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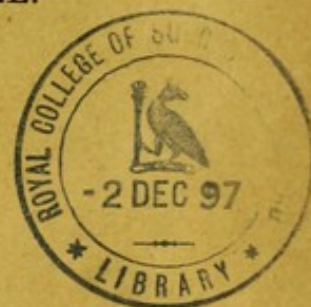
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[PLATES 1, 2.]

THE MENSTRUATION AND OVULATION OF MACACUS
RHESUS, WITH OBSERVATIONS ON THE CHANGES UNDERGONE
BY THE DISCHARGED FOLLICLE.

PART II.



BY

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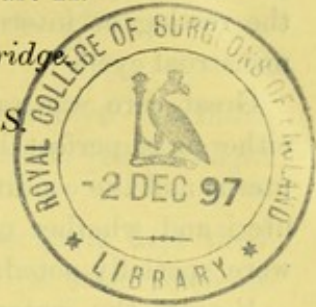
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III. *The Menstruation and Ovulation of Macacus Rhesus, with Observations on the Changes undergone by the Discharged Follicle.*—Part II.

By WALTER HEAPE, M.A., Trinity College, Cambridge.

Communicated by Professor M. FOSTER, Sec. R.S.

Received June 15,—Read June 18, 1896.



[PLATES 1, 2.]

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Introduction.

THE greater part of the material wherewith the work detailed in this paper was done, was obtained during my stay in Calcutta during the early part of 1891, and I am greatly indebted to the Committee of Management of the Calcutta Zoological Gardens, and especially to Professor D. D. CUNNINGHAM, F.R.S., both for assistance in getting the animals required and for facilities placed at my disposal for carrying on my work in that country.

Two hundred female *Macacus rhesus* were sent to me from Muttra and thirty from
 MDCCCXCVII.—B. 6.4.97

Benares. A very large proportion of these either had embryos in an advanced stage of development in utero, or had recently borne young; of the remainder many had not yet reached the age of puberty, and when all doubtful cases were excluded, seventeen specimens alone remained which could be used for the purpose of investigating the phenomena of menstruation. Five of these were referable to Stage 1, the resting or intermenstrual stage, and the other twelve to various stages of the menstrual cycle.

Great care was taken to exclude all animals about which there was any doubt either as to perfect health, premature abortion, or recent delivery. The size of the uterus and the condition of its muscular coat, the consistency of the walls of the os uteri and whether or not it was dilated, and the condition of the mammary glands, were specially noted.

Besides the material collected in Calcutta, eight female *M. rhesus* were kept by me for three to fifteen months in Cambridge, in a building heated with hot water pipes during the winter, and the menstruation of these animals was noted at various times; the climate, however, appeared to affect their health, and the results obtained cannot be considered satisfactory.

Anatomy of the Cervix.

With the exception of the cervix, the anatomy of the generative organs of *M. rhesus* is very similar to that described for *Semnopithecus entellus* in Part I. of this paper. The cervix, however, is different.

In *S. entellus* the cervix is a narrow straight canal with thick muscular walls. In *M. rhesus* a fold is formed on the anterior (ventral) wall, which projects across the lumen of the canal of the cervix and fits into a recess between two similar folds formed on the opposite wall, the whole constituting, as it were, a valve between the interna and external os uteri (figs. 3 and 4).

The canal at this intermediate point is thus rendered very narrow and convoluted; from the valve to the external os it widens out somewhat laterally and ends as a small slit on a papilla projecting into the vagina, while from the valve to the internal os it also becomes enlarged and enters the uterus by a wide mouth. The wider portions of the cervix canal have longitudinally folded walls, but in the intermediate valvular portion the folds are not present.

The position of the internal os is readily determined; the folded walls of the mouth of the cervix end abruptly at the point where the uterine cavity begins, and histological examination shows a distinct difference between the two parts; further, the various changes, which are so marked in the uterine mucosa during menstruation, do not extend to this portion of the generative canal.

The valvular structure is not confined to virgins; it is present in a specimen in my possession which has borne young, it is therefore a permanent structure.

I am not aware that this peculiar valve in the cervix canal exists in any other animal, and what its function may be I am quite unable to say; it probably serves to prevent the escape of the seminal fluid which has once been drawn into the uterus, but it is not likely this is its sole use.

Breeding and Gestation.

It is remarkable how little is known of the breeding habits of monkeys. In India, where several species abound close to native villages at all times of the year, it might be expected that their habits at least should be well known.

BLANDFORD (No. 1), in his recent work on the Fauna of British India, says there is no particular breeding season for *M. cynomolgus*, but I can find no other reference to the subject in his book.

Mr. SÁNYÁL, Superintendent of the Zoological Gardens at Calcutta, told me it was his opinion that *M. rhesus* bred at all times of the year. No doubt he has received individuals which have borne young at widely different seasons, and it was this fact, I believe, which led him to adopt his view; but that fact, in itself, is no proof that the animals breed at all times of the year in all parts of the continent of India. The specimens received at the Gardens may have been obtained from different parts of the country, where climatic and other conditions (such as food) are very different, and this circumstance would be quite sufficient to account for the widely different seasons during which the young are born at the Gardens.

Dr. AITCHISON has informed me that in Simla *M. rhesus* copulates about October and gives birth about August and September the following year. Apparently, then, these animals have a definite breeding season in Simla.

My own investigations show that the *M. rhesus*, which live on the plains about Muttra, breed at a different time of the year, and yet that they also have a definite breeding season.

The fact that a very large proportion of the adult females supplied to me during January, February, and March, bore advanced embryos in utero, and further, the fact that of those supplied in March a very large proportion had already borne young, points to the conclusion that March is the usual month when most of the young are born at Muttra.

Thus it is seen that the breeding season in Simla and in Muttra occurs at quite different times, and it would seem highly probable that *M. rhesus* living in other parts of India, may have different breeding seasons also. The geographical range of this species is very great, it is found over an area bounded by Kashmir (latitude 34) to the Godavari River (latitude 17), from Bombay (longitude 73) to Bengal (longitude 90), from an altitude of nearly 10,000 feet down to near sea-level;* and the

* See BLANDFORD (No. 1).

conditions, both of climate and of food, over this wide area, are surely various enough to account for all possible variations in the breeding time.

The period of gestation of *M. rhesus* is also by no means certainly known. BRESCHET (No. 2), who gives a fuller account of the observations which have been made on this subject than any other author with whom I am acquainted, quotes a statement made by ISIDORE GEOFFROY SAINT-HILAIRE, to the effect, that it is agreed to fix the duration of the gestation of apes at about seven months. He himself does not, however, appear to agree with this view, for after detailing the observations of other naturalists, he asserts that the period of gestation varies in different species, a conclusion which it seems to me he is justified in drawing.

With regard to *Macacus*, he remarks that FRÉDÉRIC CUVIER believed it possible to determine the gestation of "Maimon" (*M. nemestrinus*) at seven months, twenty days.

BRESCHET shows that, unlike many of the lower mammals, monkeys frequently indulge in sexual intercourse, not only at the breeding season, but also during pregnancy; and further he records F. CUVIER's observation, that menstruation takes place not infrequently during pregnancy. These facts make it doubly difficult to determine accurately the duration of gestation, and undoubtedly further investigations are required on this point.

BLANDFORD (No. 1) states for the genus *Macacus* that the period of gestation is about seven months, and that the gestation of *M. nemestrinus* has been ascertained to be seven months and twenty days, but he gives no reference to the source from whence he got his information.

The account Dr. AITCHISON gives me of *M. rhesus*, at Simla, deals only generally with the breeding season and the time of bearing young; but, from his observations, it would seem to be not improbable that the gestation of this animal occupies considerably more than seven months' time.

The fact that there is a definite breeding season for these animals, if it be true (as I cannot but think it is), conveys of course no proof that each female breeds each year.

The only evidence which I have to record which bears on this point, is the fact that menstruation undoubtedly occurs while the mother is nursing her young.

I have noted for three months the occurrence of very regular menstrual periods in the case of a specimen of *M. cynomolgus*, which was nursing a young one at the time. It is true the mother did not supply all the nourishment the young one took, but I think I am right in saying she supplied most of it.

It would seem possible therefore that the female monkey may become pregnant during the period of lactation, more than this I cannot say.

There is some reason for the suggestion that the act of copulation is dependent, quite as much upon the condition of the male, as it is upon the condition of the female. I have seen female *Semnopithecus entellus* endeavour to induce a full grown male to fertilise them without success, and this occurred at a time of year which, I was told, was somewhat less than a month before the usual breeding season began.

Menstruation.

With regard to the regularity of menstruation in Monkeys, it seems advisable I should add a word to what I have already said in Part I. of this paper (No. 8).

There is considerable evidence in favour of the view that certain monkeys menstruate regularly all the year round. GEOFFROY SAINT-HILAIRE and CUVIER (No. 7) found that in three different species, Cercopithecus, Cynocephalus, and Macacus, there was a regular monthly discharge of blood from the generative organs. SUTTON (No. 17) states that the specimens of *M. rhesus* which he investigated, and which I understand he obtained from the Zoological Gardens in London, menstruated fairly regularly; while Mr. BARTLETT, Superintendent of the Zoological Gardens in London and Mr. SÁNYÁL, Superintendent of the Gardens in Calcutta, have both assured me that monkeys menstruate regularly in their establishments.

A specimen of *M. cynomolgus* which I observed in the Gardens at Calcutta for three months menstruated regularly during that time, a bloody discharge exuding from the vagina on 20th December 1890, 20th January 1891, and about the 20th February 1891.

A specimen of *Cynocephalus porcarius* which I also noticed in the Calcutta Gardens for two months, menstruated regularly for that period, while the specimens of *Semnopithecus entellus* which I kept for observation in Calcutta, menstruated each month and the flow from the vagina lasted about four days.

The specimens of *M. rhesus* which I kept in Cambridge, were not all adults at the time they were sent to me, two of the adults, however, menstruated regularly for the three months during which they were under observation. In these animals the flow was observed to last for three to five days, and the probable mean dates were:

Specimen A. 7th May, 1892; 2nd June, 1892; and 6th July, 1892.

„ B. about 11th May, 1892; 11th June, 1892; and 6th July, 1892.

After this date until the end of the year, specimen B was irregular; she generally was found to have a secretion exuding from the vagina but it was rarely tinged with blood.

A third specimen suffered much from cold and cough and rarely menstruated, two others died, two were young ones which did not menstruate at all, and the eighth menstruated irregularly.

External Signs of Menstruation.

Apart from the menstrual flow, other signs were observed which regularly recurred with menstruation in *M. rhesus* and *M. cynomolgus*; the nipples and vulva became swollen and deeply congested, and the skin of the buttocks swollen, tense, and of a brilliant red or even purple colour; the abdominal wall also, for a short space upwards, and the inside of the thighs, sometimes as far down as the heel, and the

under surface of the tail for half its length or more, are all coloured a vivid red ; while the skin of the face, especially about the eyes, is flushed or blotched with red.

Professor SHERRINGTON has made similar observations on *M. rhesus*, and has very kindly supplied me with sketches showing the extent of the area of skin in the neighbourhood of the generative opening, which he found to be so affected. His results agree in the main with those I have described above for the buttocks, hind limbs, and tail ; but I gather from his coloured drawings, that the congested area in the animals he observed (they were kept in London), was neither so brilliant nor quite so extensive as that seen by me in specimens which lived at the Gardens in Calcutta.

This congestion of the skin of the buttocks, thighs, and tail is also observed in females during, at any rate, the later stages of gestation ; but in such animals the area of the abdominal wall which is affected, is larger than it is during menstruation, and the intensity of the colour of this part is considerably increased. The colour of the face during this later period of gestation, is also more brilliant than it generally is during menstruation. So marked is the former difference that a pregnant monkey from about the period of the fifth month of pregnancy, although not always readily distinguishable by its increased size, can be surely determined by observation of the extent of the congested area of the abdominal skin.

Nor is the brilliant colouring of these parts confined to the female *M. rhesus*. The males, when adult, are also brilliantly coloured in the region of the buttocks and over the face. For the three months during which I had them under observation, I could see little or no difference in the degree of intensity of the colouring, but whether this is a permanent characteristic of the male or not, I am unable to say.

The innervation of this congested area, which is of very considerable interest, I have drawn attention to in my former paper (No. 8).

The Menstrual Discharge.

The nature of the menstrual discharge from the vagina varies little, from time to time, in any one individual, as far as I have been able to discern during the few months in which I have had an opportunity of examining it ; and, further, the same may be said for different individuals.

The discharge consists of :—

- (1.) A somewhat viscid, stringy, opaque, white fluid. The fluid itself is transparent, and is, I believe, derived from blood serum and from the glandular cells of the uterine mucosa. The opacity of the fluid is due to the presence of great numbers of minute granules ; these have their origin chiefly from the broken down plasmodium which constitutes the bulk of the uterine mucosa. At the same time, some of the nuclei of the cast-off uterine tissues, especially the glandular epithelium nuclei, and also degenerate

leucocytes, give rise to granules. I have obtained fresh material from the uterine cavity of a menstruating monkey which shows these facts.

The glandular fluid itself, when present in the lumen of the glands, contains granules in small numbers which are apparently excreted by the glandular cells. Sometimes the discharge is more fluid, at others more viscid; sometimes it is more, sometimes it is less opaque, but the variations are not very great.

- (2.) Red blood corpuscles. These are invariably present in quantities sufficient to colour the discharge either a pale or a dark blood colour; the latter, however, is rare.
- (3.) Masses of uterine stroma tissue, pieces of uterine epithelium, both from the wall of the uterus and from the uterine glands, together with squamous epithelium from the vagina.
- (4.) Leucocytes sometimes, though not generally, in large numbers, and the isolated degenerate nuclei of broken down epithelial cells and stroma tissue. The quantity of these nuclei of the uterine tissues is various; I have seen them in very large numbers in some specimens of menstrual discharge, while in others they occur rarely.

The menstrual clot is formed of a mass of blood corpuscles, together with pieces of the various uterine tissues which are cast off by the menstrual process; it is expelled apparently at the end of menstruation, and is found in the uterine cavity in varying degrees of solidity according to the length of time it has remained there.

The variations observed in the composition of the normal menstrual discharge, may be due either to the stage of menstruation during which the specimen was obtained, or to a variation in the manner of menstruation itself.

My histological investigations of the uterine tissues during menstruation, show the remarkable uniformity of that process in the numerous specimens examined, and make it extremely unlikely that such variations as are seen in the composition of the normal menstrual discharge, should be due chiefly to variations of the manner or extent of menstruation. On the other hand, it will be readily understood that a variation in the number of leucocytes, for instance, may be accounted for by the stage of menstruation in progress at the time the specimen was taken. When the uterine epithelium first ruptures, and the mass of blood corpuscles and fresh leucocytes contained in the large lacunæ are expelled into the empty uterine cavity, the discharge will contain little else; but later, when a mass of uterine tissue occupies the cavity of the uterus, the easy flow is no doubt retarded, and disintegration of all the cellular material, epithelium, stroma, and leucocytes will take place, and will cause the discharge to assume a more viscid and more granular appearance.

Leucorrhœa.

One monkey which I kept in Cambridge, suffered, at the time I got her, May, 1892, until I killed her, August, 1893, from a discharge from the vagina other than a menstrual discharge. It occurred at first irregularly, gradually, however, it became more frequent, until eventually it was almost continuous.

This discharge had the appearance of a more or less viscid, more or less opaque white material, and consisted of a dense granular fluid in which great numbers of squamous epithelial cells were invariably present. Besides these cells there were at times a considerable number of eosinophile leucocytes, which, in some cases, contained four or more nuclei, and were therefore, according to FLEMMING, breaking down; these leucocytes were most numerous when the fluid was most viscid and thick. There were no free red blood corpuscles and no cast-off uterine tissue was to be seen; the cellular contents of the fluid, other than leucocytes, were derived entirely from the vagina and not from the uterus. The fluid itself, on the other hand, came chiefly, at any rate, from the uterus.

When the animal was killed, the vagina was full of this white, opaque, viscid fluid, and so was the cervix within the external os, while much was also found in the cavity of the uterus itself and some in the lumen of the uterine glands.

No doubt the discarded vaginal epithelium when it breaks down gives rise to a certain amount of viscid granular fluid, but as there are no glands within the vagina it is only by the former means that fluid can be formed therein, by far the greater part therefore of the fluid portion of this discharge came from the uterus. It was noticeable that the fluid contents of the glands in this specimen, contained considerably more granules than were to be seen in the glands of specimens of menstruating uteri.

In spite of this abnormal discharge, which I take to be leucorrhœa, this monkey was especially healthy and strong.

It never menstruated while I had it, but the buttocks, face, and mammæ were frequently congested, sometimes remarkably so.

On examination after death the ovaries were found to be undergoing atrophy. In one of them the external tunic of the ovary was thickened and separated from the internal stroma, while the latter had shrunk away and appeared like the kernel of a nut inside its husk, the other ovary was similarly affected, but not to the same extent.

Superficial Menstrual Phenomena.

The same grouping of menstruating uteri is adopted in the present paper as that recorded in Part I. of this work (No. 8), on *Semnopithecus entellus*, viz. :—

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

A superficial examination of the mucosa of the menstruating uteri of *M. rhesus* shows that changes take place in them which are similar to those described for *S. entellus*.

The smooth surface of the mucosa during Stage I. becomes more opaque during Stage II., and the flush which spreads over the mucosa during Stage III. gets more and more marked, until at the end of Stage IV. the mucosa may be said to be highly congested. At Stage V. the dark red spots appear on the surface of the mucosa, which are characteristic of this stage, and which are due to the formation of lacunæ, while at Stage VI. free blood is first seen in the cavity of the uterus. The formation of the menstrual clot during Stage VII., and the recuperation of the uterine mucosa during Stage VIII., are also superficially the same in *M. rhesus* as they are in *S. entellus*.

Histology of Menstruation.

The account, given below, of the histological phenomena exhibited during the menstruation of *M. rhesus* is very brief. Similar work has been undertaken for *M. rhesus*, which I have already described for *S. entellus* (No. 8). A large series of specimens have been examined in the form of serial sections, and the various phenomena compared, step by step, with those exhibited by my preparations of the menstruating uteri of *S. entellus*, and a close similarity between the two has been found to exist. While it has been thought advisable to note the points of agreement and difference, which are brought out by an examination of the process of menstruation in these two species of monkeys, and to point out the fact that the results arrived at by the study of *M. rhesus*, entirely confirm the results which my examination of *S. entellus* led me to publish, I have purposely avoided all unnecessary repetition, and have been obliged, in consequence, to assume some knowledge of the details given in Part I. of this paper (No. 8).

The advisability for this course has seemed to be the more pronounced since the results which I have arrived at differ, in various important particulars, from the accounts of menstruation which have been generally accepted, and a confirmation of the former has therefore some increased interest and importance.

With regard to the body of the uterus, I have only here to record the fact that the

mucosa is somewhat thicker than it is in *S. entellus*, and that the protoplasmic network of the stroma is more granular and is denser, and the glands more numerous and more branched than are these structures in the latter animal.

In *M. rhesus* as in *S. entellus*, there is an absence of any connective tissue framework in the stroma; we have, in fact, here, an essentially primitive tissue capable of extensive and rapid growth, and of transformation into other and more specialised tissues. The uterine and glandular epithelium, the glands devoid of a definite sheath, and the arrangement of the musculature, are all the same as are seen in *S. entellus*.

A. *Period of Rest. Stage I.*—The nuclei of the stroma at this stage are more densely packed in the lower portion of the mucosa than they are in the superficial part; in the latter situation a loose tissue exists, held together by a network of delicate protoplasmic processes.

I have observed no fibrils in the stroma of *M. rhesus*.

B. *Period of Growth. Stage II.*—There is a great increase in the number of the nuclei of the stroma, by means of amitotic division, in the upper third of the mucosa. The layer becomes in this part very densely crowded with nuclei, which, owing to the restraining pressure of the epithelium above, become elongated and flattened; they continue to exhibit great activity in division and growth. Thus hyperplasia occurs. The rapidity with which division goes on may be judged of by the proportion of very small nuclei present; they have their origin from the products of the first division of the stroma nuclei, and are in much larger proportion than the parent kind in many parts of the growing stroma layer.

Two methods of division of the nucleus occur, namely division into two and fragmentation.

The elongated nuclei of the growing stroma become constricted and divide into two, they are constantly to be seen in various stages of this process (fig. 1, Plate 1).

Division by fragmentation in the case of the nuclei of the stroma, I laid some stress upon in my former paper (No. 8), but was unable to demonstrate, to my own satisfaction, the actual separation and isolation of the various portions of the fragmented nucleus.

The same difficulty of demonstration occurs also in *M. rhesus*. Owing to the crowding together of the nuclei into what is almost a compact mass, and owing to the continuous network of protoplasm, at this stage becoming practically a solid layer without meshes and without connecting processes, I have found it impossible to prove satisfactorily the origin of separate nuclei by fragmentation. Fig. 2 will serve to show the nature of the difficulty. This drawing is made with REICHERT'S one-fifteenth immersion lens and ZEISS' No. 4 eye-piece, and it is, as nearly as I can make it, exactly similar to the actual specimen, the nuclei are very small and the scanty protoplasmic matrix is entirely devoid of cell outlines. The group of nuclei marked α , in which three nuclei are indicated still attached the one to the other, I interpret to be a nucleus undergoing fragmentation, while the groups of nuclei

marked *b, c*, in which three nuclei are seen closely allied to one another, seem very probably derived from fragmented nuclei, although it is impossible to be quite certain of the fact owing to the nature of the protoplasm, the crowding together of the nuclei and the absence of cell walls.

The growth of stroma tissue described above, causes a swelling into the lumen of the uterus and the thickness of the mucosa is in this way increased.

When the nuclei, which I believe to be formed by fragmentation (fig. 2), are compared with those which are formed by division (fig. 1), the size of the former will be seen to favour the view expressed. Both these figures are drawn on the same scale, and it is clear that the group of nuclei in fig. 2, marked *a*, are certainly not larger than a single nucleus of the dividing cells show in fig. 1.

Stage III.—The vessels increase in number and size, and leucocytes are more numerous therein than they were in the former stages.

C. Period of Degeneration. Stage IV.—No sign whatever of fatty degeneration was observed; hypertrophy, followed by degeneration of the walls of the vessels, results in the breaking down of the vessels and the escape of the blood into the meshes of the stroma tissue.

The degeneration changes are confined to the superficial part of the mucosa, while the hypertrophy is seen all through the mucosa, both in the cells forming the walls of the vessels and in the stroma tissue itself.

There is an increase in the number of leucocytes within the vessels throughout the whole of the mucosa, but no free wandering leucocytes were found in the deeper portion of the layer; they were only to be seen in the region of the broken-down vessels. Diapedesis does not take place, and it may, therefore, be assumed, that the element which the leucocytes have been summoned to attack is present within the vessels, and is not in the surrounding tissue (see Part I., p. 429).

Stages V. and VI.—Small lacunæ are first formed in the superficial stroma; they increase in size as more and more blood is poured into them, and eventually they come to lie directly below the epithelium. Eventually the epithelial layer ruptures, and the blood is poured into the uterine cavity.

Degeneration of the nuclei of the uterine epithelium and superficial stroma also takes place during this period, and is very marked during Stage VI.

The number of leucocytes is very largely increased.

Stage VII.—I have nothing to add to the description of the mucosa menstrualis already given in Part I. of this paper (No. 8). Denudation occurs in *M. rhesus* as in *S. entellus*; it is brought about in a similar manner and exists to a similar extent; a menstrual clot is also formed in the same way.

I have here very conclusive confirmation of the truth of the account given for *S. entellus*. Fig. 8, Plate 37, in my former paper might, in fact, fairly represent my specimens of the same stage in *M. rhesus*. The denudation is a remarkable process; both its completeness and extent are unquestionable.

D. *Period of Recuperation. Stage VIII.*—An account of this stage resolves itself into a repetition of what I have already written with regard to *S. entellus*.

The epithelium is re-formed, partly from the epithelium of the glands which remain *in situ*, and partly from stroma tissue.

New vessels are also formed from stroma tissue, by means of which all the blood corpuscles, included within the newly formed epithelium, are drawn again into the circulatory system.

In the deeper part of the stroma, the cells forming the walls of the hypertrophied vessels become again of normal size and consistency, and the stroma tissue is also reduced in bulk, assuming again the conditions which are found during the resting stage.

With regard to the leucocytes, I have no further evidence to offer; I would merely say that the opinion I have already expressed with regard to their presence during the menstruation of *S. entellus*, is confirmed by the observations I have made on *M. rhesus*. If METCHNIKOFF'S conclusions are to be relied upon, the presence of leucocytes in such large numbers in the vessels of the mucosa during menstruation, is evidence of a noxious material therein, while the fact that diapedesis does not occur, shows that the irritant does not extend to the surrounding tissue. Menstruation, then, cannot be considered to be an inflammatory process.

The considerable flow of blood from the ruptured vessels during menstruation would seem to get rid completely of this irritant, and this is itself sufficient to explain the disappearance of the comparatively few leucocytes which are left after denudation has taken place.

Menstruation in the Human Female.

Owing to an oversight, I omitted to draw attention in my former paper to the fact that MINOR (No. 13) divides the act of menstruation into three periods, which he calls

1. Tumefaction;
2. Menstruation;
3. Restoration of the mucosa;

and he distinguishes between these periods and a period of rest which completes the menstrual cycle.

These four periods are identical with those I have independently adopted, but the terms he has used to designate the first two of them do not appear to me to describe sufficiently accurately what takes place.

MINOR'S period of "tumefaction" must include also that most important preliminary phase which I have described as "growth of the stroma"; from my point of view, the omission to recognize this as a primary division is an error which goes to the root of a proper understanding of the forces, whatever they may be, which cause menstruation; for I hold there is no doubt that a period of growth precedes the

increased supply of blood which subsequently flows to the mucosa, and that it is to the forces which bring about this growth we must look for a solution of the origin of the process of menstruation.

Then again, MINOT's term "menstruation" omits to include the degenerative processes which occur prior to the appearance of the menstrual flow, and it seems to me important that this degeneration should be recognized as a distinct phase of the process.

MINOT describes an infiltration of blood from the vessels—no rupture of vessels at this stage having in his opinion been proved—and subsequent degeneration of the superficial layers of the mucosa, but he thinks the degenerative process is of later occurrence than the bleeding, and that it does not cause the bleeding. Here my results differ from the views this author has adopted, and it may be, that it is this difference of opinion which has prevented him from placing so much stress upon degeneration as I have done.

MINOT's description of a normal virgin uterus near the close of menstruation, and his figure of the same, though the latter is on too small a scale to admit of close comparison, show a great similarity to the description and figures given in my former paper on *S. entellus*, and give increased force to the view that, broadly speaking, the process of menstruation in man and in the monkey are practically identical.

MARTIN's article (No. 12) to which I was unable until recently to obtain access, should also be noted. He states that before the menstrual flow occurs a growth of the middle layer of the mucous membrane takes place, causing it to become five or six times thicker than before, that the lymph channels and glands become wider, that the blood-vessels become gorged and some burst, and that blood finds its way into the cavity of the uterus either by extravasation or by diaporesis, adding that possibly both, but probably the former, of these processes occur. After the blood has passed out, he says, the mucous tissue breaks down, fatty degeneration occurs, and more or less of the uterine coat is thrown off.

Here, then, we have periods of growth and of degeneration; of the former of these MARTIN's description is similar to the one I have given for monkeys, but with regard to the latter there are some differences, namely, he is of opinion that firstly, the mucous tissue breaks down only after the passage out of the blood, while I show in monkeys that degeneration occurs before the blood flow begins; and secondly, that fatty degeneration occurs, whereas I can see no trace of it.

JOHNSTONE (No. 9) reiterates the opinions he published in an earlier paper, with which I have already dealt in Part I. of this work.

CHAMPNEYS (No. 3), in an able work which escaped my attention until recently, points out that the investigation, by the histologist, of the phenomena of menstruation in the human female, necessarily neglects the peculiarities of the individual. It would seem by no means improbable, that these peculiarities are sufficiently great to cause many of the diverse views held by various investigators, who have not been able to

examine a very large number of specimens, and there is no doubt CHAMPNEYS is right when he states, that the observation of the histologist needs controlling and correcting by clinical observations.

This author seeks to show that, possibly, the menstrual flow may be determined by uterine contraction acting suddenly upon a swollen mucosa, the vessels of which are distended with blood.

I am not disposed to argue that uterine contraction does not take place during the active menstrual time, but if my observations upon the degeneration of the walls of the vessels, and of the mucosa generally, are true, and if an extravasation of blood such as I have described in the case of monkeys, also takes place in the human menstruating uterus, it follows that the menstrual flow is not dependent upon uterine contractions.

Although no doubt such a force would materially assist in the ejection, from the uterus, of the mucosa menstrualis, it must be remembered that muscular contraction of the uterus will decrease the actual flow of blood, not increase it (see Part I., pp. 436-7).

The Re-formation of the Uterine Epithelium.

I have come to the same conclusion with regard to the re-formation of the uterine epithelium after menstruation, as I detailed in Part I. of this paper. Some portions of the new layer are no doubt derived from the torn edges of the epithelium of the glands, but others, I feel confident, are derived from the elements of the stroma.

In this belief I find I am not so completely isolated as I had supposed, although many observers emphatically deny that such a process takes place.

DUVAL (No. 6), who has worked at the regeneration of uterine epithelium after delivery, comes to the same conclusion as I do. The idea of the transformation of "cellules conjonctives en cellules épithéliales," he says, was so repugnant to him that he for some time disregarded preparations which appeared to show this, and it was not until he had many preparations to study, that he convinced himself, that uterine epithelial cells are actually formed from the uterine stroma; of this fact he clearly states he has now no doubt, and he considered his evidence irrefutable.

JOHNSTONE also (No. 9) believes the epithelium of the human uterus, which takes the place of that thrown off during menstruation, is regenerated, not from the remains of the old epithelial layer, but from the connective tissue structures which underlie that layer.

KIERSNOWSKI (No. 10), on the other hand, denies the fact. He gives an historical account of the literature of the subject of the regeneration of epithelium, and a very complete list of papers. His own work was done upon the regenerating uterine tissue after delivery, of various animals, and he arrives at the conclusion, that the new epithelium is derived either from existing surface epithelial elements, or from the epithelium of the uterine glands. He points out, that in numberless places, flat epithelial cells can be demonstrated to be continuous with pre-existing columnar

epithelia cells, either of the surface or of glands, and he denies that these flat cells are formed from the connective tissue cells below them.

There is no doubt KIERSNOWSKI is quite right when he points out that much of the new epithelium is derived from pre-existing epithelial elements, but that in itself is no proof that all of it is so formed.

DUVAL'S observations, and my own, show that certain connective tissue cells are transformed into epithelial cells, and I venture to think KIERSNOWSKI'S observations in no way disprove that fact. I would go further, and would point out that in many of the figures which he gives, the epithelium is shown to be already a continuous layer, and that it is not possible to determine from such specimens the actual origin of the cells.

Again, in fig. 2, he endeavours to show the forward growth of flat epithelial cells from cubical epithelial cells; this he does show, as I have also shown it in fig. 32 of my paper on *S. entellus* (No. 8); but there are in KIERSNOWSKI'S drawing, *also* superficial flattened cells which the author obviously intends to ascribe to this forward growth, since he shades them dark as he has done the cubical epithelium; but in my opinion, it is by no means clear that these cells are derived from pre-existing epithelial elements. The drawing is not very definite, and it stops short just at the point of interest, but it shows enough to incline me to gravely doubt the interpretation KIERSNOWSKI has put upon his own preparations.

STRAHL (Nos. 15 and 16) and NOLL (No. 14) both follow in KIERSNOWSKI'S footsteps, and both lay themselves open to the same criticism. STRAHL'S figures are even less satisfactory than KIERSNOWSKI'S, as far as any proof of the origin of the new epithelium is concerned; indeed, I cannot discover that they carry any weight at all.

On the whole, therefore, while I do not deny that some new epithelium is derived from pre-existing epithelial cells, I hold that some is also formed from connective tissue cells, and I do not believe that the authors who combat this view have made out their case.

Ovulation in Macacus rhesus.

In Part I. of this paper the conclusions were arrived at: First that ovulation does not necessarily occur during each menstrual period, secondly that ovulation is not necessarily brought about by menstruation, and thirdly that the ripening of an ovum in the ovary is a process independent of the process of menstruation.

My observations on *M. rhesus* confirm these views. In consequence, however, of the very opposite views held by many investigators of this subject, it has seemed advisable to give some details here of the specimens which I have examined.

I do not propose to discuss in detail the formation of the so-called corpus luteum. During the last two years I have been engaged with a somewhat extensive series of experiments, upon the process of ovulation in the Rabbit; these seem to me to throw considerable light upon the subject, not only of the method of ovulation, but also

regarding the formation of various kinds of corpora lutea; a detailed description of these experiments I hope to publish before long, here I will treat solely of the discharged Graafian follicles in *M. rhesus*.

Out of forty-three adult females of *M. rhesus* which were examined, twenty-two of them had no sign of a corpus luteum, or as I will call it a "discharged follicle," in either ovary; of these, fourteen were menstruating females, while the remaining eight were not menstruating at the time. On the other hand in twenty-one females a more or less prominent discharged follicle was present; of these, sixteen were pregnant females, or females which had very recently borne or aborted their young; while of the remaining five, one was a female which I am inclined to think had aborted her young, but I am not certain of the fact and consider this case doubtful (fig. 7), one was a non-pregnant, non-menstruating female (fig. 8), and three only were females in which menstruation was in progress at the time they were killed (figs. 5, 6 and 9).

Thus, out of seventeen menstruating females, three only were found, in the ovaries of which there was any sign of the existence of a discharged follicle. Of these three discharged follicles, one is undoubtedly the remains of a follicle long since discharged (fig. 5), it occurred in a female killed during Stage V. of menstruation; one is equally certainly, as I will show below, not of recent origin, it occurred in a female killed during Stage IV. of menstruation (fig. 6); and one only is a recently discharged follicle (fig. 9), and it was present in the ovary of a female killed during Stage VII. of menstruation.

Thus out of the seventeen menstruating females, in one case only was a recently discharged follicle found, and in that case only is it possible to say that ovulation and menstruation were coincident. I do not myself think that we are justified in asserting, even in this case, that ovulation and menstruation are coincident; of this point I say more below, but we are undoubtedly justified in saying, that in no other of the cases before us is there any possibility of asserting that these two processes are coincident.

The presence of ripe Graafian follicles was also looked for, and in one specimen only was a follicle found which could possibly be thought to be ripe. It was enlarged and somewhat prominent, but it appears to me impossible to be assured that it was in fact a ripe follicle, ready to discharge the ovum it contained. The female in which this was found was undergoing Stage V. of menstruation.

Passing now to a histological examination of a series of discharged follicles, a glance at the figs. 5 to 9 (Plate 1) will show the various stages which the discharged follicle passes through, on its way towards complete disappearance and amalgamation with the ovarian stroma tissue.

The first point which strikes one is the difference in the size of these discharged follicles. They are all drawn with the aid of a camera lucida, with the same object glass and eye-piece.

Omitting for a time fig. 9, the size of the other four is found to be in relation to, what I have for other reasons concluded is the comparative age of these structures.

Fig. 8 represents the most recent of the four, fig. 7 the next oldest, fig. 6 the next, and fig. 5 the oldest of the four.

The reasons which have enabled me to determine the relative age of these discharged follicles are set forth below, and are, briefly, the constitution of the material contained within the wall of the follicle and the condition of that wall itself.

I am not, however, disposed to consider the size of a discharged follicle an invariable guide to its age; fig. 9 is in direct opposition to this view; in this case the discharged follicle is of very recent origin, and yet it is smaller than that drawn in fig. 8, which represents a follicle which has been discharged some time before.

I draw attention to this question of the relative size, because the age of a "corpus luteum" has, by some authors, been determined by its size, and has led to considerable confusion. I would point out that, while in certain cases the size may be to some extent an indication of age, this is surely not an infallible guide in all cases.

I will first consider the most recently discharged follicle, shown in figs. 9, 14, and 15, obtained from an animal which was undergoing Stage VII. of menstruation when killed.

The discharged follicle is prominent, and the ovarian epithelium is attenuated where it covers the greater portion of the prominent part of the wall of the ovary, but is not present at all at the point x (figs. 9 and 15).

The contents of the follicle are not cellular, but consist of a network of densely granular material, and, with the exception of a very few odd isolated nuclei and a few scattered red blood corpuscles at the edge of the cavity, it contains nothing else (fig. 14). There is no sign of a blood clot.

The follicle wall is composed mainly of branched cells amongst which blood-vessels run (fig. 14), but, at its inner edge, these cells become longitudinally disposed and form a denser, almost fibrous inner boundary, which sharply separates the wall itself from the central cavity.

Blood-vessels are present both in the wall of the follicle and in the surrounding ovarian tissue, but they are larger and more numerous in the latter position.

The appearance of this follicle, as shown in fig. 9, its prominence on the surface of the ovary, and its pear-shaped central cavity, with the apex so nearly approaching the surface, indicates a recently discharged follicle. A more detailed examination of the point x and the neighbouring tissue, leaves no room for doubt that such is the case (fig. 15).

The ovarian epithelium, which is much flattened over the prominent swollen portion, is at the point x absent altogether, and from this point downwards to the apex of the follicular cavity, the tissue there existing is very much less dense and compact than is that of the rest of the ovary, while extravasated blood is present in this region, and is connected with a lacuna close to the surface of the ovary at x . This

region seems to mark the line of rupture of the follicle, and, although one cannot say when the rupture took place, there seems good reason to believe it is of recent occurrence. The fact that this specimen was found in an animal which was menstruating at the time of death would doubtless, by many investigators, be considered sufficient evidence of the age of the structure, and it would, by such, be unhesitatingly asserted that in this case the follicle was ruptured during the act of menstruation then in course of progress.

It may be that this is the case, but I cannot admit that there is sufficient evidence of that fact. Here we have under consideration seventeen specimens of menstruating *M. rhesus*; in one of them, and in only one, a recently-discharged follicle is found; surely, then, very much stronger evidence must be adduced than is here obtainable before one can justifiably assert, that the actual date of the rupture of this follicle is in any way related to the act of menstruation going on at the time the specimen was obtained.

The second specimen is drawn in figs. 8 and 13. The animal from which this specimen was obtained, was not menstruating when it was killed, neither was it with young. It had been in my possession in Cambridge for fourteen months, and had not had access to a male during that time. It had suffered much from cold and cough, and had menstruated very irregularly while I had it.

In this case, also, the follicle is near the surface of the ovary, and forms a prominent swelling thereon. The ovarian epithelium, although much flattened, is, however, intact, and there is no evidence of the actual rupture of the follicle; at the same time there can be little doubt rupture has taken place in this case, and probably at no very distant date, at the point *y*. The wall of this follicle is much thicker than is the wall of the former specimen (fig. 9); hypertrophy has taken place; it is also characteristically folded, and contains blood-vessels. It is formed of branched cells, as in the case of the specimen just considered (compare figs. 13 and 14), but there is one prominent difference between the two: in the case now under consideration, in which hypertrophy has taken place (compare figs. 8 and 9), the inner boundary of the wall, instead of being more dense than the rest, is now irregular reticulated tissue, just like the rest (fig. 13); and, instead of being sharply defined, its cells are now continuous, with a loose wide-meshed network of cellular tissue, which now extends throughout the follicular cavity.

It would seem possible, that a certain amount of this interfollicular reticulated tissue is derived from tissue which grows in through the point of rupture, but there is abundant evidence to show that a very large portion of it, if not all, has its origin from the cells of the wall of the follicle. In every section the inward growth of these cells of the follicle wall is shown, and so also is their connection with the long-branched processes of the cells within the cavity.

There is no sign of a blood clot within the follicle; even isolated blood corpuscles are rarely met with, and only then close to the edge of the follicle wall.

The third specimen, drawn in figs. 7 and 12, shows a still further development. It is taken from a specimen, the history of which I am not quite certain about (see page 150), but for my present purpose it is of use, as showing an intermediate stage of the degeneration of the follicle.

The swelling on the surface of the ovary is not so pronounced as before, and the ovarian epithelium is formed of cubical cells. The follicular walls are more folded and the cavity smaller than before, while the blood-vessels are larger and more numerous, and exist now in the cavity as well as in the walls of the follicle. There is no blood clot, however, in the cavity of the follicle.

The cells of the wall are showing a change of arrangement; certain of them are becoming more rounded, and others are extending round these; the nuclei of the cells are noticeably reduced in size, and the tissue is more dense than it was in the second case. There is no longer any sign of hypertrophy.

The tissue within the small cavity of this follicle is also undergoing a change; the reticulated arrangement, seen in the cavity of the second specimen, is lost in this one, and minute branched nuclei, embedded in a homogeneous matrix, take its place.

Taken as a whole, this structure is smaller, and the tissue of which it is composed is denser than is the case in the preceding specimen.

The fourth specimen, drawn in fig. 6, was found in the ovary of a female which was killed during Stage IV. of menstruation. It is smaller than the previous specimen (fig. 7); the walls are less folded, and the central cavity is smaller, the blood-vessels, also, are fewer, and the whole structure lies deeper in the ovarian tissue.

The minute histology of this specimen shows similar advances. The tissue within the cavity of the follicle is now hardly to be distinguished from that composing its wall, and both are denser and more compact than has been hitherto described. Blood-vessels occur only in reduced numbers in the wall and in the tissue occupying the centre of the follicle, and they are also smaller than those seen in fig. 7.

If further evidence be required to prove that this follicle is of greater age than the one previously described, it is to be found in the occurrence of young Graafian follicles, each of which contains an ovum, which are situated between it and the surface of the ovary. These young follicles have no doubt been developed since the older follicle was discharged.

Finally, in figures 5 and 11, the fifth specimen is represented. The animal from which it was obtained I kept for some months in Cambridge; it menstruated regularly in May, June and July of 1892, and was killed in the latter month while undergoing Stage V. of menstruation.

The remains of this discharged follicle, the only one to be found in either of the ovaries, caused a slight swelling on the surface of the ovary, although the ovarian epithelial cells were not stretched and retained their usual cubical form. No central cavity is visible in this specimen, and no trace of the folded walls present in those previously described, is present in this one. A nearly solid mass of tissue (fig. 11), in

the midst of which here and there a few blood-vessels run, is all that remains of the follicle.

The cells of which it is composed scarcely differ from the cells of the ovarian stroma, and consist of polyhedral cells or multinucleated polyhedral protoplasmic masses, with intermediate finely branched connective tissue elements, bounding them, and grouping them into nests.

A thin layer of fine nucleated fibres and a few larger blood-vessels seem to separate this structure from the rest of the ovarian stroma (fig. 5), while in time even this boundary will disappear, and the remains of the follicle will no longer be distinguishable as such.

For the sake of comparison I have included here drawings of sections of a "corpus luteum," in an ovary of a *M. rhesus*, in which a six to eight weeks foetus was present (figs. 10 and 16, Plate 2). It was the only structure of the kind present in either ovary of the animal and is, no doubt, the remains of the follicle from which the ovum was discharged which gave rise to the embryo in the uterus.

This discharged follicle is sunk well within the normal boundary of the ovary and caused no swelling on its surface. The folded walls and central cavity filled with tissue, also the blood-vessels both in the central cavity in the follicle wall and in the surrounding tissue, are all here precisely as in the specimens already described.

The structure of the central tissue (fig. 16) is very similar to that shown in fig. 12, but the tissue of the wall of the follicle is more advanced than in fig. 12, and is intermediate between the latter and the specimen shown in fig. 11.

There is no central blood clot in this specimen.

In conclusion, then, we may describe the changes undergone by the discharged follicle as, firstly, hypertrophy, resulting in a folding of the follicle wall, and a filling up of the central cavity with connective tissue; and secondly, consolidation, which is brought about by the absorption of some of the elements, and the contraction of the other elements, of the tissue concerned.

The increased supply of blood to the wall of the follicle (compare figures 6, 7 and 8), indicates the method whereby the process of absorption is carried out.

Ovulation in Semnopithecus entellus.

I recorded in Part I. of this paper (No. 8), that out of forty-two menstruating specimens of this monkey, none of which had recently borne young, only two had a "recent" discharged follicle in their ovaries. This statement I must now modify.

Sections show that in neither of these cases was a recently discharged follicle present. The vascularity which had misled me was due, not to the presence of a blood clot within the follicles, as I had supposed, but to superficial hæmorrhage in no way connected with recently-discharged follicles.

Thus it is seen, that not a single one of the forty-two menstruating *S. entellus* which were examined, had a recently-discharged follicle in either ovary.

Ovulation in the Human Female.

The work of DALTON (No. 5), so frequently quoted by those who still uphold the view that ovulation and menstruation are coincident, seems to me to fail to prove the view he advanced, primarily because satisfactory proof is not given of the actual rupture of the follicles. The figures given offer no proof whatever of the minute anatomy mentioned in the text, and I know, from the experience I have had while working at the question of ovulation in the rabbit, how difficult it is always to determine satisfactorily whether or not a follicle has been ruptured.

The only corpora lutea which are definitely shown in DALTON'S works to have a ruptured wall, are those drawn in figs. 10 and 11; they were observed in women who died, the first a few hours after delivery at term, the second three days after delivery; these may therefore be disregarded. The figures of so-called corpora lutea supposed to be formed during menstruation, do not definitely show rupture. Fig. 3, nine days after menstruation, and fig. 4, ten days after menstruation, are doubtless intended to show the point of rupture, but they do not at all prove it, while fig. 1, two days after menstruation, shows no sign of rupture, and one would expect the rupture to be more easily seen then than seven or eight days later.

It is not enough to show a prominent follicle full of blood as proof that the follicle has ruptured; it is quite certain that a follicle may rupture without the subsequent formation of a blood clot within it, and it is, in my opinion, equally certain that a blood clot may be present in a degenerate follicle which has not burst and which will not burst; I have many examples of rabbits' ovaries which I think conclusively prove this latter statement.

MARTIN (No. 12) considers that menstruation and ovulation are generally coincident, but either may take place without the other, exceptionally.

CHAZAN (No. 4), after a long critical study of the subject, concludes that the ripening and bursting of Graafian follicles goes on uninterruptedly, and is in no way bound to the time of menstruation; at the same time he holds that the process of menstruation is connected with the scope of ovulation, but the connection is not one of time.

CHAMPNEYS (No. 3) is disinclined to dissociate ovulation and menstruation, and argues that the congestion which affects the uterus also affects the ovaries and the rest of the pelvic organs.

LEOPOLD and MIRONOFF (No. 11), in their recent elaborate study of ovulation in the human female, give the result of their examination of forty-two cases, which comprise examples of almost all stages of the menstrual cycle. From these results they conclude that menstruation and ovulation fall together in thirty of these cases, and that menstruation without ovulation occurs in twelve.

Unfortunately these authors do not give any satisfactory figures of the specimens from which they draw their conclusions, and it is difficult to form an opinion as to the

correctness of their interpretation of a recently-ruptured follicle, or of a ripe vesicle ready to burst.

Such statements occur as, for instance, that a certain follicle (seen in an ovary which was excised some days after menstruation) would have ruptured at the next menstrual period. As it is impossible to verify such a statement, and as its enunciation demonstrates a preconceived opinion, one naturally looks with caution upon the conclusions arrived at. The material, which these authors investigated, was most carefully chosen, and was obtained by operation from patients who were able to give satisfactory information of their menstrual history for the previous year.

The part which congestion plays in the matter of ovulation, they claim to be of very great importance. Chronic inflammation of the ovary and surrounding parts is, they say, accompanied by a rapid development and ripening of the ova; while anæmia checks, if it does not entirely prevent, the rupture of follicles. They describe a ripe follicle as thin-walled and characteristically congested with blood, and a typical corpus luteum as being, on the third day after bursting, a large cavity filled with blood; they conclude that the bursting of a follicle demands a strong blood-pressure to the generative organs, and that it is brought about by the swelling influence of menstrual congestion.

On the other hand, they state that, in spite of regular "periods," a follicle does not always rupture, and that a corpus luteum may form when menstruation does not coincide with its formation; they add that large ripe follicles are found in the ovaries at all periods of the menstrual cycle, from the third to the thirtieth day, and they own that these may rupture, and conception may take place, at any time.

Finally, they define menstruation as a period of bleeding from the mucous membrane; they add that the bleeding is connected with the presence of the ovary and with sufficient growth of uterine mucous membrane, and they conclude that, without the mutual action of both these factors, a typical menstrual bleeding does not take place. At the same time they qualify this conclusion with the remark, that uterine bleeding does not depend upon the ripening or bursting of a follicle, and that menstruation is, therefore, due less to the rupture of an ovarian follicle than to the atrophy of uterine mucous membrane.

It is not an easy matter to reconcile these various conclusions. One is forced, it appears to me, to believe that menstruation and ovulation in the human female are governed, either by individual peculiarities, or by two or more laws, which do not operate always at the same time.

The varied conclusions which many eminent investigators have independently arrived at, can only be reconciled with one or other of these assumptions, and the results of LEOPOLD and MIRONOFF'S work certainly give increased force to the latter view.

My own researches on monkeys have not been sufficiently complete to enable me to compare what happens in their case, with the story LEOPOLD and MIRONOFF tell. There is good reason to believe that the monkeys which I have investigated have a

definite breeding season, and it must be remembered that I have only had an opportunity of examining them at a time which was not the breeding time. I have found that at this period ovulation is exceedingly rare, although menstruation seems to occur regularly enough. It is quite possible that, during the breeding season, ovulation and menstruation may, as a general rule, have some definite close relation the one to the other; at non-breeding times this is certainly not the case.

Such comparison as we are able to make between the two animals, man and monkey, lies in the fact that they both may menstruate without ovulation taking place. The monkey during non-breeding times rarely ovulates, the human female also does not at all times do so; but whether these times in the human species are at regular or irregular intervals, and whether they have any relation to definite times for conception and breeding, there is no present means of knowing. Upon this latter point I have some words to add in the following section.

The Discharged Follicles of Monkeys as Compared with those of the Human Female.

In concluding this account of the discharged follicles of *M. rhesus*, which I have examined, I would especially draw attention to the absence of a blood clot in any of them. DALTON (No. 5) describes the normal human corpus luteum as filled with blood soon after rupture has taken place, and he thinks that when no blood clot is present it is probably due to abnormal menstrual conditions.

These views seem to be adopted by a considerable proportion of the medical profession, although some take the opposite view and, like COSTE, consider the presence of a blood clot in the follicle to be an abnormal condition.

I have no experience myself of the subject, but it would seem to be undoubtedly the fact that, in the human female, discharged follicles sometimes have a blood clot within them and sometimes there is no blood clot present. If the presence of a blood clot in the discharged follicle of the human female is a normal condition, then the discharged follicles of *M. rhesus* described above, differ in a marked manner from them, and yet they are both menstruating animals.

With regard to *M. rhesus* it may be suggested, in the case of the follicle drawn in fig. 8, that it was ruptured when menstruation was not going on, and that as the vessels of the ovary were not congested to the same extent as they would be during the menstrual period, the absence of a blood clot in this follicle may readily be accounted for.

LEOPOLD and MIRONOFF (No. 11) hint at some such difference in the human corpora lutea. But the follicle drawn in fig. 9 was obtained from an animal while undergoing Stage VII. of menstruation, and yet in this case no blood clot is present. A few scattered red blood corpuscles are found near the edge of the follicle (fig. 14), but there is certainly no blood clot. This would seem to show very clearly, first, that ovulation is not caused by the direct presence of free blood in the follicle, as was at

one time believed, and secondly, that the congestion of the menstrual period is not the cause of the presence of a blood clot in the discharged follicle.

There is, however, another reason which might account for the absence of a blood clot in these follicles of *M. rhesus*, and it is this, that they were not formed during the breeding season.

I have no experience myself of the relative congestion of the ovaries of monkeys during the breeding and non-breeding seasons, but I have thought it might be quite possible that there is a considerable difference in the amount of blood supplied to the ovaries at these different times, and that, during the breeding season, a blood clot might be formed within the discharged follicle.

I have enquired about this point from Professor HUBRECHT, who with untiring energy has collected a very large series of the generative organs of pregnant monkeys, lemurs, and insectivora, and he has most kindly sent me a brief account of the newly discharged follicle of *Tarsius spectrum*.

In this animal, after the ovum is discharged, the cavity of the follicle contains only an albuminous coagulum; very soon congestion of the walls of the follicle takes place, and at the same time a considerable proliferation of the cells of the wall greatly reduces the size of the central cavity; subsequently, extravasation of blood takes place into the remains of the cavity, and a small blood clot is formed there which persists for a short time only.

Thus it may be said in regard to monkeys that, while in the non-breeding season (*M. rhesus*) the discharged follicle contains no blood clot, during the breeding season (*T. spectrum*) a blood clot is formed therein.

This condition in monkeys becomes of increased interest when compared with the condition in the human female.

In both animals menstruation occurs, in both, ruptured follicles containing a blood clot and ruptured follicles without any blood clot are found.

Now, with regard to monkeys, I have shown that the evidence is opposed to the view that menstruation has anything to do with the presence or absence of a blood clot in the follicle, and I have advanced some evidence in favour of the view that it is to the presence or absence of the breeding season we must look for an explanation of the difference.

The question naturally arises, whether we may look for a similar explanation of this same variation in the human female. I do not suggest that there is evidence of the occurrence of one or other of these two kinds of discharged follicles at particular seasons, but I do suggest there is some reason to believe that the human female is not always in a condition to breed, and that it is during such times that a discharged follicle contains no blood clot.

It is possible to carry this analogy still further, and to suggest, that the occurrence of non-breeding times in the civilised woman of the present day, although it may

now be an irregular occurrence, is not incompatible with the belief that at one period of its existence the human species had a special breeding season.

Considered alone, of course, this slender evidence is of little value, but when it is placed side by side with other evidence, of which there is a considerable amount, the deduction is by no means an impossible one.

I had intended here to include a brief account of certain evidence, which I have collected, upon this question of a primitive human breeding season, but I find the subject will be better discussed in a separate paper, and I will content myself with drawing attention to this single point here.

SUMMARY.

Anatomy of the Cervix.—The existence of a valvular structure in the cervix is described. It seems probable that this valve assists in the retention of spermatozoa in the uterus.

Breeding.—The probability of different breeding times for this monkey in different parts of the continent of India is argued, and the existence of a definite breeding season maintained.

It is pointed out that further information is required to establish definitely the period of gestation.

Menstruation.—A regular menstrual flow is described.

External Signs of Menstruation.—A congestion of the skin of the abdomen, legs, and tail, a swelling and congestion of the nipples and vulva, and flushing of the face are prominent signs.

Menstrual Discharge.—This consists of a viscid, stringy, opaque white fluid filled with granules, and containing also red blood corpuscles, pieces of uterine tissue both stroma and epithelium, and also leucocytes.

Leucorrhœa was observed in one case, and consisted of a viscid, opaque fluid filled with granules chiefly derived from the uterus, and squamous epithelial cells from the vagina.

Superficial Menstrual Phenomena.—The stages of menstruation adopted in this paper are identical with those fully described in Part I., on *Semnopithecus entellus*. The smooth surface of the mucosa (Stage I.) becomes swollen, and opaque (Stage II.), then flushed (Stage III.), then highly congested (Stage IV.). Dark red spots, lacunæ, appear on the surface (Stage V.), and free blood in the uterine cavity (Stage VI.). The menstrual clot is formed (Stage VII.), and recuperation follows (Stage VIII.).

Histology of Menstruation.—The account of the histological changes which take place, resolves itself into a repetition of the description given of *S. entellus* in Part I. of this paper. The mucosa of *M. rhesus* is thicker, the protoplasmic network of the stroma denser, and the glands more numerous and more branched than in *S. entellus*.

The increase in number of the nuclei in Stage II., caused by amitotic division and fragmentation, is very marked; hyperplasia occurs, and the mucosa becomes swollen.

The vessels increase in number and size, and leucocytes increase in number in Stage III.

Hypertrophy of the walls of the vessels, followed by degeneration in the superficial part of the mucosa, occurs in Stage IV., and lacunæ are formed in Stage V., while degeneration of the epithelium and superficial stroma, followed by rupture of the lacunæ and free bleeding, is seen during Stage VI.

The denudation of the stroma and the formation of the mucosa menstrualis and clot in Stage VII. is the same as in *S. entellus*, and so also is the recuperation of hypertrophied vessels, the formation of new capillaries, and the reclamation of red blood corpuscles in the stroma during Stage VIII.

With regard to the new uterine epithelium, fresh evidence is found of its formation, partly from stroma tissue, and partly from the epithelium of portions of the uterine glands left *in situ* after denudation has taken place.

Menstruation in Man.—No recent work on human menstruation has been observed which is opposed to the account given for monkeys, while MINOT'S work gives additional reason for believing that the process in these two animals is practically identical.

The Re-formation of Uterine Epithelium from Stroma Tissue.—The opinion herein urged on this matter is also held by DUVAL and JOHNSTONE, while it is opposed by KIERSNOWSKI, STRAHL, and NOLL. It appears, however, that while the three latter observers satisfactorily show a re-formation of some uterine epithelium, by direct growth, from existing epithelial elements, yet they do not show any sufficient reason for their denial of the observations of DUVAL, while one of the figures given by KIERSNOWSKI indicates that he has probably wrongly interpreted his specimens.

DUVAL, on the other hand, only arrived at the view he now holds after examination of a large number of preparations, and he has no doubt whatever of its truth.

Ovulation in M. rhesus.—Confirmation is given of the opinions before advanced (Part I.), viz., that ovulation does not necessarily occur during each menstrual period, that it is not necessarily brought about by menstruation, and that the ripening of an ovum in the ovary may be a process independent of the process of menstruation.

In only one out of seventeen cases of menstruating *M. rhesus*, can it possibly be urged that ovulation and menstruation were coincident.

An account is given of a series of discharged follicles, and the histological changes undergone by these structures is traced, until at last they are merged into the normal ovarian stroma.

The absence of a blood clot in any of the discharged follicles is drawn attention to, and the history of the connective tissue which occupies the cavity of these follicles, is followed. The folding of the wall of the follicle and the transformation of its cells into ovarian stroma tissue are also given.

Ovulation in S. entellus.—An error made in Part I. is now corrected, and it is

shown that not a single specimen, of the forty-two menstruating *S. entellus* which were examined, had a recently-discharged follicle in either ovary.

Ovulation in the Human Female.—It is pointed out, that it is not enough to show a prominent follicle filled with blood as proof that the follicle has been ruptured. It is certain that a follicle may rupture without the formation of a blood clot (man and monkey), and it is equally certain a blood clot may be present in a degenerate follicle which has not, and which never will, rupture (rabbit). It is also shown that it is not possible to diagnose the date at which a particular follicle will rupture. Although ovulation and menstruation may be coincident, this is certainly not always the case (man and monkey), and one is forced to believe that these two processes are governed by two or more laws, which do not always operate at the same time.

The discharged Follicles of M. rhesus compared with those of the Human Female.—Attention is drawn to the fact that, in the human female, some discharged follicles contain a blood clot, whereas some do not.

In monkeys, during the non-breeding season (*M. rhesus*) no blood clot is present in newly-discharged follicles, while in the breeding season (*T. spectrum*) a blood clot is present in them. It is shown that the presence of a blood clot in monkeys is not due to the coincidence of ovulation with menstruation, and it is suggested, on the other hand, that its presence is due to the coincidence of ovulation with the breeding season. A further suggestion is then made, that the presence or absence of the blood clot in the discharged follicles of the human female, is due to the coincidence of ovulation with a favourable time for conception. It is pointed out that women are not always in a condition to breed, and that it is possible the occurrence of periods during which they do not conceive, may justly be compared with the non-breeding times of monkeys.

POSTSCRIPT.

February 17, 1897.

Since the above was written, a paper by WESTPHALEN (No. 18) has appeared. His material was obtained by curetting or from uteri amputated for chronic metritis, and did not include a complete series.

He describes the dilatation of blood-vessels before menstruation begins, the infiltration of blood in the upper part of the mucosa, and the beginning of the formation of lacunæ.

Here his observations stop until after menstruation is over, when he finds some evidence of the shedding of uterine epithelium, but does not, of course, see evidence at that stage of the discarding of stroma tissue; he does not appear to have examined the menstrual discharge to see what is thrown off, and concludes that the superficial tissue, which was raised by the formation of the lacunæ, for the most part sinks down again when the lacunæ rupture, and is rapidly covered by epithelium.

After menstruation is over, according to this author, regeneration takes place, and this process lasts until about the eighteenth or nineteenth day. During this time karyokinesis was observed in each of the structures composing the uterine mucous membrane, at first only here and there, but from the sixth to the eighteenth day in great profusion; and he points out that he saw no sign of amitotic division.

After the eighteenth day a pre-menstrual swelling of the mucosa is described; it begins gradually, and consists of a serous saturation of the stroma, and an increase in volume of the glands.

If this account be correct, there is a very considerable difference between the phenomena attending menstruation in monkeys and in the human female.

The preliminary stages of congestion of the mucosa, and the formation of lacunæ, in the woman, WESTPHALEN says, are similar to what I have described for the monkey; and as he did not observe the stage during which the lacunæ are ruptured, it is possible to account for the variation in our respective views regarding the amount of uterine tissue which is discarded at that time.

But his description of the regenerative process and of the pre-menstrual swelling is entirely at variance with my observations.

The regenerative process in monkeys consists of a *shrinkage* of the bulk of the mucosa, a return of extravasated blood to the circulatory system, and a re-formation of the uterine epithelium; while, in the human female, it would appear that profuse karyokinesis takes place during that time, and that there is an *increase* of mucosa tissue.

Again, the pre-menstrual swelling in monkeys is accompanied by a very rapid increase, in numbers, of the nuclei of the stroma tissue, by, in my opinion, amitotic division; while in the human female there is no multiplication of nuclei, and the swelling is due to serous saturation of the stroma. Thus the increase in numbers of the nuclei of the stroma, in the human uterus, occurs in the inter-menstrual period, it occupies a considerable length of time, it is a leisurely process, and it is brought about by karyokinesis; while the same process in the monkey's uterus occurs immediately before congestion begins, it is a very rapid process, and is brought about by amitotic division, and by fragmentation of the nuclei.

I have suggested in my former paper that the absence of the phenomena of karyokinesis in these dividing nuclei may be due to their minute size, and to the meagre quantity of protoplasm surrounding them; it is possible, also, that the rapidity of their increase may also have some bearing on their method of division.

In this connection it is interesting to notice that BALBIANI and HENNEGUY (No. 1A) have shown that, under certain circumstances, the ends of the tails of two tadpoles, placed in contact, will, in an hour and a half, grow together by means of the superficial growth of their epithelial cells, and that this very rapid growth is brought about by amitotic division.

STRASSMANN (No. 16A) has attempted to show that menstruation and "heat" are

brought about by the increase of inter-ovarian pressure; that the pressure exerted by the growing Graafian follicle on the sensory nerve-endings in the ovary is the exciting cause of the reflex action, which brings about congestion of the genital organs, menstruation, or "heat."

Whilst this theory is not opposed to the fact that menstruation and ovulation are quite distinct processes, since it does not presuppose that the Graafian follicle necessarily ruptures, still it is in direct opposition to the fact that menstruation may occur after ovariectomy has been performed, and I do not find that STRASSMANN has satisfactorily disposed of this objection to his theory.

Finally, I would draw attention to the fact that SOBOTTA, in his admirable work on the corpus luteum of the mouse (No. 14A), lays great stress upon the fact that the increase in size of the wall of the newly-discharged follicle is due to the hypertrophy of its cells, and not to the increase in number of those cells. This result is in accord with the view I have independently arrived at, regarding the increase in size of the wall of the newly-discharged follicles of *M. rhesus*, and has not been, as far as I am aware, drawn attention to elsewhere.

LIST OF PAPERS REFERRED TO.

- No. 1. BALBIANI et HENNEGUY. Comptes Rendus, vol. 123, 1896.
 „ 1A. BLANDFORD. The Fauna of British India, Part I., Mammalia. 1888.
 „ 2. BRESCHET. Recherches anatomiques et physiologiques sur la gestation des Quadrumanes. Mémoires de l'Académie des Sciences, vol. 19.
 „ 3. CHAMPNEYS. On Painful Menstruation. The Harveian Lectures for 1890 (1891).
 „ 4. CHAZAN. Ovulation und Menstruation. Archiv für Gynäkologie, vol. 36, 1889.
 „ 5. DALTON. Report on the Corpus Luteum. Transactions of the American Gynæcological Society, vol. 2, 1878.
 „ 6. DUVAL. De la régénération de l'épithélium des cornes utérines après la parturition. Comptes Rendus et Mémoires de la Société de Biologie, Series ix., vol. 2, Dec. 13, 1890.
 „ 7. GEOFFROY SAINT-HILAIRE et CUVIER. Hist. Natur. des Mammifères.
 „ 8. HEAPE. The Menstruation of *Semnopithecus entellus*. Philosophical Transactions of the Royal Society, vol. 185, 1894.
 „ 9. JOHNSTONE. Menstruation, its Necessity and Purpose. American Journal of Obstetrics, vol. 24, 1891.
 „ 10. KIERSNOWSKI. Zur Regeneration des Uterus-Epithels nach der Geburt. MERKEL und BONNET, Anatomie und Entwicklungsgeschichte, vol. 4, Part iii., 1894.

- No. 11. LEOPOLD und MIRONOFF. Beitrag zur Lehre von der Menstruation und Ovulation. Archiv für Gynäkologie, vol. 45, 1894.
- „ 12. MARTIN. The Physiology and Histology of Ovulation, Menstruation, and Fertilization, &c. HIRST's System of Obstetrics, vol. 1, 1888.
- „ 13. MINOT. Text Book of Human Embryology, 1892.
- „ 14. NOLL. Beiträge zur Kenntniss des Raubtier-Uterus nach dem Wurf. MERKEL und BONNET, Anatomie und Entwicklungsgeschichte, vol. 5, Part xvi., 1895.
- „ 14A. SOBOTTA. Ueber die Bildung des Corpus luteum bei der Maus. Archiv. f. Mik. Anat., vol. 47, 1896.
- „ 15. STRAHL. Die Regeneration der Uterus-Schleimhaut der Hündin nach dem Wurf. Anat. Anzeiger, vol. 9, No. 21.
- „ 16. — Die puerperale Uterus der Hündin. MERKEL und BONNET, Anatomie und Entwicklungsgeschichte, vol. 5, Part. xvi., 1895.
- „ 16A. STRASSMANN. Beitrag zur Lehre von der Ovulation, Menstruation, und Conception. Arch. f. Gynaekologie, vol. 52, 1896.
- „ 17. SUTTON. Menstruation in Monkeys. British Gynæcological Journal, vol. 2, 1880.
- „ 18. WESTPHALEN. Zur Physiologie der Menstruation. Arch. f. Gynaekologie, vol. 52, 1896.

DESCRIPTION OF PLATES 1 AND 2.

Reference Letters.

<i>bl.c.</i>	red blood corpuscles.	<i>gr.v.</i>	Graafian vesicle.
<i>bl.v.</i>	blood vessel.	<i>in.os.</i>	internal os.
<i>c.</i>	cervix.	<i>lac.</i>	lacuna.
<i>c.c.</i>	canal of cervix.	<i>muc.</i>	mucosa.
<i>cav.tis.</i>	tissue within the cavity of the follicle.	<i>o.</i>	ovary.
<i>ep.</i>	epithelium.	<i>ut.</i>	uterus.
<i>ex.os.</i>	external os.	<i>ut.c.</i>	cavity of the uterus.
<i>f.w.</i>	wall of the follicle.	<i>vag.</i>	vagina.
		<i>vl.</i>	valve.

PLATE 1.

Fig. 1. Stroma cells dividing into two. (REICHERT's Imm. $\frac{1}{5}$ occ. 4.)

Fig. 2. Showing division by fragmentation of the nuclei of the stroma. *a*, *b*, and *c*, groups of nuclei derived from a single nucleus by fragmentation. (REICHERT's Imm. $\frac{1}{5}$ occ. 4.)

- Fig. 3. The uterus, cervix, and part of the vagina of *M. rhesus*. It is cut open along the left and anterior borders of the organ, and the walls of the enclosed cavity are exposed. The uterine mucosa is smooth and soft. The canal of the cervix is longitudinally folded, and from the ventral wall of the cervix a thick lobe projects, which fits between two lobes on the dorsal wall and forms therewith a valve. ($\times 1\frac{1}{2}$ times.)
- Fig. 4. Longitudinal vertical section through the antero-posterior walls of the uterus, cervix, and part of the vagina of *M. rhesus*. The cavities of the uterus and vagina, and the long narrow tortuous canal of the cervix are shown. The valve-like structure is also shown *in situ*, the single lobe of the anterior wall of the cervix being fitted between the two lobes on the posterior wall.
- Fig. 5. Remains of a ruptured follicle, from the ovary of a *M. rhesus* undergoing Stage V. of menstruation. The walls of the follicle are no longer folded, and the central cavity is obliterated. (ZEISS, α^* , occ. 2.)
- Fig. 6. A ruptured follicle, from the ovary of a *M. rhesus* undergoing Stage IV. of menstruation. The walls are much folded, and hardly distinguishable from the central cavity. Four Graafian vesicles lie outside this follicle. (ZEISS, α^* , occ. 2.)
- Fig. 7. A ruptured follicle, from the ovary of a *M. rhesus* which had probably aborted her young. The walls are much folded, and the central cavity, though small, is distinct. (ZEISS, α^* , occ. 2.)
- Fig. 8. A ruptured follicle from the ovary of a non-menstruating *M. rhesus*. The walls are but slightly folded, and the contained cavity is wide and large. (ZEISS, α^* , occ. 2.)
- Fig. 9. A recently ruptured follicle, from the ovary of a *M. rhesus* undergoing Stage VII. of menstruation. The walls are not folded, the follicular cavity is large and pear-shaped, the apex approaching near to the surface of the ovary, which, at the point x , is devoid of epithelial covering. (ZEISS, α^* , occ. 2.)

PLATE 2.

- Fig. 10. A corpus luteum from the ovary of a *M. rhesus*, in which a six to eight weeks old embryo was found. The follicle has sunk away from the ovarian epithelium, the walls of the follicle are much folded, and the contained cavity is small and narrow. (ZEISS, α^* , occ. 2.)
- Fig. 11. A piece of the follicle represented in fig. 5, showing the nests of polyhedral cells, or of nuclei in a polyhedral mass of protoplasm, and surrounded by branched connective tissue elements. (ZEISS, C, occ. 4.)

Fig. 12. A piece of the follicle represented in fig. 7, showing the minute branched nuclei embedded in a matrix, which fills the cavity of the follicle, the branched cells of the follicle wall are also shown. (ZEISS, C, occ. 4.)

Fig. 13. A piece of the follicle represented in fig. 8; the tissue in the cavity of the follicle is a very loose, wide-meshed connective tissue, continuous with the branched cells of the follicle wall. (ZEISS, C, occ. 4.)

Fig. 14. A piece of the follicle wall represented in fig. 9. The material in the cavity of this follicle is not cellular, but consists of a network of finely granulated material. A few red blood corpuscles lie within its meshes near the wall of the follicle, but there is no blood clot.

The wall of the follicle is formed of branching cells, except along its internal edge, and here it is composed of longitudinal, finely drawn out cells, sharply marked off from the follicular cavity, but continuous with the branched processes of the deeper seated cells of the wall. (ZEISS, C, occ. 4.)

Fig. 15. A piece of the apex of the follicle drawn in fig. 9, together with the tissue intervening between it and the surface of the ovary. The ovarian epithelium is absent at the point *x*, and is much flattened on either side of this point. Between the apex of the follicle and the point *x* the tissue is loose and open; it consists of a wide-meshed connective tissue with few nuclei, and many extravasated red-blood corpuscles are scattered about therein. (ZEISS, A, occ. 4.)

Fig. 16. A piece of the follicle represented in fig. 10, showing the branched nuclei of the tissue contained within the follicle, and the early formation, in the follicle wall, of nests of nuclei surrounded by branched connective tissue cells. (ZEISS, C, occ. 4.)

Fig. 1.



Fig. 2.



Fig. 3.

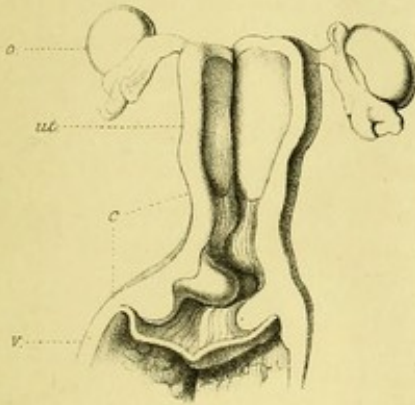


Fig. 4.

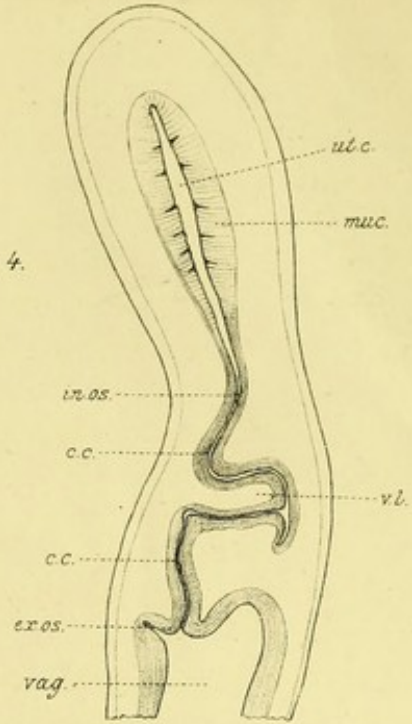


Fig. 5.

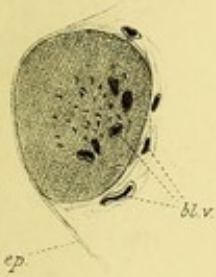


Fig. 6.

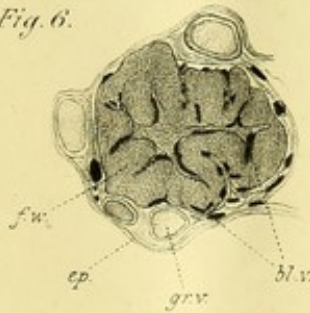


Fig. 7.

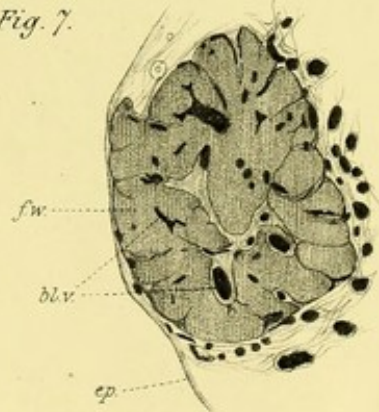


Fig. 8.

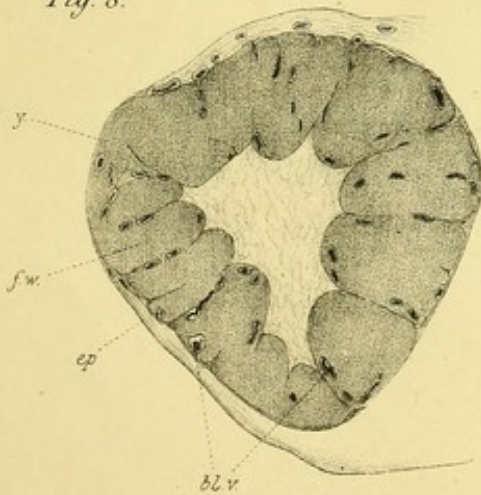
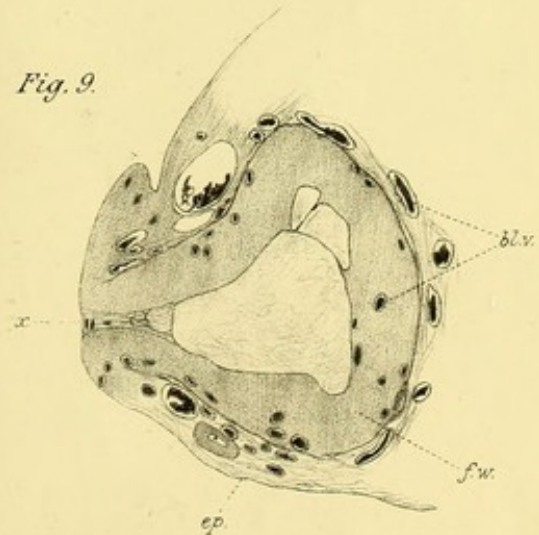


Fig. 9.



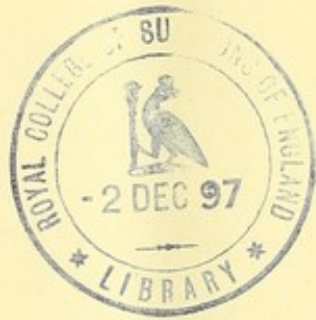


Fig. 10.

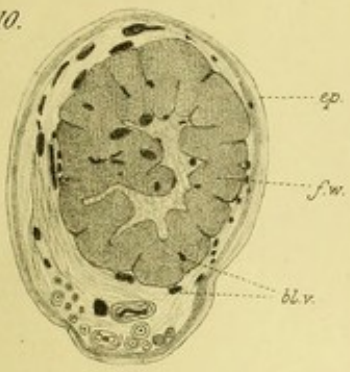


Fig. 11.

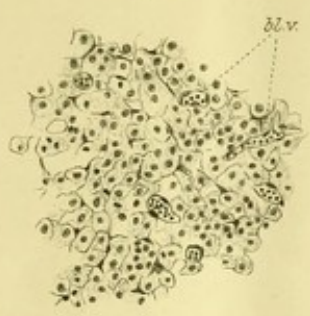


Fig. 12.

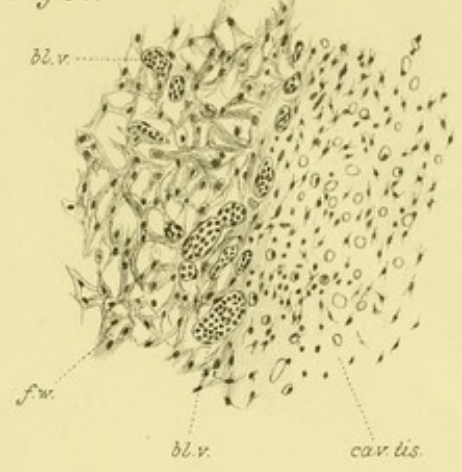


Fig. 13.

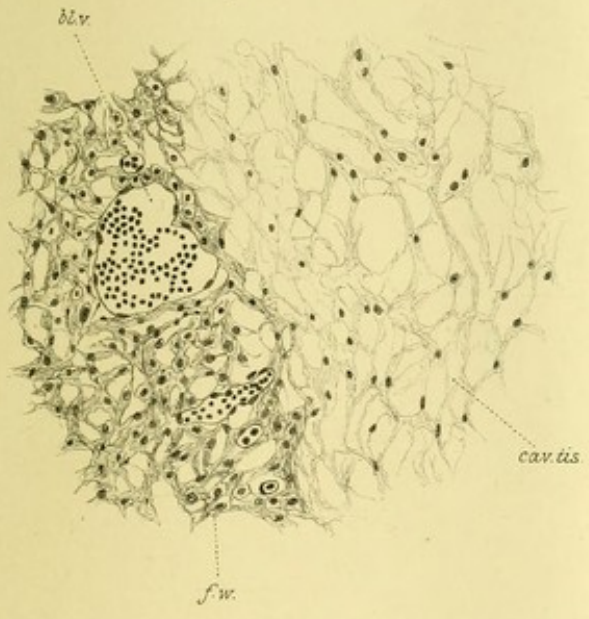


Fig. 14.

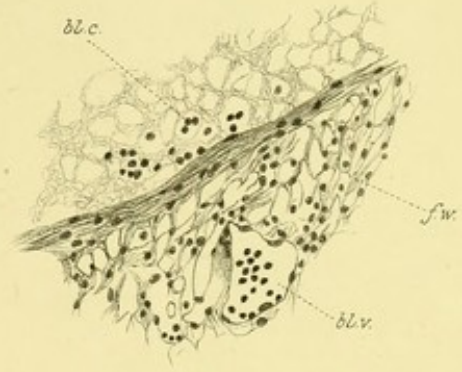


Fig. 16.

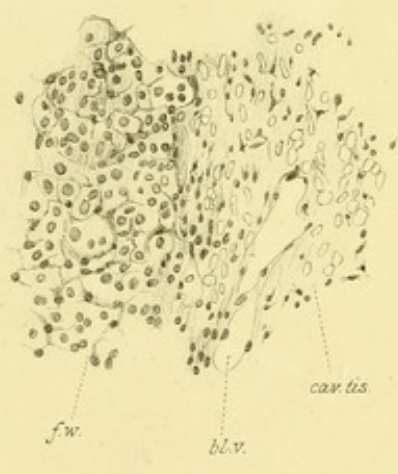


Fig. 15.

