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Elephantulus Going into Anoestrus; Menstruation and Abortion

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ELEPHANTULUS GOING INTO ANOESTRUS; MENSTRUATION AND ABORTION

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CONTENTS

Elephantulus myurus jamesoni comes into oestrus at the end of July or beginning of August. For most animals the breeding season ends in January. Some animals may go into anoestrus in December, others only in March. During the breeding season ovulation, fertilization, pregnancy, parturition, post-partum ovulation and fertilization follow each other without interruption or mishap. As at the end of the season also the males go into anoestrus (see a following paper by Miss Z. Stoch, p. 99), a female then often ovulates without being fertilized; the result is a true menstrual cycle. The female may go into anoestrus at any time at the end of the season, independent from the stage in which she happens to be, except that a menstrual cycle, once started, will be completed. Young animals may go into anoestrus directly on reaching sexual maturity; they may menstruate first or become pregnant. Similarly, an old animal may go into anoestrus directly after parturition, but it may also ovulate, menstruate or become pregnant before going into anoestrus. When anoestrus sets in, a pregnancy can be interrupted by abortion at any stage of the development of the embryo.

The events observed in *E. myurus jamesoni* have been compared with similar phenomena in other mammals. Reasons have been given why the phenomena, described in *Elephantulus*, must be considered to be a real menstrual cycle.

* Professor van der Horst died on 10 October 1951. This paper was revised and seen through the press by Dr Muriel McKerrow.

Introduction

When I published, in 1946, an account of the biology of reproduction in the female of *Elephantulus*, one section was purposely omitted. This section should have been concerned with the period when *Elephantulus* goes into anoestrus, which happens to be round about January. The material collected at that time was totally insufficient for this study; a few hundred more animals were collected therefore in December, January and February of the following years. In most of these animals, as in those previously collected, the left uterine horn, with its ovary, was serially sectioned. When the animal was heavily pregnant and the length of the embryo could readily be measured, the ovary only was sectioned, and in these cases a study of the ovary yielded sufficient information.

All animals were dated, numbered and preserved, so that if required, the other uterine horn, or any other organ, was still available for investigation. Some material collected in previous years has also been used, although it has the disadvantage that it was not dated.

When a young animal reaches sexual maturity during the breeding season, it invariably ovulates, is fertilized and becomes pregnant. However, when the young animal reaches puberty at the normal end of the breeding season, i.e. in January, various things may happen. (i) In the simplest case the animal goes into anoestrus directly for the next half-year. (ii) The animal may first ovulate and then go into anoestrus. (iii) The ovulation may be followed by a menstruation. (iv) A second, sometimes a third, ovulation, with or without succeeding menstruation, may occur. (v) An animal may be fertilized at the first or subsequent ovulation and become pregnant. (v*a*) A pregnant animal may abort during various stages of early pregnancy. (v*b*) The pregnancy may be brought to a successful end and thus the animal comes in the next category of older animals.

An old animal, i.e. one that has given birth once or more times when the normal end of the season is reached, also exhibits various potentialities, but mostly post-partum ovulation takes place. Normally, during the height of the breeding season, the animal immediately becomes pregnant again after parturition. At the end of the season post-partum ovulation may be followed directly by anoestrus, or all the other possibilities, mentioned above for the young animal, may eventuate.

Going into anoestrus without a previous menstruation

(1) *Young animal going straight into anoestrus on reaching puberty*

This seems not to be a rare phenomenon, as altogether there are forty-two series of sections that can be classified in this category. As a good example I will take an animal killed on 31 March 1942. This animal was born in the latter part of February, thus very late in the season, and it reached maturity at a time when practically all other females were already in anoestrus.

The multilayered Graafian follicles in the ovary showed that it had reached the age of puberty (figure 1). Only a very few mitotic divisions could be detected in the ovary, far less than in other ovaries at the same stage of development, and this is a reliable indication that the animal was going into anoestrus. The uterus, with its dense stroma, small, darkly staining nuclei, and low epithelium, already has all the characteristics of that of an animal during anoestrus (figure 2).

(2) *Young animal going into anoestrus directly after its first ovulation*

This seems to be a rare event; it is shown by only three specimens, two of which are rather doubtful.

The animal of series 351 was killed on 23 January 1940, and some time after its first ovulation. The corpora lutea are different to those of early pregnancy, but show the same appearance as otherwise seen during menstruation (van der Horst & Gillman 1942*a*; figure 3). The lutein cells, with their very clear cytoplasm, are arranged in trabeculae by the connective tissue that has invaded the corpus luteum from the periphery (figure 4). The practical absence of mitotic divisions in the granulosa of the Graafian follicles already indicates that the normal course of events leading up to menstruation is disturbed. This is confirmed by the appearance of the uterus. Although the deeper portion of the glands is still dilated, the stroma is dense and its nuclei small, moreover the epithelium is low (figure 5). From this it is evident that the animal is going into anoestrus. The large size of the uterus, as compared with that of an animal going into anoestrus directly on reaching maturity, is a result of the ovulation having recently taken place.

(3) *Old animal going into anoestrus directly after parturition*

This occurs, however, only rarely; altogether six cases are represented in the collection.

The animal of series 832 was killed on 21 December 1943, so at a date rather early for going into anoestrus. The ovary contains large corpora albicantia, in which even an occasional lutein cell could be detected. This shows that parturition had taken place only a few days before. There are no corpora lutea and only a few multilayered follicles, none of which shows even an indication of fluid formation. Normally fluid appears in the Graafian follicles before parturition, and ovulation takes place before the old corpora lutea are transformed into corpora albicantia. Some mitotic figures were found in the granulosa cells of the younger follicles. The uterus is still large; it is in about the same stage of involution as that shown in figure 11. Also in both these uteri the stroma is dense and darkly stained by the presence of a great number of nuclei. But differing from that of figure 11, in the present case the uterine epithelium is low, which is an indication that the animal was going into anoestrus. Moreover, the nuclei of the stroma cells are getting smaller; some of them have already attained the same size as those found during anoestrus. Taking all these characteristics together, there cannot be any doubt that this animal at the time of its death was going into anoestrus directly after parturition and without a post-partum ovulation.

(4) *Old animal going into anoestrus after post-partum ovulation*

Although it is not of frequent occurrence, yet this case is represented by eleven series in the collection, a few of which, however, are doubtful. As an example we can take series 979 from an animal killed on 3 February 1945, and series 1019 from an animal killed on 29 December 1944. The corpora albicantia are still large, and the corpora lutea of the post-partum ovulation are rather young, although completely covered over by ovarial tissue (figure 6). Unfertilized eggs were found in the upper uterus. The corpora lutea, however, show unmistakable signs of degeneration (figure 7). Cell membranes, otherwise so conspicuous, have nearly disappeared; only here and there a faint indication of a cell

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membrane could be discerned. The thecal cells, with their elongated nuclei, have penetrated, but also these are not delimited from the lutein cells. Further, the nuclei of the lutein cells have not a healthy appearance; many of them show signs of shrivelling up. The whole corpus luteum looks like a post-mortem one, but the other tissues in the ovary are quite fresh and healthy.

The uterus is not yet completely involuted after parturition; it is in a late post-partum stage (figure 8). The stroma is dense and the glands narrow. If the animal were going to menstruate, the epithelium would be high, but here it is low and that indicates that the animal is going into anoestrus.

It is clear that in this case the reaction for going into anoestrus was inaugurated at the time of, or shortly after, ovulation.

The menstrual cycle

In two previous papers (van der Horst & Gillman 1941, 1942*a*), the changes taking place in the uterus and in the corpus luteum during the menstrual cycle have been fully described. All that is needed here is to give some additional information and figures based on new material acquired since the publication of these two papers and on more experience gained.

Description of figures 1 to 11

1. Part of the ovary of a young animal going into anoestrus directly on reaching puberty. (Magn. ×75.) Series 705.
2. A cross-section of the uterus of a young animal going into anoestrus directly on reaching puberty. (Magn. ×30.) Series 705.
3. Part of the ovary of a young animal going into anoestrus after the first ovulation. (Magn. ×75.) Series 351.
4. Part of a corpus luteum of a young animal going into anoestrus after the first ovulation. (Magn. ×375.) Series 351.
5. A cross-section of the uterus of a young animal going into anoestrus after its first ovulation. (Magn. ×30.) Series 351.
6. Part of the ovary of an old animal going into anoestrus after the post-partum ovulation, showing a corpus albicans, a corpus luteum and some younger follicles. (Magn. ×75.) Series 1019.
7. Part of a corpus luteum of an old animal going into anoestrus directly after the post-partum ovulation. (Magn. ×375.) Series 979.
8. A cross-section of the uterus of an old animal going into anoestrus after the post-partum ovulation. (Magn. ×30.) Series 979.
9. Part of the ovary of an old animal after the unfertilized post-partum ovulation. A corpus albicans is shown to the right and an atretic follicle to the left. The core of elongated thecal cells reaches the base of the young corpus luteum, although this is not shown in the figure. (Magn. ×75.) Series 998.
10. Part of a corpus luteum of a young animal, after an unfertilized first ovulation. The corpus luteum is covered by a thin layer of ovarial tissue, and some elongated, darkly stained thecal cells have penetrated between the lutein cells. (Magn. ×375.) Series 81.
11. A cross-section of the uterus of an old animal some time after the unfertilized post-partum ovulation. An artery with a thick, hyaline wall enters the uterus from the mesometrium. The stroma is dense and the epithelium high. (Magn. ×30.) Series 998.

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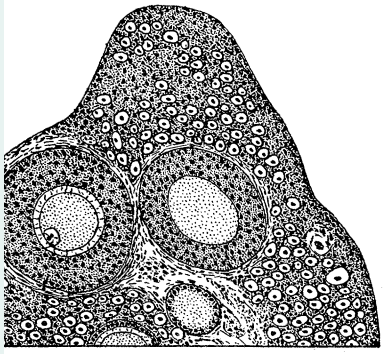

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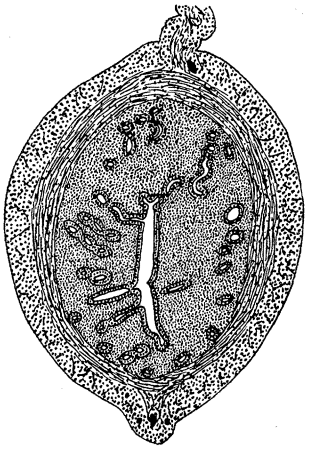

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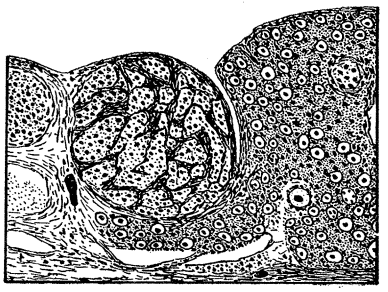

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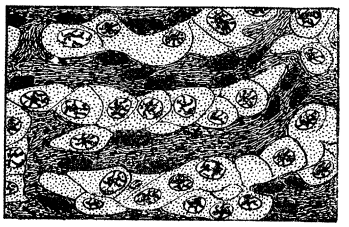

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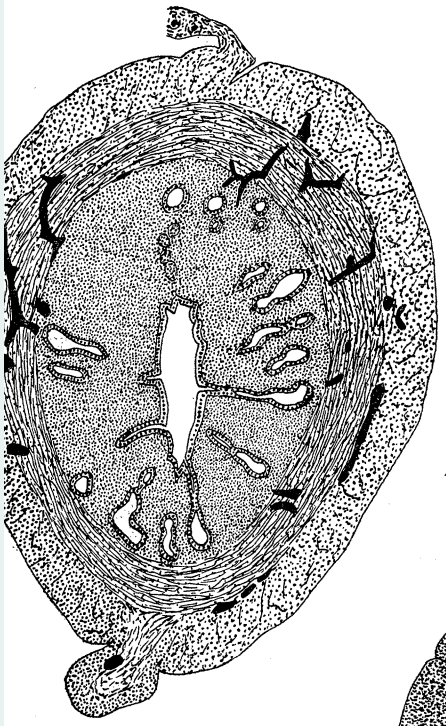

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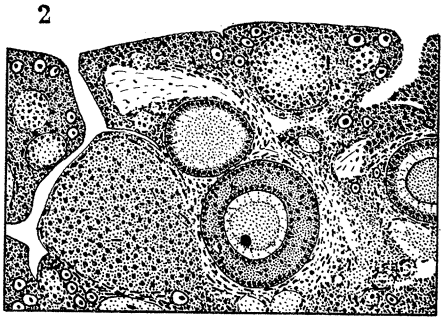

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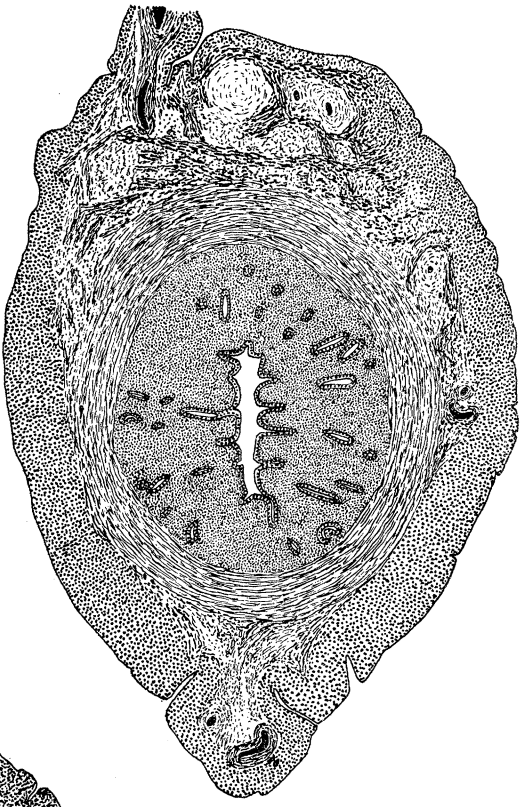

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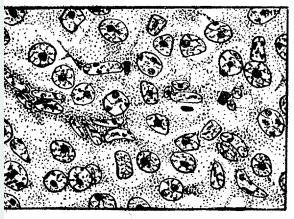

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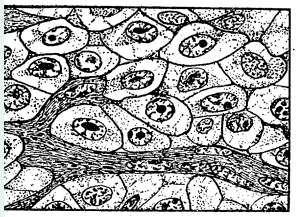

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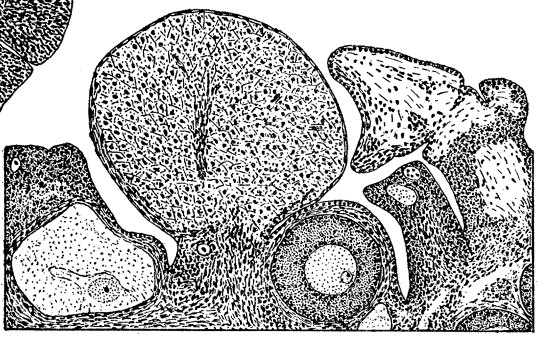

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FIGURES 1 TO 11

It is particularly noteworthy that menstruation in *Elephantulus* occurs only at the end of the breeding season. There are in the collection only one or two rather doubtful cases of menstruation during the breeding season, whereas there are many cases of the various stages of the menstrual cycle amongst the material collected at the end of the season and this equally applies to young and old animals. It follows that any animal, young or old, that ovulates during the height of the breeding season is invariably fertilized and becomes pregnant. At the end of the season, however, the female, in many cases, is not fertilized after ovulation, and then, unless the animal goes directly into anoestrus, as described above, such ovulation is followed by a menstrual cycle and sometimes by more than one cycle, before the animal goes into anoestrus.

(1) *An unfertilized ovulation*

At the time of ovulation, or very shortly afterwards, one cannot be certain whether the animal would have been fertilized, had it lived longer. Only when the eggs, accumulated in the tubal egg chamber, show unmistakable signs of disintegration, and when no sperm can be detected in the uterus, nor the result of insemination is shown by the uterine epithelium (van der Horst 1950*b*), is there certainty that we have a case of unfertilized ovulation.

There is only one young animal in the collection ovulating for the first time and falling into this category. This is series 81, but the specimen, unfortunately, is not dated. There are three cases of an unfertilized post-partum ovulation; these animals were collected on 5 March 1942, on 11 January and 3 February 1945.

A figure of the corpus luteum of the young animal was published before (van der Horst & Gillman 1942*a*, figure 7); the corpus luteum of an old animal figured here, with a corpus albicans next to it (figure 9), is in exactly the same state of differentiation. The central core of thecal cells, already considerably narrowed, is still present, and from it elongated thecal cells have penetrated between the large lutein cells (figure 10). The mass of lutein cells, however, is not yet broken up into trabeculae.

As a figure of the young animal was published before (van der Horst & Gillman 1941, figure 4), a cross-section of the uterus of one of the older animals is given here (figure 11). The latter has not yet quite recovered after parturition; it may be called a late post-partum uterus, and thus it is far larger than the uterus of the young animal. Otherwise these uteri show a striking similarity, revealing that they are in the same stage of the menstrual cycle. The stroma is getting denser, by the continued increase in the number of cells; the glands are much narrower and more coiled than at the time of ovulation, and the uterine epithelium is getting very high, consisting of thin elongated cells, with the nuclei at different levels due to the increased number of epithelial cells. Had the animals been fertilized, the epithelium would have been considerably lower (van der Horst 1950*b*). This would also have been the case had the animals gone into anoestrus directly after the post-partum ovulation (compare figures 8 and 11).

(2) *The stage of dense stroma and high epithelium*

The number of series with uteri in this stage indicates that it extends over a longer period of time than any other stage of the menstrual cycle. Thirteen series of young animals,

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having ovulated for the first time of their lives, and six series of old animals after the post-partum ovulation, can be referred to this category.

In the ovary the corpora lutea show a characteristic shape. Not only are they completely covered by the ovarian epithelium and stroma, but in contrast to an earlier stage, the main blood vessels now enter from the peripheral side and there cause a conspicuous indentation. On the other hand, the core of thecal cells, that protruded before into the mass of lutein cells from the inside, has completely disappeared and thus the corpus has assumed the form of a heart (see van der Horst & Gillman 1942*a*, figue 10). The strands of thecal cells, accompanied by capillaries, have ramified all through the mass of lutein cells, but these strands are still thin, and thus the lutein cells in the sections keep the appearance of forming a homogeneous body. The cell walls are very prominent. The large lutein cells have a finely granular cytoplasm and many vacuoles. In some cells the vacuoles predominate to such a degree that the cell seems to be nearly empty except for the nucleus.

In figure 12 a part of the ovary of an old animal at this stage is shown. Instead of a corpus luteum, a luteinized follicle is depicted. These follicles are of frequent occurrence in *Elephantulus*. However, except for the remains of the egg cell in the centre, and their spherical form, they are in no way different from a typical corpus luteum of the same stage.

Previously (van der Horst & Gillman 1941, figure 6) a cross-section of the uterus of a young animal was given. Therefore figure 13 shows a cross-section of the uterus of an old animal. Compared with that of figure 11, the uterus has contracted rather more, but still it shows the characteristic form of a post-partum uterus. In both the old and the young animal (figure 14), the stroma is densely crowded with nuclei and the epithelium is exceedingly high. At any other stage in which the animal and its uterus may be, the epithelium is of about the same height as that of the glands, but at this particular stage of the menstrual cycle, the uterine epithelium is at least twice as high as that of the glands (figure 14).

Except for this high epithelium, there is no difference at all, at this stage, either in the uterus or in the ovary, between an animal in the menstrual cycle and one that has been fertilized.

(3) *The pre-polyp stage*

During the menstrual cycle, an oedema is suddenly formed at a place in the uterus corresponding to the implantation site. The stage at which this localized oedema arises was called the pre-polyp stage (van der Horst & Gillman 1941). As can be expected it is of short duration only, and a very few animals in the collection are in this stage.

The young animal, figured before (1941, figure 8) and collected in January 1939, is really in its second menstrual cycle as shown by the presence of two generations of corpora lutea in the ovary (figure 15). As described before (van der Horst & Gillman 1942*a*), the corpus luteum is now completely embedded in the substance of the ovary, it is spherical in form, and the strands of connective tissue cells, accompanied by capillaries, have become more prominent, thus giving the corpus a trabecular appearance.

There is only one post-partum animal in the collection representing the pre-polyp stage, and this series is not dated nor is the ovary present. The form of the uterus, however, clearly shows that the animal was in the first post-partum cycle when it was killed (figure 16). Yet this series of sections is of great importance. After fertilization the arrival

of the early embryo initiates the uterine reactions. For a long time it puzzled me as to what induced the uterus to form the menstrual oedema. In series 13 an unfertilized and already degenerating egg is lying exactly at the place where implantation should take place It may therefore be assumed that here also the egg induced the uterus to form an oedema. An embryo chamber is not formed in the menstrual cycle, so the egg remains exposed in the main uterine cavity instead of being safely lodged in a niche, and thus it can readily be removed from the implantation site. In only one other instance, at a later period in the cycle, was an unfertilized egg found at the implantation site.

This removal of the egg from the implantation site is accomplished more readily during the menstrual cycle, as the formation of the oedema is not, or hardly at all, accompanied by an external swelling of the uterus. Instead of a niche being formed, the oedema at first flattens out the uterine wall towards the lumen, and in the next stage this oedematous tissue projects into the uterine cavity.

(4) *The polyp stage*

This stage is represented in the collection by five series of sections of young animals passing through their first menstrual cycle, and by nine series of old animals during the post-partum cycle. It may thus be concluded that this stage extends over a rather long time. Figures of the uteri of some young animals, in this stage, in cross-section as well as in longitudinal section, have been published before (van der Horst & Gillman 1941), but as this stage is of such great importance, another figure of the same animal figured before (1941, figure 9) is given here (figure 19).

In the ovary the strands of connective tissue carrying the capillaries have become more prominent in the corpora lutea (figure 17). The lutein cells, with their prominent cell

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DESCRIPTION OF FIGURES 12 TO 20

12. Part of the ovary of an old animal in the stage of dense stroma and high epithelium. Besides the corpora albicantia it shows a luteinized follicle, with the same structure as a normal corpus luteum at this stage. (Magn. ×75.) Series 680.
13. A cross-section of the uterus of an old animal in the stage of dense stroma and high epithelium. (Magn. ×30.) Series 680.
14. A part of the uterus of a young animal, showing the mouth of a gland, the very high uterine epithelium and the dense stroma. (Magn. ×375.) Series 602.
15. Part of the ovary of a young animal in the pre-polyp stage. It shows a larger corpus luteum corresponding to this stage of the menstrual cycle, and the small corpus of the previous cycle. (Magn. ×75.) Series 240.
16. A cross-section of the uterus of a post-partum animal in the pre-polyp stage of the menstrual cycle with an unfertilized egg in the lumen at the place where implantation of the embryo would take place after fertilization. (Magn. ×30.) Series 13.
17. Part of the ovary of a young animal during the polyp stage. Figures of the corresponding uterus have been published before (1941, figures 12, 13). (Magn. ×75.) Series 217.
18. Part of the corpus luteum of a young animal during the polyp stage. (Magn. ×375.) Series 32.
19. A cross-section of the uterus of a young animal during the polyp stage. Another section of the same uterus was published before (1941, figure 9). (Magn. ×30.) Series 257.
20. A cross-section of the uterus of an old animal during the polyp stage. (Magn. ×30.) Series 294.

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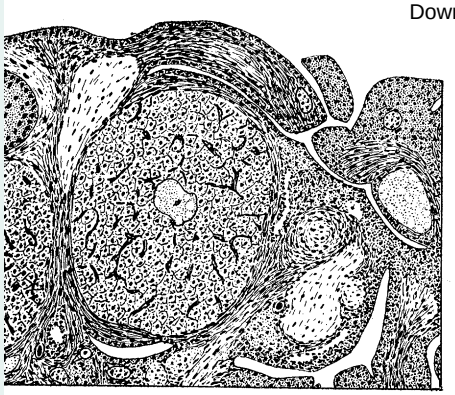

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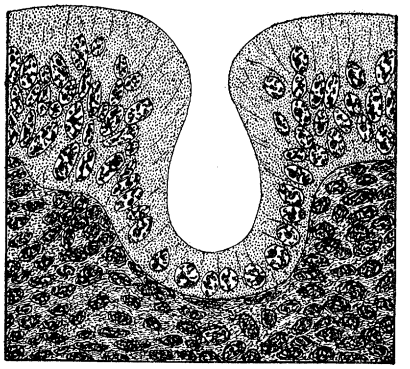

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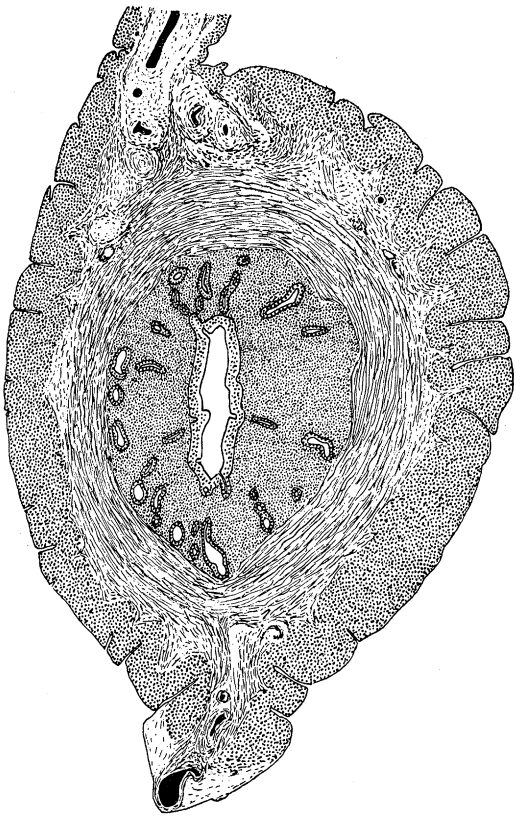

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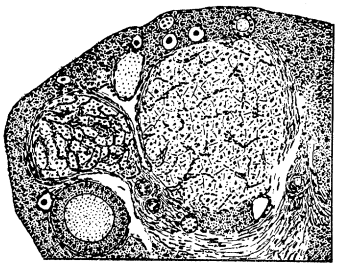

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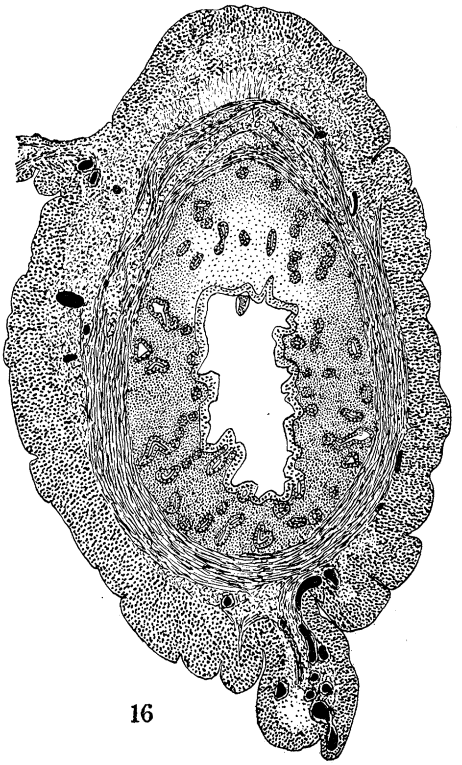

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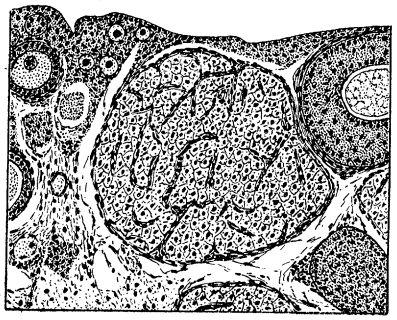

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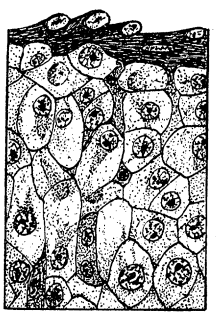

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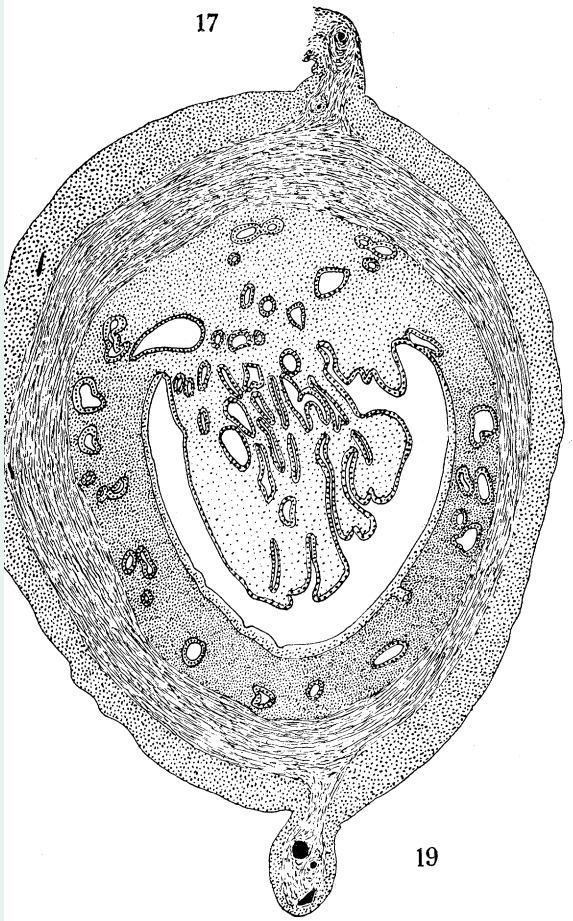

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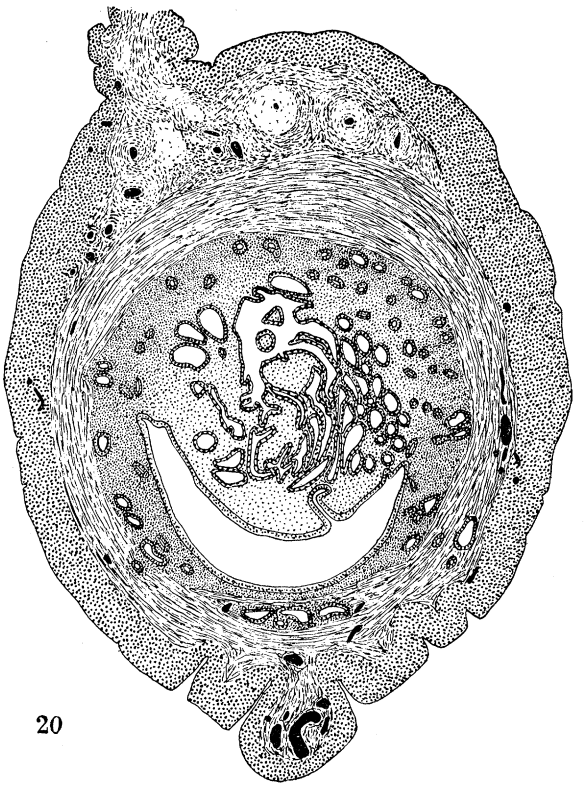

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FIGURES 12 TO 20

membranes, are highly vacuolated; in stained sections they look nearly white (figure 18). Only a flame-like condensation of finely granular cytoplasm can be seen in many cells in relation to the nucleus.

In the uterus of a young animal the stromal oedema at the mesometrial side has given rise to a large polyp-like outgrowth, hanging down in the uterine lumen (figure 19). It may be noted that the uterine epithelium is still rather high, only on the polyp is it stretched out to a thin layer of squamous cells. The glands in the polyp are at first prominent, and the deeper part of the glands, related to the polyp, starts to swell up; finally, a row of swollen glands, separated from each other only by narrow septa, is intercalated between the polyp and the rest of the uterus. As long as the polyp grows, the stromal tissue in and adjoining the polyp remains healthy, although it is highly oedematous, but no decidual reaction takes place in this tissue. Only on a few rare occasions could a young giant cell, so numerous during early pregnancy, be detected.

The polyp stage in the menstrual cycle, following the post-partum ovulation, often shows an appearance quite different from that of the same stage in a young animal. This difference may be so pronounced, depending on the degree of involution of the uterus, that in our previous paper we did not even recognize this stage.

If, by the time the polyp-like growth makes its appearance, the contraction of the uterus is well advanced, then there is not much difference at this stage of the menstrual cycle between a young and an old animal (figure 20). What is really striking is the abundance of glands in a section. This is due to the profuse branching of the glands. Also in a young animal a slight degree of branching of the glands was observed in some cases. It is noteworthy that this ramification occurs only during this latter part of the menstrual cycle. Although the glands swell considerably during early pregnancy, they never branch during the whole period of gestation. At the time of ovulation, when these glands are swollen and very conspicuous, they are simple, straight tubes.

When the involution of the uterus is less advanced at the time of formation of the polyp, the latter becomes much larger, thereby reducing the uterine lumen to a small cavity (figure 21). The glands, over the greater part of their length, are profusely branched, and

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DESCRIPTION OF FIGURES 21, 23 TO 28

21. A cross-section of the uterus of an old animal during the polyp stage. (Magn. ×30.) Series 313.
23. Part of the ovary of a young animal when the polyp in the uterus is in the process of breaking down. (Magn. ×75.) Series 171.
24. Part of the ovary of a young animal approaching ovulation after menstruation. Besides the remains of the corpus luteum of menstruation many young oocytes can be seen. (Magn. ×75.) Series 88.
25. A cross-section of the uterus of an old animal during the post-partum menstruation. (Magn. ×30.) Series 214.
26. Part of an ovary, with an old corpus luteum of menstruation, of a young animal going into anoestrus. (Magn. ×75.) Series 691.
27. A cross-section of the uterus of a young animal going into anoestrus after completing one menstrual cycle. (Magn. ×30.) Series 691.
28. A cross-section of the uterus of an old animal going into anoestrus after completing the post-partum menstrual cycle. (Magn. ×30.) Series 918.

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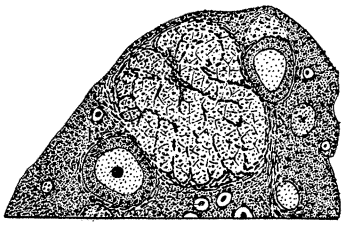

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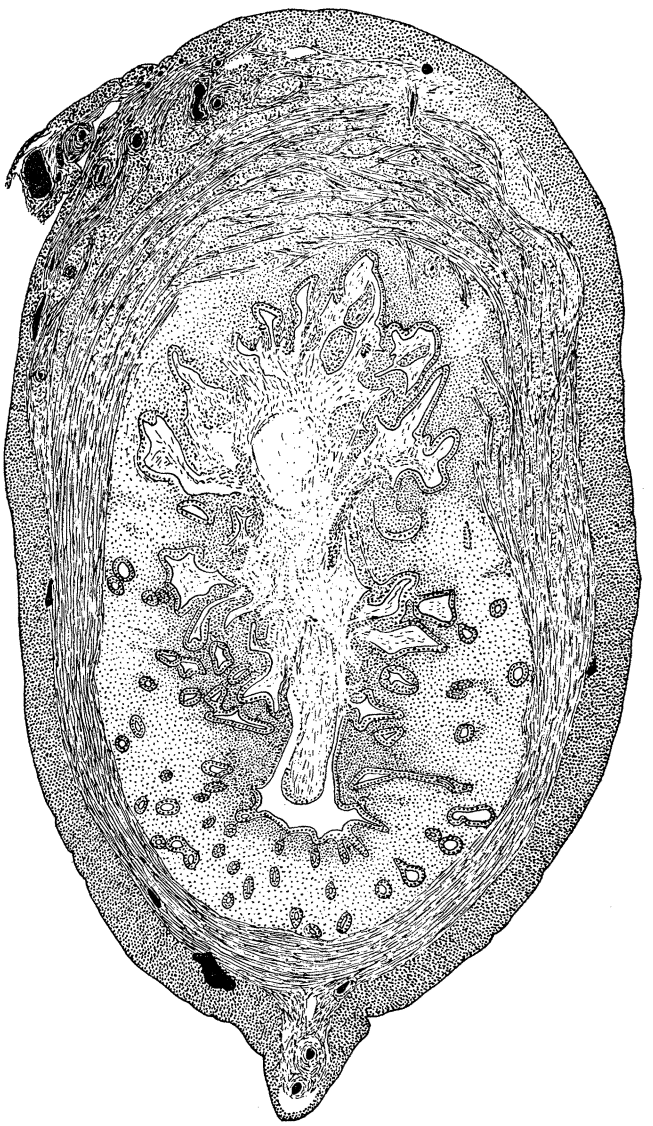

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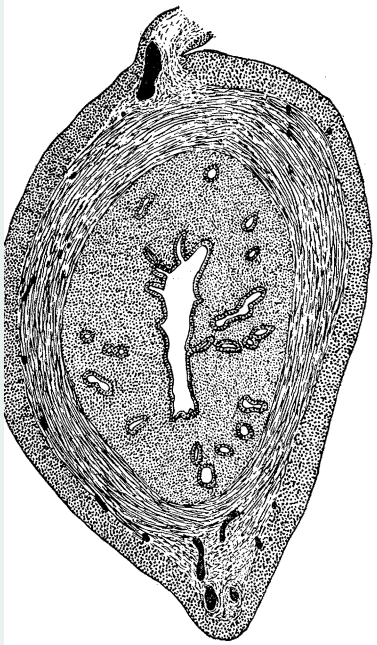

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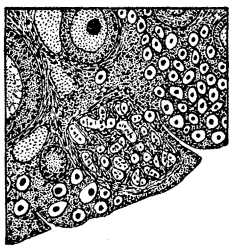

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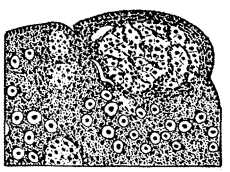

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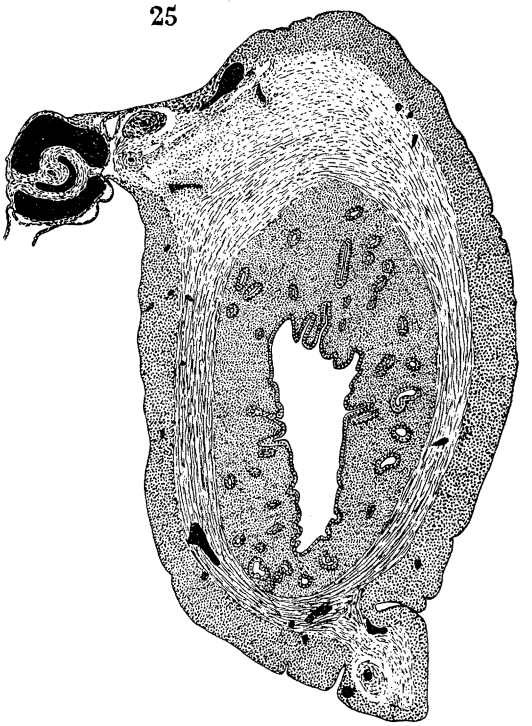

28

FIGURES 21, 23 TO 28

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as they are swollen, the stromal tissue between the glands becomes reduced often to narrow septa. This gives the polyp an appearance quite different from that of a young animal, where it consists of a more solid mass of tissue. Yet it cannot be doubted that in both cases it is one and the same thing, viz. a local growth of the mesometrial wall of the uterus hanging down into the main uterine lumen, and caused by an oedematous swelling of the stroma, and a widening of the glands. Moreover, between the two forms, as shown in figures 20 and 21, there are intermediate stages in the collection, and in none of them could a real decidual reaction, except for the oedema, be observed, neither is there any trace of an embryo chamber. Therefore it can only be concluded that the polyp-like swelling during the menstrual cycle can be very variable in size, and thus the intensity of the menstrual reaction may be greatly different in various animals.

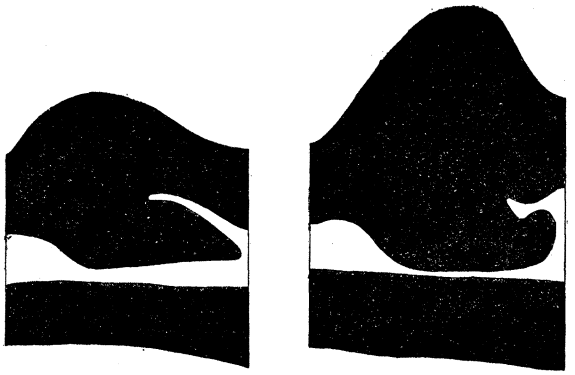

FIGURE 22. A mid-longitudinal reconstruction in outline of the swelling shown in figures 20 and 21. (Magn. ×4.)

(5) *The stage of menstruation*

This stage has been adequately described before, as well as the corpora lutea corresponding to it. It may be sufficient to repeat here that the corpora lutea, as soon as the destruction of the polyp-like growth in the uterus sets in, become progressively smaller due to a decrease in size, and in number, of the lutein cells (figures 23, 24). As long as such a cluster of lutein cells, small though it may be, remains surrounded by a layer of fibres, it can easily be recognized as the remains of a corpus luteum of menstruation, but when this fibrous layer becomes indistinct, one can only see some scattered, totally unstained cells, with small nuclei, and it becomes more and more difficult to recognize such cells as old lutein cells.

A cross-section of a large post-partum uterus during menstruation is given in figure 25. It is a further stage to that shown in figure 21. It can be seen that the whole central mass of the stroma, with the branched glands and blood vessels, is broken down.

The epithelium of the swollen peripheral part of the glands is healthy, and this will restore the uterine epithelium and glands.

(6) *Going into anoestrus after one menstrual cycle*

In a previous communication (1941) it was said that there is no lag at all between the regenerative and oestrous processes in the menstrual cycle. It may happen that a menstrua-

tion is followed by another ovulation, as will be described below; the usual procedure, however, is that the animal, having completed one menstrual cycle, goes directly into anoestrus.

There are twenty-one series in the collection of uteri of young animals that apparently have gone into anoestrus after completing one menstrual cycle. I say 'apparently' because the corpus luteum of menstruation is already very small by the time the animal has reached this period (figure 26), and soon it will become unrecognizable. It is mostly impossible to identify two successive generations of corpora lutea, and, therefore, it may be possible that some of these animals had menstruated twice before going into anoestrus. If a young animal reaches sexual maturity late in the season, like that of figures 26 and 27 (killed on 26 February 1942), then it is practically certain that it had menstruated only once. The uterus of this animal shows the features typical of a specimen during anoestrus (figure 27). In cross-section it is much smaller than at the time of menstruation, and the uterus may continue to contract. It is, however, not so small as the uterus of an animal that has gone into anoestrus directly on reaching puberty (figure 2).

In the same way the majority of old animals go into anoestrus after completion of the post-partum menstrual cycle. There are no less than forty-five series of sectioned uteri falling into this category. In figure 28 a section of the uterus is shown of an animal that has only just completed the menstrual cycle; and the dense stroma, narrow glands and low epithelium, combined with the absence of ripening follicles in the ovary, all indicate that this animal will go into anoestrus. The irregular form of the uterine lumen shows that regeneration is not yet complete.

(7) *Repeated ovulation at the end of the season*

Although the majority of animals, which may be young animals, having completed the first menstrual cycle of their lives, or old animals after one post-partum menstruation, go directly into anoestrus, quite a few enter another cycle, and all the various cases described before, after the completion of one menstrual cycle, may be repeated before the animal goes into anoestrus.

There are a few series in the collection with ripe, or nearly ripe, follicles after one menstruation, three of young animals and four of old animals, and as the follicles are normal and several mitotic figures can be found in the granulosa, as well as in the uterine epithelium and glands, ovulation would have followed in these animals.

Once the animal has ovulated after a menstrual cycle and the early corpora lutea have been formed, copulation and fertilization may take place. The two generations of corpora lutea can then be seen in the ovary (figure 29). This case is represented by six series of young animals and one series of an old animal. The presence of sperm in the uterus or the early segmentation of the eggs show that copulation has taken place. Fertilization may be followed by pregnancy, but as the corpora lutea of menstruation can be recognized only during a short time after completion of the menstrual cycle, such corpora can be identified only during the early stages of pregnancy (figure 30). In eight series of young animals and three series of old animals, very old corpora lutea of menstruation were found together with the corpora of pregnancy. In only one has the embryo reached the primitive streak stage, in all others it is younger.

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On the other hand, an ovulation following a completed menstrual cycle may again be unfertilized, and then a repetition of what has been described above, in the case of the first ovulation, can be observed. There are present five cases, two of young and three of old animals, in which the animal had only recently ovulated without being fertilized, and the two generations of corpora lutea can be found side by side in the ovaries. Four old animals, the uterine epithelium of which is very low, were apparently going into anoestrus directly after this second post-partum ovulation. In others, this second ovulation, either post-partum or of a young animal, is followed by another menstrual cycle. So we find three young animals and one old animal in the stage of dense stroma and high epithelium.

The young animal that provided series 240 was killed when the early polyp was forming as was shown in the previously published paper (1941, figure 8), and in its ovary the two generations of corpora lutea can be found (figure 15). There are two animals, one young and one old, approaching ovulation after passing through two menstrual cycles (figure 31). Another two animals, both old ones, have ovulated for the third time after parturition. Of one, series 72, the successive generations of corpora lutea, and a corpus albicans, have been mentioned and figured previously (1942*a*, figures 5, 14, 16, 17), and a part of the ovary of the other (series 51) is shown here in figure 32, in which can be seen probably two very old corpora lutea, one of which is broken up by the emergence of the new corpus, whereas that of the second generation is very large, which may be due to the fusion of two or more corpora, as often happens in *Elephantulus*. Moreover, in both these animals, the third attempt was successful and the animals were fertilized.

Description of figures 29 to 35

29. Part of the ovary of a young animal that has been fertilized after completing one menstrual cycle. The old corpus luteum of menstruation and the early corpus luteum are shown. (Magn. ×75.) Series 350.

30. Part of the ovary of a young pregnant animal, with the embryo in the early primary amniotic cavity stage, showing the corpus luteum of pregnancy, and a very old corpus luteum of menstruation. (Magn. ×75.) Series 943.

31. Parts of the ovary and uterus of an old animal, showing: a corpus albicans, a very old corpus luteum, only just recognizable, an old corpus luteum, a ripening Graafian follicle and the high epithelium, with mitotic figures, of the uterine lumen. (Magn. ×75.) Series 1039.

32. Part of the ovary of an old animal showing three successive generations of corpora lutea. (Magn. ×75.) Series 51.

33. A cross-section of the uterus of an old animal with a very small polyp-like growth of menstruation. (Magn. ×30.) Series 1032.

34. The second, exceedingly small, polyp protruding into the uterine lumen of the same uterus as shown in figure 33. The disintegrating egg-cell can be seen towards the left in the lumen. (Magn. ×187·5.) Series 1032.

35. A section of the contralateral ovary of the same animal from which figures 33 and 34 were made. Two corpora albicantia and some atretic follicles are shown. The ovary is surrounded by the bursa and attached to the peritoneum by the mesovarium; the bursa is connected to the peritoneum by the mesosalpinx. (Magn. ×30.) Series 1191.

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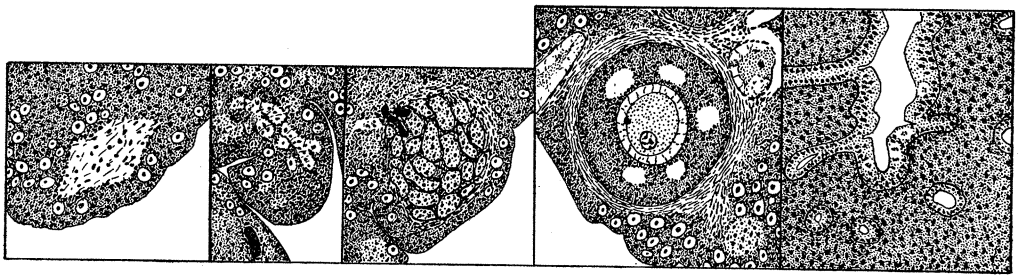

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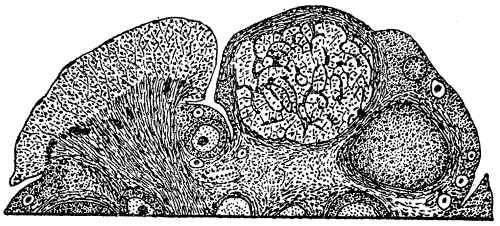

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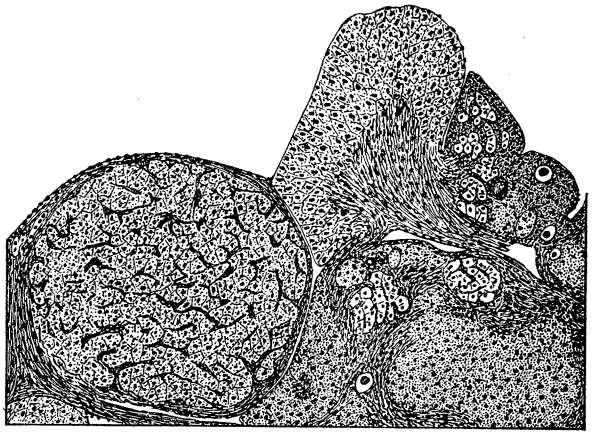

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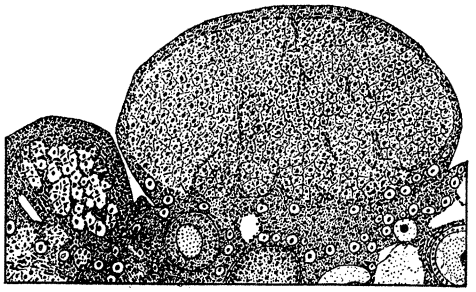

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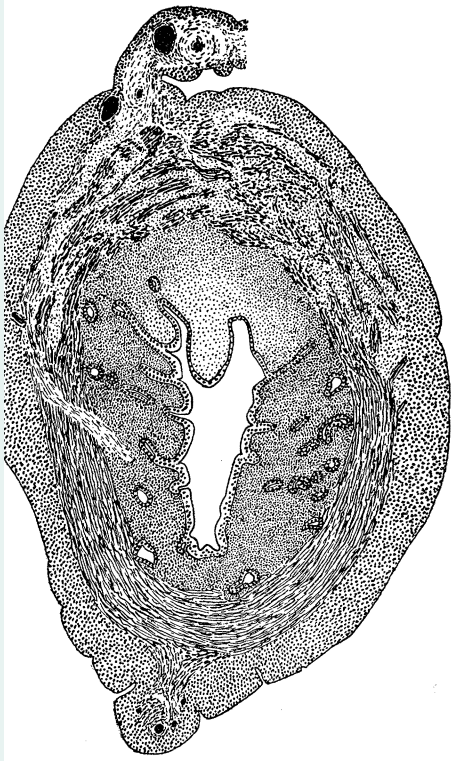

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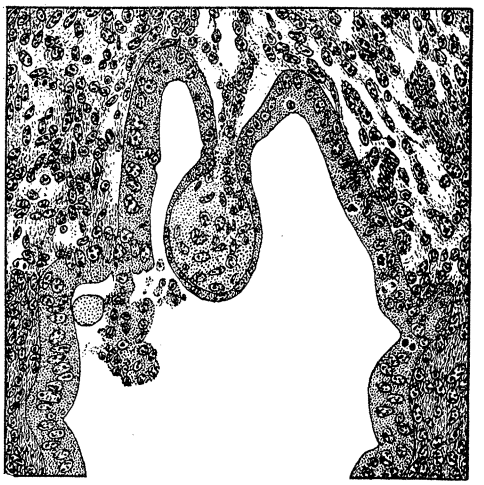

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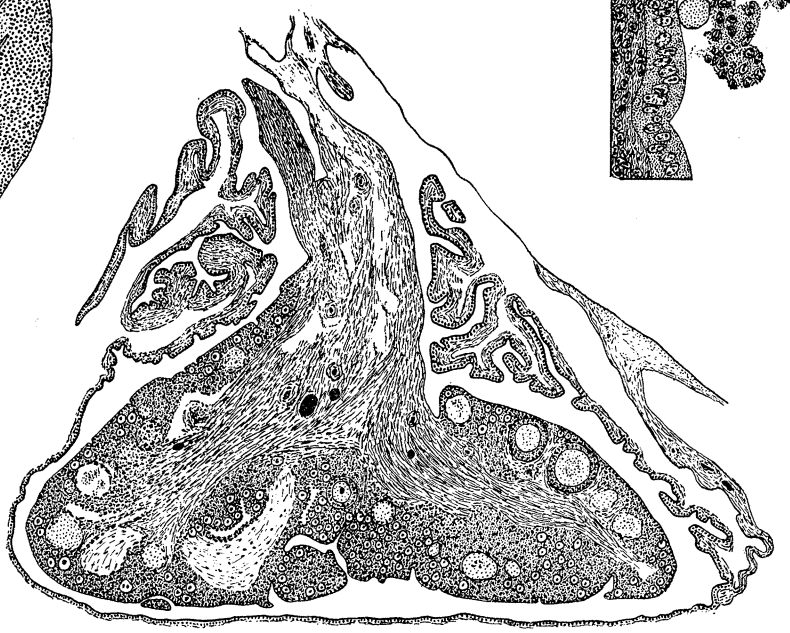

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FIGURES 29 TO 35

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(8) *Ovulation from a limited number of Graafian follicles*

Another noteworthy phenomenon may be mentioned here in addition to the account about the menstrual cycle. *E. myurus*, together with some more species belonging to the same family, the Macroscelididae, and in distinction from other species of this family, is remarkable for the great number of eggs liberated from the ovaries at each ovulation. This number is about 120 from the two ovaries, and the number of corpora lutea formed after ovulation is correspondingly high. Moreover, each corpus luteum, as well as the ripe follicle, is small as compared with the other species that liberate only a small number of eggs (van der Horst 1944).

At the end of the reproductive season and before the animal goes into anoestrus, it sometimes occurs that *E. myurus jamesoni* ovulates from a limited number of Graafian follicles. These follicles; and the ensuing corpora lutea, then have the usual small size normally found. It may, therefore, be assumed that the amount of hormone, oestrogen or progesterone, as the case may be, produced by these follicles or corpora lutea is correspondingly reduced, and this as will be seen, affects the reaction of the uterus.

The most interesting case of this type is presented by series 1032 of an old animal killed on 15 January 1945. Besides corpora albicantia the ovary contains one single corpus luteum. Yet the animal had not gone into anoestrus, but had entered upon a menstrual cycle. In the uterus a very small, but otherwise normal polyp could be seen protruding into the lumen, together with a typical oedema confined to the mesometrial side (figure 33). This polyp extends over a few sections only. Behind it, and a few sections removed, a second, exceedingly small polyp is found (figure 34). Next to the latter a slight proliferation of the uterine epithelium can be seen and also the egg itself. It is very rare to find an egg at the site where the polyp forms (see figure 16), but in a case like this with one egg only, it is more than one can hope for. The presence of this egg may have caused the proliferation of the uterine epithelium, as normally such a growth does not occur.

The other ovary and uterine horn of this animal were also sectioned (series 1191). In the ovary the corpora albicantia of the previous pregnancy were present, together with some atretic larger follicles, and the usual large number of oocytes (figure 35). However, there is not one corpus luteum present and the uterus shows all the characteristics of anoestrus. Apparently this animal was on the way to going into anoestrus, but one egg escaped at the critical moment, and this caused the animal to pass into a partial menstrual cycle.

To this may be added another remarkable case, that of series 1054 of a young animal killed on 11 January 1946. Here the usual large number of Graafian follicles ripened, but, except for a few, ovulation did not take place and the follicles underwent luteinization and formed corpora lutea with an egg in the centre (see figure 12). Four healthy, and as yet unfertilized, eggs were found in the Fallopian tube. In this case, notwithstanding the small number of eggs liberated at ovulation, the uterus shows the normal characteristics of oestrus, with a general oedema and many mitotic divisions in the stroma, the epithelium and the glands.

(9) *The duration of the menstrual cycle*

As all animals in the collection were caught in the wild, and by far the greater number were killed immediately after capture, no direct data about the duration of the menstrual

cycle were available. Some animals were kept in captivity and remained alive for a considerable time. In captivity, however, *Elephantulus* goes into anoestrus directly; all attempts to breed them have failed utterly. Thus in this way too it was impossible to collect information about the length of the menstrual cycle.

In a few instances, animals were caught in the last stages of pregnancy, and after giving birth, these animals were kept alive for a number of days before being killed. These animals give at least an indication of the duration of the menstrual cycle in an indirect way, by comparing their ovaries and uteri with those of other animals that were killed during the post-partum menstrual cycle.

An animal killed 4 days after parturition had a uterus slightly larger than that shown in figure 11. The eggs were still in the tubal egg chamber, whereas in the animal of figure 11 they had already entered the uterus. From this it might be concluded that the animal of figure 11 was killed more than 4 days after parturition.

Another animal killed 7 days after parturition had a uterus of about the same size and configuration as that shown in figure 16, and in both these animals the eggs had reached the lower part of the uterine horns. Thus the animal of figure 16, in which the formation of the polyp-like growth is just initiated was probably killed about 7 days after parturition.

No further data are available. After the stage shown in figure 16 the polyp has to be formed. This will then break down and the uterine tissues regenerate. If it is permissible at all to make a guess from these meagre indications, I would say that the duration of the whole menstrual cycle is about 14 days.

Abortion

Elephantulus is liable to commit abortion, at any time during the season of reproduction, when placed in adverse circumstances. A good number of the collected animals were sent to me alive, and they had to travel in a small box for a day before reaching me. In that way I got more cases of abortion than I really liked, and serial sections were made of the uterus in only a few instances.

This type of abortion is fundamentally different from that which may be called natural abortion, as it often occurs at the end of the season. In some cases, however, it is not easy to differentiate between the two types, especially in the case of an animal captured and kept alive for some time towards the end of the breeding season. During the height of the breeding season natural abortion was never observed.

All uteri that were apparently in the stage of early pregnancy were cut into serial sections. Macroscopically, however, one cannot see whether a uterus contains an early embryo, or whether one has a case of menstruation or of abortion. On microscopical examination it then appeared that all cases of abortion of an early embryo occurred only at the end of the breeding season, in the same way as was found in cases of menstruation. For the few exceptions, a ready explanation could be given; two or three, for example, were obvious abnormalities. It may therefore be concluded that normally abortion of a young embryo takes place only towards the end of the season.

This leaves two possibilities: (1) *Elephantulus* is likely to commit abortion particularly at the end of the season when placed in adverse circumstances. (2) At this time some

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natural cause affects the animal, with the result that an early pregnancy is broken off by an abortion, and the animal then goes into anoestrus.

The great majority of animals were killed and preserved shortly after capture, or at least on the same day. Those that were sent to me alive may have been killed two days after being caught. Thus if the abortion was the result of captivity, all animals should have been in about the same early stage of abortion. This is not the case. As we will find below, all stages, from the first beginnings of abortion until the animal is practically in anoestrus after abortion, are represented in the collection. Therefore the conclusion is warranted that abortion at the end of the season, i.e. round about the month of January, is a natural phenomenon.

I can now proceed to the description of the abortion during the successive stages of embryonic development.

(1) *Abortion during the transportation of the eggs*

In the case of an animal killed on 22 January 1942 (series 663 and 847, both horns and the median uterus being sectioned) the pregnancy was the result of post-partum ovulation. The corpora lutea have not got a healthy appearance; the nuclei, some of which have an irregular form, have the chromatin all concentrated in one or a few nucleoli; there are large, but ill-defined, vacuoles in the cytoplasm; some cells are nearly empty shells with a nucleus. The upper uterus is not contracted; normally it contracts when the first blastula reaches the implantation site. Fertilization had taken place as was revealed by the presence of numerous one- to four-celled stages or blastulas, and even of several large swollen blastulas (see van der Horst & Gillman 1944). Furthermore, these eggs and early embryos were scattered indiscriminately in both horns over the whole length, from the Fallopian tube to the median uterus, so some of them had passed the implantation site. Yet, at this place no reaction had taken place; there is no mesometrial oedema nor is an embryo chamber formed. Otherwise the uterus is a normal, late post-partum one. It is evident that this animal went into anoestrus after ovulation and fertilization, but before nidation.

Series 933 was prepared from an old animal killed on 20 December 1944. As in the previous case there are one- to four-celled stages, blastulas and swollen blastulas over the whole length of the uterus, but the animal was killed at a slightly later stage, when the embryo had arrived at the implantation site (figure 36). Apparently at that moment the animal had gone into anoestrus. A mesometrial oedema, characteristic of early pregnancy, is being formed, but not an embryo chamber. Neither could the embryo advance beyond

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DESCRIPTION OF FIGURES 36 TO 39

36. A section of the uterus of an old animal that committed abortion and went into anoestrus at the moment the embryo arrived at the implantation site. (Magn. ×30.) Series 933.

37. A cross-section of the uterus of a young animal, a case of early abortion of a four-celled embryo. (Magn. ×30.) Series 344.

38. A cross-section of the uterus of an old animal, a case of more advanced abortion of a four-celled embryo. (Magn. ×30.) Series 809.

39. A cross-section of the uterus of an old animal; the abortion is slightly more advanced than in the case of figure 38. (Magn. ×30.) Series 312.

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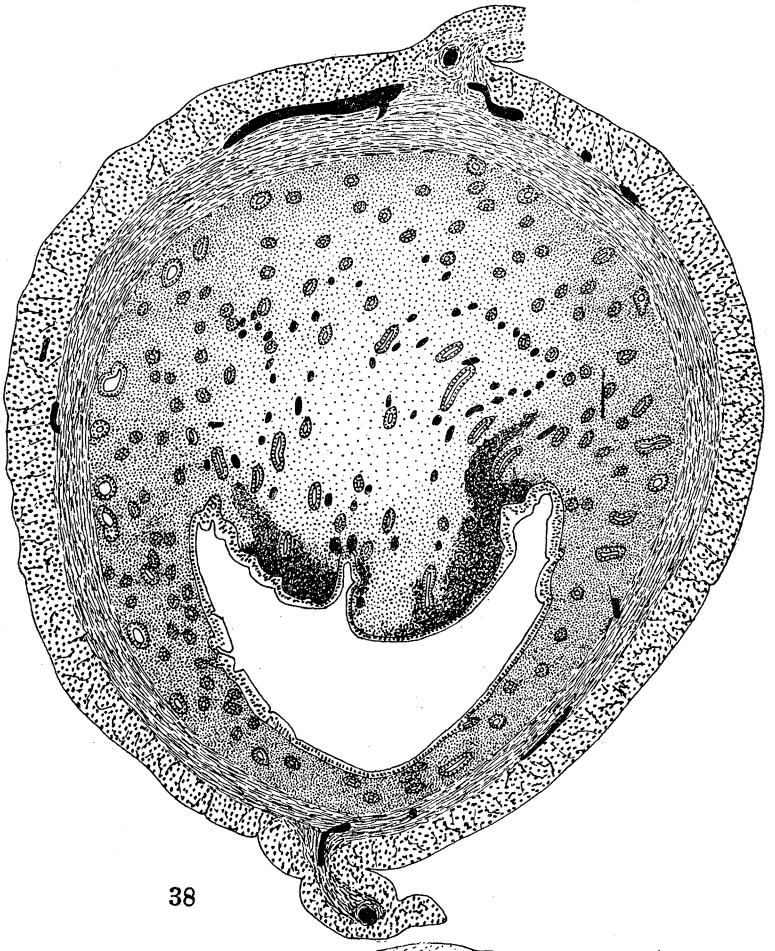

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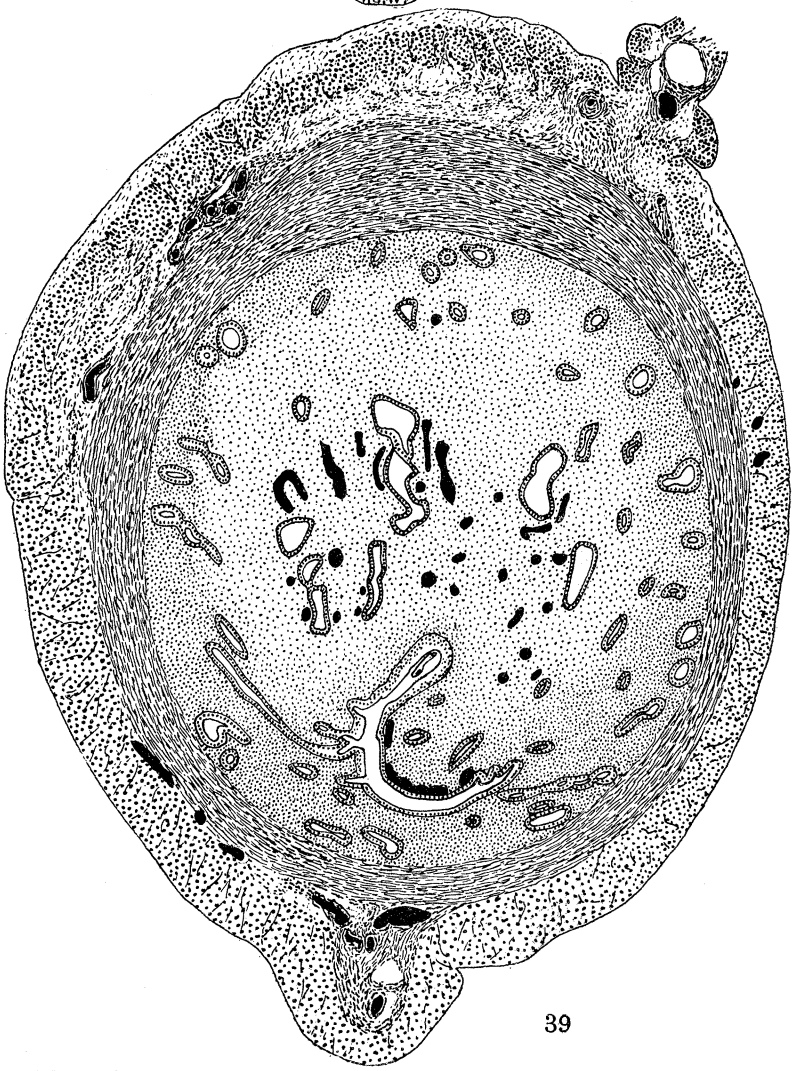

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FIGURES 36 TO 39

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the four-celled stage, it is only greatly swollen. Normally an embryo can only proceed in its development after arrival at the implantation site; a healthy embryo that does not arrive there can accumulate fluid and swell up to a large four-celled blastula.

(2) *Abortion of an embryo in the blastula stage*

It rather frequently occurs that abortion takes place shortly after the arrival of the four-celled embryo at the implantation site, when the embryo chamber has already been formed. Some cases of this nature have been mentioned in a previous publication (van der Horst & Gillman 1942*b*), but at that time not enough material was available for study, so that some mistakes in that paper can now be rectified.

Abortion at this stage of development can be initiated in two different ways. In the first place the embryo itself may, for some reason or other, die. This may happen at any time during the breeding season. A good example is given by an animal, killed on 3 November 1937, in which the broken up remains of an early blastula were found near the embryo chamber. In the second place the mother may interrupt the early pregnancy; the embryo, often already ejected from the embryo chamber, then has a healthy appearance. As far as it occurs in our dated material, this is confined to the end of the breeding season. Taking dated and undated material together, there are fifteen cases in old, and five cases in young animals, of this early type of abortion.

The difference between these two eventualities is not only the presence of a dead or of a living embryo, if an embryo can be found at all. In the case where the death of the embryo is the cause, one can find nuclear divisions in the stroma and the glands of the uterus, at least if the mother was killed shortly after the death of the embryo; in the other case such divisions are absent, indicating that the cause of the abortion was something happening to the mother.

On the other hand, the reactions taking place in the uterus are very similar in both cases. The living embryo, upon arrival at the implantation site, had initiated the reactions of the uterus, and these reactions, once set in motion, continue. However, when the four-celled embryo dies, or is removed, the later reactions, do not take place. The first reactions then continue unimpeded by the following. The result is an excessive oedema, extending from the chamber through the whole thickness of the endometrium to the muscle layer, and the formation of a very wide embryo chamber (figure 37). In a normal case the embryo about fills the embryo chamber.

DESCRIPTION OF FIGURES 40 TO 44

40. Part of a corpus luteum of a young animal in the process of aborting a later blastula stage. (Magn. × 375.) Series 226.

41. A cross-section of the uterus of a young animal in the process of aborting an embryo in the later blastula stage. (Magn. × 30.) Series 226.

42. A cross-section of the uterus of a young animal when the abortion of an early embryo is nearly completed. (Magn. × 30.) Series 856.

43. A cross-section of the uterus of an old animal going into anoestrus after the abortion of an early embryo. (Magn. × 30.) Series 1017.

44. A cross-section of the uterus showing an early stage of abortion of a blastocyst. (Magn. × 30.) Series 254.

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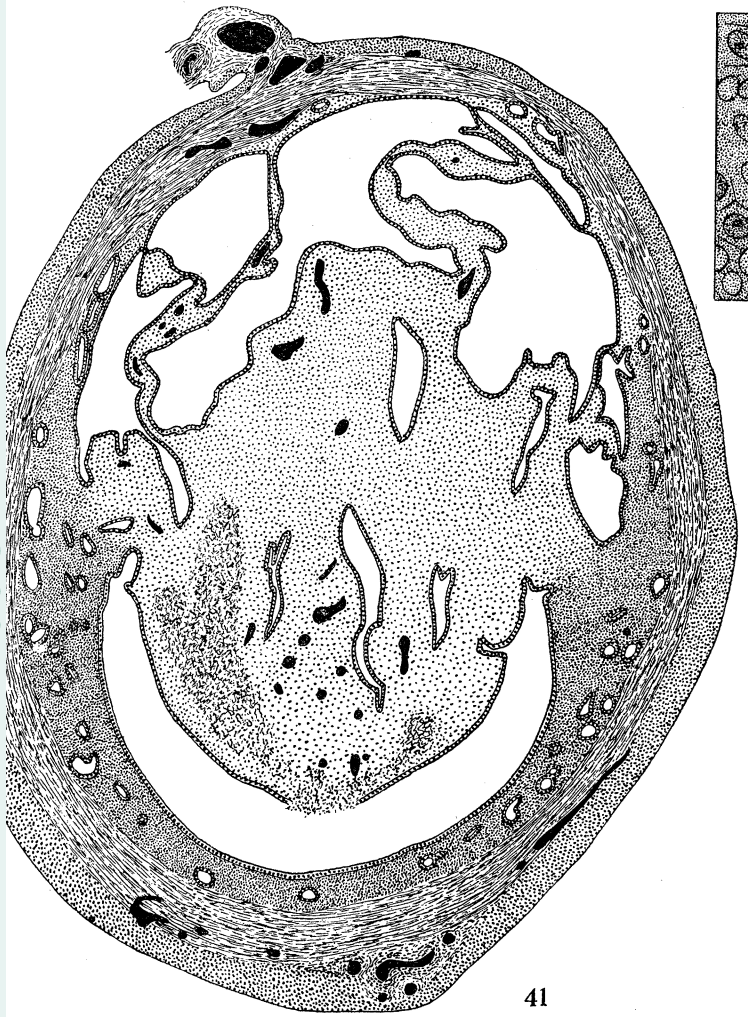

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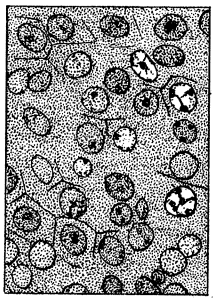

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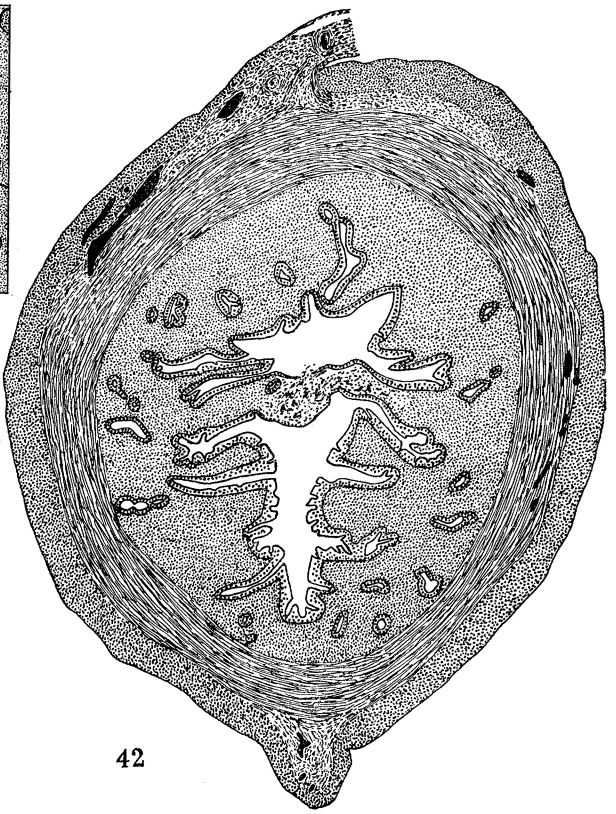

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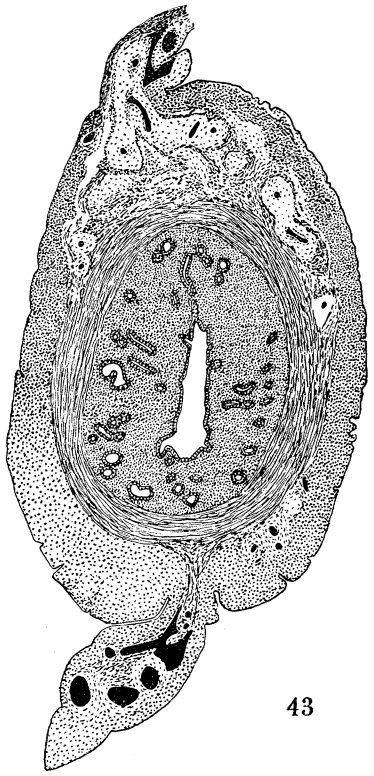

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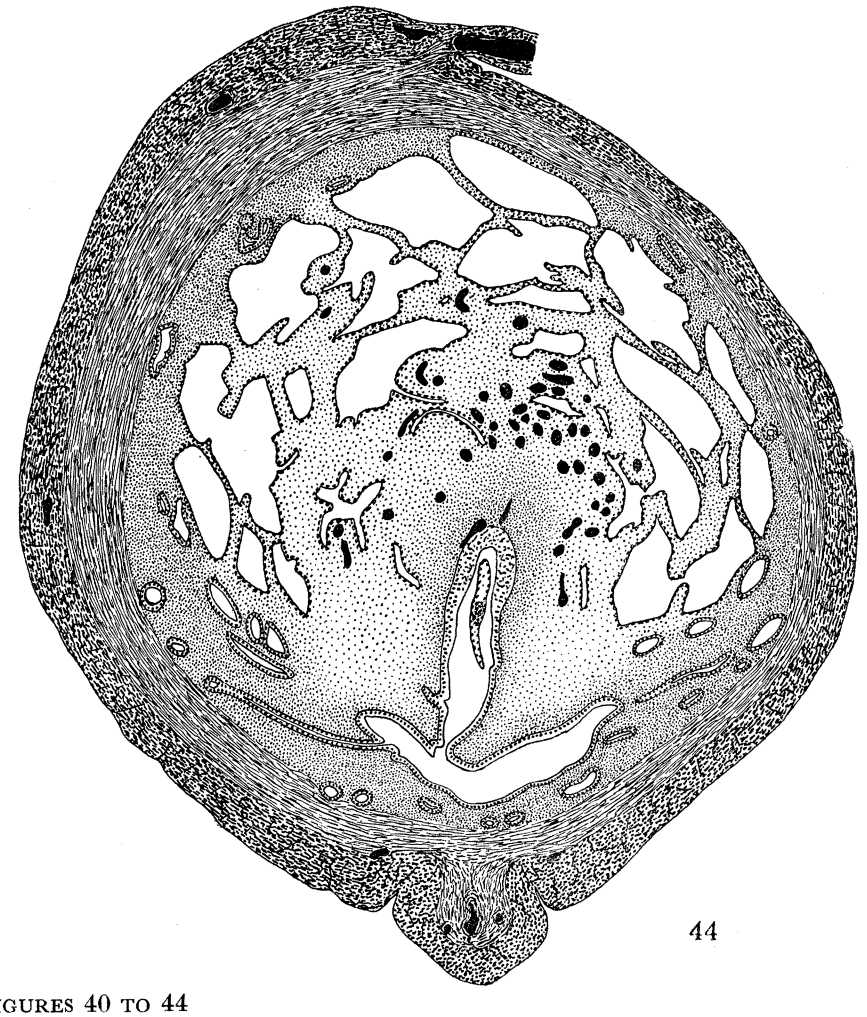

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FIGURES 40 TO 44

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Series 94, accurately described and figured before (1942*b*, figures 1, 2), represents the same stage in an old animal. Here the embryo was ejected from the chamber, but it was found in the median uterus in a healthy condition.

A later stage in this process is shown in figure 38. The very oedematous mesometrial stroma is protruding into the uterine lumen, in the same way as the polyp-like growth during the menstrual cycle (figures 19, 20). In the present case, however, there is a clear embryo chamber, although it is compressed, indicating that an early embryo had reached the implantation site. The blood vessels are slightly swollen and extravasates occur in the neighbourhood of the chamber. On the other hand, the glands are narrow, from which it can be concluded that, when the abortion set in, the embryo was only in the four-celled stage.

The animal of series 312 (figure 39) is slightly more advanced than the previous case, although here the early embryo is still contained in the embryo chamber; apparently it is dying. The blood vessels are somewhat wider and the glands are starting to swell. The corpora lutea of this animal clearly show signs of disintegration; the cell membranes, otherwise so conspicuous, have practically disappeared, and many nuclei are reduced to empty vesicles.

A good example of an abortion at the stage of a late blastula is presented by series 226, of January 1939, which, at the same time, illustrates what occurs when the abortion is further advanced. In the ovary the disintegration of the corpora lutea is well advanced (figure 40); a few nuclei may still have a healthy appearance but most of them are dead, and the cell membranes are disappearing. That an older blastula was aborted, although no embryo could be found, is revealed by two facts: the chamber epithelium was already in an advanced state of decomposition, so that it was easily pressed out of its place by the increasing oedema and the extravasated blood, leaving a wound facing the uterine lumen (figure 41). Further, the decidual reaction of the stroma had started, there are pear-shaped cells and some of them could be recognized as early giant cells. This reaction is so far advanced in series 226, as is normally the case when the embryo is in the early blastocyst stage.

What is particularly striking in figure 41 is the enormous swelling of the glands, so that the mass of decidual tissue is suspended from the mesometrial wall of the uterus by narrow strips only, which consist almost of glandular epithelium alone. For comparison with the next case, it is noteworthy that the connexions of the central mass of tissue to the lateral walls are much stronger. The narrow strips of tissue between the swollen glands next break up and the confluent lumina of the glands then form a new lumen of the uterus at the mesometrial side. The old uterine lumen remains at the antimesometrial side, but by the decomposition and ejection of the decidual mass, these two parts fuse to one cavity. In figure 42 (animal killed on 21 December 1944), a bridge of decomposed tissue is still connecting the lateral walls of the uterus. When also this bridge is removed, the uterus contracts further, the epithelium becomes low and the glands narrow, as shown in series 904 of an animal killed on 15 January 1945. Finally, the uterus assumes a form characteristic for anoestrus (figure 43) (animal killed on 15 January 1945). At this stage only the disintegration of the corpora lutea indicates that the animal went into anoestrus after an abortion of an early embryo, and not after the completion of a menstrual cycle.

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(3) *Abortion of an embryo in the blastocyst stage*

Abortion at this stage of development of the embryo is represented by eight series of sections in the collection. This is considerably less than the numerous cases of abortion during the blastula stage of the embryo, yet these eight cases show a considerable variety, which allows us to come to some conclusion about the sequence of events.

A good stage to begin with, anyhow the earliest present, is given in series 254 of an old animal; the date of capture is unknown. Here a healthy blastocyst is lying in the embryo chamber (figure 44). It is, however, somewhat compressed, which is apparently due to the peculiar swelling of the glands, and the differentiation of the decidua compacta. The epithelium of the embryo chamber is multi-layered, eosinophilic and vacuolated; it shows the same signs of disintegration as seen in a normal pregnancy at the same stage of embryonic development (compare with that of van der Horst 1950*a*, figure 28). The decidual reaction of the stroma also corresponds to that seen in a normal case (van der Horst 1950*a*, figure 9), with an accumulation of pear-shaped cells surrounding the embryo chamber, and some early giant cells. Towards the periphery the stroma is highly oedematous. The blood vessels in the decidua start swelling. The glands on the other hand, are more swollen than in a normal case, with the result that the whole decidua compacta, with the embryo chamber, is pressed into the main uterine cavity, which is thereby reduced to a narrow horizontal slit. When comparing the normal case (van der Horst 1950*a*, figure 9), with figure 44, it is evident at once that something has gone wrong with the latter specimen, which is corroborated by the ovary, in which the corpora lutea show definite signs of disintegration. And that series 254 represents an early stage of abortion of a blastocyst, is revealed by comparing it with the following stages of abortion.

Figure 45 shows the next stage in this process. It is of a cross-section of the uterus of an old animal, of unknown date. A healthy, early blastocyst is here ejected from the embryo chamber and is lying in the main uterine lumen. In comparison with the previous case the decidual reaction has further advanced; there are a good many giant cells in the stroma. The decidua compacta is completely surrounded by the much enlarged, but greatly flattened, glands of the decidua spongiosa. These glands are separated from each other by narrow septa only. The corpora lutea in the ovary are, as before, disintegrating.

Series 91, the ovary and uterus of an old, undated animal and series 879, of an old animal, collected on 10 January 1945, are exactly the same and they represent a stage following that of series 93. Series 91 was described in a previous publication (van der Horst & Gillman 1942*c*), when, curiously enough, we did not realize that series 93, with a well-preserved embryo, represented a slightly earlier stage of abortion.

In the ovary the corpora lutea are greatly reduced in size (figure 46), and they are in an advanced state of disintegration (figure 47). The nuclei are of irregular form, and several of them are broken up; the cell membranes have disappeared completely. The embryo could not be found any more in the uterus, but a comparison with series 93 does not leave any doubt that the embryo was in the blastocyst stage when it was ejected from the embryo chamber. This chamber is still recognizable; in figure 48 it can be seen in the form of an indentation in the decidual mass towards the antimesometrial side. The septa between the flattened, swollen glands have broken down, except where the now large blood

vessels pass through them on their way from the muscularis to the decidua compacta. The result is that a new uterine lumen is formed in which the globular decidual mass is lying, connected to the uterine wall in only a few places where the blood vessels pass. The number of giant cells has greatly increased, and they are as densely packed in the decidua compacta as is normally the case when the embryo is in the primitive streak stage.

(4) *Abortion of an embryo in the primary amniotic cavity stage*

This case is represented by twelve series of sections in the collection. A few of them are somewhat doubtful. At the beginning of the process it may be difficult to decide whether the embryo will be pushed out, or whether it is only more loosely attached than is usually the case. And at the end, when there is no embryo to be found, and the uterus is regenerating, one cannot always be quite certain that the embryo actually was in the primary amniotic cavity stage. I will select two series that illustrate the process very well.

The animal that provided series 246 was collected in January 1939. It had been pregnant before. The corpora lutea, otherwise typical for this stage of pregnancy, show early indications of disintegration; the cell membranes are beginning to disappear. The uterus shows the configuration that is normally found at this stage, with enlarged but greatly flattened glands separated from each other by narrow septa, and surrounding the decidua compacta (figure 49). A number of giant cells are very obvious in the decidua compacta. The epithelium of the embryo chamber is completely destroyed, and the embryonic villi have made contact with, and opened up, the swollen capillaries that surround the chamber. Apparently the uterus, at the time of fixation, had already contracted to some extent, thereby compressing the embryo; otherwise the embryo is completely healthy. However, the embryo is pushed out of the chamber, and the villi, by

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DESCRIPTION OF FIGURES 45 TO 53

45. A cross-section of the uterus showing a healthy blastocyst being ejected from the embryo chamber into the main uterine lumen. (Magn. × 27.) Series 93.
46. Part of the ovary of an old animal aborting an embryo in the blastocyst stage. (Magn. × 27.) Series 879.
47. Part of the corpus luteum shown in figure 46. (Magn. × 333.) Series 879.
48. A cross-section of the uterus of an animal aborting an embryo in the blastocyst stage. (Magn. × 27.) Series 91.
49. A cross-section of the uterus of an animal beginning to abort an embryo in the primary amniotic cavity stage. (Magn. × 27.) Series 246.
50. A cross-section of the uterus of an animal aborting an embryo in the primary amniotic cavity stage. (Magn. × 27.) Series 258.
51. Part of a corpus luteum of an animal about to abort an embryo, 5·47 mm in length. (Magn. × 333.) Series 876.
52. Part of a corpus luteum of a pregnant animal with an embryo 6·14 mm in length. (Magn. × 333.) Series 567. (See van der Horst 1950*a*, figure 19.)
53. A schematic longitudinal section of the posterior end of the uterine horn and the anterior part of the median uterus of an animal about to abort an embryo 5·47 mm in length. Reconstructed from cross-sections. (Magn. × 10.) Series 876.

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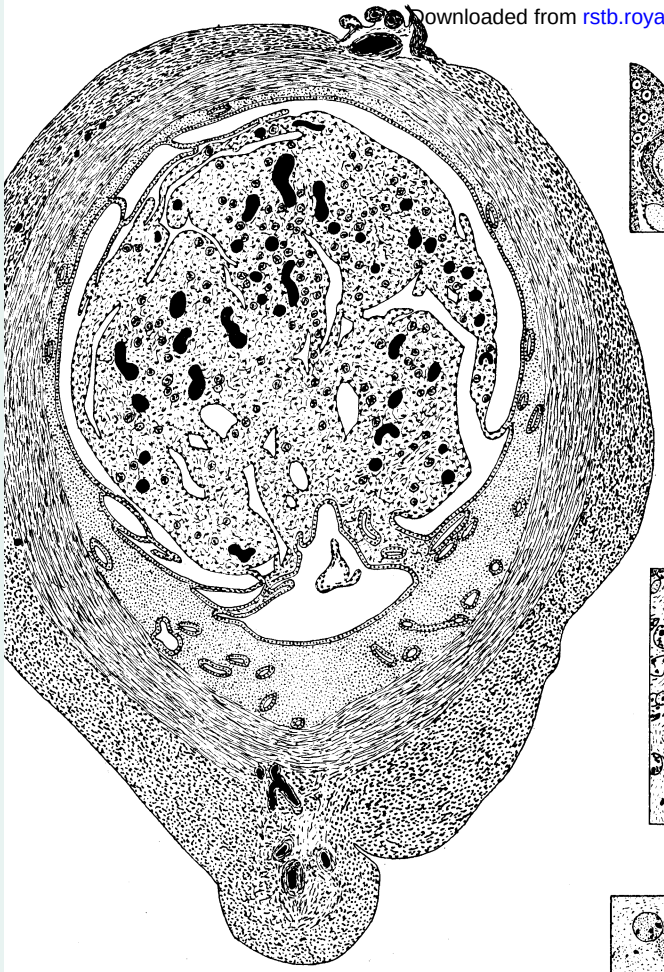

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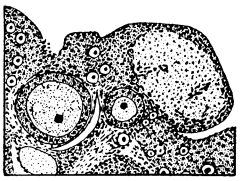

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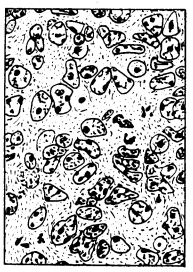

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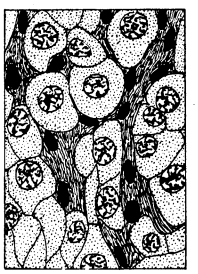

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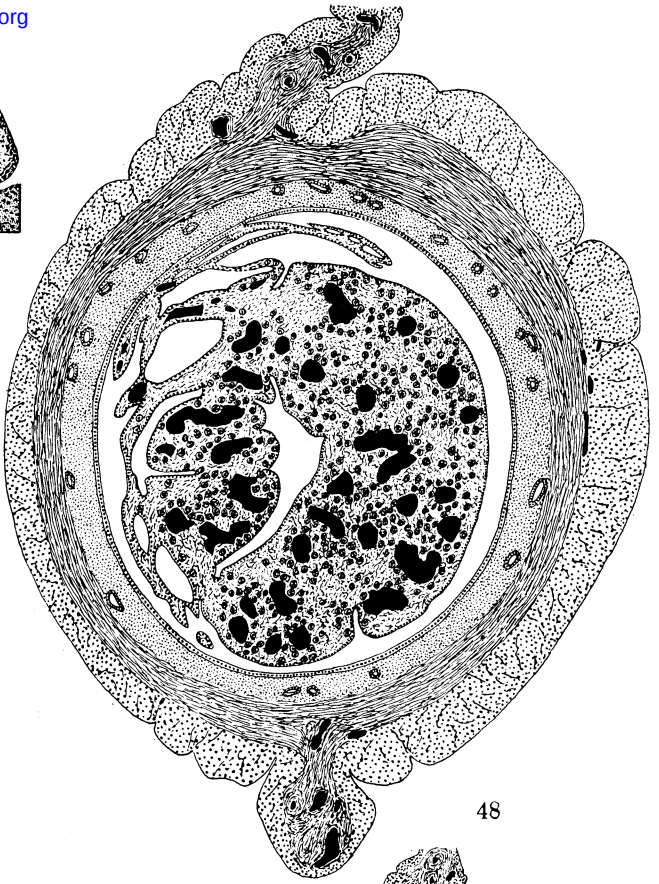

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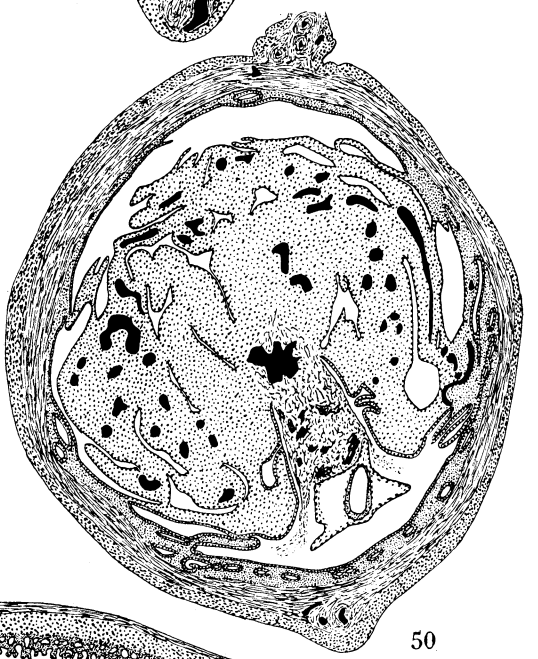

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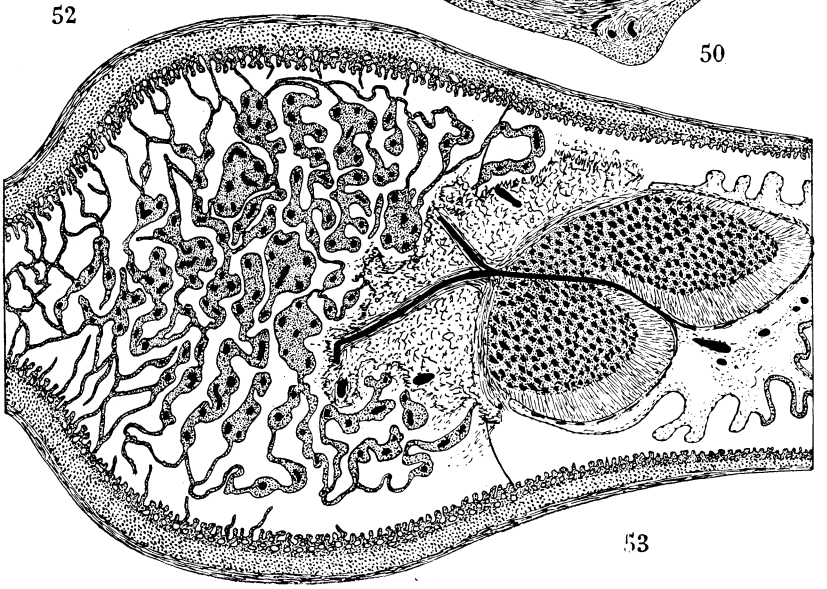

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FIGURES 45 TO 53

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which it was attached, are broken off. The loose ends of these villi can be seen between the swollen capillaries, and other villi, still attached to the embryo, are completely detached from the wall of the uterine lumen. It is quite evident that this embryo would have been aborted had the animal lived some time longer.

Series 258, of an animal collected on 23 January 1940, clearly shows the next stage of abortion. The corpora lutea are disintegrating. The uterus has contracted and many of the septa between the enlarged glands have broken up (figure 50), so that the decidua compacta is largely lying loose in the extended uterine lumen. Compared with series 246 the number of giant cells has increased, and the blood vessels are more swollen. The embryo has been completely pushed out of the original embryo chamber and is lying in the main uterine cavity. It is somewhat depressed, but otherwise it is healthy, and mitotic figures are present in the tissue. Also following the embryo the decomposed mass of maternal tissue, the swollen, opened capillaries that originally surrounded the chamber and broken-off embryonic villi, are being pushed out.

(5) *Abortions of older embryos*

When the embryo grows larger, it becomes increasingly more difficult to decide whether an abortion is a natural one, occurring at the end of the season, or an induced one which may occur at any time of the breeding season when the animal is in adverse circumstances. When the uterus starts to contract the growing embryo is pushed out at once and there are no preliminary stages in the uterus as are found when the embryo is still small. The corpus luteum only may give an indication, and enable one to decide whether the abortion was a natural one or not. Even so, one has to be careful because the disintegration of the corpus luteum may be the result, and not the cause, of the abortion.

A very good example of a natural abortion is given in series 876, of an animal collected on 10 January 1945. The uterus of this animal was found to be asymmetrical, which is a rare occurrence in *E. myurus jamesoni*. Therefore both uterine horns with a part of the median uterus were sectioned. In the one horn a normal embryo was found, the length of which, in sections, could be measured and appeared to be 5·47 mm. The embryo of the other horn had been aborted.

The corpora lutea of both ovaries are well on the way to complete disintegration. In figure 51 part of a corpus luteum of the ovary corresponding to the still healthy embryo is given, and all corpora lutea of both ovaries are exactly the same. The cytoplasm is decomposed and the cell membranes have disappeared. Some of the nuclei are of irregular form, others are breaking up, and in those that still have a regular form, the chromatin is clustered together in one or a few clumps. For comparison, a section of a corpus luteum corresponding to a normal embryo, in length 6·14 mm, is given in figure 52. In this corpus luteum the lutein cells are circumscribed, surrounded by obvious membranes, and the nuclei and cytoplasm are perfectly healthy. It has the same appearance as shortly after ovulation (figure 4), except that the lutein cells are larger in relation to the general increase in size of the corpora lutea.

The uterine horn, still containing the embryo, shows the normal appearance found at this stage of pregnancy. The decidua spongiosa is at the height of its development, whereas the decidua compacta is completely decomposed, so that the decidual arteries follow a

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straight course through it. The placenta consists of a spongy and a columnar part, and the allantois has surrounded the yolk-sac. The embryonic membranes, followed by the embryo itself, have penetrated into the main uterine lumen, and here the trophoblast has thickened to form the rudimentary secondary placenta.

The other uterine horn has contracted considerably (figure 53). The decidua spongiosa, with a normal structure, has been pressed together in the centre of the uterus; here and there it is still connected to the uterine wall by delicate strands of tissue, the septa between the enlarged glands. The decomposed decidua compacta is pressed downwards, and the placenta is completely pushed down into the median uterus. The thickened trophoblast has burst open and the embryo itself has been ejected, leaving the umbilical vessels hanging down in the median uterus.

This case shows better than anything else that a natural abortion can occur in *Elephantulus* at the end of the reproductive season. Had the animal lived longer, no doubt the other embryo would have been ejected soon, and the animal would have gone into anoestrus.

A similar case, although much further advanced, is given in series 1034 and 1212, collected on 9 January 1945. In both ovaries the corpora lutea are far disintegrated. The two uterine horns are again asymmetrical. The one is still wide, although the stroma and the glands have regenerated; the low epithelium indicates that the animal is going into anoestrus. The other horn has nearly reached the small size found during anoestrus, and only a small amount of decayed material is left in the lumen.

Discussion

The breeding season in general

In this respect a certain amount of variation is found in various mammals, data of which are available. In *Microtus agrestis* (Brambell & Hall 1939), and in *Evotomys glareolus* (Brambell & Rowlands 1936), a young female frequently fails to become pregnant at the first oestrus, and may experience one or more dioestrous cycles, as shown by the presence of more than one set of corpora lutea in the ovary. Also in the hedgehog (Deanesly 1934) successive ovulations take place before the animal finally becomes pregnant. In *Elephantulus*, without exception, in the young as well as the old animals, only one generation of corpora lutea was found during early pregnancy at the height of the breeding season. Therefore ovulation takes place only once, and as in *Sorex araneus* (Brambell 1935) ovulation is always accompanied by copulation and fertilization.

In *Elephantulus* fertilization is facilitated by the long duration of the process of ovulation. The great number of eggs, about one hundred and twenty from the two ovaries, are not liberated simultaneously; some eggs may be found in the Fallopian tubes, while others are still contained in the Graafian follicles. The ovulation may extend over one or more days, and thus some eggs are available for fertilization at any time. On the other hand, several of the eggs, which may have been liberated too early or too late, are not fertilized at all. In the hedgehog, according to Deanesly (1934), a number of ovulations occurs in rapid succession before copulation takes place, and this may correspond to the one ovulation as found in *Elephantulus*.

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In the shrews, ovulation is caused by the stimulus of copulation. In *Sorex* (Brambell 1935) only one copulation is sufficient. In *Blarina* (Pearson 1944) many matings are necessary to cause ovulation. In *Elephantulus* ovulation is spontaneous and may take place in special circumstances without any copulation.

Like several other mammals, *Elephantulus* ovulates shortly after parturition. As in the case of the first ovulation of the season, copulation and fertilization take place, and thus the post-partum ovulation is directly followed by another pregnancy. A lactation anoestrus does not occur in *Elephantulus*.

In the hedgehog (Deanesly 1934) there is no post-partum oestrus, and a lactation anoestrus follows parturition also in the middle of the breeding season. *Sorex araneus*, on the other hand (Brambell 1935), normally becomes pregnant at the post-partum oestrus, and several successive litters are born to this animal during one breeding season. Some females, however, have a lactation anoestrus, according to Brambell, having failed to ovulate after parturition, and he thinks it probable that at the end of the season animals, in lactation anoestrus, pass directly into winter anoestrus when the young are weaned. I doubt this interpretation as being correct, as this, so-called, lactation anoestrus in *Sorex* apparently occurs only at the end of the season. It is more likely that *Sorex* passes into winter anoestrus directly after the last parturition of the season, and that the young are fed during the first part of this period of anoestrus. The same may happen in *Elephantulus*.

In its way of reproduction, *E. myurus*, on the whole, closely corresponds to *Sorex araneus*. The female of *E. myurus jamesoni* comes into oestrus and ovulates at the beginning of the breeding season in July or August; it is fertilized and becomes pregnant. Pregnancy is immediately followed by a post-partum ovulation, when the animal is fertilized again, and becomes pregnant for a second time, etc. A young animal coming into oestrus for the first time in its life at the beginning of the breeding season, thus passes through three pregnancies without interruption. It then goes into anoestrus in some way or other, or it may die. This species of *Elephantulus* has only three pregnancies in its whole life. However, as a young animal reaches sexual maturity, in the remarkably short time of about five weeks after birth, it may become pregnant once or even twice in the same breeding season in which it was born; the remaining one or two pregnancies then are postponed until the next breeding season after a six months' period of anoestrus.

In this respect *E. myurus* is quite different from *Sorex araneus*, in which animal, according to Brambell (1935), there is no evidence that any young females attain oestrus in the same season in which they are born; and all old animals die off after the breeding season. In the hedgehog also young animals do not reach maturity in the season of their birth (Deanesly 1934). On the other hand, the American shrew, *Blarina brevicauda*, closely corresponds to *Elephantulus myurus* in this respect (Pearson 1944). And in *Evotomys glareolus* (Brambell & Rowlands 1936), young animals may breed in the same season in which they are born, and parous animals frequently survive the winter and participate in a second breeding season, just as in *Elephantulus*.

The above-mentioned facts about the breeding habits of the female *E. myurus jamesoni* need particular emphasis, because at the end of the breeding season, about January, the regular continuity of events is suddenly disturbed when the animal prepares to go into anoestrus, in one of the various ways described in the first part of this paper.

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Going into anoestrus

Going into anoestrus is a rather sudden process in an individual animal; it may be achieved in a few days. On the contrary, taking the population as a whole, the period of reproduction fades out gradually. Some animals, described above, were found to go into anoestrus as early as December. On the other hand, pregnant animals were collected on the fifth of March. The great decline in sexual life is in January. There is not much point in speculating about external factors that may cause the end of reproduction. Suffice it to say that January is in the middle of summer and in the middle of the rainy season, when there is abundance of food available for the animals.

Whereas at the height of the breeding season a female is invariably fertilized at each ovulation, at the end of the season infertile ovulations are of frequent occurrence. A female may ovulate once or twice before she goes into anoestrus; it may even happen that a female becomes pregnant after a second or third ovulation. This indicates that not only the females go into anoestrus one after the other, but the males also. A female may still be sexually active, but towards the end of the season its chance of finding a suitable male decreases gradually. Miss Z. Stoch recently investigated this problem of the males going into anoestrus, and actually found that they do; moreover, the males go into anoestrus in quite an unexpected way. The results of her investigations are published in a following article (p. 99).

The approach of anoestrus is more pronounced in the uterus than in the ovary. A narrow uterus, a dense stroma with small nuclei, and a low uterine epithelium are all indications that the animal is going into anoestrus. In the corresponding ovary there are certainly no ripening follicles, but mitotic divisions can still be found in the granulosa cells. These features, however, make it difficult, or even impossible, to decide whether a young animal is preparing for its first ovulation or is going into anoestrus directly on reaching puberty. In both cases the uterus is small, with a dense stroma and a low epithelium, and any mitotic divisions that can be observed in the ovary do not give sufficient indication. In old animals, with a post-partum ovulation, the same difficulty does not arise; even if there are some mitotic divisions in the granulosa cells, the structure of the uterus reveals at once whether the animal will go into anoestrus, or ovulate and pass through another cycle.

Gradually these divisions of the granulosa cells decrease in number, and finally all activity in the ovary comes to an end. Only then can it be said that the animal is in anoestrus.

The follicular inactivity of the ovary during anoestrus is complete as far as can be ascertained in sections. Even the corpora albicantia, resulting from the last pregnancy, do not change at all but persist in the ovary until the first pregnancy of the following season. During the breeding season corpora albicantia are conspicuous only in the first half of a subsequent pregnancy; in the second half they become obliterated completely, so that not more than one generation is present. Thus, in the breeding season, corpora albicantia do not last longer than six weeks; during anoestrus they persist six months or longer.

Going into anoestrus is independent of the other sexual activities of the animal. A cycle in which a female happens to be can be interrupted at any stage. That there are few instances of an interruption at some particular stage, as, for instance, directly after parturition,

may only be an indication that such a stage is normally only of short duration. There is, however, one exception to this rule. Unless a female goes into anoestrus directly after an infertile ovulation, the menstrual cycle, following such an ovulation, will be completed. This shows that, whatever may be the direct cause of this interruption of sexual activity, the menstrual cycle, once it has started, is independent of this cause. The most drastic effect is reached when the animal goes into the stage of anoestrus during pregnancy. Then, unless the animal is near term, the inevitable result is abortion of the embryo.

Whereas the primary cause of going into anoestrus is probably an environmental one, the more direct cause of the interruption of sexual activity is most likely a change in the function of the pituitary gland.

Mr Hoogstraal informed me privately that the species of *Elephantulus* he collected in the Sudan breeds all the year round. I have an idea that some South African species may also breed at any time of the year; at least I found all stages of pregnancy in *E. intufi* during July, and I obtained an immature animal in May. This will be investigated when adequate material is available. It may be, however, that the Sudan species, and maybe others, behave in this respect as does *Mastomys erythroleucus*, in which animal the females may cease breeding for a period, at different, and apparently not fixed, times of the year (Brambell & Davis 1941). Also in the wild brown rat (Perry 1944), individuals may cease to ovulate for a considerable period at any time of the year. The latter two cases indicate that the primary cause of going into anoestrus may not be an environmental one but something in the animal itself.

The menstrual cycle

The uterine reactions during the menstrual cycle of *E. myurus*, and a comparison between *Elephantulus* and other mammals, were described and discussed in a previous paper (van der Horst & Gillman 1941). Also the life history of the corpus luteum of menstruation has been dealt with before (van der Horst & Gillman 1942*a*). Only a few remarks have to be added to this previous work.

When these papers were written, no material had as yet been collected systematically all the year round. Therefore, we did not realize that menstruation in *Elephantulus* is confined to a short time towards the end of the breeding season. Of course, theoretically, the possibility exists that the animal can menstruate at any time during the season. However, as has been stated above, the female is fertilized at every ovulation during the height of the season, so in practice it has no chance to menstruate. Only when the males go into anoestrus is an infertile ovulation usually followed by a menstrual cycle in a still sexually active female.

All examples and figures published before were taken from young animals, menstruating after they had reached puberty, with one exception (van der Horst & Gillman 1941, figure 10), and that concerned a not quite normal case with a small number of corpora lutea only. However, a post-partum ovulation at the end of the season may also not be accompanied by a copulation, and then mostly results in a post-partum menstrual cycle. The picture shown by the uterus may then be widely different from that of the uterus of a young animal, depending on the degree of contraction of the uterine wall as shown in figures 21 and 25. These are rather extreme cases, and they were not recognized by us as stages in the menstrual cycle at all. With more material available for comparison, it became clear that the picture might

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look more like a menstruation stage as it is found in a young animal, had the uterus strongly contracted (figure 20). Several intermediate stages were also found.

In the absence of fertilization, the corpora lutea, once they have assumed their definite form, do not increase in size, and indications of their degeneration can already be observed at the time the menstrual polyp is being formed. By the end of the menstrual cycle usually many lutein cells have already broken down, the corpus luteum becomes correspondingly smaller, although retaining its cellular structure. Usually, when a second menstrual cycle follows, the corpus luteum completely disappears, as an entity, during that cycle. Only in a few cases could three generations of corpora lutea be identified.

It has been shown before (van der Horst & Gillman 1946) that the behaviour of the corpus luteum of pregnancy is totally different from that of the corpus luteum of menstruation; it increases in size and remains functional during nearly the whole period of pregnancy.

In a few cases, described above, ovulation had taken place from a few Graafian follicles, or even a single one, at the end of the season, and the number of corpora lutea is correspondingly small. The menstrual reaction in correlation with the minimum amount of hormone produced by the few, or even one, corpora lutea, is very slight, as is so well illustrated by series 1032 (figures 33, 34).

The all-important question may be raised whether or not the phenomena, observed in *Elephantulus*, can be regarded as a process of menstruation. It might be an abortion of a very early embryo or a pseudo-pregnancy.

Taking the mammals as a whole, menstruation is rare. It is confined to the Catarrhina and Anthropomorphae, in a very weak form it occurs in the Platyrrhina. *Tarsius* also menstruates, but the Lemuroidea do not. It is possible that *Galeopithecus* menstruates, but *Tupaia* does not (van Herwerden 1905). The placentation of *Tupaia* and the absence of coiled arteries in this animal (van der Horst 1949) also indicate that *Tupaia* does not menstruate.

There seems to be a close relation between the occurrence of menstruation and the presence of coiled arteries in the uterine wall (van der Horst 1950*a*). It is known that in Catarrhines and in Anthropomorphae these arteries are well developed. In Platyrrhines the menstrual process is very weak indeed, and the 'coiled arteries', although otherwise exhibiting the features of coiled arteries, are short and straight.

Further coiled arteries are known to exist in the Macroscelididae (*Elephantulus*), the Centetidae and the Erinaceidae, all families belonging to the order of the Insectivora, or in any case, if that order is no longer recognized, they are amongst the most primitive of the placental mammals. No data are available about the presence of coiled arteries in *Galeopithecus*.

In *Elephantulus* menstruation is very vigorous, accepting for the moment that we may designate the process as such, but it is strictly localized and limited to a small area of the uterus. Only in this same area are coiled arteries found and, compared with other animals, they are enormously developed.

It is unknown if menstruation occurs in the Centetidae.

The hedgehog, Erinaceidae, also has coiling arteries and, differing from *Elephantulus*, they are present in great number. According to Deanesly (1934) in the mated, but

non-pregnant, hedgehogs there are large, or well-vascularized, developing corpora lutea, totally different from those of ovulation, and indistinguishable from those of pregnancy. The number of these large corpora lutea, in May and June, of hedgehogs whose uteri show no trace of recent pregnancy, make it clear that a succession of two or three pseudo-pregnancy cycles is by no means uncommon before implantation takes place. The histological changes in the uterus during these pseudo-pregnancies were not described by Deanesly. It occurs to me that one may not have to do with pseudo-pregnancies at all, but that the female passes through a few menstrual cycles before it becomes pregnant. In *Elephantulus* also the corpora lutea of menstruation are at first indistinguishable from those of pregnancy; a difference between them revealing itself only after the embryo has reached the implantation site. There is, however, this difference between *Elephantulus* and *Erinaceus*. In the latter animal a number of ovulations follow each other in rapid succession if the animal is not mated, and the suggestion has already been made above that these ovulations correspond to a single ovulation of *Elephantulus*. Also the time interval between these ovulations, 7 to 10 days in *Erinaceus*, corresponds more with the estimated duration of the menstrual cycle of *Elephantulus* than with that of a pseudo-pregnancy.

Real pseudo-pregnancy extends over a much longer time than 7 to 10 days, as mentioned by Deanesly in the case of *Erinaceus*. According to Hammond & Marshall (1930) pseudo-pregnancy lasts $5\frac{1}{2}$ to 6 weeks in the ferret, and also in the bitch, pseudo-pregnancy equals pregnancy in duration. In the rabbit pseudo-pregnancy lasts up to the sixteenth day after sterile mating, and during this time the growth of the uterine mucosa and the hypertrophy of the mammary glands are the same as during real pregnancy.

We may, therefore, conclude that the reactions observed in *Elephantulus* are not a case of pseudo-pregnancy, and probably the same holds true for *Erinaceus*. Now we can consider the possibility of explaining these reactions as an abortion of a very young embryo.

In *Elephantulus* the uterine reactions during the menstrual cycle are different from those in early pregnancy. Only in the formation of a localized, mesometrial oedema, and in the swelling of the blood vessels is there correspondence between the two cycles. Even so, the coiled arteries do not become so conspicuous and do not swell so regularly over their whole length in the menstrual cycle as they do during early pregnancy. Whereas, in early pregnancy, the uterine stroma and epithelium withdraw in front of the embryo in order to form a niche at the implantation site, no indication of such an embryo chamber can be observed after an infertile ovulation. Neither does the uterine lumen extend to accommodate the growing embryo. On the contrary, although there is a slight local swelling of the uterus, the greater part of the oedematous stroma protrudes, as a polyp-like growth, into the lumen of the uterus from the mesometrial side, thereby reducing the lumen, in a cross-section, to a crescent.

It has been pointed out in a previous article (van der Horst 1950*b*) that the height of the uterine epithelium is considerably reduced by insemination. During the menstrual cycle the epithelium remains very high, except where it covers the polyp-like outgrowth. Thus it may be concluded whether an ovulation was fertile or infertile from the height of the epithelium.

The behaviour of the corpus luteum in the menstrual cycle is different from that in abortion. The corpus luteum of menstruation stops growing at an early stage, before the polyp is being formed, which corresponds to the time when the early embryo reaches the

implantation site, and although it retains the same size to about the next ovulation, it apparently does not function any more. It remains cellular as long as it can be recognized in the ovary, but the cells become smaller and disappear one after the other. After an abortion, the corpus luteum disintegrates as a whole, the cell membranes break up and the nuclei become irregular in form.

Therefore the reactions observed in the uterus cannot be explained as an abortion of an early embryo.

As the phenomena observed cannot be interpreted as a pseudo-pregnancy nor as an abortion, it can only be concluded that menstruation occurs in *Elephantulus*, which contention is supported by the presence of coiled arteries, by the height of the uterine epithelium and by the behaviour of the corpora lutea.

What, however, is the stimulus that initiates the formation of the polyp during the menstrual cycle? In *Elephantulus* a menstruation without a previous ovulation was never observed. It is, therefore, possible that an unfertilized egg has to reach the implantation site to initiate the menstrual reaction, which would indicate a great difference between the action of an unfertilized egg and an early embryo. In two cases an unfertilized egg was found attached to the polyp during the menstrual cycle.

On the other hand, it is possible that a menstrual reaction, without such an additional stimulus provided by the egg, sets in at a certain time after ovulation.

Abortion

Abortion at the end of the breeding season, which occurs regularly in *Elephantulus*, is a phenomenon that has not been recorded from any other mammal. Yet it may not be only of theoretical significance. Only one instance of a similar nature was found in the literature. Brambell & Rowlands (1936) obtained one pregnant female of *Evotomys glareolus* in October containing two blastocysts free in the uterine lumen. The uterus of the animal was exceedingly small and histologically resembled that of an animal in anoestrus, so that this initial pregnancy would not have been maintained. This seems to be a case of pre-implantation abortion as recorded for *Elephantulus* (van der Horst & Gillman 1942*b*).

In *Sorex araneus*, according to Brambell (1935) the falling off in the litter size, as shown by the mean number of embryos *in utero* towards the end of the season, is probably due to an increase in the embryonic mortality, and not to a decrease in the number of ova ovulated. Here it is only the size of the litter that is reduced and it is not a complete interruption of pregnancy. Brambell does not mention how the dead embryos are removed from the uterus, but as some of the embryos are retained, one cannot call this an abortion.

Abortion occurs in the wild rabbit according to Brambell & Mills (1948). In this animal a good many pregnancies are interrupted, either by the death of individual embryos, or by the death of whole litters, and then, in the latter part of pregnancy, abortion is a more frequent means of removal of the dead embryos than reabsorption. This embryonic mortality and abortion in the wild rabbit, being not confined to the end of the breeding season, is of a different character from that which happens in *Elephantulus*.

Pre-natal mortality, and reabsorption of the embryos, seems to be of frequent occurrence in rodents; it has been mentioned by several authors, the last being Purdy & Hilleman (1950), who found it in the golden hamster.

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Abortion as found in *E. myurus jamesoni* is a seasonal phenomenon. Whatever the ultimate cause may be, it affects only a good many of the pregnant animals, particularly during the earlier stages of pregnancy. Others, however, escape the influence and bring their pregnancy to a successful end. This abortion, therefore, is in some respects different from a spontaneous abortion as may occur in man and other mammals.

This type of abortion, found in *Elephantulus*, is a phenomenon so unexpected and so different from anything found in other mammals, that previously it was only recognized as such when it occurred in very early stages of pregnancy, before the embryo had implanted (van der Horst & Gillman 1942*b*). A slightly later case, that of series 91 (figure 48), was described as a spontaneously developed deciduoma, as no embryo could be detected (van der Horst & Gillman 1942*c*). Series 93 (figure 45) might have given us the answer, but here we thought that the embryo was only in a somewhat abnormal position. In reality series 93 shows a stage of the abortion of a blastocyst, and in series 91 the blastocyst had already been expelled but the decidual tissue was still retained in the uterus. Only after much more material had been collected and studied was this remarkable phenomenon of abortion, before going into anoestrus, recognized as such.

In *Elephantulus*, the death of the embryo is certainly not the cause of the abortion. In every case, where the embryo was still in the uterus, even if it was no longer in its normal position, the embryonic tissues had a perfectly healthy appearance. In the case of series 876 (figure 53) the embryo, that had already advanced at least to mid-term, was expelled, but the placenta and membranes looked quite healthy, and, moreover, nothing seemed to be wrong with the embryo in the other uterine horn of the same animal.

As far as can be ascertained up till now, the direct cause of the abortion in *Elephantulus* is the disintegration of the corpora lutea. The size of the corpora lutea was found to correspond to the age of the embryo at the time of abortion, from which it can be concluded that the corpora lutea had grown and functioned normally to a period shortly before the abortion. These corpora lutea have an aspect totally different from the corpora lutea of menstruation that do not grow but gradually degenerate.

Elephantulus may abort occasionally at any time of the breeding season, and a few cases of such an abortion are represented in the collection. Then a definite cause of such an abortion, a dead embryo, an abnormal uterus, etc., can generally be found. *Elephantulus* often aborts when kept in captivity. The shock of being caught and confined to a narrow cage is then probably the cause of the abortion. Corresponding cases occur in man also.

In *Elephantulus* the corpus luteum remains active during the greater part of pregnancy. In man the corpus luteum is essential during the first 10 weeks of pregnancy only. We have seen above that the disintegration of the corpora lutea is the direct cause of abortion in *Elephantulus*, the primary cause may be found in the pituitary gland, or finally in the environmental circumstances.

I do not know whether a human corpus luteum has ever been investigated after an abortion at an early stage. It is, however, possible that in such a case the same direct cause, namely, the disintegration of the corpus luteum, as in the seasonal abortion of *Elephantulus*, is effective. Abortion in man during the later stages of pregnancy cannot be compared with abortion as it occurs in *Elephantulus*.

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