OBSERVATIONS ON THE ORIGIN OF METRIAL GLAND CELLS IN THE RAT PLACENTA

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The development of metrial gland cells in the pregnant rat was studied by Baker (1948), who traced their origin to mesenchyme-like connective tissue cells in the mesometrial triangle (i.e. the region between the muscle layers at the attachment of the mesometrium to the uterus—Young, 1956), which became basiphilic, rounded and enlarged. He stated that the basiphilia was short-lived, for it declined with the appearance of eosinophilic granules and glycogen. He found cells with the characteristics described not only in the mesometrial triangle but also in the decidua basalis, which led him to conclude that the same stimulus causes the formation of both the metrial gland cells and the decidua. Baker, like Selye & McKeown (1935), who worked on the metrial gland of pseudo-pregnancy, did not mention one of the striking features of metrial gland cells, namely the high frequency of binuclearity.

Our interest in the origin of metrial gland cells was aroused when it was noticed that cells with all the characteristics of metrial gland cells had appeared in the decidua basalis, and also in the ectoplacental cone at a time when none was to be found in the proper site of the definitive metrial gland, the mesometrial triangle. Several features are typical of the fully developed metrial gland cell (Pl. 1, fig. 1). It is a large cell (about 18 to 20 μ in diameter), it is binucleate (Velardo, Dawson, Olsen & Hisaw, 1953) and there is a perinuclear aggregation of acidophilic, PAS-positive, diastase-fast granules surrounded by a rim of apparently clear cytoplasm, which has a high content of glycogen. There are, unfortunately for purposes of certain identification of cell types, numerous cells throughout the pregnant rat's uterus which possess one or other, or even more than one, of these features. It was decided, therefore, in this investigation of the metrial gland in pregnancy, to accept as metrial gland cells only those which were large and binucleate, with acidophilic or PAS-positive diastase-fast granules (according to staining method) as well as a rim of clear cytoplasm. The second type of metrial gland cell (Ellis, 1957) which contains lipid, is usually mononucleate and develops later than the granular type, is not dealt with in this paper.

MATERIAL AND METHODS

In addition to the rat placentae of 12, 14 and 17 days which were examined in a study of carbohydrate materials (Bulmer & Dickson, 1960), there were available also placentae of 9 and 10 days which had been fixed in 10 % formalin. This material was serially sectioned at 3, 5 or 7 μ, with the exception of one 10-day specimen sectioned at 10 μ and one 12-day placenta from which sections were cut at 10, 20 and 30 μ. Series of sections extending through each placenta, stained by the trichrome and PAS (with diastase digestion) methods, were examined. The PAS

technique combined with dimedone blockade (Bulmer, 1959) was used for the demonstration of glycogen. Acidophilia of metrial gland cell granules was shown by staining with orange G. The performic acid-alcian blue method of Adams & Sloper (1956) was used to demonstrate protein-bound disulphide groups, a marked positive reaction indicating the presence of at least 4% cystine (Pearse, 1960). Occasional sections were stained for reticulin fibres by the methods of Long (1948) and Gomori (Lillie, 1954). In attempts to demonstrate sex chromatin the techniques of Klinger (1957) and Klinger & Ludwig (1957) were employed.

OBSERVATIONS

At 9 days cells which conform to all the criteria listed above as characteristic of the typical metrial gland cell are situated in the decidua basalis adjacent to the ectoplacental cone (Pl. 1, fig. 2) and, less frequently, in the ectoplacental cone itself. Those in the decidua basalis (Text-fig. 1) are scattered inside a cone, the apex of which is against the apex of the ectoplacental cone. The base of this cone, which will be referred to as the decidual cone to distinguish it from the ectoplacental cone, is in the position shortly to be occupied by the capsule (Bulmer & Dickson, 1961) which will separate the decidua basalis from the inner layer of uterine muscle until this portion of the decidua disappears (Dickson & Bulmer, 1960). The decidual cone is surrounded by the glycogen tissue of the decidua basalis. Approximately in its axis, which coincides with the mesometrial-antimesometrial axis of the uterus, lie the arteries constituting the maternal supply to the developing placenta (Holmes & Davies, 1948). These arteries pierce the inner muscle layer at the centre of the base of the decidual cone.

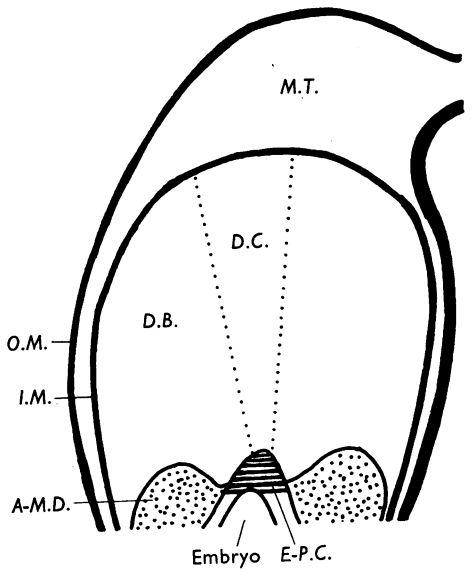
Inside the decidual cone are found decidual cells and typical metrial gland cells. The latter are densely packed at the apex and scattered in decreasing numbers towards the base. It is noticeable that, while all the metrial gland cells in the apical portion of the decidual cone are, like those in the ectoplacental cone, typical, there are towards the base considerable numbers of cells which possess some, but not all, of the features of the typical metrial gland cell. These cells cause difficulty, for it is impossible to be certain whether they should be regarded as developing metrial gland cells or as cells which, since binuclearity and a content of PAS-positive granules are not infrequently to be observed in any region of the pregnant rat uterus, fortuitously resemble metrial gland cells.

At this 9-day stage there is no typical metrial gland cell in the mesometrial triangle, that is, in the connective tissue between the muscle layers at the base of the mesometrium which will later be occupied by the metrial gland. Further, at this time cells possessing even one of the features of the typical metrial gland cell are infrequent in this region.

At 10 days metrial gland cells are common in the ectoplacental cone (Pl. 1, fig. 3) and also in the trophoblastic spur which projects from its apex into the decidual cone in the line of the central artery. This artery, approaching from the maternal side of the developing placenta, stops at the tip of the spur, the cells of which, like those of the ectoplacental cone itself, are bathed by maternal blood without an intervening endothelium. The lack of endothelium makes it difficult, in the case of

occasional metrial gland cells, to decide whether the cell lies in the substance of the trophoblastic spur or ectoplacental cone or whether it lies in the maternal blood bathing these tissues. It seems safe to say that at least the majority of these cells are in the embryonic tissues and not in the maternal blood.

Beyond the termination of the trophoblastic spur the endovascular plasmodium (Duval, 1891; Bridgman, 1948), which, as pointed out by Pritchard (1947), is continuous with the trophoblast, lines a short segment of the supplying artery (or arteries, for there may be more than one). The cells of the endovascular plasmodium



Text-fig. 1. A section illustrating the decidual cone on the ninth day of gestation.

A–M.D.	Antimesometrial decidua	*I.M.*	Inner layer of muscle
D.B.	Decidua basalis	*M.T.*	Mesometrial triangle
D.C.	Decidual cone	*O.M.*	Outer layer of muscle
E–P.C.	Ectoplacental cone		

—the word plasmodium indicates incorrectly that this tissue is a syncytium (Bulmer & Dickson, 1960)—are large and, in common with the trophoblast, which may now be distinguished as junctional or spongy zone trophoblast from the syncytiotrophoblast on its foetal aspect, show intense cytoplasmic basiphilia due to ribonucleic acid (Bulmer & Dickson, 1960) and alkaline phosphatase activity (Pritchard, 1947). Not all the cells in the endovascular plasmodium are typical. Some show a clear rim like a metrial gland cell, some are binucleate and some have perinuclear aggregations of granules which give cytochemical reactions similar to those of metrial gland cells round about. Some are, indeed, indistinguishable from typical metrial gland cells (Pl. 1, fig. 4). All these types occur in the endovascular plasmodium, separated only by the basement membrane from the surrounding concentration of metrial gland cells in the decidual cone. It is noteworthy that there are gaps in the basement membrane.

At 10 days typical metrial gland cells make their first appearance in the mesometrial triangle. They are situated close to the external surface of the inner muscle layer and in close proximity to the central arteries perforating this layer. They are in very small numbers—one or perhaps two in a section. At this stage smooth muscle cells of unusual form may be seen in the vessels further out in the mesometrial triangle. In transverse section (Pl. 2, fig. 5) they are seen to have a central nucleus and a rim from which the cytoplasm appears to have retracted. The cytoplasm concentrated round the nucleus tends to be broken up into small discrete masses or granules. These would seem to be the cells which Selye & McKeown (1935) considered to be one of the types of forerunner of metrial gland cells. They have not, however, been observed to be binucleate and, unlike metrial gland cell granules, the broken-up cytoplasm does not stain with the performic acid-alcian blue technique. Further, arteries with similar muscle cells are to be found in the antimesometrial wall of the uterus, where metrial gland cells do not occur. It is considered that the appearance of discrete masses of cytoplasm simulating granules is artefactual.

The number of metrial gland cells in the decidual cone has, by the 10-day stage, undergone an increase which results in a greater number of them being found in the outer, basal part of the cone.

At 12 days, metrial gland cells are scattered with decreased density through a decidual cone which has enlarged with the growth of the placenta. They occur in all parts of the decidual cone, being seen, at the two extremes, close to the juctional zone trophoblast and near to the capsule (Bulmer & Dickson, 1961). They may also be found, infrequently, among the cells of the maternal glycogenic tissue surrounding the decidual cone. The mesometrial triangle is almost completely filled by a mass of metrial gland cells, which tend to have a perivascular arrangement. The inner muscle layer is disrupted into bands scattered in the inner part of the metrial gland. Not all the metrial gland cells are typical, for some display mononuclearity. Thicker sections of 10, 20 and 30 μ were examined in an attempt to determine whether this mononuclearity was apparent only and due to thin sectioning. Lack of transparency, however, in the thick sections prevented clarification of the problem.

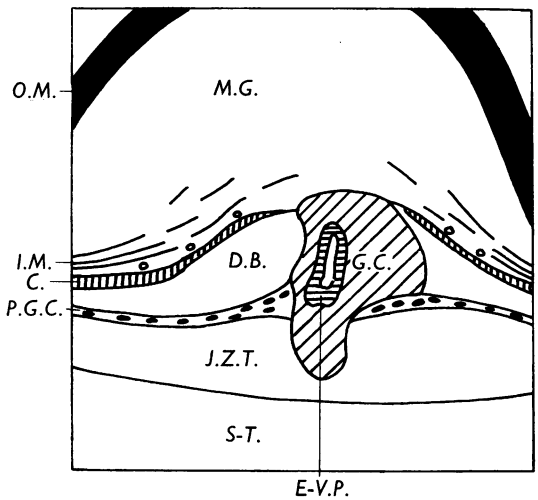
At 12 days all stages intermediate between endovascular plasmodium and typical metrial gland cells are found inside the basement membrane of the supplying arteries (Pl. 2, fig. 6). Occasional typical metrial gland cells are found free in the lumina of these vessels, but they are so few in number that it is difficult to assess their significance. Into this category come also the occasional metrial gland cells in the junctional zone trophoblast. More significance is attached to apparent continuities between endovascular plasmodium and metrial gland cells through breaks —often wide gaps—in the basement membrane of the supplying vessels. These continuities are seen as tongues of endovascular plasmodium projecting into the surrounding metrial gland tissue in the inner part of the mesometrial triangle (Pl. 2, fig. 7). Along the tongue cytoplasmic basiphilia decreases, while the granules, binuclearity and clear periphery of the typical metrial gland cells appear.

At 14 days no metrial gland cell is to be found in the decidua basalis, a finding which, since the decidua basalis is itself disappearing, applies to all later stages. At this time occasional metrial gland cells (indicated by circles in Text-fig. 2) are found at the junction of the decidua basalis with the uterine wall proper, that is, between

the developing capsule (Bulmer & Dickson, 1961) and the disrupted inner layer of smooth muscle which separates them from the vast number of their fellows in the mesometrial triangle.

Continuities between endovascular plasmodium and metrial gland cells in the mesometrial triangle are now even more marked than at 12 days, there being wide openings in the basement membrane (Pl. 2, fig. 8). It can be exceedingly difficult to judge whether a given metrial gland cell is in the endovascular plasmodium of the supplying vessel or in the tissues of the mesometrial triangle outside the vessel.

Many of the cells of the junctional zone trophoblast have become glycogen cells. These cells and the junctional zone trophoblast containing them are separated from



Text-fig. 2. A section illustrating the placenta on the 14th day of gestation. Circles represent metrial gland cells between the capsule and the disrupted inner layer of uterine muscle.

C.	Capsule	*J.Z.T.*	Junctional zone trophoblast
D.B.	Decidua basalis	*M.G.*	Metrial gland
E–V.P.	Endovascular plasmodium	*O.M.*	Outer layer of muscle
G.C.	Cuff of glycogen cells	*P.G.C.*	Placental giant cells
I.M.	Inner layer of muscle	*S–T.*	Syncytiotrophoblast

the decidua basalis, over the whole of the placenta except a small central area, by the layer of trophoblastic giant cells. At the central area the maternal vessels reach the embryonic tissues of the placenta by passing through a hole in the giant cell layer (Dickson & Bulmer, 1960). As mentioned above, these arteries are lined by endovascular plasmodium which is limited externally by a tube of basement membrane. At this stage, the tube of basement membrane no longer extends as far as the embryonic side of the placenta, its end having receded to the level of the capsule. The endovascular plasmodium, which is indistinguishable from junctional zone trophoblast, is not, however, left in contact with maternal tissues by the recession of the basement membrane, for a cuff of glycogen cells is now present, intervening between the endovascular plasmodium and the decidua basalis (Text-fig. 2). A framework of PAS-positive diastase-fast intercellular substance lies among these

glycogen cells. Its continuity with the placental end of the tube of basement membrane suggests that it may be derived from that structure. The appearances indicate that the glycogen cells of the periarterial cuff originate from the endovascular plasmodium and that their outgrowth breaks up the basement membrane. By 17 days, the termination of the tube of basement membrane is in the mesometrial triangle. The cuff of glycogen cells, with their intercellular substance, has advanced *pari passu*, and as a result glycogen cells are now found in the mesometrial triangle. Bridgman (1948) points out that the picture is a confusing one, for it is difficult to determine whether one is dealing with foetal glycogen cells which have grown out from the junctional zone trophoblast or with maternal glycogen cells which, remaining after the disappearance of the rest of the decidua basalis, have migrated into the mesometrial triangle.

An attempt was made, using the techniques for the demonstration of sex chromatin, to discover whether the cells of the outwardly extending cuff are of maternal or foetal origin. There are difficulties in employing the presence or absence of sex chromatin as a criterion for establishing the origin of rat placental cells. First, in the early stages, when the gonad is morphologically indifferent, comparison must be made between embryonic cells which, according to sex, may or may not contain sex chromatin and maternal cells which have no male counterpart. Secondly, reports of the demonstration of sex chromatin in rodent tissues are very few. Klinger (1957) mentions his unpublished findings of sex chromatin in rat nerve cells. In a study of sections of spinal cord of 17-day male and female rat embryos we found that, in each interphase nucleus, three or four bodies could be identified with the appearances and staining characteristics of the sex chromatin described in other mammalian forms. Though counts of male and female nuclei showed that on the average the female nucleus contained one more such body, it was impossible to identify one particular body as the sex chromatin. Examinations of placentae associated with male and female embryos proved similarly unsuccessful. The nuclei of junctional zone trophoblast cells, each with several nucleoli, contained numerous particles resembling sex chromatin. While, on the average, more such particles could be counted in a series of female than in a series of male nuclei, the variation from nucleus to nucleus was so great as apparently to render this an unreliable method for the identification of sex. On the other hand, cells of the mesometrial decidua showed a single intra-nuclear particle situated at either the nuclear or the nucleolar membrane, but it is impossible to be certain that this body is the sex chromatin. There is, nevertheless, a marked difference in nuclear morphology between the trophoblast cells and the cells of the decidua basalis. The glycogen cells of the junctional zone trophoblast and of the outwardly extending periarterial cuff have nuclei which become smaller and more densely staining as the glycogen content increases. They are occasionally binucleate. Many of these cells, however, show nuclei with a morphology similar to that of the adjacent trophoblast nuclei. Intermediate stages can be seen between cells with large granular nuclei, each containing several nucleoli, and cells with small, densely staining nuclei. None of these cells showed any nuclear resemblance to the decidual cells. These findings, such as they are, seem to indicate that these glycogen cells are foetal in origin. Furthermore, the decidual glycogen cells have a supporting network of reticular fibres, which is

absent from the glycogen cells of both the junctional zone trophoblast and the periarterial cuff. At 14 days the few decidual glycogen cells which persist retain their reticulin network but at 17 days, when the decidua basalis has disappeared, there are no longer any glycogen cells with a reticular framework, suggesting that at this stage only foetal glycogen cells are present.

One other observation on the 17-day material is worthy of note. Some of the glycogen cells of the cuff, especially those situated in the region of its advancing edge, that is to say outside the capsule and in the mesometrial triangle, are binucleate and possess granules giving histochemical reactions similar to those of the neighbouring metrial gland cells. A few of these cells are apparently typical metrial gland cells.

DISCUSSION

The observations described above indicate that typical metrial gland cells appear first in the decidua basalis close to the ectoplacental cone and in the cone itself at about 9 days, that at 10 days a very few and at 12 days (when the decidua basalis still contains many) a multitude are found in the mesometrial triangle and that at 14 days none remains in the decidua basalis. Typical metrial gland cells, then, appear from within outwards and disappear from within outwards. The straightforward conclusion to be drawn from these observations is that metrial gland cells are formed in the region of the ectoplacental cone and migrate outwards, formation stopping at about 12 days and migration being complete at about 14 days.

The cell type which is parent to the metrial gland cell is not obvious. At 9 days suspicion must fall on decidua basalis cells and, since metrial gland cells appear in our material as early in embryonic as in maternal tissues, also on the trophoblast cells of the ectoplacental cone. Evidence supplied by later stages supports an embryonic origin, for at 10 days some cells with one or two, and a few cells with all, of the characters of the typical metrial gland cell are found among the cells, generally accepted to be embryonic in origin, of the endovascular plasmodium lining the maternal arteries supplying the placenta. The significant point is that these apparent metrial gland cell precursors are separated from the many mature metrial gland cells in the surrounding decidual cone only by a basement membrane with holes in it. At the 12- and 14-day stages there is even better reason for thinking that endovascular plasmodium gives rise to typical metrial gland cells, for the holes in the basement membrane are much bigger than before and are occupied by tongues of endovascular plasmodium projecting into the metrial gland tissue in the mesometrial triangle. One interpretation of these appearances is that the cells of the tongues gradually lose the characters of endovascular plasmodium and acquire those of metrial gland cells.

It appears that metrial gland cells may be produced by trophoblast which at first lies against the decidua basalis and then grows into the mesometrial triangle, being called in the former situation ectoplacental cone and in the latter endovascular plasmodium. On this view it is not metrial gland cells which migrate outwards but rather their source and another interpretation of their disappearance from the decidua basalis by the 14-day stage is possible—that they are short-lived. It may be reasonable to postulate that they are short-lived because they are polyploid,

and Sachs & Shelesnyak (1955) used the same postulate to explain the short life of deciduoma cells.

Another possible explanation of the apparent outward spread of metrial gland cells is that a substance spreads out from the region of the ectoplacental cone, inducing decidua basalis and mesenchyme cells in the mesometrial triangle to become metrial gland cells. It is difficult to explain on this basis why the main concentration of metrial gland cells is in the mesometrial triangle and not close to the origin of the supposed inducing substance. It is, of course, easy to manufacture hypotheses which circumvent this difficulty but not nearly so easy to obtain evidence which will prove whether the movement is of cells or of an inducing substance.

The apparent origin of metrial gland cells from endovascular plasmodium does not fit easily into a hypothesis of the outward spread of an inducing substance from the region of the ectoplacental cone. The evidence presented in favour of an origin from endovascular plasmodium might sufficiently satisfy a morphological histologist for him to postulate that metrial gland cells can arise from embryonic cells. All metrial gland cells are not embryonic in origin, for it has been shown by Selye & McKeown (1935) that an apparently normal metrial gland develops in association with the traumatic deciduoma of pseudopregnancy. These authors, who did not mention that metrial gland cells are binucleate, stated that they may arise from the endothelial and 'adventitious' cells of vessels, from decidual cells which migrate into the mesometrial triangle and from smooth muscle cells of the uterine wall. They considered that, in fact, no particular mother cell was responsible and that almost any cell in the region could become a metrial gland cell, having first de-differentiated into a cell type resembling a small fibroblast. It must be very difficult to distinguish between a de-differentiated cell resembling a fibroblast and a real fibroblast. Their identification of smooth muscle cells as fore-runners of metrial gland cells is perhaps unreliable. They observed that both typical spindle-shaped smooth muscle cells and round or polygonal metrial gland cells contained glycogen. They also observed glycogen-containing cells of shapes intermediate between the spindle and the round or polygonal and concluded that this represented a change from muscle cells into metrial gland cells. It would seem that these observations merit only a conclusion that the long axes of all the muscle cells are not parallel. Examination of material shows this to be so, after the dispersion of the inner muscle layer during the growth of the metrial gland. We feel that it is impossible to identify a particular cell as a metrial gland cell unless it is large, binucleate and has a perinuclear aggregation of acidophilic or strongly PAS-positive diastase-fast granules. A cell possessing some of these features may be considered a differentiating metrial gland cell, but a cell which possesses none of them cannot possibly be so identified. The adoption of strict criteria may make difficult the locating of the source of metrial gland cells, but it should prevent a problem being accepted as settled when it is in fact unsolved. Velardo *et al.* (1953) adopted criteria similar to ours for the identification of metrial gland cells, although they did not employ the PAS technique. They suggested that the metrial gland cells associated with deciduomata arise from mesenchyme cells. Ellis (1957) also ascribed the source of these cells to mesenchyme cells or alternatively to fibroblasts. He traced the differentiation of the metrial gland cell through stages of cytoplasmic basiphilia, glycogen accumulation and granule for-

mation. The description by Baker (1948) of the development in pregnancy was essentially similar. As indicated above, we are not satisfied that the early stages described by these authors can be accepted without reservation, for there can be no proof that a cell which, in a section, exhibits cytoplasmic basiphilia would have become a metrial gland cell. Neither can there be proof that the cells we describe in our sections as intermediate between endovascular plasmodium and metrial gland cells actually have this relationship to these cell types. We have preferred another characteristic of metrial gland cells, namely, granularity, as an indication of a possible relationship, since cytoplasmic basiphilia is shared by many cell types and cannot therefore be used as a criterion for identification.

While there may be doubts about the recognition of the precise cell types which become metrial gland cells, there is no doubt that in deciduomata granulated metrial gland cells are of maternal origin. One should not, however, take the view, as Selye & McKeown did, that this evidence is sufficient to exclude an embryonic origin for metrial gland cells in pregnancy. There are, as described, appearances which can be interpreted as indicating such an origin. It is fully realized that these appearances can be interpreted in other ways. It is, however, probably not going beyond what is reasonable to say that cells are passing through the holes in the basement membranes of the endovascular plasmodium-lined arteries. We have chosen to suggest that the movement may be outwards, the endovascular plasmodium differentiating into metrial gland cells. Others have suggested that it is inwards. Selye & McKeown, supported by Pritchard (1947) and Bridgman (1948), have suggested that metrial gland cells pass into the endovascular plasmodium-lined arteries and lodge as glycogen cells in the junctional zone trophoblast of the placenta, where their glycogen is released for the nutrition of the embryo. Since we have put forward an opposite hypothesis we must criticize this one, but would emphasize that criticism of one hypothesis and advocation of another are equally sterile when matters involving cell movements have to be considered in sectioned material. One can expect solutions of such problems only by experimental methods, unfortunately of such technical difficulty in this case that a negative finding is more likely to be an indictment of the technique than a revelation of the truth. Selye & McKeown were of the opinion that they had proved the existence of this two-step passage of glycogen from the metrial gland to the embryo, via the junctional zone glycogen cells, when they removed an embryo, but not its placenta, at operation and found that junctional zone glycogen cells accumulated. They gave no information about the methods they adopted to assess the number of glycogen cells before and after operation. If it did occur, an increase would not be evidence that metrial gland cell glycogen reaches the junctional zone glycogen cells but only that junctional zone glycogen cells may be concerned in embryonic nutrition. The observation of Selye & McKeown that junctional zone glycogen cells never contain the granules characteristic of metrial gland cells might seem to indicate that metrial gland cells do not become junctional zone glycogen cells. These glycogen cells are now generally believed to be embryonic in origin (Bridgman, 1948), though this cannot be regarded as proved. Selye & McKeown were apparently firmly convinced that they are not embryonic cells, for they suggested a second maternal source for them—islets of decidua basalis cut off by invading cords of trophoblast. However,

in the rat placenta trophoblast does not invade the decidua basalis but always maintains a plane surface of contact between maternal and foetal tissues (Dickson & Bulmer, 1960). In any event, the 'small cellular' (Selye & McKeown) junctional zone trophoblast should not be held responsible for invading the decidua basalis, since it is separated from the decidua over the whole area of the placenta, with the exception of the central vascular hiatus, by the layer of trophoblastic giant cells.

In short, then, we believe that the view of Selye & McKeown on the metrial gland as a supplier of nutriment to the embryo is, like their view of the origin of its cells, not well substantiated. The only basis for their hypothesis is the finding of metrial gland cells free in the maternal arteries supplying the placenta. We have seen them in this position but, as stated earlier (Bulmer & Dickson, 1960) they are in our material so infrequent that we are not prepared, without more information than is available at present, to attempt to assess their significance. We prefer to present an alternative suggestion, depending on the more striking apparent relationship between endovascular plasmodium and metrial gland cells.

Our suggestion implies that in the metrial gland there are granular cells of both maternal and foetal origins. Examination of all the material used in our studies of the rat placenta, stained by a wide variety of histological and histochemical procedures, does not reveal two types of cell responding differently to any procedure. This may mean that a procedure adequate for the purpose has not been found, that cells of maternal and of foetal origins have so submerged their differences as to seem identical, or that the cells of the metrial gland are all maternal (assuming that the evidence from deciduomata is sufficient to exclude the possibility that all are embryonic). The only evidence in favour of an embryonic origin for some metrial gland cells is the apparent metamorphosis of endovascular plasmodium (which we believe to be trophoblast) into metrial gland cells. It is admitted that this is an interpretation, and that it might be claimed that the evidence is equally suggestive of a metamorphosis of metrial gland cells into endovascular plasmodium. This seems to be a *reductio ad absurdum*, for it would mean that the trophoblast called endovascular plasmodium is of maternal origin. There is no evidence against an embryonic origin, since evidence derived from deciduomata cannot bear directly on conditions in a normal pregnancy. It would seem that the problem is only soluble by direct differentiation between maternal and embryonic tissues in sections by an immunological method, or by demonstrating the growth *in vitro* of metrial gland cells in explants of ectoplacental cone which contain no decidual cells.

The function of the metrial gland remains an enigma. The suggestion by Selye & McKeown (1935) that it is a source of nutrient for the embryo is unsubstantiated. They suspected also an endocrine effect on lactation. Velardo *et al.* (1953) suggested that this activity might be 'to furnish a factor (possibly relaxin) that synergizes with estrogen and progesterone to produce better development of the mammary glands and consequently lactation'. Wislocki, Weiss, Burgos & Ellis (1957) postulated that the acidophilic granules might represent relaxin, though the histochemical grounds for their suggestion were hardly adequate. If some of its cells are embryonic in origin, a luteotrophic activity, direct or indirect, might be suspected in addition to a mammotrophic activity.

SUMMARY

Certain observations suggest that some metrial gland cells in the pregnant rat may be of embryonic origin.

1. Typical metrial gland cells appear as early in the ectoplacental cone as in the decidua basalis and before any are present in the mesometrial triangle, the site of the definitive metrial gland.

2. There is apparently an outward migration of metrial gland cells from the region of the ectoplacental cone to the mesometrial triangle.

3. Developing and fully developed metrial gland cells are found among the endovascular plasmodium, which is believed to be of trophoblastic origin.

4. There are gaps in the basement membranes of the endovascular plasmodium-lined arteries, through which the metrial gland cells developed inside appear to pass outwards into the metrial gland.

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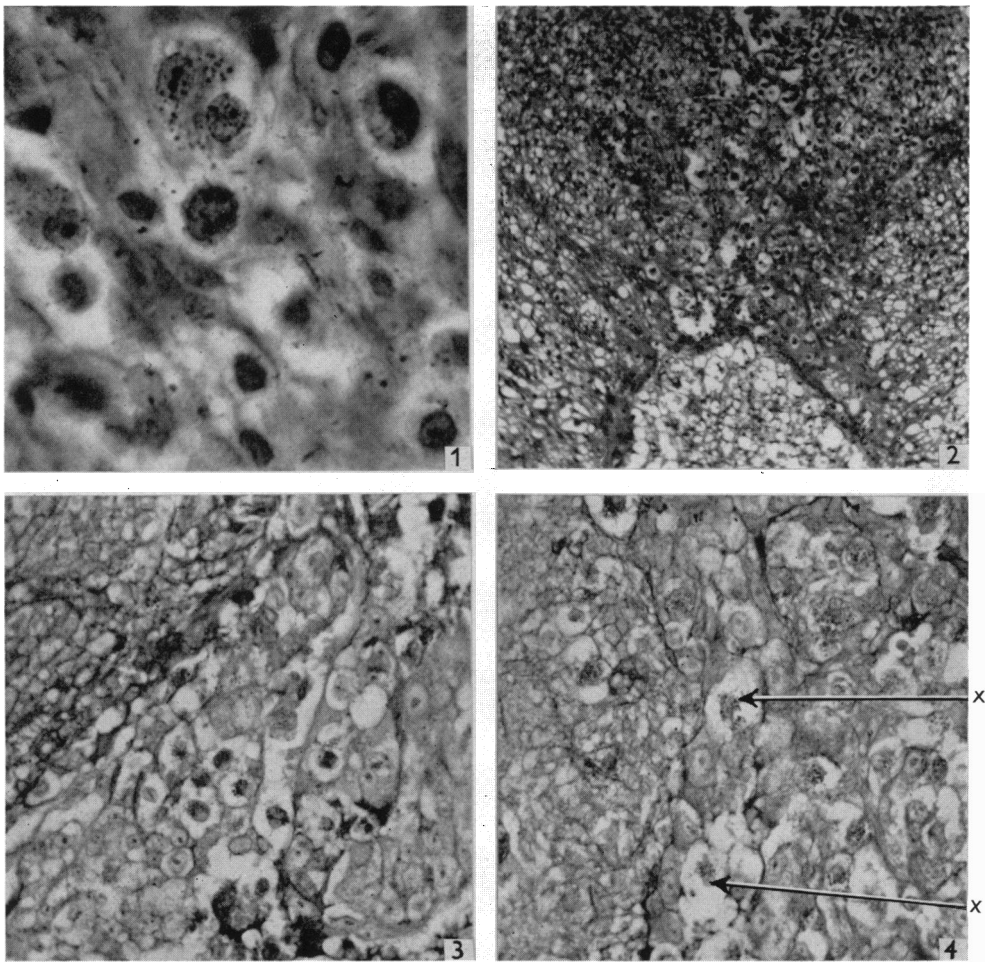
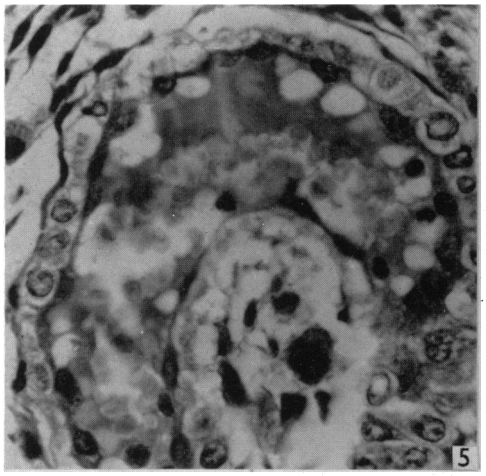
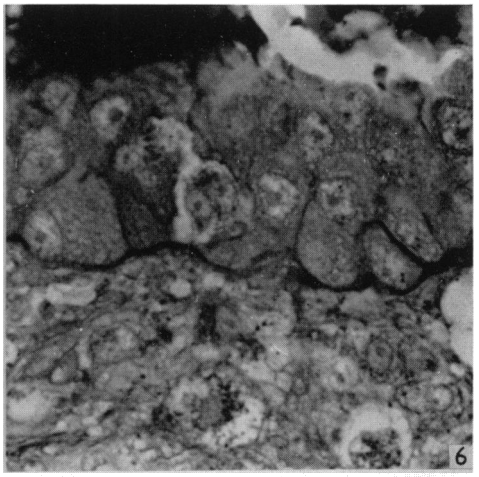
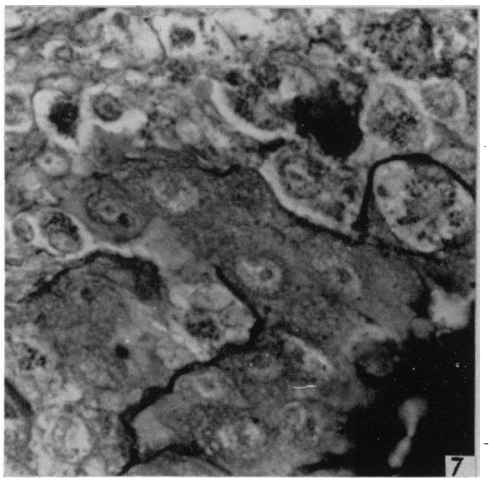


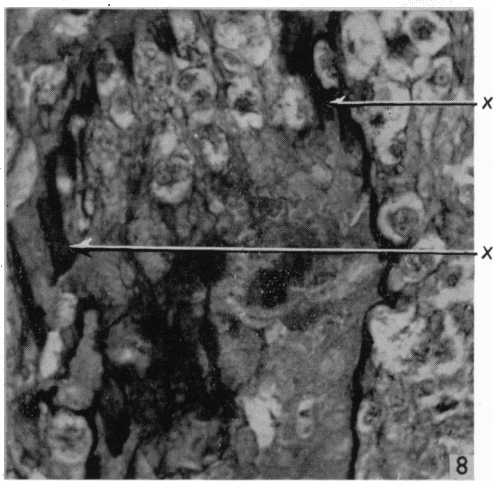
DICKSON AND BULMER—ORIGIN OF METRIAL GLAND CELLS IN THE RAT PLACENTA

(*Facing p.* 272)









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EXPLANATION OF PLATES

PLATE 1

Fig. 1. A metrial gland cell in the mesometrial triangle of a 12-day rat placenta. Trichrome, ×1000.

Fig. 2. The apices of the ectoplacental and decidual cones of a 9-day rat placenta. Trichrome, ×65.

Fig. 3. Metrial gland cells in the ectoplacental cone of a 10-day rat placenta. PAS diastase, ×200.

Fig. 4. Metrial gland cells (*x*, *x*) among the cells of the endovascular plasmodium in a 10-day rat placenta. PAS diastase, ×200.

PLATE 2

Fig. 5. A cross-section of a blood vessel in the outer part of the mesometrial triangle of a rat on the 10th day of gestation, showing muscle cells with their cytoplasm aggregated into granules. Trichrome, ×350.

Fig. 6. A metrial gland cell lying among the cells of the endovascular plasmodium in a 12-day rat placenta. PAS diastase, ×350.

Fig. 7. A tongue of endovascular plasmodium projecting into the metrial gland through a deficiency in the basement membrane. PAS diastase, ×350.

Fig. 8. A section showing continuity of endovascular plasmodium and metrial gland cells at the 14th day of gestation. The basement membrane is deficient between the points *x*, *x*. PAS diastase, ×250.