above; nevertheless there are certain facts shown in my preparations which are not without interest.

The peculiarities of the nucleus or nuclei of leucocytes and the readiness with which they stain, make them very prominent objects in section, and serve to distinguish them readily from the cells of the surrounding tissue; so that I have some confidence in stating they do not appear, in my specimens of recuperating mucosa, to take any part whatever in the re-formation of that tissue.

As I have already pointed out, the greatest proportion of leucocytes are always found in the vessels, not in the tissue. Further, not only is there no evidence of diapedesis of leucocytes, but they show no signs of taking advantage even of ruptured vessels in order to migrate into the surrounding tissue; their presence outside the ruptured vessels appears to be due either to the force of the rush of blood which sweeps them from their hold upon the walls of the vessels, or to the fact that they

are scattered by the breaking up of the tissue itself. At all events their dissipation either causes their degeneration *in situ*, or the loss by the menstrual flow of all those which are not included again in the circulatory system.

Under these circumstances the presence of leucocytes in such large numbers would appear to be unnecessary.

According to METCHNIKOFF, the congregation of the leucocytes in the vessels near the surface, indicates the presence there of noxious material. The casting off of the menstrual mucosa together with this irritating substance, and the rapid, clean healing of the wounded surface would have the effect of clearing away that which the leucocytes were summoned to absorb; their protective presence in this instance then is not required, and they may be said to have been induced to appear on the scene to undertake duties which are otherwise performed.

In a case of suppressed menstruation, possibly the leucocytes would play a very different part, and it would be a matter of great interest to determine what that part might be; but where menstruation is normal and where there is a sufficiently complete denudation, it does not seem improbable that the necessity for the presence of the leucocytes is by this means greatly reduced, if not altogether removed.

If this suggestion is correct, the absence of wandering leucocytes in the tissues and the freedom from pus on the wounded surface is rendered more intelligible; while the already noticed remarkable peculiarities which are observed during the process of menstruation are accentuated, and we have increased reason for the belief that we have here a recurrent process which is unique in the animal economy.

OVULATION.

The relation of ovulation to menstruation has long been, and still is, a matter of controversy, and I therefore paid some attention to the matter when removing the generative organs from the specimens of *S. entellus* obtained in Calcutta.

The results of these observations are as follow :—

In Stage I., of which stage six specimens were examined, no discharged follicles were seen in either ovary of any of them; in three specimens there were prominent Graafian vesicles, and in the remaining three there were none visible.

In Stage II. there were also six specimens; in none of them was there any sign of recent discharged follicles; but in one specimen two old cicatrices were seen in one ovary. In four specimens prominent vesicles were seen in one ovary or the other, and in two there were none visible.

In Stage III. there were four specimens, of which one showed a red corpus luteum in the right ovary. The fimbriated extremity of the Fallopian tube was remarkably pronounced, and spread out as if it had been recently active; but there was no sign of cilia on its epithelium, and no trace of an ovum either in the uterus or in the

Fallopian tube itself. The other three specimens had no discharged follicles; in one of them two prominent Graafian vesicles were present, but in the other two, none.

In Stage IV., of which there were six specimens, one showed a large pendent corpus luteum on the right ovary, and one showed evidences of cicatrices in the right ovary. Five specimens showed no discharged follicles, four of them no prominent vesicles, and two a few vesicles which were somewhat prominent.

In Stage V. there were five specimens, in none of which was a discharged follicle visible; in one there were, however, several small cicatrices in the right ovary. In three specimens there were more or less prominent Graafian vesicles, but in the other two none which were raised.

In Stage VI. there were five specimens also, one of which had an old corpus luteum in the left ovary, and one a cicatrice in the left ovary. None, however, had any recently discharged follicles; two were possessed of prominent vesicles, and the other three had none prominent.

In Stage VII. there were four specimens, in none of which was there a sign of a discharged follicle. Two of them had prominent vesicles and two none prominent.

In Stage VIII. there were twelve specimens; in none of them were there either corpora lutea or recently discharged follicles or cicatrices to be seen; in four of them there were prominent vesicles in one or other ovary, in four, semi-transparent spots could be discerned, and in the remaining four, none.

Besides these, in a specimen in which an embryo in utero was being aborted, there was a large reddish-yellow corpus luteum in the left ovary, and in two more specimens, which had recently borne young, there was a large corpus luteum in the left ovary of each of them; while in three specimens, which had borne young some time ago, and were then suckling them, no corpora lutea were seen, and no prominent Graafian vesicles.

Thus, as far as discharged follicles are concerned, it is seen that out of forty-two menstruating specimens, none of which had recently borne young, only two had a recent corpus luteum in their ovary. Such a result appears to me amply sufficient to warrant the statements:—

First, that ovulation does not necessarily occur during each menstrual period; and

Secondly, that menstruation is not brought about by ovulation.

It will be observed, however, that the only two recently discharged follicles which were seen, occurred in specimens of Stages III. and IV. of menstruation; and it will be remembered that the first great increase of the blood supply to the uterine mucosa takes place at these stages. It is no doubt possible that this increased blood supply may affect the ovary, and may have a tendency, by means of pressure to induce ovulation where an ovum in a sufficiently advanced stage of development is present. In my opinion, this is a very probable view; it does not, however, permit of the inference that an ovum is actually dehisced at each menstrual period, but rather that

if an ovum in a sufficiently ripe state be present, the congestion which occurs during the menstrual period may cause it to be shed.

It is quite possible such a circumstance may occur in animals which menstruate and whose generative organs are gorged with blood at these times, though I do not consider there is any definite proof of the fact: at any rate, it is generally believed that in the lower Mammals "heat" is coincident with ovulation, and in these animals it would seem highly probable that the congestion which occurs during "heat" may bring about the rupture of ripe follicles in the ovaries.

With regard to the prominent Graafian vesicles, it may be urged that these vesicles are on the point of discharging the ova contained therein, and that they would have done so before menstruation was over.

During Stages II. to VIII., that is during menstruation, eighteen specimens were seen in which there were prominent vesicles in one ovary or the other, while twenty-two specimens, during the same stages, had no prominent vesicles at all. So that it would seem quite certain that twenty-two of these individuals, out of a total of forty, would not have undergone ovulation during the menstrual period then in progress, under any circumstances; and this evidence is again sufficient to show that ovulation and menstruation are not necessarily simultaneous processes.

But I do not believe that the prominence of a vesicle is any proof whatever of its complete maturity.

It is not at all unusual to find very prominent Graafian vesicles alongside of newly discharged follicles in Rabbits' ovaries 36 hours after copulation, at which time fertilized ova are found already part way down the Fallopian tubes, and I question very much the value of results which have been deduced from assumed knowledge of the degree of ripeness of a Graafian vesicle.

The evidence here offered then, points to the conclusion that the ripening of an ovum in the ovary is independent of the process of menstruation, and that ovulation is neither the cause nor the necessary result of menstruation. It is possible, however, that the increased blood supply to the generative organs during menstruation may induce ovulation when a sufficiently ripe ovum is present.

To what extent coitus may exert influence in the same direction I am not in a position to say from observations on *S. entellus*. PLAYFAIR (54) seems to think the stimulus of sexual excitement may cause the rupture of a ripe follicle; and certain observations I have made on Rabbits, lead me to think this view is possibly correct.

ACCOUNT OF RECENT LITERATURE AND CONCLUSIONS.

1. *Menstruation in Monkeys.*

On the subject of the menstruation of Monkeys, little has been hitherto written. RENGGER (62) observed a discharge from the vagina of a species of *Cebus* which

recurred at intervals of three, six, or ten weeks, the periods being irregular and the amount of discharge small.

GEOFFROY SAINT-HILAIRE and CUVIER (16) described a discharge of blood, with enlargement of the sexual organs each month, in *Cercopithecus*, *Macacus*, and *Cynocephalus*—three species of Monkey. [See also EHRENBERG (9) and NUMAN (51)].

Recently J. BLAND SUTTON has paid some attention to the subject, and in a paper published in the 'British Gynæcological Journal' (74) has given an account of his observations.

He finds that *Macacus* menstruates fairly regularly, and that there is a discharge of blood. He states there is no shedding of the lining epithelium of the uterus, and no disintegration of the mucous membrane; the latter, however, becomes congested, and blood emerges therefrom in much the same way as blood escapes from the nasal or buccal cavities in Man, during congestion.

SUTTON'S results, then, differ much from those detailed in the present paper for *S. entellus*. His figures are too diagrammatic to enable one to form a very definite opinion, but it would appear probable he has missed my Stages IV., V., VI., and VII., unless, indeed, the menstrual process in *Macacus* is very much curtailed when the animal is kept in this country.

A cursory examination of the menstruating uteri of *M. rhesus*, which I collected in India, gives me very strong reason to believe that a process, almost identical with that described for *S. entellus*, takes place also in *M. rhesus* during menstruation.

Possibly the cold climate of England acts as a check on the free menstruation of animals which naturally live in a much warmer climate, and this may be the reason why SUTTON, who, I fancy, obtained all his material in London, did not see in them the denudation process.

The above is the only paper I know of in which any attempt is made to describe the histological changes which take place in the uterus of the Monkey during menstruation.

2. *Menstruation in Man.*

I pass now to the phenomena of menstruation as described for the human female. An immense amount of work has been done in this connection. I do not propose to enter here into an exhaustive criticism of the voluminous literature of the subject. From time to time critical accounts have been published, the most recent with which I am acquainted being MEYER'S (46) and STEINHAUS' (70), both of which appeared in 1890.

It appears to me advisable, however, to refer briefly to the work of some of the more recent authors, and to point out where their results and the results arrived at in the present paper differ or are in accord.

There are few observers who now hold the view that no denudation takes place during menstruation; most of them consider that, at any rate, the epithelium, or part

of it, is cast off, and many have come to the conclusion that, although WILLIAMS (78, 79, and 80) has possibly exaggerated the extent of the denudation, yet still a certain portion of the stroma is expelled as well as the epithelium of the mucosa.

It does not seem to be improbable that the extent of the denudation normally varies in different individuals, and, further, that the same individual experiences more or less severe menstrual denudation at different times. This variation, in the severity of the process, may possibly account for much of the difference of opinion found amongst gynæcologists on this matter; but a more probable cause of the various views held appears to me to be the fact, that a sufficient number of specimens of human menstruating uteri, in good preservation, are rarely obtainable by any one investigator. For instance, it is not unfrequently stated that uteri at the height of the menstrual period, and filled with blood, are found to be possessed of uterine epithelium intact, and such evidence is considered sufficient to prove that neither the epithelium nor the underlying stroma is cast off during the process. The evidence I have brought forward in this paper, however, shows that, although it is quite true the uterus may be filled with blood while the epithelium is apparently intact—the blood being derived from the lacunæ through minute ruptures in the epithelial covering—examinations of later stages do show denudation, and prove that the full height of the menstrual cycle is not reached when the blood first flows into the uterine cavity.

DE SINÉTY (68) examined the uteri of many women during different stages of menstruation, and he asserts that in no case was desquamation observed, and that the epithelium was always present. DE SINÉTY explains that the specimens he examined were taken from women who had died from severe cold, and were practically frozen; he claims that, on this account, his material was in a better state of preservation than could possibly be obtained in any other manner, and decides that when the uterine epithelium is shed it is due to pathological conditions.

It appears to me more than probable that the severe cold which caused the death of the women, also arrested the progress of menstruation, and that the uteri he examined were in a state of suppressed menstruation; if this is so, his results would be sufficiently explained.

The suppression of menstruation in consequence of a chill is a matter of very frequent occurrence, how much more then would cold which was sufficient to cause the death of the subject, serve to arrest the progress of a function which may be so very readily disarranged.

An extraordinary theory, broached by Dr. HOTTENIER, and drawn attention to by DE SINÉTY, is founded on these results. It claims that, as the menstrual blood cannot be shed between the epithelial cells, it follows that the glands are the channels through which the blood escapes; there appears, however, to be absolutely no evidence in favour of this view.

The work of KUNDRAT and ENGELMANN (34), reproduced in an article by the

latter author (11), is perhaps the most important contribution that favours the view that no denudation takes place; these authors state there is no shedding of mucous membrane; cells, however, were found among the débris of the menstrual flow, presumably epithelial cells, but it is denied that the whole of the epithelium is cast off.

A swelling of the mucosa is described by these authors, due to the growth of the stroma of the upper part of the mucosa, also an increase of intercellular substance, and an enlargement of glands and vessels, followed by hæmorrhage. The hæmorrhage, it is claimed, is always confined to the surface of the lining membrane, and is caused by the rupture of the vessels in that region; this rupture of vessels being due to disintegration changes (fatty degeneration) which is specially marked upon the surface of the uterus. It is concluded that the hæmorrhage is not due to congestion of the organ, because far greater hyperæmia exists in pregnant uteri without any hæmorrhage.

Much of this work is very much in accord with my own results, but appears to stop short at my Stage IV. The period of growth is fully described, but the period of degeneration is not completed, the swelling of the stroma, increase of vessels, their congestion and hæmorrhage due to hypertrophy and degenerative causes (not fatty degeneration, however) being described in the account I have given above, for *S. entellus*.

I fully agree with these authors that the rupture of the vessels is ultimately due to degeneration, but cannot go so far as to say it is not primarily due to congestion; hyperæmia undoubtedly precedes the rupture of the vessels, and there seems to be good reason to suppose that a state of congestion is naturally followed by degeneration of the walls of the vessels and the surrounding tissue. The fact that increased hyperæmia exists in pregnant uteri without hæmorrhage, may be readily accounted for by the presence of the embryonic membranes over the surface of the uterus.

Möricke (50) is more emphatic in his statement that the mucous membrane is neither partly nor wholly cast off during menstruation. He says that the inter-glandular stroma is not increased, and that fatty degeneration, except perhaps to a trifling degree, is never shown. He also describes an increase in the homogeneous ground substance of the mucosa, and states that the vessels enlarge, become filled with blood, and there is an occurrence of extravasation of blood in the upper layer of the mucosa.

This author, then, does not appear to distinguish a period of growth of the same extent as I have described, and denies the existence of a period of degeneration altogether.

More recently Oliver (52) has expressed somewhat similar views, and states that he has examined uteri (*post-mortem*) both before and during the menstrual period, and has never found evidence of any change in the tissue. So that here we find even a period of growth denied.

It is impossible to reconcile these results with my own researches or with those of the authors quoted below, and one can only suppose, either that the specimens examined were uteri of individuals who were all suffering from suppressed menstruation, a very improbable supposition, or that these authors have not been fortunate enough to obtain a complete series of menstruating uteri.

AVELING (1) urges the view that there is a periodical formation of a membrane lining the body of the uterus, the development taking place during the intermenstrual period; that in the absence of a fertilized ovum, degeneration, caused by a cessation of nutrition, loosens its attachments, and it is expelled by contractions of the uterus, generally in small portions, but sometimes whole, as a three-cornered bag.

Finally, he believes that menstruation is probably determined by the act of "denidation," as he calls it, because it is from the denided surface that the menstrual flow comes.

This author considers the formation of the membrane and menstruation as two separate processes, the former being a preparation of the uterus for the reception of an ovum, while the latter is a secondary process due to denidation.

I will refer to this view later on, and will here merely remark that my own results are to some extent in accord with those of AVELING. He finds and differentiates periods of growth and degeneration as I do, but he appears to consider them less closely allied than my observations allow me to admit.

WILLIAMS (78, 79, and 80) describes a period of growth in the mucous membrane prior to menstruation, and describes the latter as produced by fatty degeneration of the uterine mucosa. This degeneration, he says, commences within the internal os and extends to the fundus, is followed by disintegration; which includes the whole of the mucous membrane, the glandular and mucous elements, and the walls of the superficial vessels; and thus causes hæmorrhage. In this author's opinion the denudation is so complete that the muscular coat is laid bare. The re-formation of the mucous membrane is described as beginning at the internal os and extending gradually towards the fundus, the new tissue being produced partly from the fibres of the muscular coat and partly from the stroma.

WILLIAMS' results have not been generally accepted; it has been argued that his material, mostly derived from subjects who died from fever, was unsatisfactory, and that doubtless the completeness of the denudation was due to disintegrating changes produced, not by menstruation, but by the disease from which the patient suffered. Exception has also been taken to his description of the re-formation of the mucosa from the muscle layer.

WILLIAMS has attempted to meet this latter objection (79) by arguing that the inner muscle layer of the human uterus is really a portion of the mucosa, and he has presented a comparative account of the structure of the uterus in various animals in support of his view.

I have not myself had an opportunity of investigating the comparative anatomy of

the uterus, nor, what is more important, the comparative development of the mucosa, and cannot offer an opinion on the relation of the muscular layer of the human uterus, I can only say that in *S. entellus* the denudation is superficial and does not approach the internal muscle layer.

I do not agree with WILLIAMS in ascribing the degeneration to fatty degeneration, but that is a small point; our results agree as regards the occurrence of periods of growth, degeneration, and recuperation; but WILLIAMS denies there is any period of rest, and states the nearest approach to uterine rest is during the menstrual flow when disintegration is going on.

Here, again, our results differ; I find that the epithelium begins to re-form while the menstrual flow is still going on, and that there is certainly no sign of rest at that stage.

WILLIAMS appears to think the process of growth in the mucosa occupies the whole of the time after the cessation of the menstrual flow until degeneration again occurs; whereas I find there is a space of time after the flow has stopped, and after the recuperation has concluded, during which the tissue of the mucosa is in a state of rest.

UNDERHILL (77) finds in the uterus of a woman who died immediately after menstruation, that the superficial part of the mucosa was wanting, but he disagrees with WILLIAMS in stating that all the mucous layer is shed.

LEOPOLD'S researches (38) lead that author to express the view that pieces of the superficial mucosa are cast off, and that the bleeding is derived from the capillaries, which are much swollen, by diapedesis; and he denies that bleeding is due to fatty degeneration. He describes a growth of the mucosa which is so considerable that it almost entirely fills up the cavity of the uterus, prior to the bleeding, and a subsequent return to its normal thickness.

The regeneration of the mucous membrane, he states, begins at the close of the bleeding stage. The swollen vessels of the upper surface are partly resorbed, partly broken off, and the gaps left in the superficial mucosa by denudation are filled up by the growth of neighbouring cells, and the cylindrical epithelium of the glands. The author gives a description of the histological elements of the human mucosa which is very different from that which obtains in the mucosa of *S. entellus*.

I cannot but think it will be found that LEOPOLD'S results are based upon an incomplete series of menstruating uteri.

WYDER (82, 83) believes there is a variable amount of the upper part of the mucosa cast off in different cases, sometimes the whole of it being denuded, at other times the amount is minimal (SPIEGLEBERG (69)). In all cases, however, a well preserved portion is left behind. The denudation he considers due to menstrual bleeding and not to fatty degeneration, the latter, in his opinion, being a consequence of the destruction and denudation of the tissue after the bleeding. The regeneration of the

epithelium he describes as due, as much to the glandular as it is to the remaining epithelial cells of the surface of the uterus, which remain behind.

WYDER calls attention to the marked difference between the cells of the upper and middle layer of the mucosa of the menstruating uterus and the cells of the decidua of a pregnant uterus, and suggests the cast-off portion should be called mucosa menstrualis instead of decidua menstrualis, in order to avoid confusion. This suggestion I have adopted in the account given of my own observations. I cannot agree with this author that degeneration of the mucosa is due to the denudation process; in my preparations degenerated tissue is undoubtedly present before denudation takes place.

JOHNSTONE (29) describes the mucosa of the menstruating uterus as similar to that of the non-menstruating organ, except that the epithelium is cast off and washed away. He considers the material used by WILLIAMS to be unsatisfactory, and criticises AVELING'S observations as entirely erroneous. He believes the growth of the corpuscular element of the mucosa ("endometrium") is continually going on by means of the gradual growth of the granular elements contained in the "sustentacular threads," and not by division of the cells themselves; and that the products of this growth in the non-pregnant uterus are washed away by the menstrual flow. I cannot discover that JOHNSTONE presents sufficient evidence to render his views of the formation of cells *de novo* at all probable: and his description of the "continual" growth of the mucosa is probably due to the fact that he has not seen menstruating uteri throughout the whole of the denudation period.

OVERLACH (53) finds the upper surface of the mucosa is almost entirely cast off. He considers the cause of menstrual bleeding to be venous congestion, brought about by the compression of the veins in the muscular wall of the uterus, and the actual escape of blood to be derived from the capillaries within the mucosa by diapedesis, and from those on the surface by rupture. In contradistinction to WYDER, OVERLACH believes that a formation of decidual tissue does take place. (See also GUSSEROW (19), and LEVY (40)).

FEOKTISTOW (13) believes there is no doubt that fatty degeneration may appear in the menstruating mucosa, and that there may be a loss of uterine epithelium, but the menstrual bleeding he considers an inconstant and immaterial symptom.

KAHLDEN (30) says that in all probability the whole of the epithelium of the surface, together with a considerable part of the mucous membrane, is cast off during menstruation; a conclusion with which LÖHLEIN (41) does not agree.

Thus it is seen there are a great variety of views held by modern investigators of the process of menstruation in the human female, as to the actual phenomena which occur, almost as many views indeed as there are writers on the subject.

The extreme view on the one hand that there is no change in the tissue during menstruation is opposed by the extreme view on the other hand that highly specialized decidual tissue is formed in the mucosa at that time. Again, the statement that not even a portion of the epithelium is lost by denudation is opposed by

the statement that the whole of the epithelium, together with all the underlying mucous membrane, is discarded during menstruation.

To reconcile such diametrically opposite views is impossible. It is no doubt possible that all these extreme cases may have occurred, though, in my opinion, that is doubtful; but it is quite certain that neither the one nor the other is descriptive of the phenomena which normally occur in menstruating uteri. The majority of writers appear to hold that a growth of the stroma takes place, and that it is followed by more or less complete denudation of the epithelium and the superficial stroma; that the denudation is preceded by or accompanied by bleeding from the congested capillaries in the superficial mucosa, either by diapedesis or by rupture of the vessels, or by both processes; that more or less degeneration of the tissue of that region occurs, and that the denudation is due either to the extravasation of blood, or to the degeneration of the tissue.

These views are, in a general way, similar to those advanced by me for *S. entellus*; the details are very variably described however, and only extended researches can satisfactorily determine which are correct.

The difficulty experienced by any one investigator in obtaining a sufficient number of specimens of human uteri, and the rare opportunities which present themselves of getting healthy uteri immediately after death, have no doubt been the main causes of the different descriptions given, and the diversity of views held, of the changes which take place during menstruation; but it is also very possible that different individuals experience more or less severe menstrual periods, or that the same individual experiences more or less severe periods at different times.

In comparing the results arrived at by my investigations on *S. entellus* with the records of writers on menstruation in the human female, it should be remembered that I was fortunate enough to get an ample supply of well-preserved material and that the material was derived from healthy females, killed for the purpose.

This being so I have some confidence in my belief that the various phases represented in my figures are not abnormal phases, though I cannot assert they invariably occur in the same individual, or in another individual to the same extent. As a matter of fact, however, I have in no case relied upon a single specimen to prove the existence of any one stage; I have always had three or four, and generally more, specimens referable to the same stage.

3. *The Period of "Heat" in Animals.*

A comprehensive account of the period of "heat" in animals has still to be written. I do not attempt here to present an adequate account of what is known of the subject, but some interesting work has been done recently which has no little interest to students of gynæcology, and requires mention here.

Bonnet (3 and 4) describes the formation of pigment in the uterine mucous membrane of the Sheep from extravasated blood-corpuscles which he says are first

seen in the deeper part of the layer and are subsequently carried to the surface by wandering cells.

KASSANDER (31) finds scattered blood-corpuscles lying in the midst of the tissue of the uterine mucous membrane of the Sheep in an early stage of hæmorrhage; he states they rarely occur in the deeper tissue but they are seen in numbers near the surface; he denies the existence of the wandering cells described by BONNET, but agrees that the corpuscles give rise to pigment in the tissue.

ELLENBERGER (10) describes congestion of the sexual organs and secretion from their glands during "heat," he states also the mucous membrane of the uterus is swollen and reddened, and a little bleeding takes place on the surface of the organ. In Ruminants the bleeding occurs at the cotyledons.

BONNET in an article in the same work (5) confirms ELLENBERGER and adds, the bleeding may occur within the mucosa of the uterus.

RETTERER (63) again confirms ELLENBERGER'S statement of the modification of the mucous membrane, and describes other changes which take place in the mucosa of the Bitch during "heat," which are of great interest.

The capillaries, it seems, which are rare and small when the uterus is in a quiescent state, become during "heat" much more numerous and larger; their dilatation results in rupture in the superficial part of what he calls the "chorion," in which numerous spots of extravasated blood are formed. Blood, he adds, is poured into the cavity of the uterus, but he does not believe the uterine epithelium is shed. He finds the epithelium is less firmly attached to the "chorion" during "heat," and that it is absent here and there, but he attributes its disappearance to faulty manipulation. Finally he describes hypertrophy of the "chorion" during "heat," and shows that pigment is formed in the hæmorrhage centres from masses of red blood-corpuscles.

These observations of RETTERER'S are very interesting and do much to prove that menstruation and "heat" are processes very closely allied. They show that the mucosa of the Bitch undergoes changes probably (in the absence of figures it is not possible to say more) very similar to those described in the present paper from Stage I. to Stage V. or even VI., that is, as far as the formation of lacunæ (RETTERER'S "spots"), and probably as far as the escape of blood from the lacunæ into the uterine cavity. The denudation stage is not represented in the Dog according to RETTERER, although it seems to me very probable that the loss of epithelium, which he thinks due to faulty manipulation, may well be caused by denudation. This view is rendered all the more probable because the epithelium is described as less firmly attached to the "chorion" during "heat."

We may say then, that a period of growth followed by a period of degeneration occurs in the Dog during "heat," probably in much the same way as they occur in menstruation, except that the degenerative changes are not carried so far.

4. *Ovulation in the Human Female and other Animals.*

On the subject of ovulation in the human female, STEINHAUS (70) gives a very excellent *résumé* of the literature, and concludes that the evidence brought forward shows, in the first place, that ovulation in Man is a spontaneous occurrence, in so far as it is due to internal energy without the concurrence of provocation from the exterior; and in the second place that ovulation is not periodic, and does not necessarily occur in connection with menstruation.

REEVES JACKSON (59), who also gives a critical account of previous writers, concludes that ovulation and menstruation may occur independently, that ovulation is an irregular but constant function of the ovaries, while menstruation is a rhythmical function of the uterus. He considers that the maturation and rupture of the Graafian vesicles is not necessarily connected with menstruation, and that menstruation may persist after the removal of the ovaries. AVELING (1) says it seems certain that ova are discharged from the ovaries at irregular periods, and not once a month at or near the menstrual period. LAWSON TAIT (37) also believes that menstruation and ovulation are not concurrent; and a similar conclusion is come to by RAYMOND (58).

GUSSEROW (19) and LEVY (40), on the other hand, believe ovulation and menstruation are coincident; WILLIAMS (81) that they are closely connected, while LEOPOLD (38 and 39), after closely investigating the material at his command, considers there is not sufficient evidence to determine the question with certainty.

LÖWENTHAL (42) holds that the condition of bleeding of the uterus induces a force which acts as a cause for the bursting of a ripe follicle; but he considers the menstrual bleeding may appear without the simultaneous bursting of a follicle. Finally, SANDERS (64) seems to think that coitus is an excitable cause of ovulation.

The conclusion, that the majority of recent writers are in favour of the view that ovulation is not necessarily coincident with menstruation, is in harmony with the result at which I arrived after examining the ovaries of *S. entellus* in connection with menstruation; further, my suggestion that the increased blood supply to the generative organs during menstruation may induce ovulation when a sufficiently ripe ovum is present, receives the support of LÖWENTHAL'S observations.

The method adopted to determine the question of the connection between ovulation and menstruation is beset with much difficulty. It is desired to know the age of corpora lutea, and the condition of ripeness of prominent Graafian vesicles. In the first place I greatly doubt the possibility of determining accurately when a Graafian vesicle is perfectly ripe, and in the second place I doubt if it is possible to be assured of the exact age of a "false" corpus luteum.

LEOPOLD in his earlier paper makes allusions to corpora lutea one to two days old, three weeks old, or four weeks old; and states with regard to the Graafian vesicle of a girl who died just before menstruation, that if the girl had lived the follicle would have burst the next day; and WILLIAMS makes assumptions somewhat similar.

I would suggest that such statements can only be made if it is already assumed that the process of ovulation takes place at certain known times, only then, with the knowledge at present at our command, can the age of a corpus luteum or the date of the bursting of a follicle be determined. To assume this knowledge is, however, to presume acquaintance with the problem it is desired to solve, and I venture to think that results founded on this method are not trustworthy.

Ovulation in the lower Mammals is generally, if not universally, considered to be coincident with the period of "heat." RETTERER (63) says this is so in the Dog. He draws attention to the fact that if the ovum of a Fowl be prevented from entering the oviduct, albumen is still secreted by the latter, and round the albumen a shell is formed and it is laid. The author thinks the congestion of the uterus of the Dog is due to an analogous mechanism, and appears to assume that ovulation produces menstruation in Woman, and that "heat" and menstruation are analogous processes.

In the lower animals then, ovulation and "heat" are said to be coincident, but whether the latter induces the former, or the former the latter, there is no evidence to show.

5. *Some Theories of the Cause and Function of Menstruation and "Heat."*

With regard to the cause of the hæmorrhage :—AVELING (1) considers "denidation" is caused by a cessation of nutrition. KUNDRAT and ENGELMANN (34) go farther and urge the view that fatty degeneration is the cause of menstrual bleeding, an opinion shared by WILLIAMS (78) and opposed by WYDER (83). GOODMAN (17) holds that congestion is the principal factor in, if not the sole cause of hæmorrhage, and that congestion is produced by the contraction of involuntary muscles round the vessels. OVERLACH (53) also thinks congestion, caused by compression of veins in the muscle coat of the uterus, is the cause of menstrual bleeding.

JACOBI (28) suggests that the mechanical effects of pressure caused by the growth of the opposite walls of the uterus against each other, described also by LEOPOLD (38), is sufficient to bring about rupture.

Although I find congestion in the superficial vessels, I have no evidence of any compression of the veins in the muscular coat which would cause congestion, and HELME'S work (21) appears to be unfavourable to such a view ; also I cannot agree with JACOBI'S suggestion of the mechanical effect of pressure, there is no evidence whatever that any pressure is exerted in the case of *S. entellus*, the cavity of the uterus is not obliterated at any stage of menstruation, until the menstrual clot is formed and the period of recuperation sets in, and yet very extensive bleeding occurs in this animal. My own preparations show that hyperplasia of the vessels followed by congestion and degeneration is the immediate cause of the extravasation of blood and subsequent menstrual hæmorrhage.

The primary cause of menstruation remains unexplained ; the old view that ovula-

tion is the cause of menstruation is, in my opinion, no longer tenable. OLIVER (52) considers menstruation has a nervous origin.

The function of menstruation seems more capable of explanation. AVELING (1) broadly states it is a primary reproductive function. GEDDES and THOMPSON (15) that it is a means of getting rid of anabolic surplus in the absence of the consumption thereof by an embryo.

KUNDRAT (KUNDRAT and ENGELMANN (34)) more particularly defines menstruation as designed to prepare the uterus for the reception of an ovum, while his fellow author, ENGELMANN (11), does not share that view. LAWSON TAIT (37) also considers that menstruation is in reality a preparation of the surface of the mucosa for the retention of an ovum, while at the same time he draws attention to the fact that pregnancy is possible without menstruation. LÖWENTHAL (42) goes so far as to propound the belief that the menstrual "decidua" is actually produced by the embedding therein of an unfructified ovum, and that the pregnancy decidua is built up if the ovum is fertilized, whereas, if it is not fertilized, the decidua falls to pieces. He brings forward no evidence which, in my opinion, supports the first part of his theory.

JOHNSTONE (29) considers that the design of menstruation is to change the uterine mucosa, a view also held by FEOKTISTOW (13) and others.

In strong contrast with these views is that of KING (32). He considers menstruation is a disease, an abnormal, unnatural, acquired habit, due to the fact that Women do not breed early enough. The fact that vessels rupture during menstruation, he argues, is proof that the process is an unnatural one, and in support of his argument he urges that abnormal congestion in organs gives rise to fibroid growth, and that fibroid growths in the uterus are common.

The evidence which KING brings in support of his theory is criticized by STUDLEY (73), and shown to be capable of other interpretation, while the work of RETTERER (63) on the Bitch, my own researches on *S. entellus*, and KRIEGER (33), TILT (75), RACIBORSKI (57), PLOSS (55), VON ICARD (26), and many others on the human female, may be quoted as directly opposed thereto.

Finally, PLAYFAIR (54) says the purpose of the loss of blood in menstruation is quite unknown.

The view that menstruation is designed to prepare the uterus for the reception of an ovum, seems to be the view most generally maintained; it is held by those who believe denudation takes place and by those who believe no denudation occurs. The one presumably believes it is the growth of tissue which prepares the uterus for the reception of the ovum, the other that it is the changing of the tissue by denudation, which is the important phase of the preparation. These views are, therefore, contradictory, and, doubtless, the contradiction is due to the fact that the period of growth and the period of degeneration have not been clearly recognized. For my part, I consider there is strong reason to think that the growth of the stroma is, in fact, a

preparation of the uterus for the reception and retention of an ovum, and that the subsequent degeneration, bleeding, and denudation are due to the absence of a fertilized ovum in the uterus at that time.

6. *The Connection between "Heat" and Menstruation.*

Reeves Jackson (59) and Lawson Tait (37) deny that "heat" and menstruation are homologous, while Playfair (54) considers they are probably analogous functions. Retterer (63), who believes in the ovulation theory of menstruation, considers "heat" and menstruation are analogous; and certainly his work on the Bitch, and mine on *S. entellus*, show there is a marked similarity between the histological processes which occur during the period of "heat" and menstruation of these animals. This similarity is especially emphasized in regard to the period of growth, and I am much inclined to think it will be found that growth of the mucosa universally occurs in the uterus of animals "on heat." I have observed in the uterus of the Mole at breeding time and prior to fertilization that the mucosa is swollen and tumid; the same appearance is also present in the uterus of the Rabbit when "on heat"; and Playfair (54) says the mucous membrane of the human uterus becomes thickened and vascular before the ovum reaches the uterus.

The relation of "heat" to fertility, the accompanying desire for sexual intercourse, a desire which is absent in the females of the lower Mammals at all other times, and the coincidence of "heat" and ovulation, make it not surprising to find that this growth of the mucosa is recognized as one of the earliest phenomena attending the formation of the placenta. I have observed that this is so in the Mole (see also Strahl's figures (72)); Minot (47) and Masquelin and Swaen (43) find it in the Rabbit, and Heinricius (20) in the Dog.

So that in these animals, whatever may be the cause of this growth of the mucosa during "heat," its probable function is the preparation of the uterus for the reception of fertilised ova, which the coincidence of ovulation and "heat" enables the uterus to anticipate with some certainty.

I think it may be assumed that the majority of females "on heat" in the wild state are impregnated whenever their condition renders copulation possible, and this being so, it is not surprising to find the uterus anticipating the arrival of fertilised ova. In human beings, however, these relations no longer exist; menstruation is not coincident with ovulation nor does a desire for sexual intercourse prevail during menstruation; further, Ercolani (12) states that the growth of tissue to form the placenta in the human female is quite distinct from that of other animals; but in view of the most interesting researches of Hubrecht (25) on the Hedgehog this statement requires confirmation.

I conclude then, that the similarity of the histological processes which occur in "heat" and menstruation is enough to show that they are analogous processes, and I believe

that the differences which exist are referable to the increased complexity of the phenomena attending breeding in the higher animals.

I do not know whether Monkeys copulate during menstruation or not; that they have a special breeding season or seasons appears certain, but whether sexual intercourse is admitted at other times or not, is not, as far as I am aware, known.

In connection with this subject the nervous relation between the flushed area on the buttocks, thighs, and tail of *M. rhesus* and the vagina is of interest. The joint researches of LANGLEY and SHERRINGTON (36) and SHERRINGTON (66 and 67) show that the motor roots of the Ist, IInd, and IIIrd sacral nerves supply the vagina, while the sensory roots of these nerves supply the flushed area described above. This area is always more or less flushed in *M. rhesus*, but is specially noticeable in the female during menstruation and pregnancy, when it is very highly congested, and would undoubtedly appear to be influenced by sexual phenomena.

The uterus of the Rabbit, however, according to LANGLEY'S (35) observations, receives motor fibres from the sympathetic chain, from about the IVth to the VIth lumbar ganglia, and is not certainly affected by stimulation of the sacral nerves.

I have mentioned these facts because the swelling which is observed round the external generative organs of animals during the season of "heat," is probably homologous with the enormously swollen area exhibited by certain Baboons during menstruation, and with some portion, at any rate, of the flushed area of *M. rhesus* at this time, and it is of interest to know that there is a nervous connection between these parts and the vagina.

A further examination of the physiological relation between the vagina and the uterus would probably throw much light upon the origin of menstruation and "heat."

In conclusion, it appears to me that sufficient stress has not been laid upon the different periods of the menstrual process, and that a consideration of them, although it does not explain the origin, leads to an explanation of the function of menstruation.

The period of growth of the stroma is the primary phenomena attending menstruation. I cannot admit that AVELING (1) is right to separate the growth of the stroma from what he calls the "denidation." This growth of tissue is closely bound up, indeed is indissolubly connected, with the phenomena which subsequently appear; it is the primary phase of menstruation, and I am convinced it is to a determination of the cause or causes regulating and inciting this growth we must look for an explanation of the origin of the process.

NOTE.

Since finishing this paper, I have seen MARSHALL'S recent book on 'Vertebrate Embryology' (42A). In it he divides menstruation into four stages identical with the four periods into which I have divided the process in the present paper.

MARSHALL is also of opinion that the period of growth is in effect a preparation of the uterus for the reception of an embryo, but he goes further and seeks to show that

the degeneration stage is not to be regarded as an undoing of the preparation made during the period of growth, but as a further continuance in a modified form of the act of preparation, leaving the uterus in a condition in which, for further elaboration to occur, the presence of an embryo is necessary.

I do not understand from this account whether MARSHALL believes that the uterus is in a condition to receive an ovum during the period of degeneration, or whether, after the recuperation period is over, the uterus is in a condition in which, for further elaboration to occur, the presence of an embryo is necessary.

Neither of these views, however, appear to me tenable.

With regard to the first view, a glance at my fig. 8 will, I think, show that it is exceedingly improbable an embryo would be retained in the uterus in the face of the active denuding process which is there going on; and, in regard to the second view, its adoption seems to me to entail the rejection of his previous assertion that the period of growth is in effect a preparation of the uterus for the reception of an embryo.

It is true that ERCOLANI (12), MINOT (47), and others have shown that degenerative changes do occur in the mucosa during the formation of the placenta soon after the embryo becomes attached to the maternal tissue, but, as far as I can understand, the changes are due to absorption by the embryo, and are not in any way similar to the degeneration which precedes and accompanies denudation.

SUMMARY.

The phenomena of menstruation are grouped into four periods which are subdivided into eight stages.

A. Period of Rest.
    Stage I. The resting stage.
B. Period of Growth.
    Stage II. The growth of stroma.
    Stage III. The increase of vessels.
C. Period of Degeneration.
    Stage IV. The breaking down of vessels.
    Stage V. The formation of lacunæ.
    Stage VI. The rupture of lacunæ.
    Stage VII. The formation of the menstrual clot.
D. Period of Recuperation.
    Stage VIII. The recuperation stage.

Superficial Phenomena of Menstruation.

External.—A swelling of the labia and of the nipples takes place, and a discharge from the vagina, consisting of mucus, leucocytes, blood, stroma, and epithelial cells.

Internal. Stages I. and II.—Mucosa an opaque white colour, either smooth or swollen into folds, ridges, or polygonal areas by the growth of the stroma during Stage II.

Stages III. and IV.—Mucosa uniformly flushed when smooth, but when folded the flush is concentrated on the edge of the ridges. The flushing is exaggerated during Stage IV.

Stage V.—Dark red spots are seen on the mucosa—lacunæ. The increased supply of blood affects the dorsal before it affects the ventral wall of the uterus.

Stage VI.—Free blood is found in the cavity of the uterus, and is due to the rupture of the lacunæ.

Stage VII.—Shows the formation of the menstrual clot, which consists of red blood corpuscles, leucocytes, epithelial cells, and stroma.

Stage VIII.—The mucosa appears at first with a ragged surface, and then with a smooth one, the latter stage being due to the growth of the epithelium. The menstrual clot is still in the uterus at the early part of this stage, at the latter part the mucosa has a transparent appearance.

Histology of Menstruation.

General.—The body of the uterus consists of mucosa and muscle layers.

The mucosa is formed of uterine and glandular epithelium, a primitive tissue consisting of a network of protoplasm in which nuclei are embedded and which I have called stroma, blood vessels, and a few radial muscles.

The internal muscle layer is composed chiefly of circular bundles with fewer longitudinal bundles; the external muscle layer chiefly of longitudinal bundles with fewer circular bundles amongst them. The sheath is a thin layer of scattered circular and longitudinal muscle fibres, together with a few connective tissue cells, and is covered by a flat epithelium.

In the cervix, the mucosa gives place gradually to a layer of denser material, the cylindrical epithelium of which is not cast off during menstruation. The walls of the Fallopian tubes carry a continuation of the uterine mucosa as a thin layer of stroma surmounted by cylindrical epithelium. There is no change of structure in the tubes during menstruation.

A. *Period of Rest.*

Stage I.—The uterine epithelium is a single row of cubical or columnar cells, containing round nuclei, the outer edge of the epithelium is sharply defined in section, the protoplasm of the inner edge is continuous with the protoplasm of the stroma network below. The uterine epithelium is continuous with that of the glands, the latter rest on a basement membrane but have no sheath. The stroma

has round nuclei embedded in a continuous network of protoplasm, the processes are very fine and delicate.

For one-third of the depth of the mucosa the stroma is regularly disposed, below that, fibrils run through it fan-wise, they are formed of processes of the stroma joined together. The blood vessels are small, but fairly numerous.

B. *Period of Growth.*

Stage II.—An increase in the number of stroma nuclei by amitotic division, and probably fragmentation, causes swelling and increase of the density of the upper third of the mucosa—hyperplasia. Owing to pressure the nuclei become fusiform. In the deeper layer there is no change in the stroma. An enlargement of vessels in the deeper mucosa follows the growth of the stroma in the upper part. The swelling takes place in the interglandular regions. The epithelium of the uterus and glands is very little altered.

Stage III.—The dense layer of nuclei of the last stage is rendered less dense on account of the swelling of the stroma and the stretching of the epithelium covering it. Hyperplasia of the vessels takes place below the epithelium, giving rise to the flush seen on the surface.

The swelling of the stroma causes an increase in the thickness of the mucosa and a widening of the glands. The hyperplasia of the vessels is a natural result of hyperplasia of the stroma. The size of many of the stroma nuclei is reduced.

C. *Period of Degeneration.*

Stage IV.—Simple hypertrophy of the uterine epithelium, stroma, and walls of the vessels now appears all over the mucosa, followed by degeneration in the superficial region where the dilated, congested capillaries break down, and the blood contained therein is extravasated. I see no signs of fatty degeneration, and am inclined to consider the degeneration observed to be of the amyloid or hyaline type. There is a decided increase in the number of leucocytes, which travel to the surface of the mucosa by the blood vessels, collecting there in the dilated capillaries.

There is no sign of migration of leucocytes or diapedesis of red blood corpuscles, but where vessels are ruptured, leucocytes are swept out, together with red blood corpuscles, into the surrounding stroma tissue. The congregation of leucocytes in the dilated capillaries near the surface probably indicates the occurrence there of an inflammatory substance.

Stage V.—The extravasated blood collects into lacunæ, which are first formed within the stroma, but gradually extend themselves superficially, displace the intervening stroma tissue, and come to lie directly below the epithelium. All superficial dilated capillaries now break down, but vessels in the deeper mucosa remain intact. There is no trace of leucocytes or red blood corpuscles in the tissue of the deeper mucosa.

Certain stroma cells and free leucocytes now appear to be undergoing degeneration.

Stage VI.—The uterine epithelium and superficial stroma now shrivel up and become degenerate. The lacunæ increase greatly in size, and, in consequence of the rupture of the degenerated uterine epithelium covering them, the blood contained within them is poured into the uterine cavity.

The lacunæ are generally in the neighbourhood of glands, and sometimes they entirely surround a gland, so that when rupture takes place the whole gland is washed away. Large numbers of leucocytes are seen, for the most part within vessels, and, if the latter are ruptured, the leucocytes seem to stick to the remains of their walls rather than to migrate into the tissue.

Vigorous nuclear reproduction takes place in the leucocytes, but no division of the leucocyte cell was seen. It is probable the increased number of leucocytes is due to an increased supply rather than to reproduction *in situ*.

Stage VII.—Denudation now takes place, and is very complete; all the uterine epithelium, a portion of the glands, and in some places a whole gland, and a portion of the stroma layer are torn away, together with ruptured vessels, red blood corpuscles, and leucocytes—a severe, devastating, periodic action which is very remarkable. Much of the mucosa menstrualis consists of shrivelled degenerated cells, but there are many normal cells amongst them. A ragged surface is left behind, and the remaining stroma contains masses of extravasated blood. In the deeper parts of the mucosa there is no further change in the tissue.

D. *Period of Recuperation.*

Stage VIII.—The recuperation consists of the re-formation of the epithelium, partly from the torn edges of the glands and partly by means of the transformation of stroma elements into flat epithelium cells. Gradually the flat cells become more cubical. There is no pus formed on the wounded surface. There is a cessation of the blood flow, probably owing to uterine contractions. New capillaries are formed superficially from stroma cells surrounding intercellular spaces in which blood corpuscles lie. Great activity is exhibited in enclosing all the extravasated blood corpuscles which remain in the tissue, and in returning them to the circulatory system. These capillaries eventually disappear. There is a recuperation of the vessels in the deeper mucosa; they return to their normal size and consistency.

Further, there is a return of the stroma to its condition of rest, accompanied by a limited amount of multiplication of nuclei by amitotic division, and probably also fragmentation. A general shrinkage of the mucosa takes place, the stroma first retiring, the epithelium following, the cells of the latter becoming columnar in the process, and folds in that layer being formed which give rise to new glands.

The leucocytes which were left with the extravasated blood in the tissue are returned to the circulatory system by means of the new vessels; they do not form new tissue *in situ*, nor migrate, and seem to have been induced to appear on

the scene, in such large numbers, unnecessarily; the casting away of the menstrual mucosa, together with all noxious material, and the clean healing of the wounded surface, rendering their protective presence unnecessary.

Ovulation.—There appears to be sufficient proof that ovulation is neither the cause nor the necessary result of menstruation. It is possible, however, that the increased blood supply to the generative organs during menstruation may induce ovulation when a sufficiently ripe ovum is present.

Account of Recent Literature and Conclusions.

1. *The Menstruation in Monkeys.*—The only paper on the history of this subject is by SUTTON, who describes a discharge of blood into the uterus, but denies that any denudation takes place in *M. rhesus.* I have got menstruating uteri of *M. rhesus,* however, in which denudation is shown.

2. *The Menstruation in Man.*—On this subject a great variety of opinions are held. The majority of authors, however, hold that growth of the tissue of the mucosa takes place, followed by more or less denudation, and accompanied by bleeding from congested capillaries, either by diapedesis or rupture, or both processes; that degeneration occurs, and that denudation is due either to degeneration of tissue or extravasation of blood. These views are very similar to those advanced for *S. entellus* in this paper. The variety of views on human menstrual phenomena is probably due to the difficulty of obtaining a complete series of healthy uteri properly preserved.

3. *The Period of "Heat" in Animals.*—RETTERER'S observations show that the mucosa of the Bitch during "heat" undergoes changes probably very similar to those described for *S. entellus* from Stages I. to VI., the denudation not being represented according to this author, although there is an escape of blood. Periods of growth and degeneration, therefore, both occur in the mucosa of the Bitch during "heat."

4. *Ovulation in the Human Female and in other Animals.*—It is found that the majority of writers are in favour of the view that ovulation is not necessarily coincident with menstruation in the human female, a view in harmony with that expressed by me for *S. entellus,* whereas in the lower Mammals ovulation and "heat" appear to be inseparable.

5. *Some Theories of the Cause and Function of Menstruation and "Heat."*—The hæmorrhage during menstruation is chiefly attributed to either congestion or degeneration. The primary cause of menstruation remains unexplained. The function of menstruation is variously represented, but it is largely believed to be a preparation by the uterus for the reception of an ovum. I myself hold that the period of growth is a preparation for the reception and retention of an ovum, and that the subsequent degeneration is due to the fact that a fertilised ovum is not present in the uterus at the time.

6. *The Connection between "Heat" and Menstruation.*—The period of growth is found

alike in the phenomena attending "heat" and menstruation, and in the lower Mammals, at any rate, a similar growth is found in the early development of the placenta. The function of this growth I consider to represent the preparation of the uterus for the reception of an ovum, which the coincidence of "heat" and ovulation enables the uterus in these animals to anticipate with some certainty. The histological similarity of the mucosa during the period of "heat" in the Dog and menstruation in *S. entellus* shows that these processes are analogous, while the differences which exist are, in my opinion, referable to the increased complexity attending the process of breeding in the higher animals.

Conclusion.

In the description which has been given of the menstruation of *S. entellus*, attention has been drawn to the primitive nature of the stroma, of which the mucosa is largely composed. The most remarkable changes which take place in the mucosa have been indicated, and some idea given of the part played by the various tissues concerned. An endeavour has been made to establish the fact that the monthly history of the adult non-pregnant uterus consists of four periods, namely, A, rest; B, growth; C, degeneration; and D, recuperation. The existence of these periods, although they cannot be quite sharply defined, are, nevertheless, very marked and real, and they indicate that a substantial periodic growth of the mucosa is arrested by degenerative changes when a fertilised ovum is not present.

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DESCRIPTION OF PLATES.

Reference Letters.

a.	Artery.
b. m.	Basement membrane.
bl. ex.	Extravasated blood in stroma.
bl. fr.	Free blood in uterine cavity.
bl. r.	Red blood corpuscles.
bl. v.	Blood vessels.
cap.	Capillaries.
dor.	Dorsal.
ep.gl.	Glandular epithelium.
ep.ut.	Uterine epithelium.
gl.	Gland.
lac.	Lacuna.
leu.	Leucocyte.
mc.	Mucosa.
msl.cl.	Circular muscles.
msl.lg.	Longitudinal muscles.
msl.rd.	Radial muscles.
sh.	Sheath.
str.	Stroma.
v.	Vein.
vent.	Ventral.

The sections are cut through the body of the uterus at right angles to its antero-posterior plane, and vertical to the wall of the uterus.

The figs. 1 to 11 are drawn with ZEISS' E. objective and No. 4 eye-piece; fig. 12 with ZEISS' *a** objective and No. 2 eye-piece; figs. 13 to 30 and 32 to 39 with REICHERT'S $\frac{1}{16}$th oil immersion objective and No. 4 eye-piece; and figs. 31 and 40 with the same objective and No. 2 eye-piece.

All the drawings were made with the aid of the camera lucida. In the coloured drawings the yellow colour represents blood; in most of the figures the blood corpuscles are not indicated individually.

PLATE 35.

Fig. 1. A section through the vertical wall of a uterus, Stage I. Showing a portion of the mucosa and a small portion of the inner muscular layer. The thin lines running from the deeper part of the stroma outwards are fibrils only present at this stage.

Fig. 2. A section through the ventral wall of a uterus, Stage II. Showing a portion of the mucosa and a small portion of the inner muscular layer. The nuclei of the superficial portion of the stroma are densely packed and fusiform in shape.

Fig. 3. A section through the dorsal wall of a uterus, Stage III. Showing a portion of the mucosa only. The dense layer of the stroma nuclei is more restricted, the blood vessels are larger, and many lie flattened out close beneath the epithelium.

Fig. 4. A section through the dorsal wall of a uterus, Stage IV. Showing a portion of the mucosa only. Many of the superficial vessels have broken down, and extravasated blood lies amidst the stroma network.

PLATE 36.

Fig. 5. A section through the dorsal wall of a uterus, Stage V. Showing a portion of the mucosa only. A lacuna in the midst of the stroma is seen, with extravasated blood around, in the network of the stroma. The nuclei of the stroma superficial to the dense layer, are again more rounded.

Fig. 6. A section through the dorsal wall of a uterus, Stage V. Showing a portion of the mucosa only. The vessels are more numerous, and larger and more congested. Much extravasated blood is in the stroma, and lacunæ are shown below the epithelium.

Fig. 7. A section through the lateral part of the ventral wall of a uterus, Stage VI. Showing a piece of the mucosa, and subjacent muscle layer. Large lacunæ are shown, which include nearly all the extravasated blood. Some free blood is seen in the cavity of the uterus, which has escaped through ruptures in the epithelial wall of the lacunæ.

PLATE 37.

Fig. 8. A section through the dorsal wall of a uterus, Stage VII. The lower part of the section shows a small part of one of the lateral walls of the uterus. A portion only of the mucosa is shown. Denudation is here represented,

and the severity of the process is shown. A few pieces of the uterine epithelium, *ep.ut*$_1$, remain *in situ*, the rest is cast off. The glands are much distorted; the cavity of the uterus is filled with débris, which will form the menstrual clot. Extravasated blood still remains in the stroma, but most of it is now free in the uterine cavity. The vessels in the deeper mucosa remain intact, there is no extravasated blood in that region.

PLATE 38.

Fig. 9. A section through the dorsal wall of a uterus, Stage VIII. Showing a portion of the mucosa only. Recuperation of the epithelium is in progress; it is much flattened, *ep.ut.* Pieces of the mucosa, *x*, are still being cast off; but the denuding process is almost over. The menstrual clot was still in this uterus. Extravasated blood is present in the stroma tissue.

Fig. 10. A section through the dorsal wall of a uterus, Stage VIII. Showing a portion of the mucosa only. The epithelium is now re-formed, but is not yet cubical. The stroma layer is shrinking, but remains attached to the epithelium by long protoplasmic processes. Extravasated blood is still present in the stroma, but numerous capillaries are being formed.

Fig. 11. A section through the dorsal wall of a uterus, Stage VIII. Showing a portion of the mucosa layer and subjacent muscles. The epithelium has followed the stroma, and is now closely attached to the latter; its cells are cubical and columnar, and it is folded in many places to form new glands. The vessels are more numerous, and larger than in fig. 1, but otherwise this uterus is very like a specimen of Stage I. There is now no extravasated blood present in the stroma.

PLATE 39.

Fig. 12. A section through the body of a uterus towards the close of Stage VIII. Showing the epithelium, glands, and stroma of the mucosa, the muscle layers and sheath, and the blood vessels in the external muscle layer. The vessels are not shown in the internal muscle layer, nor in the mucosa, for the sake of clearness.

Fig. 13. A piece of glandular epithelium from the same uterus drawn in fig. 1, Stage I. The basement membrane and ragged processes on the surface of the cells (cilia?) are shown.

Fig. 14. A piece of uterine epithelium and stroma from the same uterus, Stage I. The delicate protoplasmic processes of the stroma are shown in connection with the epithelial cells. The nuclei are round or oval, and have a nuclear network.

Fig. 15. A piece of the densely packed stroma seen in fig. 2, Stage II. The elongated nuclei are shown, many of which are undergoing amitotic division, *d*. Three stages of division are shown by d_2.

Fig. 16. Cells from the same uterus, Stage II.

a. Part of a capillary containing a leucocyte (*leu.*) and blood corpuscles.

b. Part of a capillary showing the nuclei of the cells forming its wall, b_1, b_2, b_3.

b_1 is at right angles to the flat plane of the cell.

b_2 is more oblique, and b_3 is a surface view of the nucleus of a cell forming the lower wall of the capillary, which the section cuts at the end of a curve.

c. Series of elongated nuclei of the stroma, showing amitotic division. $c_{2,\ 3,\ 4,\ 5}$ different stages of division.

d. Series of nuclei undergoing fragmentation. d_1 is a typical nucleus. $d_{2,\ 3,\ 4}$ show the fragmentation process.

h. Series of small nuclei undergoing division.

f_1. Is probably a similar cell to those of the *c* series, but shows fragmentation.

The *c* series, *h* series, and f_1 are commonly seen; $d_{2,\ 3,\ 4}$ rarely seen.

Fig. 17. Nuclei of the stroma, from the same uterus drawn in fig. 4, Stage IV. Showing amitotic division. They are commonly seen in the dense area of the stroma.

Fig. 18. Piece of glandular epithelium and stroma from deep down in the mucosa; from the same uterus as fig. 17 is taken, Stage IV. There is a basement membrane but no sheath. The stroma nuclei are elongated in the region of the gland. They are not dividing.

Fig. 19. A piece of lining epithelium from the same uterus as fig. 18 is taken, Stage IV. The nuclear network is barely visible in some, and not at all in other nuclei. One large nucleolus is present at the base of each cell in place of the nuclear network and chromatin granules seen in fig. 14. The protoplasm of the cells is still continuous with the stroma network.

Fig. 20. A piece of the stroma from near the surface of the same uterus as fig. 7 is taken, Stage VI. Some nuclei, st_1, remain like those in fig. 14, but many, st_2, show degeneration changes; they are shrivelled and stain darkly. The protoplasm of these latter cells is much reduced in amount, st_2.

Fig. 21. A piece of uterine epithelium from the surface of a lacuna, Stage VI., together with shrivelled stroma elements and blood corpuscles. The nuclei of the epithelium are also shrivelled and degenerating.

PLATE 40.

Fig. 22. An artery and vein from just below the dense area of the stroma, Stage III. Showing the multiplication of the cells forming the walls thereof, a and v_1.

Fig. 23. Part of the wall of a capillary from near the surface of the mucosa, Stage IV. Showing hypertrophy of the nuclei. This shows the condition of the cells prior to rupture of the vessel.

Fig. 24. A ruptured capillary and stroma, from near the surface of the mucosa, Stage IV. Hypertrophy of the nuclei and protoplasm of the stroma and vessel wall is shown, and the wall of the vessel has broken down, allowing the blood corpuscles to be extravasated in the meshes of the stroma. A leucocyte remains attached to the remnant of the ruptured vessel. The protoplasm of the cells is less sharply defined than it is in fig. 22.

Fig. 25. An artery and vein with stroma from the deeper part of the mucosa of the same uterus as fig. 24, Stage IV. The vessels are not ruptured, but the nuclei and protoplasm of the stroma and of the walls of the vessels are hypertrophied, and strands of protoplasm are stretched across the lumen of the vessels. A leucocyte is shown in the vein (*leu.*). The other cell in the vein belongs to the wall of the vessel which has been cut in section owing to the irregular bulging of the wall. The walls of the vessels are not so solid and compact as they are in fig. 22.

Fig. 26. A piece of the superficial stroma at Stage VIII. Showing newly formed capillaries. The nuclei and protoplasm of the cells are now no longer hypertrophied.

Fig. 27, A and B. An artery and vein from the deeper part of the mucosa, Stage VIII. Showing the recovery of hypertrophied vessels. The nuclei and protoplasm still show signs of the swelling seen in fig. 25, but not nearly to the same extent.

Fig. 28. A piece of the upper part of the mucosa from the same uterus as fig. 11, Stage VIII. Showing the newly-formed cubical epithelium; the nuclei of the stroma are now almost the same as in fig. 14, but still somewhat irregular in shape, and a definitely formed capillary is present.

Fig. 29. Stroma cells from the same uterus as fig. 9, Stage VIII. Showing, a, hypertrophied nucleus; *b.b.*, irregular nuclei, probably dividing; c_1, c_2, regular nuclei dividing; d_1, d_2, fragmentation of the nucleus.

Fig. 30. Débris from the cavity of the same uterus as fig. 8, Stage VII. Uterine and glandular epithelium, stroma nuclei, leucocytes, and red blood corpuscles; nearly all in degenerate condition.

PLATE 41.

Figs. 31 to 36 are taken from various uteri during Stage VIII., to illustrate the re-formation of the epithelium. The nuclei marked *d* are undergoing division.

Fig. 31. A section through a piece of growing epithelium connected with a gland at the lower end of the figure, *ep.ut.* The close connection between the stroma and the growing epithelium at the upper end of the section is shown, the two being in fact continuous there.

Fig. 32. A section through the growing point of epithelium, showing the amitotic division of the terminal cell.

Fig. 33. A section showing the flattened epithelium seen in fig. 9, and the scattered stroma nuclei with long protoplasmic processes, below. Blood corpuscles in great number are enclosed within the stroma network—extravasated blood. *x* is a stroma cell; *y*, a cell of the epithelial layer derived from the stroma; *z*, an epithelial cell.

Figs. 34 and 35. Sections of a slightly later stage, in which the flattened cells of the epithelium are becoming columnar. The nuclei are still of irregular shape and size.

Fig. 36. A section through the epithelium and superficial stroma, from the same uterus as fig. 10. Showing the more regular epithelium and the scattered nuclei and long processes of the underlying stroma. The nuclei of these layers are still irregular, but are more nearly approached to those seen in fig. 14 than heretofore. Minute capillaries are seen, *cap.*, and a few isolated blood corpuscles.

Figs. 37 to 40 are drawings of leucocytes.

Fig. 37 shows a leucocyte with stellate processes, adhering to the remains of an hypertrophied and broken down capillary, Stage IV.

Fig. 38. A colony of leucocytes within a vessel, Stage VI. The nuclei are in various stages of division. A sharp outline is invariably present round the cell; *d* indicates a cell whose single nucleus is dividing into two.

Figs. 39A and 39B are drawings of leucocytes which were situated within vessels at Stage VIII. Showing the various shaped nuclei seen, and leucocytes with one, two, three, and four nuclei within them; 39B shows a leucocyte whose single nucleus is dividing into four simultaneously—fragmentation. The chromatin within this nucleus is confined to the boundary-wall of the nucleus.

Fig. 40. Outline of a vessel, Stage VIII. Showing the very large proportion of leucocytes to red blood corpuscles, viz., 47·115 per cent. of leucocytes.

Fig. 1.

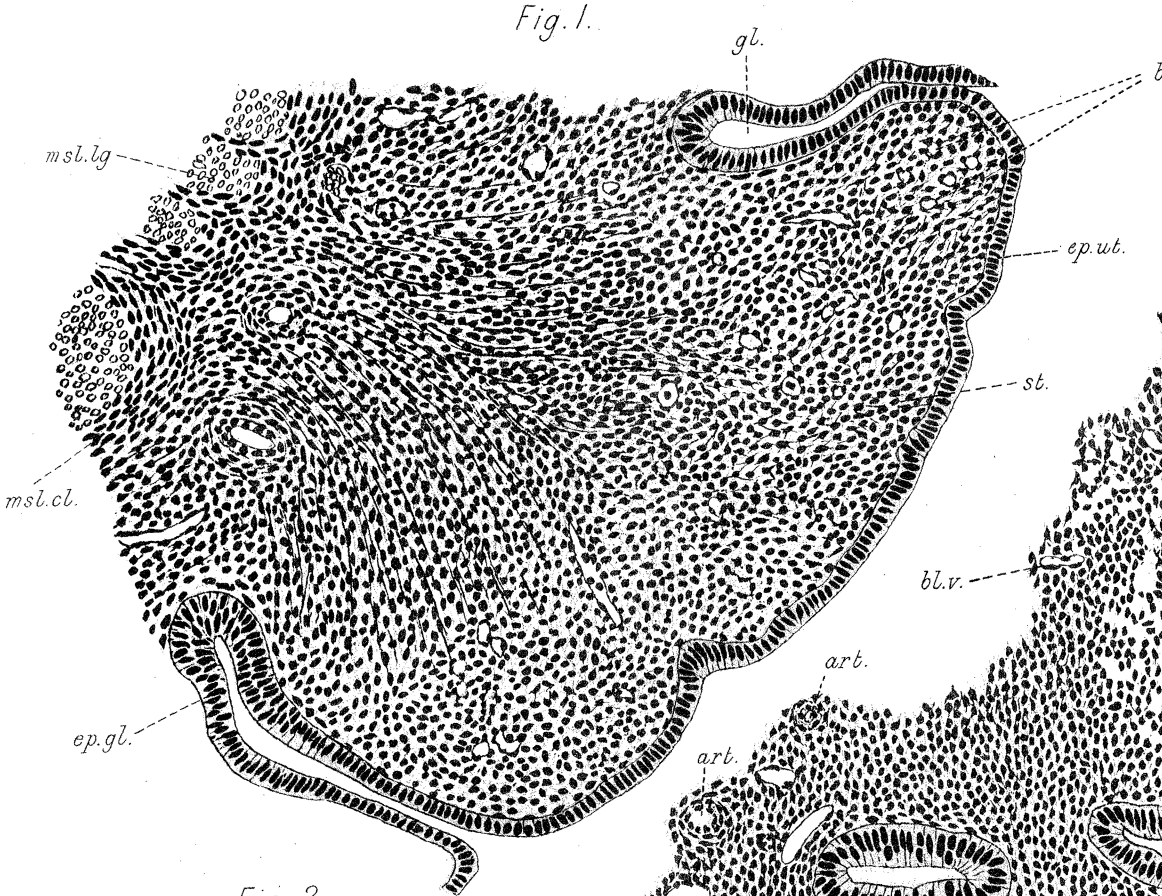
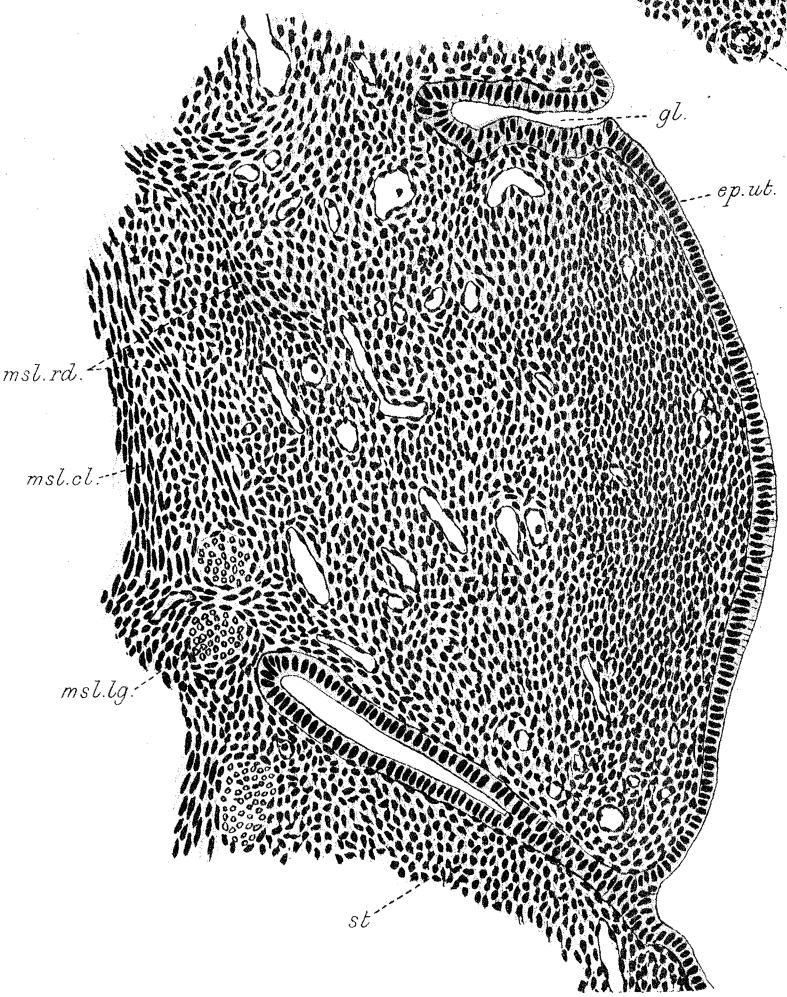


Fig. 4.

Fig. 2.



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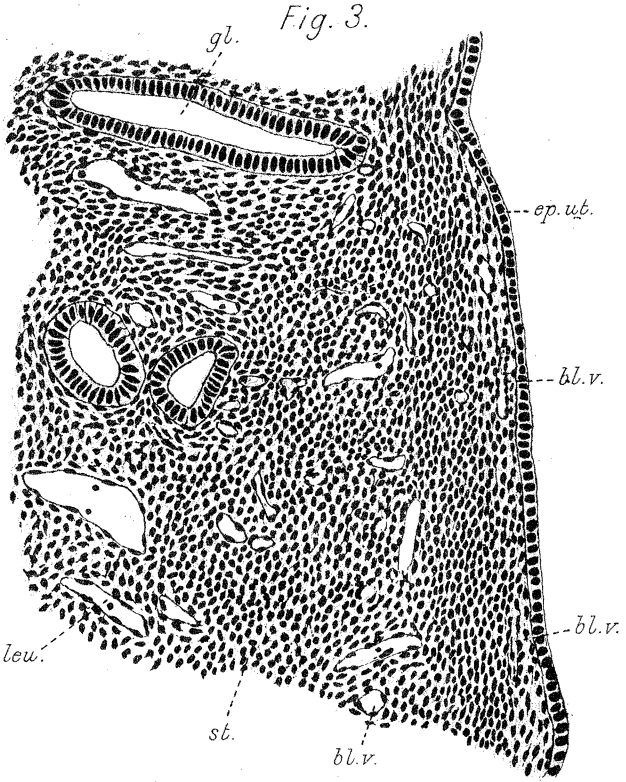

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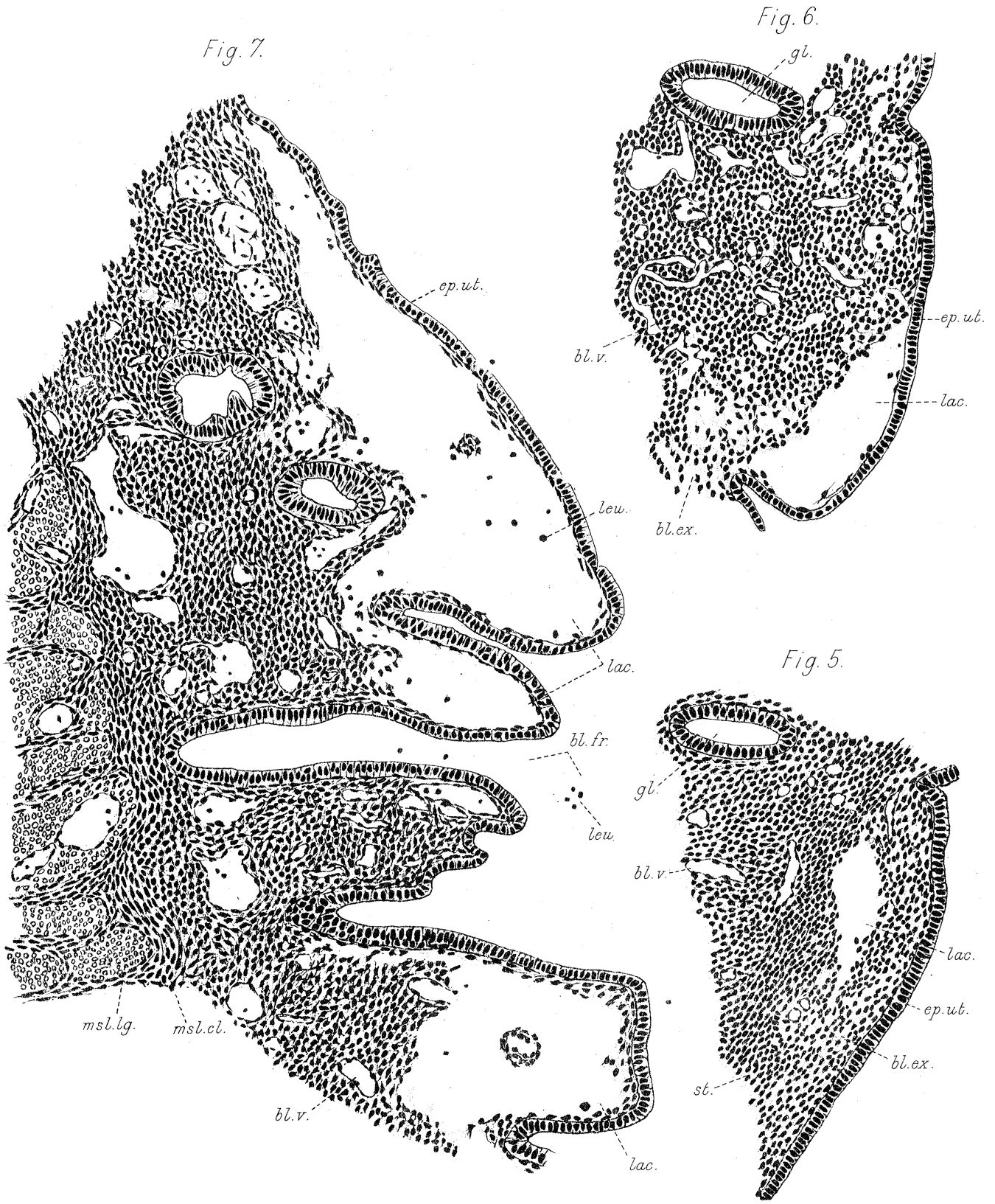
Fig. 7.
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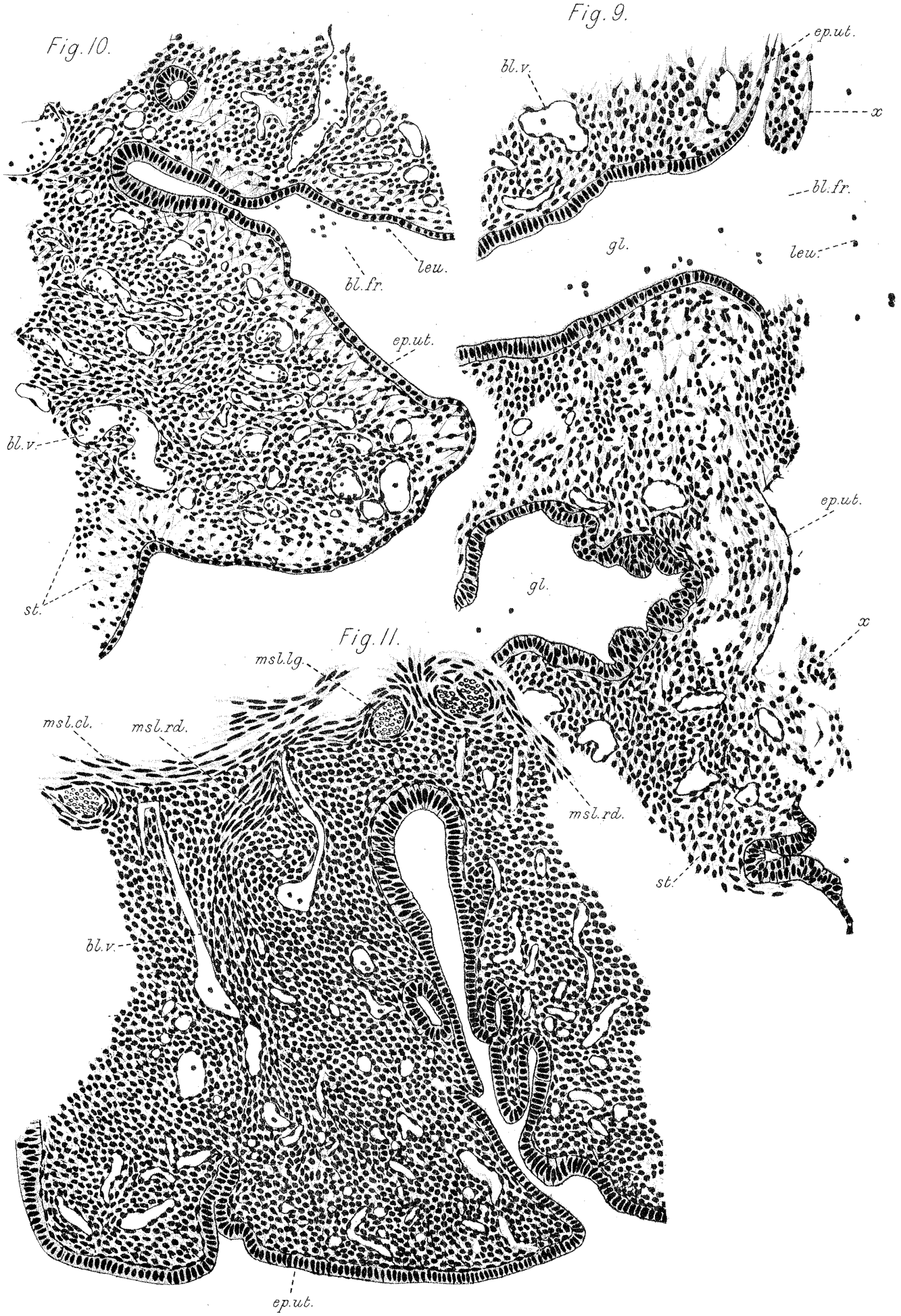

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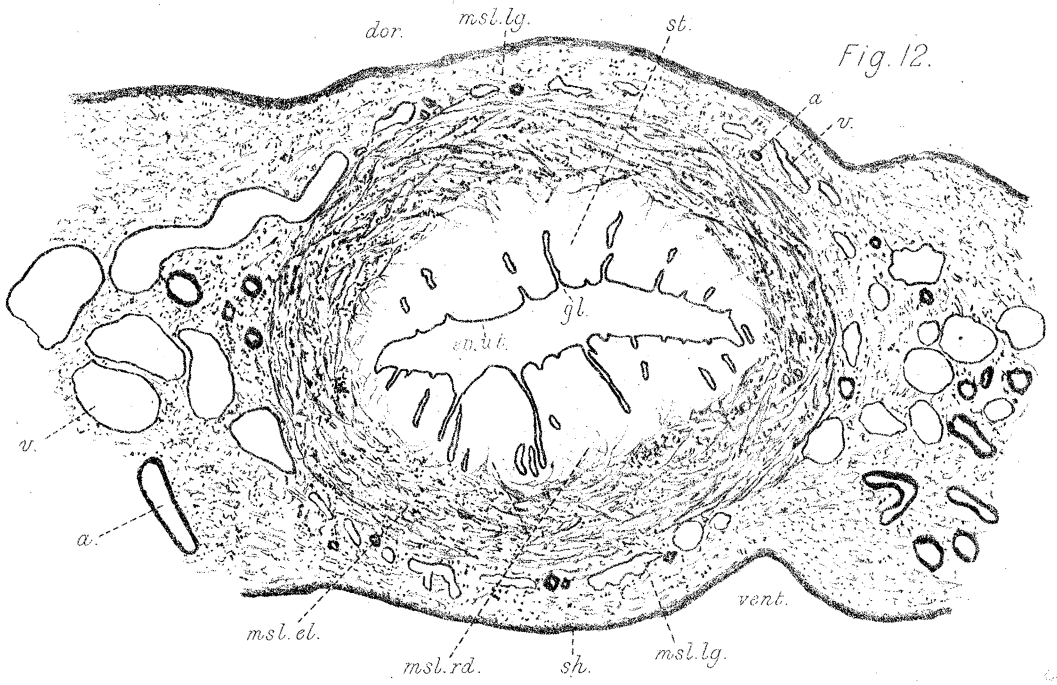
Fig. 12.



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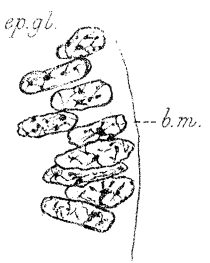
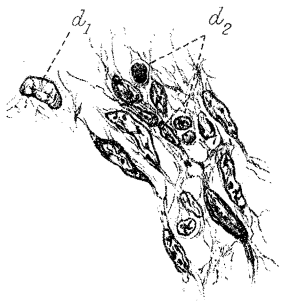


Fig. 14.

Fig. 15.



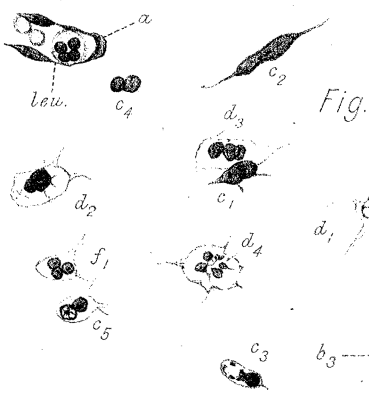


Fig. 16.

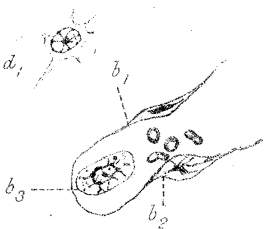
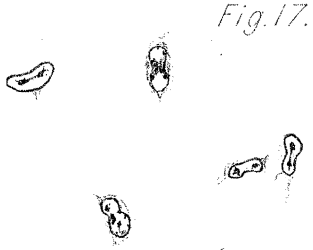


Fig. 17.



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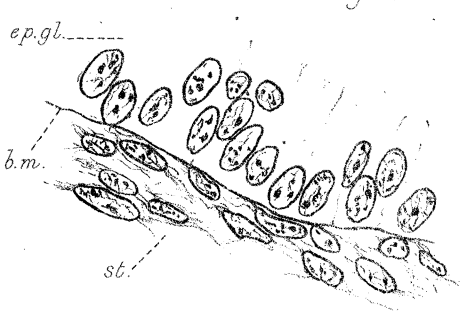

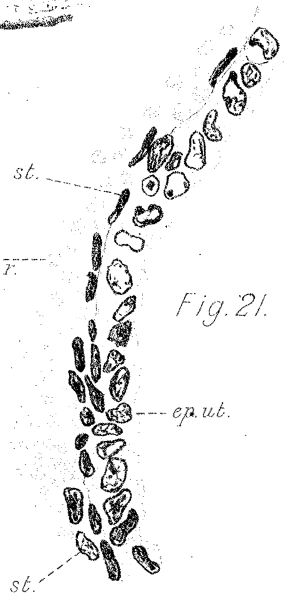

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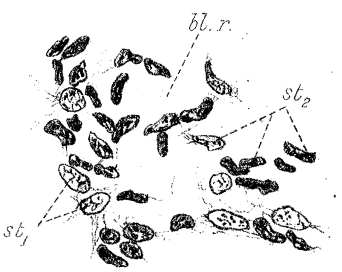

Fig. 20.

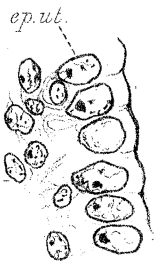

Fig. 19.

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Fig. 22.

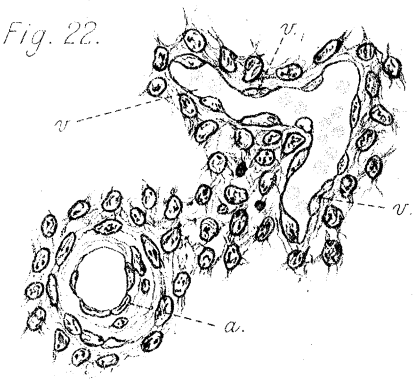
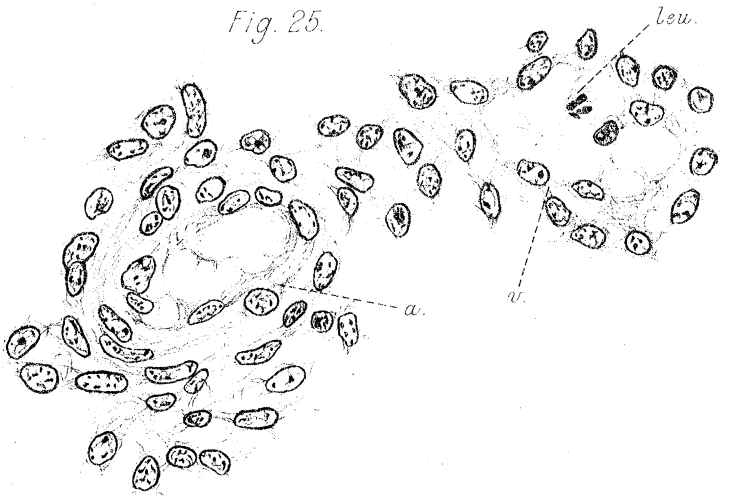


Fig. 25.



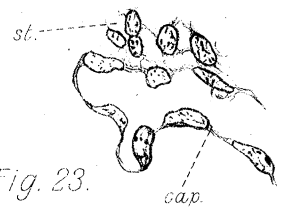
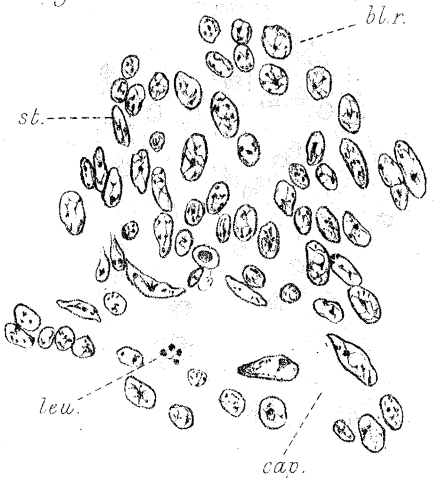


Fig. 23.

Fig. 24.



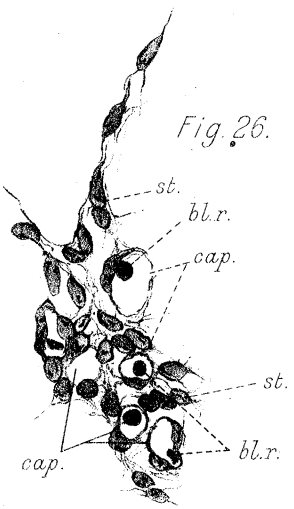
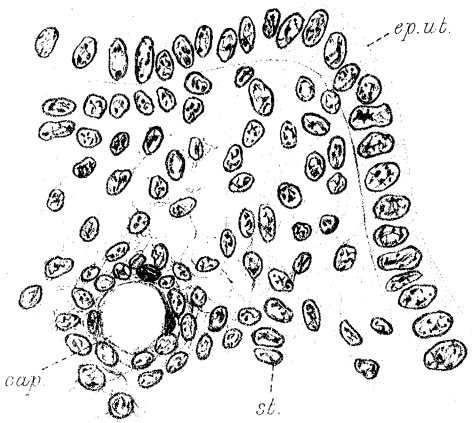


Fig. 26.



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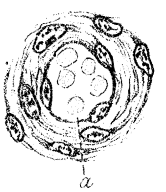
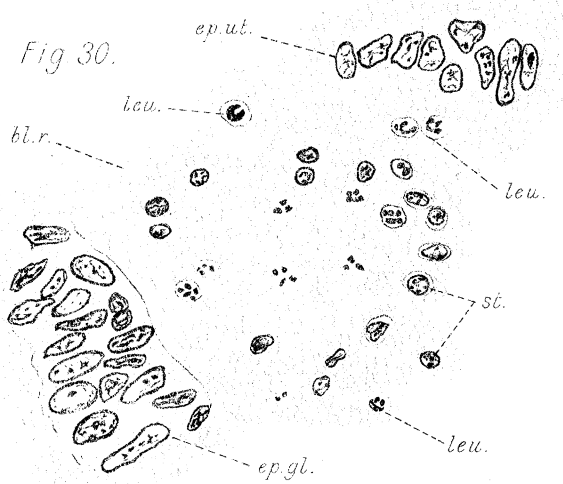


Fig. 27a.

Fig. 30.



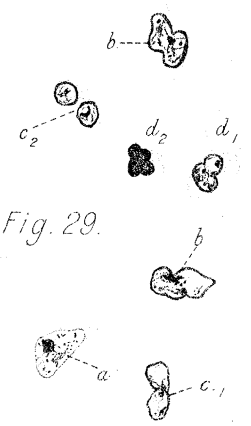


Fig. 29.

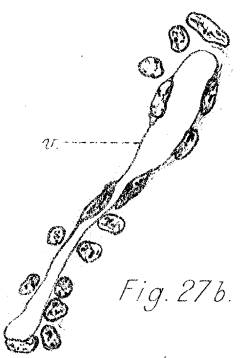


Fig. 27b.

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Fig. 31.

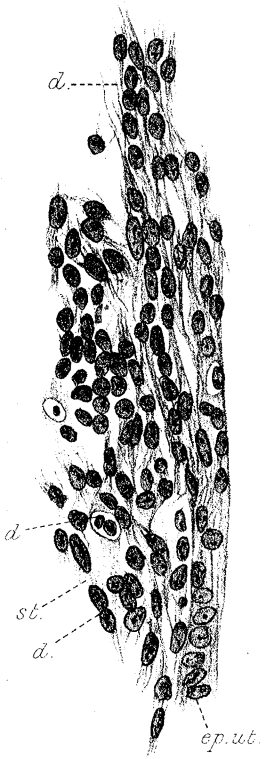


Fig. 36.

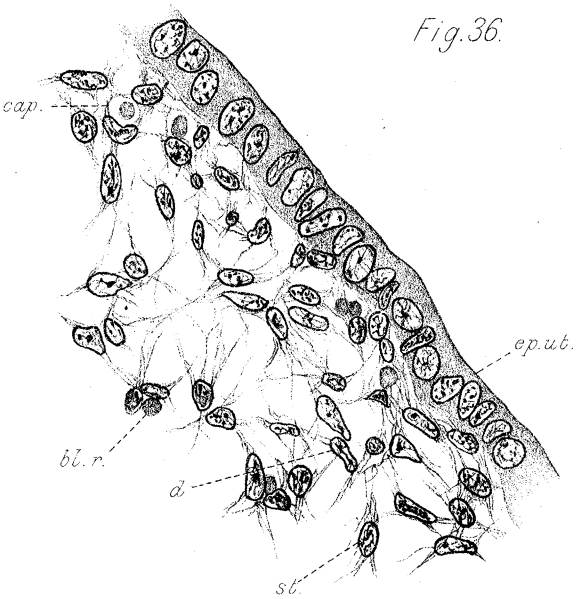


Fig. 33.

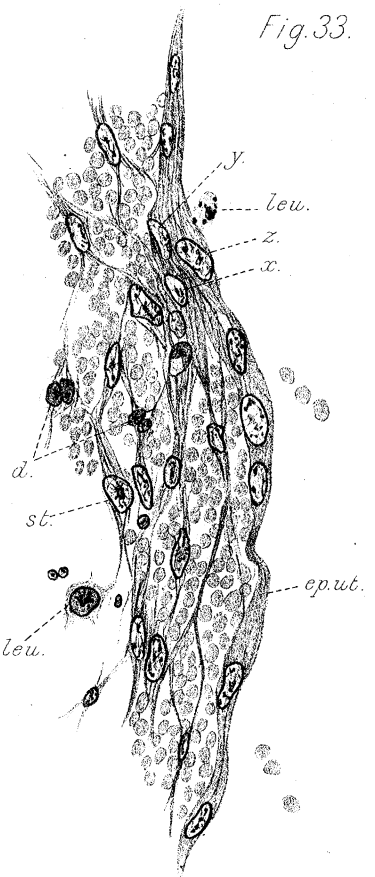


Fig. 35.

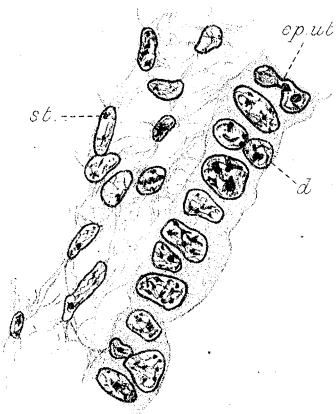


Fig. 32.

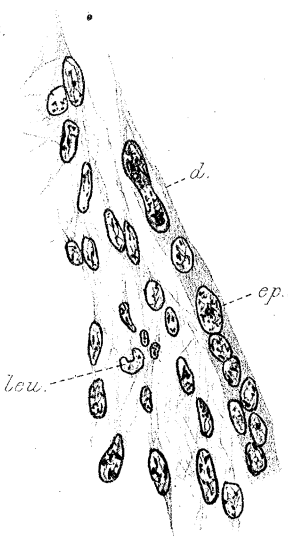


Fig. 34.

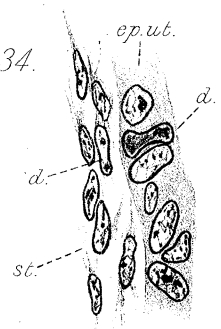


Fig. 37.

Fig. 39 b.

Fig. 39 a.

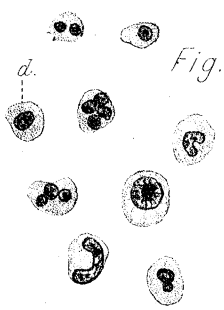


Fig. 38.

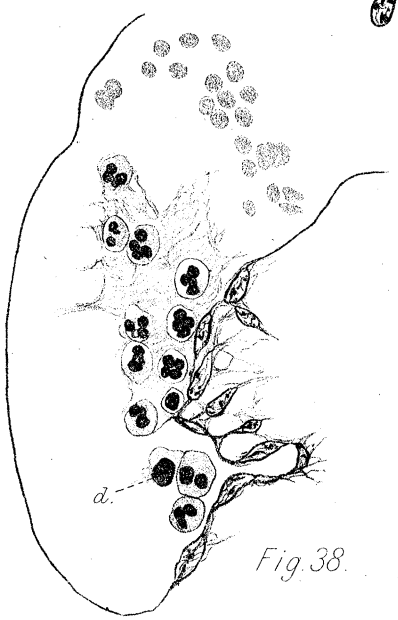
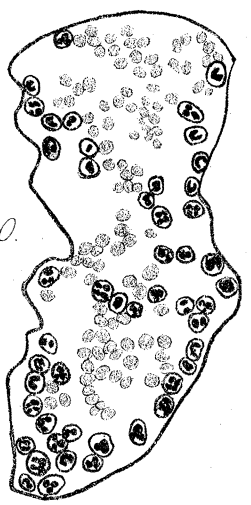


Fig. 40.



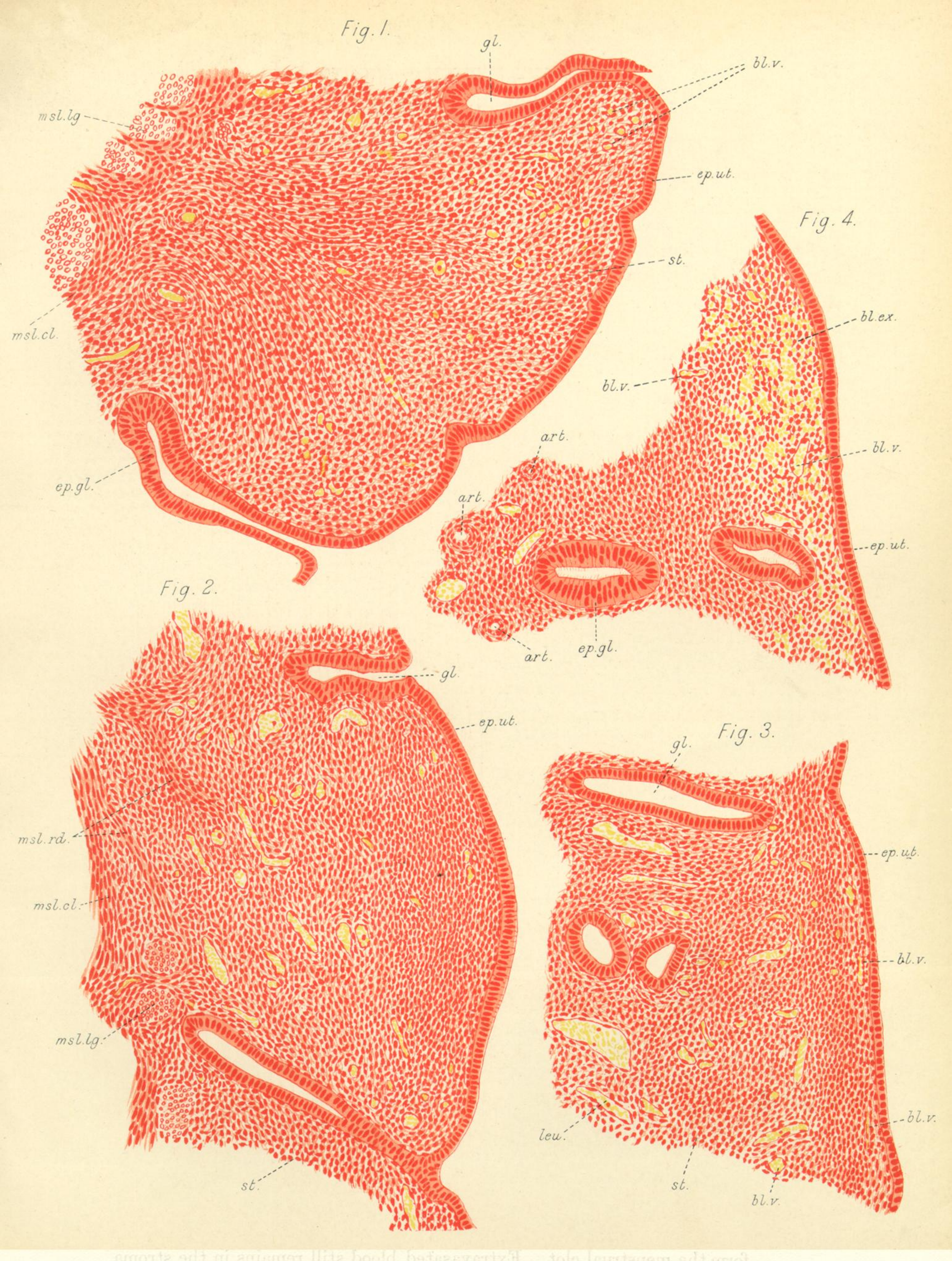


PLATE 35.

Fig. 1. A section through the vertical wall of a uterus, Stage I. Showing a portion of the mucosa and a small portion of the inner muscular layer. The thin lines running from the deeper part of the stroma outwards are fibrils only present at this stage.

Fig. 2. A section through the ventral wall of a uterus, Stage II. Showing a portion of the mucosa and a small portion of the inner muscular layer. The nuclei of the superficial portion of the stroma are densely packed and fusiform in shape.

Fig. 3. A section through the dorsal wall of a uterus, Stage III. Showing a portion of the mucosa only. The dense layer of the stroma nuclei is more restricted, the blood vessels are larger, and many lie flattened out close beneath the epithelium.

Fig. 4. A section through the dorsal wall of a uterus, Stage IV. Showing a portion of the mucosa only. Many of the superficial vessels have broken down, and extravasated blood lies amidst the stroma network.

Fig. 7.

Fig. 6.

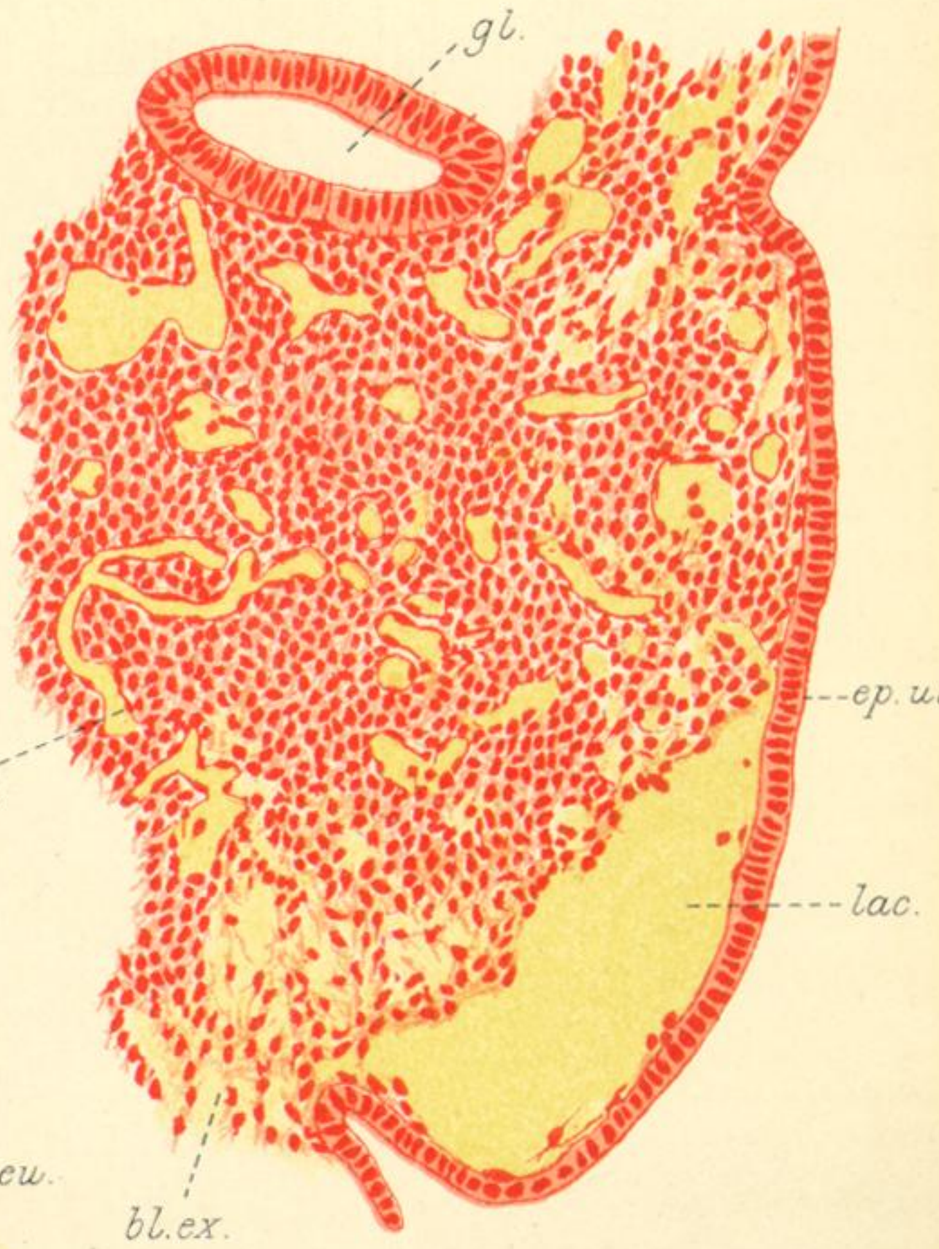


Fig. 5.

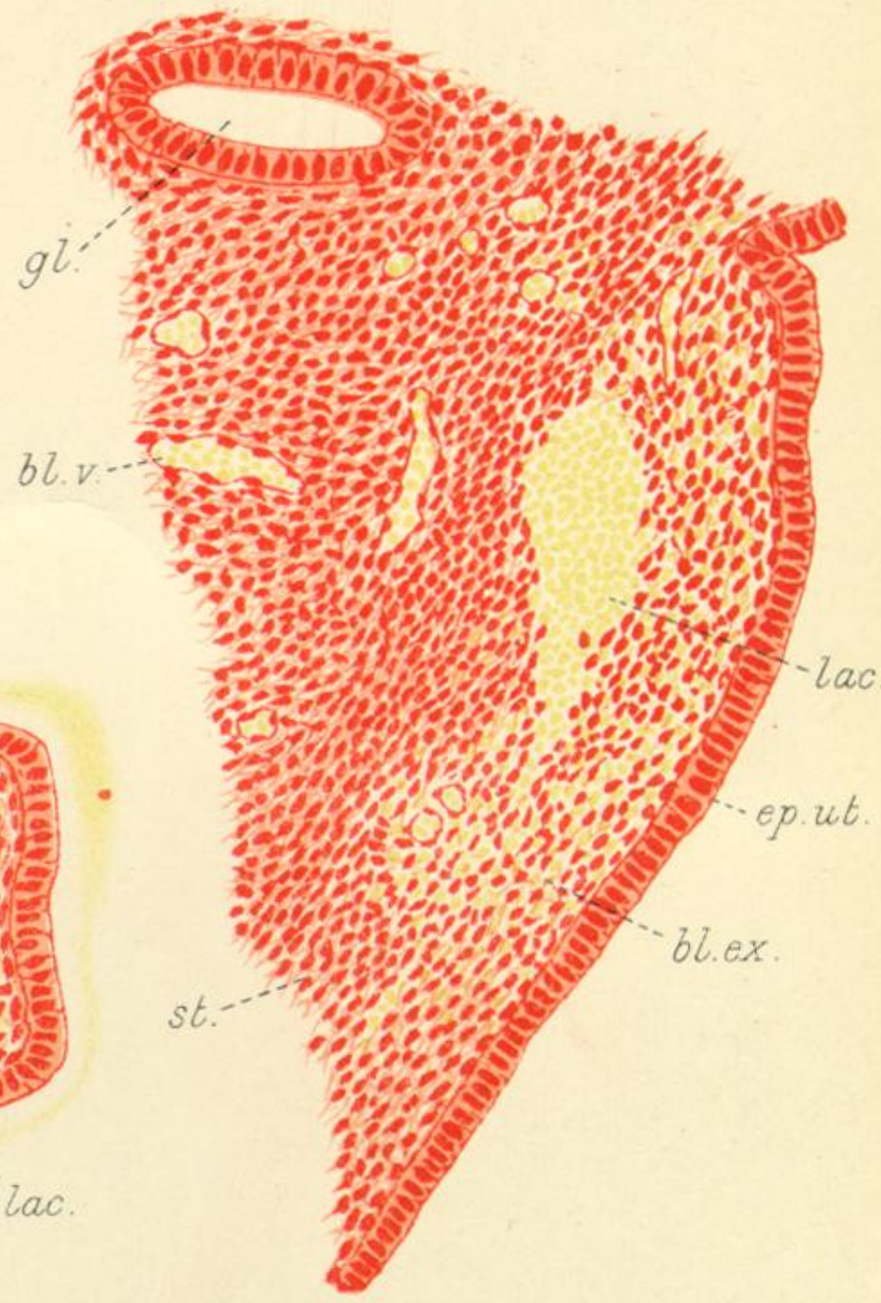


PLATE 36.

Fig. 5. A section through the dorsal wall of a uterus, Stage V. Showing a portion of the mucosa only. A lacuna in the midst of the stroma is seen, with extravasated blood around, in the network of the stroma. The nuclei of the stroma superficial to the dense layer, are again more rounded.

Fig. 6. A section through the dorsal wall of a uterus, Stage V. Showing a portion of the mucosa only. The vessels are more numerous, and larger and more congested. Much extravasated blood is in the stroma, and lacunæ are shown below the epithelium.

Fig. 7. A section through the lateral part of the ventral wall of a uterus, Stage VI. Showing a piece of the mucosa, and subjacent muscle layer. Large lacunæ are shown, which include nearly all the extravasated blood. Some free blood is seen in the cavity of the uterus, which has escaped through ruptures in the epithelial wall of the lacunæ.

Fig. 8.

PLATE 37.

Fig. 8. A section through the dorsal wall of a uterus, Stage VII. The lower part of the section shows a small part of one of the lateral walls of the uterus. A portion only of the mucosa is shown. Denudation is here represented, and the severity of the process is shown. A few pieces of the uterine epithelium, *ep.ut*$_1$, remain *in situ*, the rest is cast off. The glands are much distorted ; the cavity of the uterus is filled with débris, which will form the menstrual clot. Extravasated blood still remains in the stroma, but most of it is now free in the uterine cavity. The vessels in the deeper mucosa remain intact, there is no extravasated blood in that region.

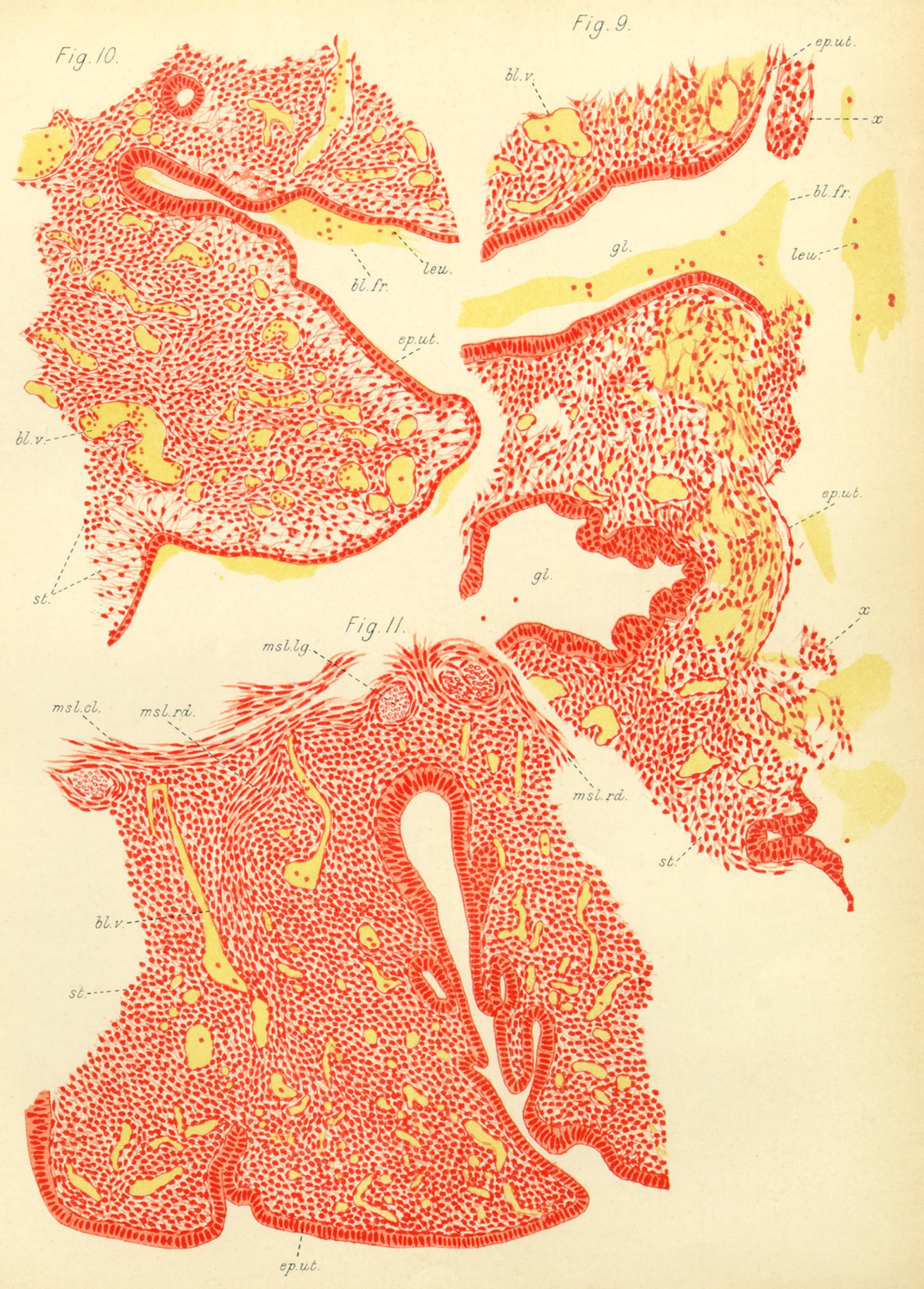


PLATE 38.

Fig. 9. A section through the dorsal wall of a uterus, Stage VIII. Showing a portion of the mucosa only. Recuperation of the epithelium is in progress; it is much flattened, *ep.ut.* Pieces of the mucosa, *x*, are still being cast off; but the denuding process is almost over. The menstrual clot was still in this uterus. Extravasated blood is present in the stroma tissue.

Fig. 10. A section through the dorsal wall of a uterus, Stage VIII. Showing a portion of the mucosa only. The epithelium is now re-formed, but is not yet cubical. The stroma layer is shrinking, but remains attached to the epithelium by long protoplasmic processes. Extravasated blood is still present in the stroma, but numerous capillaries are being formed.

Fig. 11. A section through the dorsal wall of a uterus, Stage VIII. Showing a portion of the mucosa layer and subjacent muscles. The epithelium has followed the stroma, and is now closely attached to the latter; its cells are cubical and columnar, and it is folded in many places to form new glands. The vessels are more numerous, and larger than in fig. 1, but otherwise this uterus is very like a specimen of Stage I. There is now no extravasated blood present in the stroma.

PLATE 39.

Fig. 12. A section through the body of a uterus towards the close of Stage VIII. Showing the epithelium, glands, and stroma of the mucosa, the muscle layers and sheath, and the blood vessels in the external muscle layer. The vessels are not shown in the internal muscle layer, nor in the mucosa, for the sake of clearness.

Fig. 13. A piece of glandular epithelium from the same uterus drawn in fig. 1, Stage I. The basement membrane and ragged processes on the surface of the cells (cilia?) are shown.

Fig. 14. A piece of uterine epithelium and stroma from the same uterus, Stage I. The delicate protoplasmic processes of the stroma are shown in connection with the epithelial cells. The nuclei are round or oval, and have a nuclear network.

Fig. 15. A piece of the densely packed stroma seen in fig. 2, Stage II. The elongated nuclei are shown, many of which are undergoing amitotic division, *d*. Three stages of division are shown by d_2.

Fig. 16. Cells from the same uterus, Stage II.

a. Part of a capillary containing a leucocyte (*leu.*) and blood corpuscles.

b. Part of a capillary showing the nuclei of the cells forming its wall, b_1, b_2, b_3.

b_1 is at right angles to the flat plane of the cell.

b_2 is more oblique, and b_3 is a surface view of the nucleus of a cell forming the lower wall of the capillary, which the section cuts at the end of a curve.

c. Series of elongated nuclei of the stroma, showing amitotic division. $c_{2,\ 3,\ 4,\ 5}$ different stages of division.

d. Series of nuclei undergoing fragmentation. d_1 is a typical nucleus. $d_{2,\ 3,\ 4}$ show the fragmentation process.

h. Series of small nuclei undergoing division.

f_1. Is probably a similar cell to those of the *c* series, but shows fragmentation.

The *c* series, *h* series, and f_1 are commonly seen; $d_{2,\ 3,\ 4}$ rarely seen.

Fig. 17. Nuclei of the stroma, from the same uterus drawn in fig. 4, Stage IV. Showing amitotic division. They are commonly seen in the dense area of the stroma.

Fig. 18. Piece of glandular epithelium and stroma from deep down in the mucosa; from the same uterus as fig. 17 is taken, Stage IV. There is a basement membrane but no sheath. The stroma nuclei are elongated in the region of the gland. They are not dividing.

Fig. 19. A piece of lining epithelium from the same uterus as fig. 18 is taken, Stage IV. The nuclear network is barely visible in some, and not at all in other nuclei. One large nucleolus is present at the base of each cell in place of the nuclear network and chromatin granules seen in fig. 14. The protoplasm of the cells is still continuous with the stroma network.

Fig. 20. A piece of the stroma from near the surface of the same uterus as fig. 7 is taken, Stage VI. Some nuclei, st_1, remain like those in fig. 14, but many, st_2, show degeneration changes; they are shrivelled and stain darkly. The protoplasm of these latter cells is much reduced in amount, st_2.

Fig. 21. A piece of uterine epithelium from the surface of a lacuna, Stage VI., together with shrivelled stroma elements and blood corpuscles. The nuclei of the epithelium are also shrivelled and degenerating.

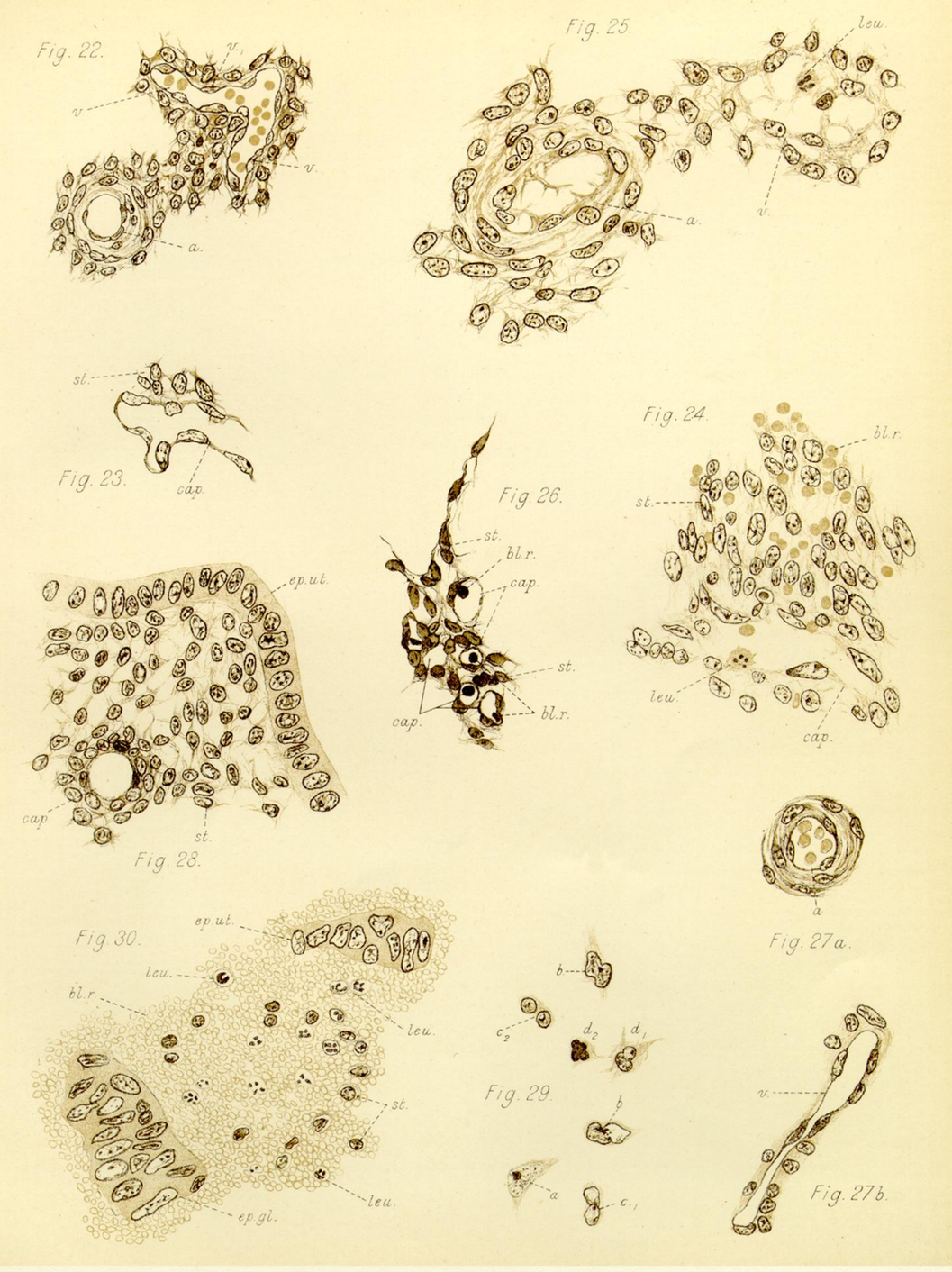


PLATE 40.

Fig. 22. An artery and vein from just below the dense area of the stroma, Stage III. Showing the multiplication of the cells forming the walls thereof, a and v_1.

Fig. 23. Part of the wall of a capillary from near the surface of the mucosa, Stage IV. Showing hypertrophy of the nuclei. This shows the condition of the cells prior to rupture of the vessel.

Fig. 24. A ruptured capillary and stroma, from near the surface of the mucosa, Stage IV. Hypertrophy of the nuclei and protoplasm of the stroma and vessel wall is shown, and the wall of the vessel has broken down, allowing the blood corpuscles to be extravasated in the meshes of the stroma. A leucocyte remains attached to the remnant of the ruptured vessel. The protoplasm of the cells is less sharply defined than it is in fig. 22.

Fig. 25. An artery and vein with stroma from the deeper part of the mucosa of the same uterus as fig. 24, Stage IV. The vessels are not ruptured, but the nuclei and protoplasm of the stroma and of the walls of the vessels are hypertrophied, and strands of protoplasm are stretched across the lumen of the vessels. A leucocyte is shown in the vein (*leu.*). The other cell in the vein belongs to the wall of the vessel which has been cut in section owing to the irregular bulging of the wall. The walls of the vessels are not so solid and compact as they are in fig. 22.

Fig. 26. A piece of the superficial stroma at Stage VIII. Showing newly formed capillaries. The nuclei and protoplasm of the cells are now no longer hypertrophied.

Fig. 27, A and B. An artery and vein from the deeper part of the mucosa, Stage VIII. Showing the recovery of hypertrophied vessels. The nuclei and protoplasm still show signs of the swelling seen in fig. 25, but not nearly to the same extent.

Fig. 28. A piece of the upper part of the mucosa from the same uterus as fig. 11, Stage VIII. Showing the newly-formed cubical epithelium; the nuclei of the stroma are now almost the same as in fig. 14, but still somewhat irregular in shape, and a definitely formed capillary is present.

Fig. 29. Stroma cells from the same uterus as fig. 9, Stage VIII. Showing, a, hypertrophied nucleus; *b.b.*, irregular nuclei, probably dividing; c_1, c_2, regular nuclei dividing; d_1, d_2, fragmentation of the nucleus.

Fig. 30. Débris from the cavity of the same uterus as fig. 8, Stage VII. Uterine and glandular epithelium, stroma nuclei, leucocytes, and red blood corpuscles; nearly all in degenerate condition.

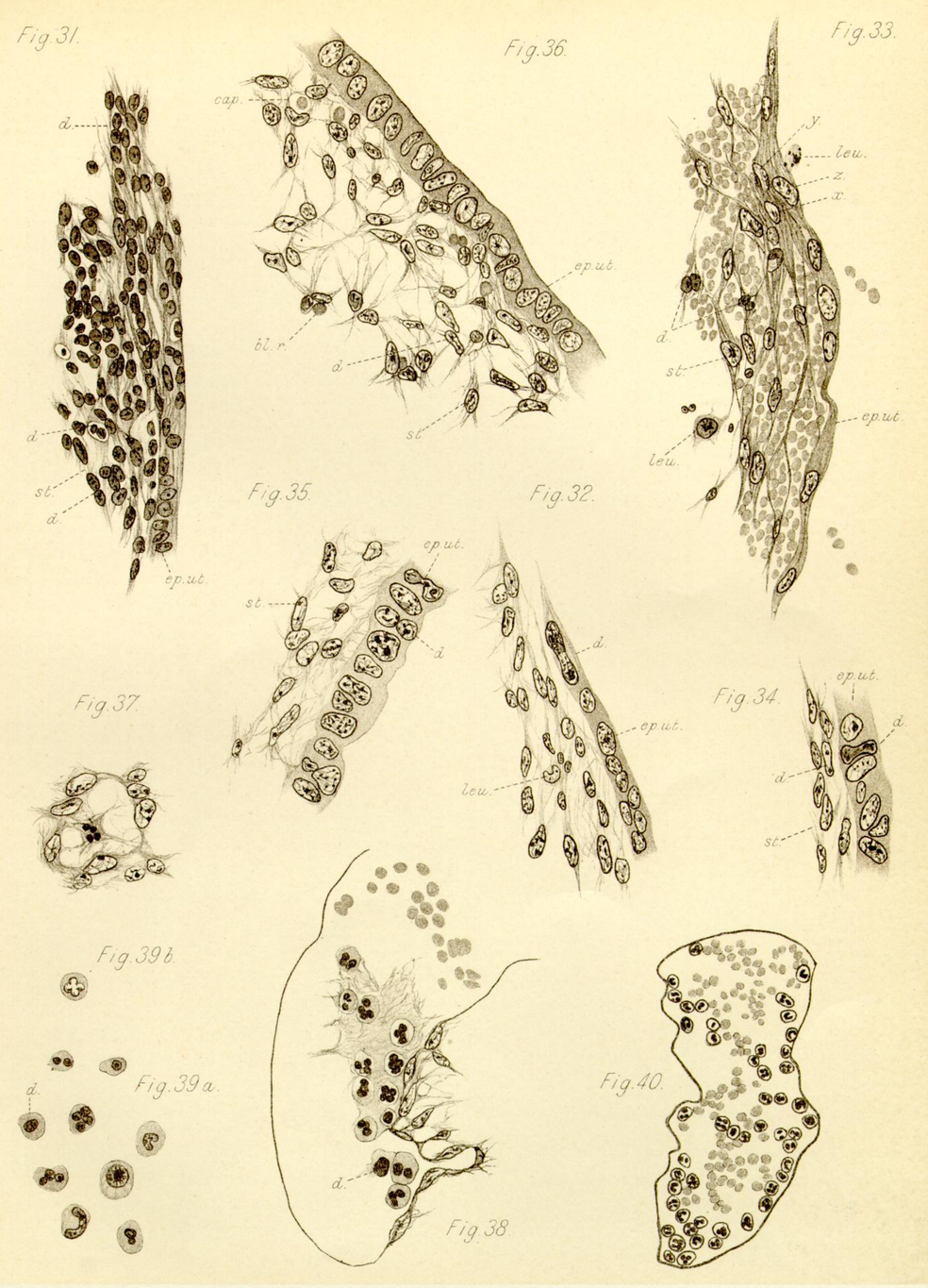


PLATE 41.

Figs. 31 to 36 are taken from various uteri during Stage VIII., to illustrate the re-formation of the epithelium. The nuclei marked *d* are undergoing division.

Fig. 31. A section through a piece of growing epithelium connected with a gland at the lower end of the figure, *ep.ut.* The close connection between the stroma and the growing epithelium at the upper end of the section is shown, the two being in fact continuous there.

Fig. 32. A section through the growing point of epithelium, showing the amitotic division of the terminal cell.

Fig. 33. A section showing the flattened epithelium seen in fig. 9, and the scattered stroma nuclei with long protoplasmic processes, below. Blood corpuscles in great number are enclosed within the stroma network—extravasated blood. *x* is a stroma cell; *y*, a cell of the epithelial layer derived from the stroma; *z*, an epithelial cell.

Figs. 34 and 35. Sections of a slightly later stage, in which the flattened cells of the epithelium are becoming columnar. The nuclei are still of irregular shape and size.

Fig. 36. A section through the epithelium and superficial stroma, from the same uterus as fig. 10. Showing the more regular epithelium and the scattered nuclei and long processes of the underlying stroma. The nuclei of these layers are still irregular, but are more nearly approached to those seen in fig. 14 than heretofore. Minute capillaries are seen, *cap.*, and a few isolated blood corpuscles.

Figs. 37 to 40 are drawings of leucocytes.

Fig. 37 shows a leucocyte with stellate processes, adhering to the remains of an hypertrophied and broken down capillary, Stage IV.

Fig. 38. A colony of leucocytes within a vessel, Stage VI. The nuclei are in various stages of division. A sharp outline is invariably present round the cell; *d* indicates a cell whose single nucleus is dividing into two.

Figs. 39A and 39B are drawings of leucocytes which were situated within vessels at Stage VIII. Showing the various shaped nuclei seen, and leucocytes with one, two, three, and four nuclei within them; 39B shows a leucocyte whose single nucleus is dividing into four simultaneously—fragmentation. The chromatin within this nucleus is confined to the boundary-wall of the nucleus.

Fig. 40. Outline of a vessel, Stage VIII. Showing the very large proportion of leucocytes to red blood corpuscles, viz., 47·115 per cent. of leucocytes.