plant residues are converted by bacterial action in the soil into calcium carbonate.

(5) The return of base by the growth of plants and the production of calcium carbonate by the decay of plant residues are sufficient to maintain soils neutral which are poor in calcium carbonate, and to replace the bases which have been consumed in nitrification and similar changes.

On the Origin and Life History of the Interstitial Cells of the Ovary in the Rabbit.

By Janet E. Lane-Claypon.

(From the Physiological Laboratory, University College. Communicated by Professor E. H. Starling, F.R.S. Received June 16, 1905.)

[Plate 1.]

The majority of the investigators of the subject consider that the cells of the germinal epithelium arise by differentiation of the peritoneum, and become embedded in the subjacent mesoblast, there being probably a dual process, namely, the downgrowth of the cells themselves and a simultaneous upgrowth of the subjacent mesoblast.

The fate of the cells thus embedded has given rise to much discussion. All observers agree in stating that they give rise to the ova, and most observers consider that they give rise also to the follicle cells; but de Foulis (8),* Schrön (16), and Wendeler (20), believe these cells to be derived from the connective tissue.

Pflüger (15) and Waldeyer (18), although differing in regard to the development of the ovary, both consider that the germinal cells give rise to the cells of the follicular epithelium, there being most probably a previous division of the original cells.

Nagel (14) also agrees that the follicle cells are derived from the germinal epithelium. Balfour (4) believed that some of the cells of the egg-clusters became ova by differentiation, and he described besides a number of small cells, of which some formed the follicular epithelium and the others probably either served as foodstuff for the rest, or eventually themselves formed ova or follicle cells.

Bühler (7) describes the formation of the follicular epithelium by the

* These numbers refer to the entries in the bibliography at end.

streaming inwards from the periphery of some of the cells of the germinal epithelium.

The changes connected with ovogenesis have been very fully described by v. Winiwarter (19). They may be briefly summarised as follows. The germinal cells of the second invagination are rather small and show a nucleus with some lumps of chromatin, being also rather granular. These he calls *protobroque* cells of the *a* variety. These divide, giving rise to other protobroque cells *a*, and also to a *b* variety. These last divide again giving rise to more cells of the *b* variety and to a new form of cell, *deutobroque*. The last are larger, and the nucleus more transparent. The deutobroque cells give rise to the ova by nuclear differentiation by means of the following stages. 1. The chromatin breaks up into fine filaments, which are distributed over the whole nuclear area; this is the *leptotenic* stage. 2. The filaments become gradually massed together until they show as a compact lump at one side of the nuclear area. This transformation is the *synaptenic* stage, which is succeeded by 3, the *pachytenic*. Here the filaments become again spread out, but they are much coarser than in the previous stages The 4th stage, or *diplotenic*, is so called on account of the tendency of the chromatin strands to lie in pairs. In the final or *dictyate* condition the chromatin is distributed in a reticulum over the greater part of the nuclear area

Balfour describes protoplasmic masses of young ova where the cells appear fused, and he suggests that one of these ova may grow at the expense of the rest. Van Beneden (5) describes multinucleated masses in the ovary of the adult bat, which he suggests may give rise to an ovum and its follicular epithelium.

The formation of follicles, which proceeds rapidly, gives rise in the ovary to two zones, an external or parenchymatous zone in which the follicles lie, and an interstitial vascular zone; these have been described with some modifications by various workers and for different animals. (His (11), Waldeyer, Born (6), Macleod (13), Van Beneden.)

The question of the post-natal formation of primordial ova has been the subject of many isolated observations. Pflüger believed he had evidence of the return of the ovary to the tubular formation at the rutting season, the object of the return being the formation of fresh ova. Waldeyer believed that all ova were formed in the young animal, and for this reason called all ova "primordial ova."

Schrön noticed an increase in the number of clear cells, presumably ova, near the periphery in cats and rabbits at the rutting season, and in women at the menstrual periods. Koster (12) describes prolongations of epithelium with formation of fresh ova and follicles in the ovaries of several recently

pregnant women; Wagener (17) records the thickening of the germinal epithelium near the attachment of the Fallopian tube in the pregnant bitch, a condition which he thinks denotes the formation of ova.

Amann (1) describes the presence of follicles in the ovaries of a woman of 63, where there was incipient cystadenoma, the follicles being in all stages of formation by means of invagination of the germinal epithelium. The interest of this observation lies in the age of the woman and in the apparent formation of fresh ova consequent on the stimulus caused by the incipient cystadenoma.

V. Winiwarter was not able to trace any of the stages of ovogenesis in any of the adult ovaries he examined, and considers this a necessary condition for the formation of ova. As far as the literature goes, we may consider the ovary to be formed by the embedding in the underlying mesoblast of the cells of the germinal epithelium, the embedding being brought about by a process of ingrowth of the cells and of upgrowth of the mesoblast. The cells thus embedded are oogonia, which give rise to ova by division, as also to the follicle cells, the future ova undergoing considerable nuclear transformation before reaching the condition of the fully-formed primordial ovum.

The post-natal formation of primordial ova has been recorded in certain cases, but there is not much evidence either in favour of or against it.

Object of the Investigations.—Certain features which I observed in the interstitial cells of the ovaries of rabbits at a late period of pregnancy led me to study the origin of these cells. This question would appear to have been neglected by previous workers on the ovary. The formation of an internal ovarian secretion (*cf.* Andrews (3)), which by analogy with the interstitial gland of the testis might be presumed to be derived from the interstitial cells (*cf.* Ancel and Bouin (2)), gives considerable interest to their origin.

This was studied by examining (1) the ovaries of rabbits from the twentieth day embryo up to those of the young rabbit about three weeks after birth; (2) the ovaries of pregnant rabbits at all stages.

Methods.—It is not easy to find a really good fixing agent for ovaries, especially adult ovaries. Hermann's, Flemming's (strong formula), Podwyssoski's and Altmann's fluids, were all used. The last was found satisfactory for cytoplasm, but the sections obtained with the other fixatives were not good. The tissue was osmicated outside and insufficiently fixed inside. Finally,* Gilson's fluid was used exclusively for all nuclear figures, and a

* Gilson's fluid = abs. alc., 1 part;
glacial acetic, 1 part;
chloroform, 1 part;
the whole saturated with sublimate.

mixture of sublimate (saturated) 4 pints, formol 1 pint, and 1 per cent. glacial acetic for other purposes.

The sections fixed in Gilson's fluid were stained with iron hæmatoxylin, or hæmalum; those fixed in the other solution stain well either with iron hæmatoxylin, hæmalum and eosin, or toluidine blue and eosin.

Changes in the Cells of the Germinal Epithelium in the Immature Rabbit.

The origin of the germinal epithelium from the peritoneum by a process of differentiation has been so fully shown by several observers, that it will not be necessary to deal any further with the origin of the germinal cells. Also it has been shown that these cells become embedded in the underlying mesoblast; this state of affairs is seen in an embryo of the twentieth day.

The ovary is by this time a definite organ; it is intensely vascular, showing large blood spaces, especially in the parts lying immediately round the mesoblastic core. At this period the main mass of the germinal cells is situated peripherally, only a few isolated ones having penetrated into the core, which last is sending processes of connective tissue in between groups of germinal cells. Of these there are present a large number of protobroque and a few deutobroque; also a certain number of mitotic figures, but these are not numerous. (See Plate 1, fig. 1.)

From this time onward until after birth the changes in the ovary, as seen under the low power of the microscope, are not striking; there are more deutobroque cells, characterised by their transparent appearance, and there is an increase in the number of mitotic figures.

Studied under the high power of the microscope some of the deutobroque cells are seen to have entered upon the early stages of ovogenesis, and to have reached the leptotenic stage. There are large numbers of round cells showing a nuclear structure differing from either the protobroque or the deutobroque cells. The mitoses are chiefly found near the periphery, and the greater number of them seem to be taking place in the large cells. I do not altogether agree with v. Winiwarter on the question of mitosis in these cells. In the first place there appears to be very little distinction between the varieties of protobroque cell, *a* and *b*, and I shall not dwell upon it. The mitosis in the protobroque cells does not appear to be sufficient to account for the large number of deutobroque cells which are formed, and my observations are to the effect that by far the greater number of mitoses are taking place in the deutobroque cells themselves. Each class of cell divides, the protobroque less copiously than the deutobroque, giving rise to two cells of their own variety. There can be no doubt that the deutobroque cells are modified

germinal cells, but I hope to show that the process is one of differentiation, and not of division.

The protobroque cell is the type of the original germinal cell; it is small, generally oblong or oval, and contains a large nucleus. The nucleus shows a number of chromatin masses of varying sizes, and the whole nuclear area gives a general impression of granulation (represented by shading in the figures (Plate 1, fig. 2 (*a*)). There are no chromatin filaments.

The deutobroque cell is very much larger, and the nucleus has for the most part a strikingly transparent aspect, the granular appearance noticed in the protobroque cell being confined to the periphery of the nuclear area. The chromatin is quite differently arranged; there are one or two irregular chromatin masses, and strands showing nodular enlargements where they intersect. See fig. 2 (*f*).

Sections of a young ovary very soon before or after birth show a large number of cells whose nuclei exhibit every phase of transition between these two varieties. These changes in the nucleus may be classed broadly into three divisions:—

1. The chromatin masses become fewer and larger.
2. There is considerable formation of chromatin strands.
3. The granular appearance gradually passes away from the centre of the nucleus towards the periphery, leaving the centre clear.

Some of these changes are shown in fig. 2 (*b*), (*c*), (*d*), (*e*). In the first stage the whole cell becomes rounder, as also the nucleus, and the chromatin has begun to aggregate, and there are traces of strands passing away from the masses. These features increase in intensity until there are only a few chromatin masses, but the strands are passing between them and intersect in parts. The granular appearance has begun to leave the centre, which is clear.

A further process on these lines brings the cell into the typical deutobroque condition. It would therefore seem that the change from the protobroque type is accomplished by means of transformations in the nuclear area, accompanied by a growth in size of the cell, and it is unnecessary to suppose, under these circumstances, that mitosis is also a method of formation. The protobroque and deutobroque cells are therefore all oogonia, either potential or actual, the transition from the one class to the other being probably accomplished by processes of nuclear differentiation.

At this period in the life of the ovary there is no appearance which could be characterised either as egg-tubules or egg-clusters; there are large collections of epithelial cells bounded centrally by the mesoblast, which presents the appearance of connective tissue. This tissue penetrates but slightly into the region lying peripherally to the main central core, but careful

inspection shows that there are a few fine processes pushing their way outwards and more or less enclosing large numbers of germinal cells. The latter are of all shapes and sizes, from the typical protobroque to the deutobroque type.

By the third day after birth the general configuration of the ovary has changed very considerably. There is still the central mesoblastic core, but the germinal cells have become more marked off than in the embryo, presenting the appearance of a definite zone of germinal epithelial cells. The cells are arranged, especially in the more central parts of the zone, in the form of solid rods or clusters, several cells thick, which press their rounded ends into the central mesoblast. Some of them might fairly easily be mistaken for tubules without a lumen, and there can I think be little doubt that these are what Pflüger took for tubules. Around the periphery the tubular formation is not so marked, the cells lying in irregular aggregations (fig. 3). As the mesoblast is centrally situated those parts of the germinal zone lying towards the centre get divided up earlier than the more peripheral parts, which retain the formation of an earlier stage. This lagging behind, as it were, of the periphery is quite characteristic of all the changes taking place in the young ovary; it applies to the formation of tubules and clusters, to the processes of ovogenesis, as pointed out by v. Winiwarter, as well as to the formation of interstitia cells, which will be dwelt upon later on.

From this time onwards up to about the twelfth day after birth the changes in the general configuration of the ovary are brought about by an amplification of the processes already described, namely, continued upgrowths of connective tissue, cutting off the tubules and clusters. The connective tissue likewise presses into the larger collections of germinal cells, thus cutting them off and dividing them again into smaller portions, so that as time goes on the clusters near the central parts consist of less cells, but are present in much greater number, while those parts more peripherally situated are in a somewhat earlier stage, the cluster formation being still fairly evident close to the periphery as late as the sixteenth day.*

Before proceeding to the changes in the egg-clusters about the fifteenth

* Too much stress, however, should not be laid upon the exact date of the young ovary in relation to its structural aspect. There seems to be an appreciable difference in the extent to which the ovary is developed in different animals about this age. v. Winiwarter does not describe any ovary between the tenth and the eighteenth day, because he does not consider the changes to be sufficiently striking to call for any description. Of two litters of rabbits I found slight differences in the ovaries of the same date, the sixteenth day, the changes being rather more advanced in one than in the other, and both were almost as advanced as v. Winiwarter's figure of the eighteenth day. The differences are probably determined by the varying nutrition of the animal, as also possibly by the kind of rabbit, some being far more advanced in outward aspect at this age than others.

day, the transformations which have been taking place in the deutobroque cells must be briefly touched upon, but they have been so fully described by v. Winiwarter that a lengthy exposition is quite unnecessary. I shall adopt his nomenclature throughout. It has already been stated that almost immediately after birth changes begin to take place in the deutobroque cells, which enter upon the leptotenic phase, the transformations beginning centrally. This is succeeded by the synaptenic, and by the third day there are already a very great number of this variety.

The leptotenic phase is characterised by the absence of visible nucleolus, and by the spreading out of the chrcmatin in the form of fine filaments over the whole nuclear area. This stage is evidently only a further step in the differentiation which has already taken place. It has been shown that the change from the protobroque to the deutobroque type is accomplished by the chromatin masses becoming gradually broken up into strands. In the leptotenic phase the process is merely carried further. Whereas in the deutobroque stage there are still one or two chromatin masses which have not become broken up into strands, in the leptotenic this is not the case, the whole chromatin being present in the form of filaments. The transition stage can be seen in an ovary of a few days after birth (fig. 6 (1)). These filaments become gradually aggregated, passing to the synaptenic state. The leptotenic condition is a very fugitive one, whereas the synaptenic, owing presumably to the great variety of aspects through which the aggregation passes is very much more prolonged. The synaptenic is succeeded by the pachytenic, where the filaments are coarser, then by the diplotenic, and this in its turn by the dictyate condition, which is the typical nuclear appearance of the young ovum.

These changes pass gradually outwards, and by the tenth day even the cells quite at the periphery have passed through the earliest phases, whilst the central cells are reaching the final ones. By the fourteenth day there are a certain number of dictyate nuclei towards the centre. At this stage the central mesoblastic core is becoming obliterated, the egg-clusters of either side of the ovary very nearly meeting. The clusters are much smaller, having been split up by the ingrowing mesoblast. The number of dictyate nuclei now increases at a surprising rate, there being a great number by the fifteenth day, and a still greater number by the sixteenth day, by which time the clusters are almost indistinguishable, except round the periphery, their place having been taken by dictyate cells, some of which now show a surrounding follicular epithelium. There are also collections of small more or less rounded cells lying in between the young follicles, but not forming any part of the follicular epithelium. These are the interstitial cells of the ovary, and I propose now to trace their origin in detail.

Origin of Interstitial Cells.—By about the tenth day the ovogenetic processes in the central egg-clusters are at their height, and continue in this condition, passing through the various phases, until about the fourteenth day, when, as already stated, some have reached their final stage. Throughout the whole period, however, there are in almost all the clusters some three or four cells, or perhaps more, which remain in the ordinary deutobroque state, and do not undergo any of the ovogenetic phases, the number of these being greater in the peripheral clusters than in the central ones; by the fifteenth and sixteenth days, when the number of dictyate nuclei is increasing, there are few, if any, of the deutobroque cells to be found in the central parts, but instead, there is an increasing number of the small round cells already referred to. As the days pass on the number of the former decreases, and the number of smaller cells increases. Thus, there is throughout the ovary, but in different parts at slightly different periods, a reduction in the number of deutobroque cells, which have remained unchanged, and an increase in the number of small round cells.

Examination of sections of the fourteenth, fifteenth, and sixteenth days near the centre of the ovary, leaves no room for doubt that some of these cells form the follicular epithelium, gradually passing towards and arranging themselves around the young ova. At the fourteenth day the number of these cells to be found near the centre is not nearly sufficient to form the follicular epithelium for the large number of young ova, while near the periphery there are many more than would appear to be necessary for the requirements of this part. By the fifteenth day the number of these cells near the centre has increased very largely, still more so by the sixteenth day, by which time many of the young ova are surrounded with follicle cells, and there are also the collections of these cells already referred to. Their number has meanwhile diminished somewhat at the periphery. The appearance in the intermediate parts gives the key to the whole question. Here are seen large numbers of these cells streaming inwards from the periphery and making their way between the egg-clusters of the periphery towards the centre, where the cluster formation can now be scarcely recognised. Here they arrange themselves around the young ova, or pass into little groups by themselves. These groups are the first beginnings of the real interstitial tissue of the ovary, and mark the commencement of the adult aspect of the organ.

There are thus two main points to be emphasised at this period in the life of the ovary. First, the passage inwards of a large number of cells from the periphery, and secondly, the commencement of the adult formation by the formation of young follicles, and the appearance of interstitial cells.

This passage inwards of cells from the periphery was noticed by Bühler; he realised that the number of small cells near the centre during the height of ovogenesis was not enough to provide a follicular covering for all the young ova which were there, and he describes the streaming inwards of the cells from the periphery, and their passage to the young ova, around which they arranged themselves, and formed the follicular epithelium.

Balfour noticed that in the later periods of ovogenesis there were present too many of the small cells, like the follicle cells, for them all to become arranged around the ova and give rise to the follicular epithelium. He was at a loss to account for the destiny of these supernumerary cells, and supposed that they must either eventually become ova or follicle cells, or be used up as food-stuffs for the other cells.

It seems to me, however, that these cells, supernumerary as far as the follicular epithelium is concerned, are in reality very important. They form the groups which represent the interstitial tissue of the fully-formed ovary, and thus, far from being unimportant, are absolutely essential for the performance of the functions of the ovary.

The question which now arises is, where do these cells come from, and what is their history of formation? It has already been indicated that the number of unchanged deutobroque cells varies inversely with the number of these cells, since these last are greater in number in the region where there are most deutobroque cells present, namely, at the periphery, especially in the region of the poles, and the high power of the microscope reveals the fact that these cells are indeed metamorphosed deutobroque cells.

The ordinary deutobroque cell presents one or two irregular chromatin masses, from which pass out filaments of varying degrees of coarseness and fineness with nodules at their intersections. The centre of the nucleus is clear, whilst around the periphery is the granular appearance already described. See fig. 2 (*f*). In the ovary of about the eighteenth day the only regions where these cells are to be seen in any appreciable numbers are round the periphery and at the poles. They stand out even under the low power on account of their general transparent aspect as compared with the surrounding cells, and also in many cases on account of their rather larger size. There are also cells whose transparency is not so great, but which show up quite markedly in contrast to the rest and are rather smaller in size than the more transparent ones. These cells are transformation stages between the deutobroque and the ordinary interstitial type, and the process resembles very much in the inverse order that which has been already described for the deutobroque formation from the protobroque.

The first stage is the gradual massing of the chromatin into irregular masses

and the thinning of the chromatin strands, which become rather less in number, as do also the nodules (fig. 4 (*c*)). At the same time the granular appearance extends gradually towards the centre, although it is not until quite a late stage that it reaches the centre itself (fig. 4 (*f*) and (*g*)). The size of the cell becomes gradually less, and the amount of protoplasm relatively greater.

The retraction, as it were, of the filaments and strands towards the chromatin masses is very much more marked in the cells of smaller size, where there is a tendency for the masses to pass towards the periphery, leaving the centre clear (fig. 4 (*d*) and (*e*)).

These changes continue until nearly all the chromatin is massed, the masses becoming rounder as the process goes on. There are always traces of strand formation left, in contrast to the protobroque nucleus, where it is markedly absent. Thus the small cell derived by differentiation from the deutobroque cell does not return to the characteristic protobroque type, but shows traces of its intervening deutobroque condition in the shape of strands of chromatin, and nodules on the strands. See fig. 4 (*g*).

The cells, once reduced in size, become true ovarian cells, and may either function as follicle cells or as interstitial cells (fig. 4 (*h*) and (*k*)).

Thus we find the following processes taking place in connection with the formation of the mature ovary. The cells of the germinal epithelium become embedded in the underlying mesoblast, and, once there, may either undergo differentiation, or apparently may remain in the protobroque condition. If the former be its fate, it must undergo nuclear transformation, together with growth in size, until it reaches the deutobroque stage. Arrived at this condition it probably divides, although possibly this is not an essential, and the two cells formed by this division are of the same type. There are now two courses open for the cells thus produced; they may undergo the nuclear transformations of ovogenesis, and become primordial ova, or they may rest for a time, and finally undergo regressive transformations, becoming either follicle cells or interstitial cells. Every cell of the germinal epithelium is probably a potential ovum, relatively very few remaining in the protobroque state, although some may still be seen at the periphery in ovaries of the eighteenth day. Incomparably the greater number pass to the deutobroque state, preparatory doubtless to the formation of ova. All cannot become ova, for the other forms of cell are necessary for the maintenance of the ovarian functions; possibly, therefore, only the most robust cells, and those which are most conveniently situated for obtaining nourishment undergo the ovogenetic changes. This would seem to be borne out by the fact that many more of the central cells, which are nearer their food supply, undergo ovogenesis, than

of the peripheral ones. The rest of the cells which are not able, for one cause or another, to undergo these changes, appear to remain quiescent for a while, until finally they regress and pass into a condition of subserviency to the needs of those which have become ova. Both follicle cells and interstitial cells are, however, still potential ova. They have passed through the initial stages, and only need enlargement and nuclear transformations in order to become ova, should the appropriate stimulus be given. This chance is not given to the follicle cells. As soon as the follicle begins to grow, they multiply rapidly, and probably provide, by their disintegration, the follicular secretion upon which the ovum feeds and grows. In the ripe follicle of the rabbit there is almost complete disintegration of the membrana granulosa, and the remains of the discus proligerus is presumably extruded with the ovum, perhaps serving it as food material prior to its fertilisation, and subsequent attachment to the uterine wall. The interstitial cells, however, have possibilities before them, being still capable of carrying out any function belonging to the true ovarian cell.

All the true ovarian tissue is derived from the germinal epithelium, this tissue forming in the adult rabbit by far the greatest part of the whole ovary. There is relatively little mesoblast, which subserves solely the function of support and of nutriment-carrier to the rest of the organ. We may, therefore, look upon the whole ovary as consisting of two classes of cells and of two only, namely, (1) those derived from the germinal epithelium and performing all the ovarian functions, and (2) those derived from the original mesoblast, which are supporting and vascular.

There remains only one feature to be dealt with in the immature ovary, one that has already been described by Balfour, namely, the protoplasmic masses formed by the aggregations of young ova. In the ovary of the sixteenth day the ova are all separate, but a day or two later this is not the case. There are now a large number of these masses of various sizes. They appear to consist of two, three, four, or even five young ova, to judge by the number of nuclei seen, but it is impossible to distinguish any trace of cell-boundary between them. Balfour suggests that these may either form as many ova as there are nuclei, or that one ovum may develop at the expense of the rest. This last point of view appears to be the more probable. It is evident that the massing takes place subsequent to the formation of the young ova, since it is not seen until after the appearance of the ova, and it would appear rather purposeless if they merely separated again a little later on. Moreover, in these masses one or two of the nuclei often look as if they were disappearing by gradual dissolution, and it is, therefore, probable that they will all ultimately serve as food-stuff for the one ovum

whose condition happens to have been best, and will, therefore, survive in the struggle for existence.

This cannibalism on the part of the young ovum is not surprising, if the life of an ovum be considered. It is really but the normal condition of the cell at all its stages of development; it grows and fattens at the expense of other cells. In the young ovary it is starting its first stage of growth and must devour other cells; later on, when it grows during the growth of the follicle, it lives upon the follicle cells, and later still, when, after fertilisation, the ovum in its extended sense refers to the young fœtus, it lives on the material provided by the cells of the maternal organism.

This massing of cells and subsequent demolition of some of them for the benefit of one will be again dealt with in connection with the ovary of the pregnant rabbit.

Changes in the Ovary during Pregnancy.

The young ovary, after the period when it has reached a stage where the general aspect is that of an adult ovary, enters upon a period of slow growth, during which there is a continual formation of a considerable number of follicles, which having reached a state of partial maturity then begin to atrophy and finally disappear, leaving only a faint trace of their former existence in the shape of a scar.

Having reached sexual maturity, the ovary becomes subject to periodic influences, of the nature of which little, if anything, is known. According to Fraenckel (9), they are intimately connected with the hypertrophy of the mucous membrane of the uterus. The sum total of the influences at work results in the production of "heat," which occurs in the rabbit about once a fortnight, but the external changes in the vulva by which this is judged take place very gradually, so much so, that in the spring and summer time, when breeding is most prolific, the adult rabbit is scarcely ever out of one or other stage of "heat." It is fairly certain, therefore, that whatever changes may take place in the ovary during "heat," the condition recurs too frequently for these to be very marked. This does not refer in any way to the formation of the corpora lutea of "heat," which are, of course, very definite. It has recently been stated by Heape (10) that unless impregnation occurs the ripe follicles of "heat" do not burst, in which case, presumably, there can be no formation of corpora lutea. If this is the case it would seem that there can be no such thing as the corpus luteum of "heat," and the changes in the ovary during this period must be considered to consist merely of those taking place before sexual maturity, only rather more marked, namely, the formation of follicles, but after puberty these

reach the ripe state, since they will burst if impregnation occur, whereas this is probably not the case in the immature ovary. There would then, on this view of the case, be no ovulation except in the impregnated rabbit. It is quite possible that the additional stimulus of impregnation may hasten the bursting of the follicle, but it seems somewhat unlikely that without impregnation there should never be ovulation.

The changes resulting in the production of "heat" are obviously those preparatory to a possible pregnancy. Fertilisation appears to be in itself a stimulus, and sets up general hypertrophy of the entire genital apparatus, producing likewise an improved condition of the animal; as to the mechanism of the production of this hypertrophy, however, our knowledge may be said to be nil, and we are reduced to classifying the whole as the changes brought about by the stimulus of pregnancy.

Naked Eye Changes.—Fraenckel describes and figures very accurately the naked eye changes in the pregnant ovary of about the fifteenth day in his paper on the function of the corpus luteum.

These changes are very striking, and indicate in themselves some very definite alteration or increase in the function of the gland; apart from the formation of the corpora lutea, there is an immense increase in absolute size, the gradual occurrence of which will now be described.

The ovary of the non-pregnant rabbit is a small yellowish body, lying on either side against the posterior abdominal wall, a little below the kidney. It is usually about $\frac{1}{2}$ inch in length and thin, being slightly wedge-shaped in transverse section and rather pointed longitudinally at either end; upon its surface may be seen clear round spots, showing the locality of the larger follicles, some of which, if they are nearly ripe, may even project slightly from the surface.

The bursting of the follicles and fertilisation lead to the formation of the corpora lutea, the so-called "true" corpora lutea of pregnancy, and the growth of these bodies during the early period are undoubtedly the most characteristic feature in the naked eye appearance of the ovary. If the pregnancy be one with a large number of fœtuses, the ovary often looks gnarled, so large and numerous are the excrescences produced upon its surface by these bodies. If these, however, be cut off, and if the organ be carefully examined at about the fourteenth day, when the corpora lutea are at their maximum state of development,* it will be readily seen that the ovary itself has increased in size, quite apart from the formation of the lutein tissue. The whole gland has a more swollen and rather less compact aspect; it is larger both in length and girth, and the wedge-shape of the

* *Cf.* Fraenckel, *loc. cit.*

transverse section is less marked; there are also in many cases fewer follicles in an advanced condition than in the non-pregnant state. Just at this period the energies of the gland have apparently been directed rather to the formation of the lutein tissue than new follicles.

From the fourteenth to the eighteenth day the corpora lutea remain at their maximum, and then begin to diminish rapidly in size. Instead of being very vascular whitish bodies, projecting in many cases to the extent of three-quarters of their whole extent beyond the surface of the gland, they gradually diminish both in size and vascularity, until by about the twenty-second day of pregnancy they are merely elevations on the surface, showing the faintest possible trace of vascularity; this diminution continues steadily until, a little while before birth, the locality of these striking features of the fourteenth day of pregnancy is only seen by the presence of an opaque whitish circular area upon the surface of the ovary. The changes are so marked that it is possible after a little experience to diagnose very approximately the previous duration of the pregnancy from the appearance of the corpora lutea.

Whilst these external changes are taking place in the lutein tissue, the rest of the ovarian tissue has been also undergoing changes, which, if not so striking in appearance, are none the less evident. It has already been stated that the organ at the fourteenth day shows marked increase in size apart from the corpora lutea; whereas, shortly after this period, these bodies begin to diminish in size, the reverse takes place in the rest of the ovarian tissue; and whereas growth of the ovary as a whole has been slow up to the present, it now becomes rapid and continues until close upon the time of parturition.

By about the eighteenth or twentieth day all trace of wedge-shape in cross-section has completely gone, and the organ is nearly circular, the girth is much greater, and this increase extends right up to the poles. These changes become more and more marked, until at about the twenty-sixth day the organ is well over an inch in length, sometimes about $1\frac{1}{2}$ inches, showing a proportionate increase in its other measurements, and having a shape very much resembling a spindle with blunted ends. The number of clear round spots has meanwhile been increasing rapidly, so that in the majority of cases the greater part of the surface is taken up either by them or by the round whitish patches, which mark the spots where the corpora lutea have been projecting above the surface. The formation of follicles appears to be somewhat inhibited during the rapid growth of the corpora lutea, but to be resumed with greater energy when these have reached their maximum development. At the time of parturition there are a large number of

follicles which have almost reached full maturity, and it is a well-known fact that rabbits can be readily fertilised immediately after parturition.

The gland, although soft, is not in any way brittle, and in spite of its great general enlargement retains on the whole the same shape, the most marked change being that from the wedge-shaped to the circular transverse section.

Changes in Size of the Interstitial Cells.—This great increase in size must be the result either of a large numerical increase, or of a very great increase in the size of the individual ovarian cells. The latter is at any rate the main, if not the only factor concerned, the change in size of the cell under the microscope being so marked as to attract attention even apart from any actual measurement.

The measurements were made with a micrometer eye-piece, gauged against a micrometer slide, this method being found quite sufficiently accurate for the purpose. It was not intended to record exactly the size of each individual cell, but rather by taking the measurements as accurately as possible of a large number, to find the average increase in size at different stages of pregnancy. In taking the measurements considerable selection was exercised in the cells measured; only those whose area in section was approximately circular, and where the nucleus was centrally situated being used, as it was hoped by these precautions to obtain measurements passing as nearly as possible through the centre of the cell. The measurements are given below of 10 cells from each date of pregnancy, but this does not by any means represent the number actually measured, but the same figures recur again and again, and the average works out to almost precisely that given.

Towards the end of pregnancy there is considerable difficulty in finding the right kind of cells to measure, nearly all of them being angular and irregular in outline, giving as a whole somewhat the appearance of a tesselated surface. The changes in general aspect of the sections, produced by the change in the size of the cells, will be returned to later on.

Interstitial Cells of a normal Rabbit.

Diameter in mm.		Diameter at 14th day of pregnancy. mm.	
0·0162		0·0225	
0·0180		0·0216	
0·0171		0·0243	
0·0189		0·0207	
0·0180	Average = 0·0177 mm.	0·0252	Average = 0·0234 mm.
0·0153	= 17 μ	0·0216	= 23·4 μ
0·0180		0·0225	
0·0198		0·0270	
0·0171		0·0252	
0·0189		0·0243	
0·1773		0·2349	

Diameter at 18th day. mm.		Diameter at 20th day. mm.	
0·0252		0·0342	
0·0279		0·0333	
0·0288		0·0306	
0·0279		0·0306	
0·0270	Average = 0·0272 mm.	0·0297	Average = 0·0319 mm.
0·0288	= 27·2 μ	0·0315	= 31·9 μ
0·0270		0·0324	
0·0252		0·0315	
0·0270		0·0324	
0·0279		0·0333	
0·2727		0·3195	

Diameter at 22nd day. mm.		Diameter at about 26th day. mm.	
0·0324		0·0306	
0·0315		0·0288	
0·0324		0·0297	
0·0315		0·0342	
0·0315	Average = 0·0326 mm.	0·0270	Average = 0·0318 mm.
0·0306	= 32·6 μ	0·0333	= 31·8 μ
0·0360		0·0360	
0·0351		0·0351	
0·0342		0·0315	
0·0315		0·0324	
0·3267		0·3186	

Diameter just before birth, at 28th or 29th day. mm.
0·0288
0·0315
0·0270
0·0297
0·0288
0·0315
0·0288
0·0306
0·0315
0·0306
0·2988

Average = 0·0298 mm. = 29·8 μ

Diameter a few hours after parturition. mm.
0·0270
0·0279
0·0279
0·0270
0·0270
0·0261
0·0252
0·0279
0·0270
0·0279
0·2709

Average = 0·027 mm. = 27 μ

Diameter after 3 days' lactation. mm.
0·0270
0·0252
0·0279
0·0270
0·0270
0·0252
0·0279
0·0261
0·0270
0·0279
0·2682

Average = 0·0268 mm. = 26·8 μ

Diameter after 6 weeks' lactation. mm.
0·0180
0·0171
0·0162
0·0180
0·0171
0·0153
0·0180
0·0171
0·0162
0·0180
0·1710

Average = 0·0171 mm. = 17·1 μ

Tabulating these results, one gets—

Approximate age of pregnancy.	Diameter of cells in μ.
0 (= normal)	17·0
14th day	23·4
18th „	27·2
20th „	31·9
22nd „	32·6
27th „	31·8
Shortly before birth	29·8
„ after „	27·0
3 days „ „	26·8
6 weeks „ „	17·1

Taking the radius of the cells it is seen that the increase in its length in the cell during pregnancy is from 8·5 to 16·3 or very nearly double.

If the volume of the sphere be taken as $\frac{4}{3}\pi \, . \, r^3$ and the cell be taken as a sphere, the ratio of the non-pregnant cell to the cell at the maximum size attained during pregnancy becomes almost exactly 1 : 7, which would allow sufficient enlargement of the ovary to account fully for the increase in size. It is not to be supposed that all the cells enlarge to the same extent, but it may reasonably be supposed that they enlarge to about five times their normal size. This will account for the enlargement of the whole ovary, and there would seem therefore to be no necessity to seek any further cause of the enlargement of the ovary during pregnancy.

The only other possible cause which suggests itself at once is of course the division of cells, but although I have examined some hundreds of sections of pregnant ovaries, I have not found any trace of this happening. In giving the above figures I do not wish to suggest that the measurements are absolute. They are subject most probably to individual variations, depending possibly upon the number of fœtuses in each pregnancy, and on various other circumstances. The ovaries in question were, however, taken quite haphazard in regard to all external causes, which allows some scope for differences in the ovary, and the results are fairly definite. They show a great increase in the size of the ovarian interstitial cells during pregnancy, and that the main increase is reached by about the twenty-second day, and is sustained until just before birth, when there is a slight diminution in size.

In this connection there is one feature to be dealt with, namely, the shape of the cell. Up to about the twenty-fourth or twenty-fifth day it is not difficult to find approximately spherical cells to measure. After this period, however, the difficulty of doing so becomes very great, if not impossible. The cells are angular and seem crushed together, and I would suggest that possibly the cells may be really still undergoing slight increase in size, but that the capsule having almost reached its maximum stretching capacity does not admit of the desired expansion, and the cells instead of being spherical become more closely packed in order to find room for the additional bulk, filling in as it were the interstices rather than causing an increase in size in the spherical direction.

The rounded appearance is resumed very shortly after birth, and there is also a slight decrease in size. Why there should be a decrease before birth is a point upon which I feel it is impossible to offer any suggestion. The mechanism of the production of labour is a question upon which very little is definitely known; if, however, it be the function of the ovary to cause the adhesion of the fœtus to the uterine wall (Fraenckel), a function carried out

presumably by means of the interstitial cells, since these probably furnish the internal secretion of the organ, it seems not impossible that the diminution in size may be indirectly connected with the onset of labour.

The Formation of "Primordial" Ova from the Interstitial Cells.

In addition to the increase in size there are other changes taking place in some of the interstitial cells near the peripheral parts of the ovary, during the later third (approx.) of the period of gestation. It is a matter of common histological knowledge that over the surface of the ovary there is a layer of epithelial cells, roughly about two cells deep, although varying slightly in thickness at different places. Immediately below this is a layer of tissue in which are embedded the primordial ova in their early stages, when they have not yet acquired a follicular epithelium or when that epithelium is not very highly developed. There are in addition groups of small ovarian cells which will eventually, as occasion arises, form the follicle cells for the primordial ova. This whole layer together with the germinal epithelium varies very considerably in thickness in different animals, the variation having possibly some relation to the age of the animal under investigation (*cf.* v. Beneden).

In the non-pregnant animal and in the early periods of pregnancy, there is a fairly sharp boundary between these outer layers and the deeper lying interstitial cells. By about the twentieth day of pregnancy this state of affairs is seen to be gradually changing, and some of the interstitial cells are becoming surrounded by the connective tissue of the inner layer and thus getting cut off from their fellows below. Whether this is brought about by the passing outwards of the cells themselves or by the growth inwards of the connective tissue is very difficult to decide quite satisfactorily; but I think it is reasonable to suppose that both processes are involved. It has already been shown that there are two means whereby the germinal cells of the embryo become embedded in the subjacent mesoblast, namely, by an ingrowth of the germinal cells and by a simultaneous upgrowth of the mesoblast lying below. Here we have an analogous condition, but the positions are reversed; the germinal cells are now inside and the mesoblast outside.

This process, which is beginning to be evident about the twentieth day, continues throughout the rest of pregnancy, so that as the days go on more cells become cut off and press outwards, in many cases reaching almost to the periphery. The number of cells thus cut off varies appreciably in different animals, probably depending upon the age of the animal, but it is not excessive at any time; I have never found more than three or four rows

of cells cut off, and these rows do not form continuous layers round the ovary (*vide* fig. 5).

About the twenty-third or twenty-fourth day, and in ovaries of later dates of pregnancy, a somewhat striking feature about some of these cells is that they are no longer mononucleated; two nuclei are frequent, three quite common, whilst in some cases there may be as many as six. These nuclei are not massed together as in a giant cell, but lie separate in the cell protoplasm. The latter is very much greater in amount than in an ordinary interstitial cell, and is irregular in outline. The appearance of these multinucleated cells suggests that they have been derived from the fusion of the same number of interstitial cells as there are nuclei in the cell. It will be remembered that van Beneden pointed out this appearance in the bat's ovary, when he found in some cases as many as eleven nuclei, and he suggested that possibly one of them grew at the expense of the others, whom it used as food, or that one might become an ovum and the others the follicle cells.

Examination of a large number of these cell masses shows that in many cases there is undoubted atrophy of one or more of the nuclei going on. In some there is a clear space where a nucleus might have been expected, in others the nucleus stains very faintly or only in parts, whilst there is usually one nucleus which stains intensely, especially in the iron hæmatoxylin specimens, and in which the staining, even after extreme differentiation, is still so dark as to remove all possibility of tracing any nuclear structure. This points to some difference of metabolic condition, and the conclusion seems obvious that this nucleus is growing strong at the expense of the others; one is reminded of the protoplasmic masses described by Balfour in the young ovary and to which reference has already been made in this paper. Here we have a number of potential ova (for the fact has already been emphasized that all interstitial cells being derived from the germinal epithelium are potential ova) massed together, of which the nucleus of one of them grows at the expense of the others, which it uses as food material; in the young ovary the end-product is a primordial ovum. In the pregnant ovary the end-product is likewise a "primordial" ovum. The cells of these aggregations are all quite clearly ordinary interstitial cells, and the surviving cell is also an interstitial cell differing only in the intensity of its staining reaction.

It has I hope been conclusively shown, in the earlier part of this paper, that the interstitial cells have all been derived from the cells of the germinal epithelium, and have all passed through the deutobroque condition, and it has been pointed out by v. Winiwarter that if there is to be ovogenesis subsequent to the first great ovogenetic period, the cells which are to become

ova must pass through the requisite nuclear changes. Also it is obvious, although this is not a point which he brings out, that there is a very great difference in size between the primordial ovum and the interstitial cell in a non-pregnant animal, and it is therefore necessary for the cell to enlarge at some period of the transformation. This requirement is fulfilled, as has already been shown, in the case of the pregnant ovary. The interstitial cell of the non-pregnant ovary has approximately a diameter of 17 μ, but increases up to 29 μ or even rather over 30 μ in the pregnant animal. The size of a primordial ovum before it begins to grow, preparatory to becoming a Graafian follicle, is very constant; I have taken measurements of a large number of ova both in the young ovary and in the pregnant as well as the non-pregnant animal, and the average diameter is 27 μ, the diameter reached by the interstitial cells about the eighteenth day of pregnancy.

It is about the twentieth day of pregnancy that the cutting off of the interstitial cells towards the periphery begins to be noticeable—that is to say, shortly after they have reached a diameter about equal to that of a primordial ovum. It is not, however, until a little later that the cells thus cut off begin to show any nuclear differentiation, in fact this is perhaps best seen in the ovary of a rabbit whose time of parturition has almost arrived. These changes are identical with those taking place in the deutobroque cells of the young ovary during the period of ovogenesis. The only difference lies in the fact that whereas in the pregnant ovary the process is taking place only at the periphery, and in relatively very small numbers, in the young ovary there may be 20 or 30 nuclei undergoing changes in the same field. The fact of their presence at all in the pregnant ovary is, however, all proof that is necessary for the formation of ova. It is not for a moment to be supposed that any formation of fresh primordial ova after the first great period should take place to anything like the same extent. Probably the actual changes only occur over a period of a few days, commencing about the twenty-fifth day of pregnancy, or rather earlier, and extending probably to a little after parturition. In the young ovary the changes do not commence until after birth, and some of the cells have completed their changes by about the tenth or eleventh day, the process being probably considerably less lengthy than this for the individual cells, and taking still less time, if anything, in the pregnant rabbit, where there is obviously a state of stimulation during the whole period of pregnancy.

The first change passed through by the nucleus of an interstitial cell, which has passed to the periphery in order to become an ovum, is shown in fig. 6 (1). The nucleus shows chromatin filaments, in the middle of which are seen irregular lumps of chromatin. (In the diagrams the analogous stage of the

young ovary has been given side by side with that in the adult, and does not call for any special description.) This is a transition form from the interstitial nucleus to the leptotenic stage in the process of ovogenesis, and appears to be brought about by the breaking up of the nuclear chromatin into an immense number of filaments. The arrangement of the chromatin in the interstitial cells is, as a rule, discrete either in a rather loose reticulum or round the edges, usually the former.

The first change is therefore the formation of fine filaments. The *leptotenic* stage of v. Winiwarter is brought about by the enlargement of the nuclear area and the spreading out of the filaments over this increased space, thus producing a looser arrangement which consists of fine filaments with a rather nodular appearance where they intersect (fig. 6 (2)). This state would appear to be a very fugitive one (as observed likewise by v. Winiwarter), judging by the rarity of its occurrence. It is quickly passed through, and the nucleus enters upon the *synaptenic* condition (fig. 6 (3)). This stage occupies much longer than the last, and a relatively large number of nuclei are found in this condition, which has many modifications. The filaments at the leptotenic stage are spread out over the nuclear area, whilst at the final synaptenic the chromatin is massed into a lump at the side of the nucleus. All stages may be traced both in the adult pregnant ovary and the young ovary, but only the most characteristic phase is figured, namely, that where a very appreciable amount of massing has already proceeded, the mass being connected to the sides of the nucleus by a few very fine filaments.

The massing completed, there seems to be a rearrangement of the chromatin, and it becomes spread out again, but this time the filaments are thicker. This is the *pachytenic* stage (fig. 6 (4)). The number of nuclei found in this stage is less than in the synaptenic, but still there are a fair number in various conditions. The filaments are so markedly thicker and more bulky generally that it is impossible to confuse it in any way with the leptotenic phase. The chromatin does not fill the nucleus quite so much as in the young ovary, but I have found sections where this was more the case than in the one figured; moreover in some the chromatin seems to have a more continuous disposition than is here represented.

The transition stage between the pachytenic and dictyate or final stage is not, according to my observations, quite analogous to v. Winiwarter's, and I rather hesitate to call it diplotenic, as the duality of the filaments is not well marked (*see* fig. 6 (5)); the chromatin is still arranged in thick strands, and there is some trace of nucleoli, whilst at the same time there are a very few thinner nodulated strands, foreshadowing the condition called by v. Winiwarter *dictyate*, and which represents that of the young ovum.

The nucleolus in the dictyate condition (fig. 6 (6)) is very definite, and the chromatin is arranged more or less all over the nuclear area (which is now very large), and shows a number of small nodules both at what appear to be free ends and at the points of intersection. There can, in fact, be not much doubt that the changes taking place are identical with those seen in the young ovary, which lead to ovogenesis, and therefore it would appear that ovogenesis also takes place in the adult animal during pregnancy.

Previous observers on this subject appear to have all considered that formation of ova must be accomplished by means of fresh invaginations of germinal epithelium, and those who thought they saw invaginations concluded at once that there was therefore a formation of ova in later life, whilst those who failed to find them denied the possibility on this account. My observations show that fresh invaginations of the germinal epithelium are not a necessity, but that the "invagination" has taken place already in the embryo. The invaginated cells of the germinal epithelium give rise to all the cells of the true ovarian tissue, which are all capable of functioning in any true ovarian capacity—that is, they may become ova or follicle cells, or interstitial cells, and most probably also lutein cells, their destiny appearing to be a matter of chance. The interstitial cells, however, are still capable of becoming ova, and of undergoing the changes requisite for ovogenesis should the appropriate stimulus be given. This stimulus is supplied when the animal becomes pregnant, and the ovarian cells enlarge in size. Towards the end of the time of pregnancy some of them press towards the periphery and undergo the necessary changes, becoming true ova. Thus every pregnancy would seem to be a stimulus for the next, in the way of providing new ova, although even of the relatively small number found probably very few ever reach maturity.

Conclusions.—Summing up the conclusions reached in this paper we find—

1. That a large number of germinal cells become embedded in the subjacent mesoblast. Of these the great majority undergo transformations up to a certain stage. This stage having been reached, they may pass through the necessary processes of ovogenesis, or they may become modified to form either follicle cells or interstitial cells, this last process being the chief fate of the cells near the periphery, whilst ovogenesis is that of the more centrally situated ones.

2. The interstitial cells are thus potential ova, capable of becoming ova should the appropriate stimulus be given.

3. This stimulus is provided by pregnancy, during which period the interstitial cells undergo enlargement in size, exceeding that of a primordial ovum.

4. About the twenty-third day some of the interstitial cells become cut off near the periphery and pass through the nuclear transformations of ovogenesis, becoming true ova.

I wish to express my deep obligation to Professor Starling, under whose supervision this research has been carried out, and without whose never-failing assistance, interest, and sympathy at each step of the work it would have been impossible to carry out the investigations described above.

Also I desire to thank Mr. H. G. Plimmer for his kindness in giving me much valuable information in regard to the carrying out of the histological details.

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DESCRIPTION OF PLATE 1.

Fig. 1.—Ovary of 20th day embryo (rabbit). Fixed in Gilson's fluid :—

a = protobroque cells.
b = „ (in mitosis).
c = deutobroque cell.
d = connective tissue cell.
e = position of mesoblastic core.

Fig. 2.—Cells in ovaries of rabbits just before and after birth. Fixed in Gilson's fluid :—

a = protobroque cell.
b, *c*, *d*, *e* = transition forms between (*a*) and (*f*).
f = deutobroque cell.

Fig. 3.—Ovary of three days old rabbit showing formation of egg-clusters. Fixed in sublimate solution :—

a = protobroque cell.
b = deutobroque cell.
c = „ in mitosis.
d = leptotenic stage in ovogenesis.

Fig. 4.—Cells in ovaries of young rabbits. Fixed in Gilson's fluid :—

a = deutobroque cell in ovary of three days old rabbit.
b = „ „ about 18 days old rabbit.
c, *d*, *e*, *f*, *g* = transition stages from deutobroque to ovarian cell in ovary of about 18 days old rabbit.
h = interstitial cell, *k* = follicle cell } from ovary of young rabbit (18 days).

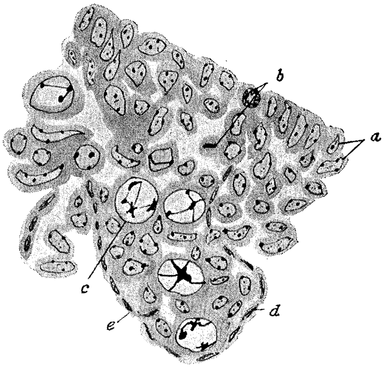

FIG. 1.

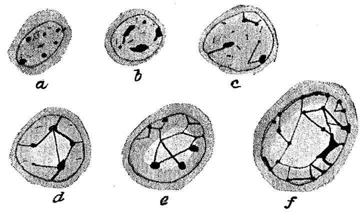

FIG. 2.

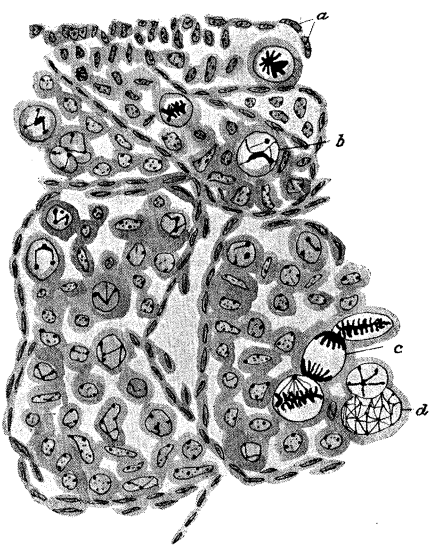

FIG. 3.

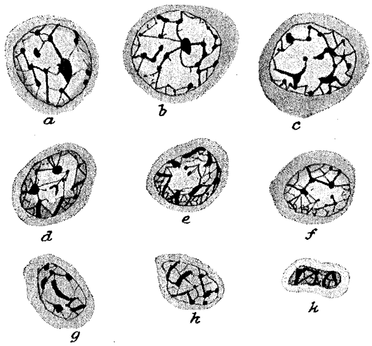

FIG. 4.

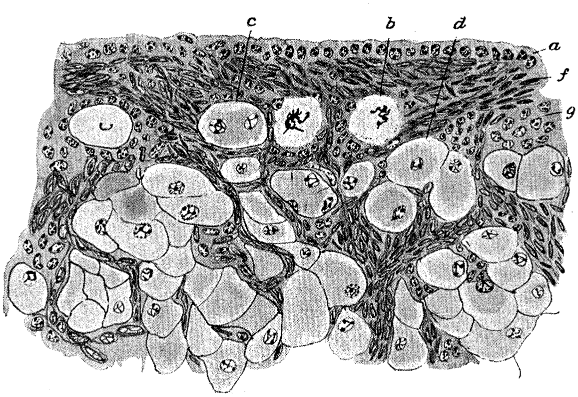

FIG. 5.

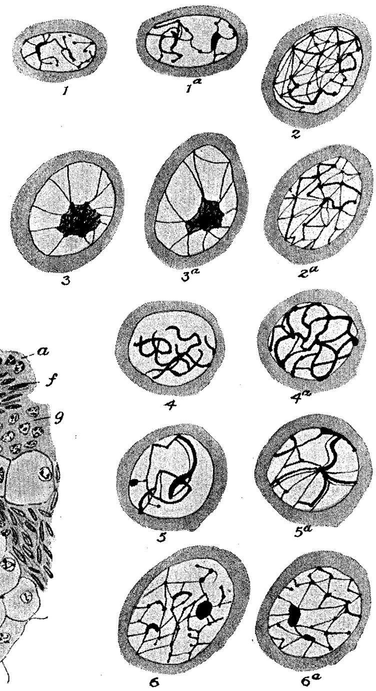

FIG. 6.

FIG. 5.—Ovary of rabbit about 22nd day of pregnancy. Taken from the cortical region. Fixed in sublimate solution :—

a = germinal epithelium.
b = primordial ovum.
c = multi-nucleated interstitial cell.
d = interstitial cell, becoming isolated.
f = connective tissue.
g = modified germinal cells.

FIG. 6.—1—6 are taken from the ovaries of rabbits in the later stages of pregnancy. 1*a*—6*a* from ovaries of young rabbits : showing ovogenetic changes for comparison with 1—6. Fixed in Gilson's fluid :—

1 = transition from interstitial to leptotenic phase in pregnant ovary.
1*a* = " " young "
2 = Leptotenic phase in pregnant ovary.
2*a* = " young "
3 = Synaptenic phase in pregnant ovary.
3*a* = " young "
4 = Pachytenic phase in pregnant ovary.
4*a* = " young "
5 = Diplotenic phase in pregnant ovary.
5*a* = " young "
6 = Dictyate phase in pregnant ovary.
6*a* = " young "

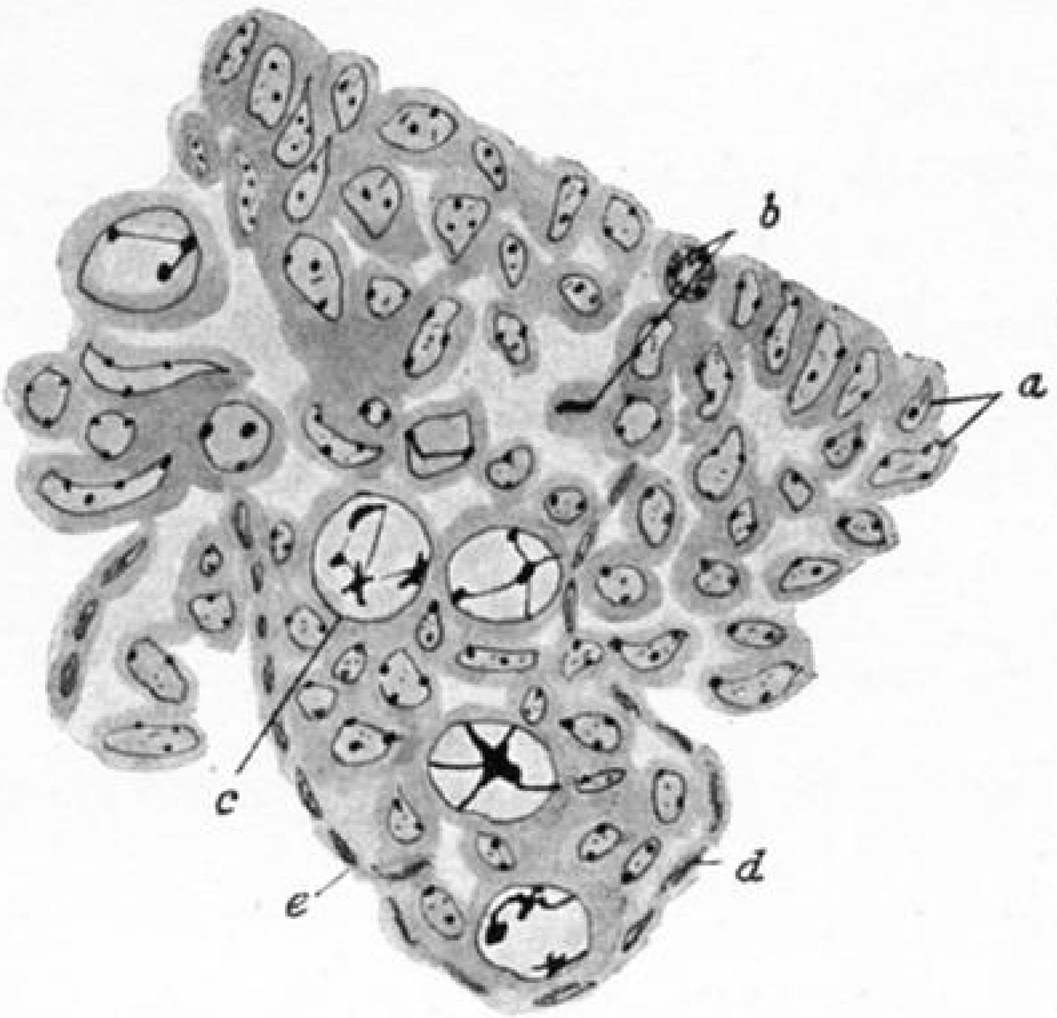

FIG. 1.

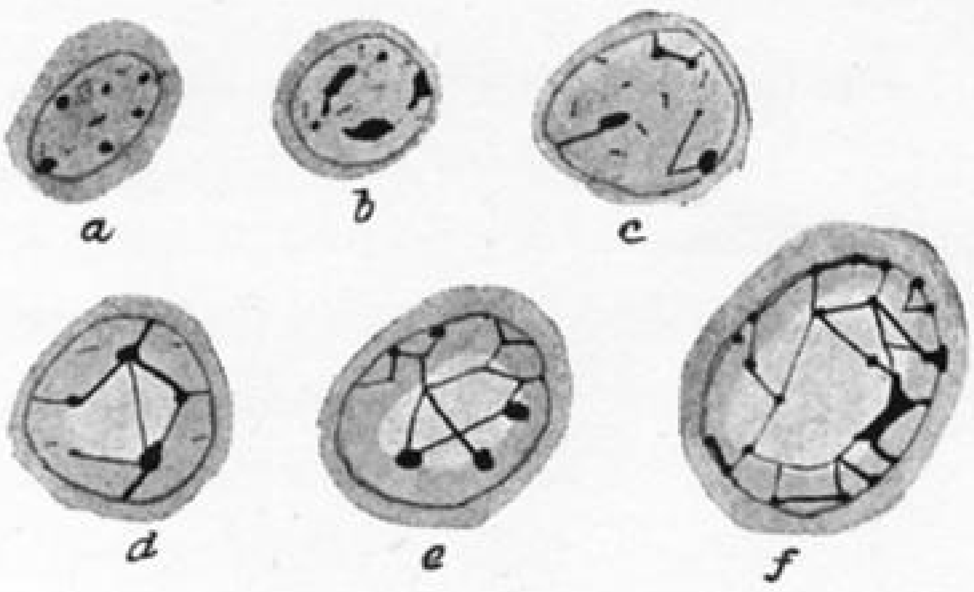

FIG. 2.

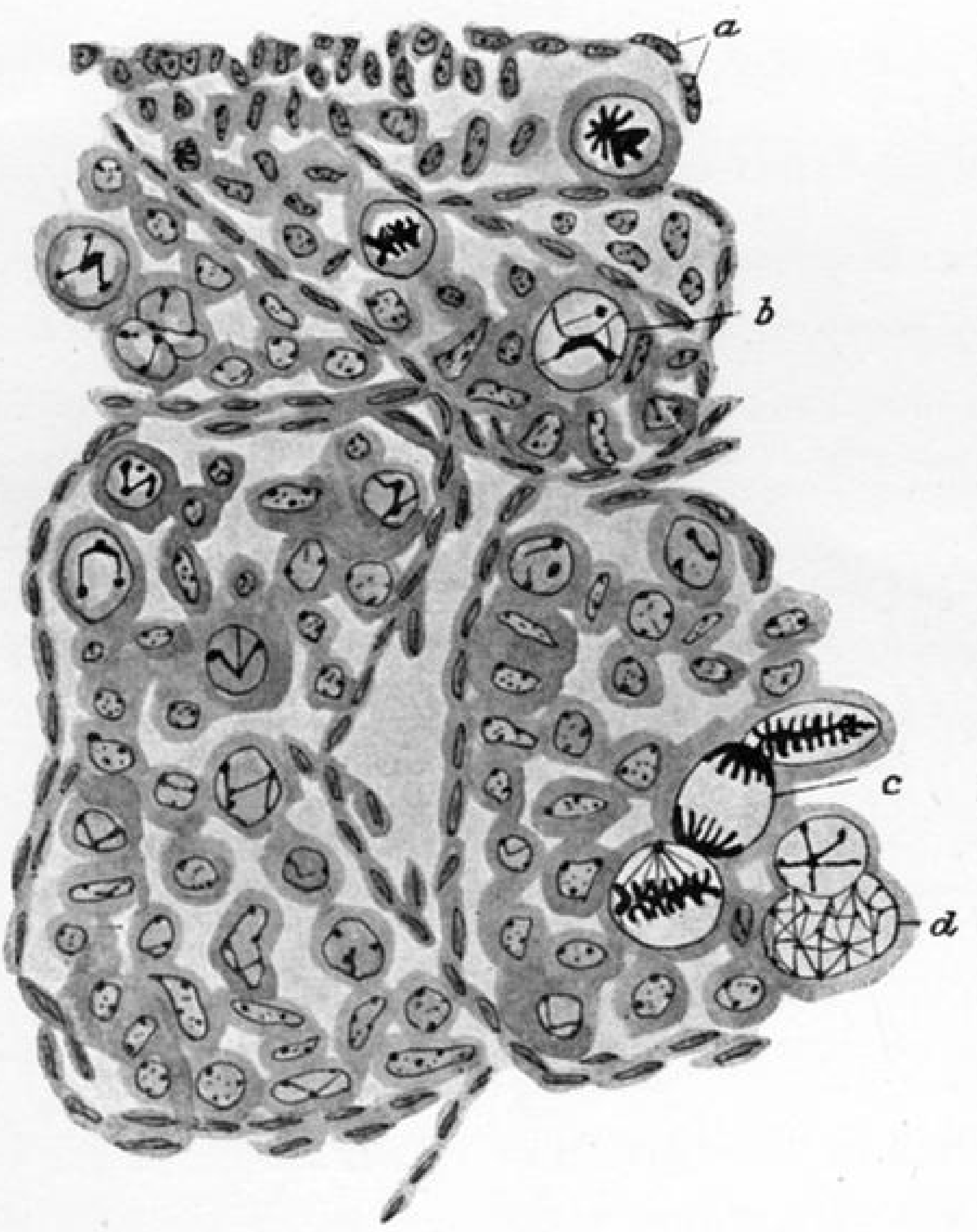

FIG. 3.

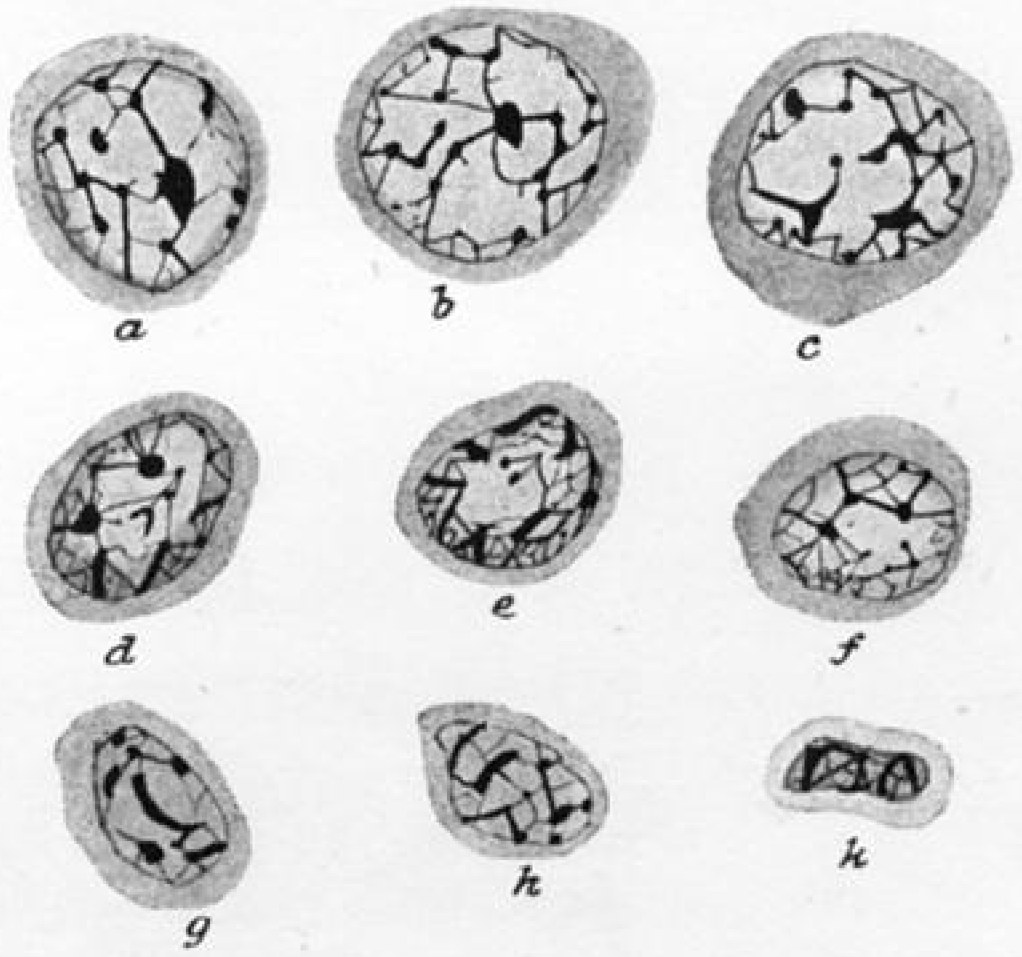

FIG. 4.

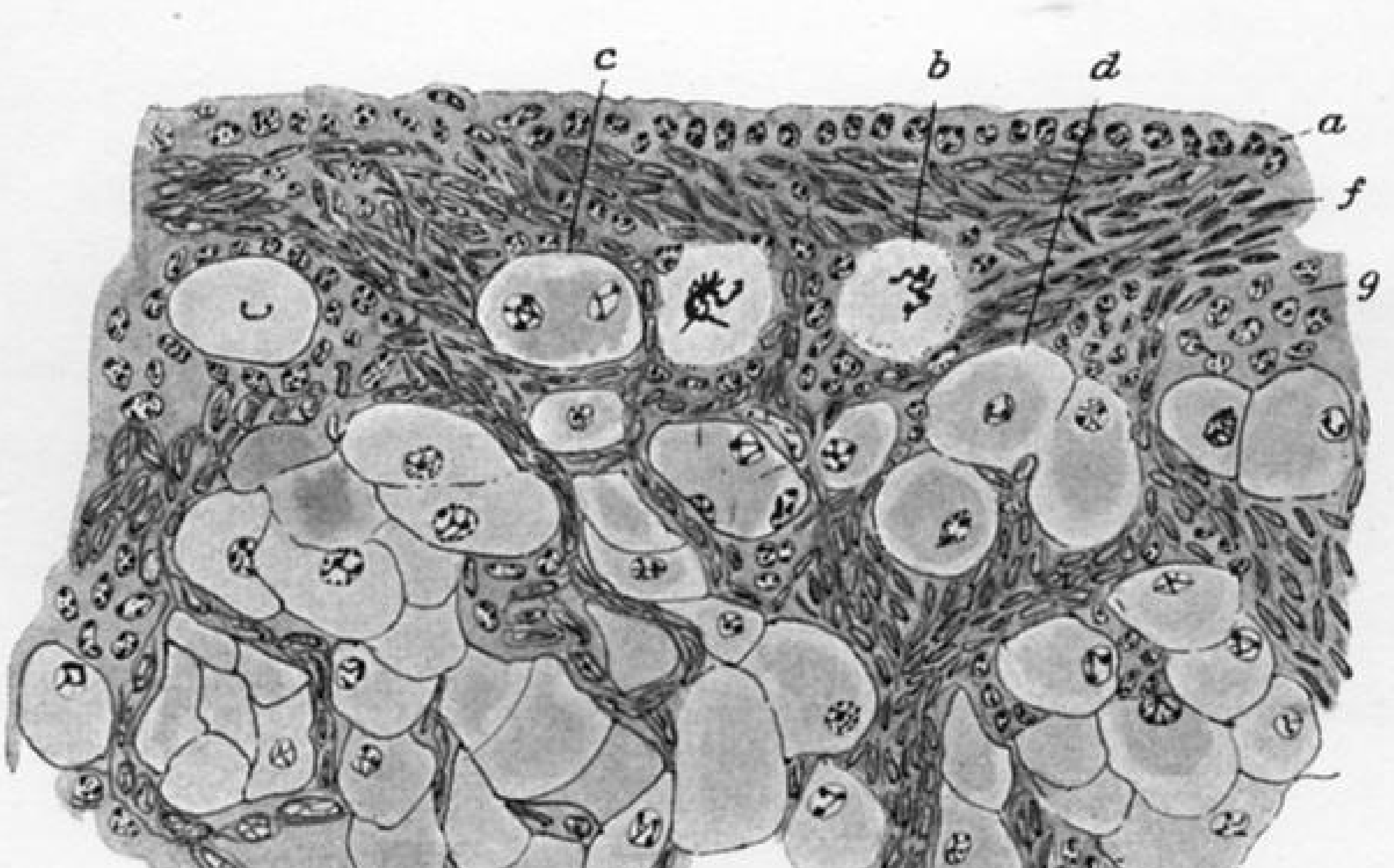

FIG. 5.

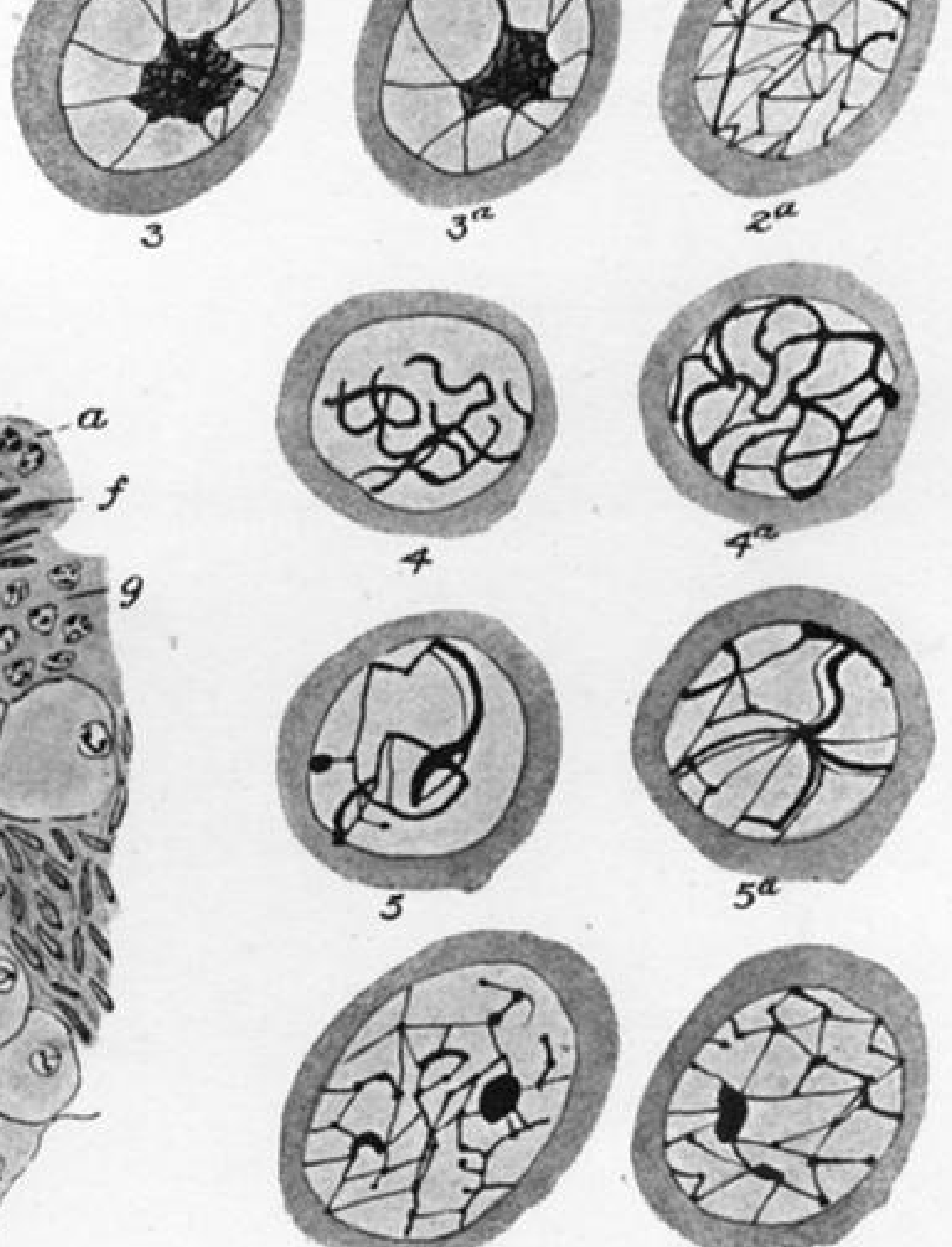

FIG. 6.