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Numbers of metrial gland cells in the maternal placental supply and drainage vessels of Swiss Webster and C57B1 mice

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INTRODUCTION

The finding (Dickson, 1980) that, from the eleventh to the sixteenth day of gestation, Swiss Webster albino mice have, overall, more metrial gland cells in the maternal interchange vessels of the chorio-allantoic placenta than do C57B1 mice, has led to investigation of the numbers in the main vessels carrying blood to and from the placenta during the same period. It has been suggested that these cells, which develop in both the metrial gland and the decidua basalis of the rat and the mouse (Bridgman, 1948*a*, *b*; Dickson & Bulmer, 1961; Stewart & Peel, 1978), arise from lymphocytes (Smith, 1966; Peel & Bulmer, 1977). Their entry into the maternal vessels passing through the decidua basalis to supply the placenta was described by Selye & McKeown (1935) and Bridgman (1948*a*, *b*) in the rat and by Stewart & Peel (1978) in the mouse. Although it is not known why metrial gland cells migrate to the labyrinth, a recent suggestion was that they carry a blocking antibody to the trophoblast (Bulmer & Peel, 1977). Sharma & Peel (1979) expressed the opinion that they synthesize the immunoglobulin they contain. The difference in numbers in the labyrinth between an inbred and an outbred mouse strain (Dickson, 1980) is at least consistent with an immunological role for these cells. This study was undertaken in the belief that further knowledge of their migration would permit formulation of clearer hypotheses about their role in reproduction.

Metrial gland cells are more frequent in the lungs of C57B1 mice than in those of Swiss Webster mice on the eleventh day of gestation and, after that, are uncommon in this situation in both strains (Dickson, 1980). In order to acquire further information about the magnitude and duration of this migration out of the uterus, counting of metrial gland cells was attempted in the veins draining the placenta and uterus.

MATERIALS AND METHODS

The histological sections of 36 conceptual sites used in this study were those in which metrial gland cells were counted in the labyrinth and lungs (Dickson, 1980). They were obtained daily from the eleventh to the sixteenth day of gestation from each of 3 Swiss Webster/ALAS and of 3 C57B1/HPB (C57B1) mice. The details of the preparation have been described (Dickson, 1980).

Metrial gland cells were counted in the placental supply vessels (*a*) passing through the metrial gland, (*b*) passing through the decidua basalis and (*c*) being distributed to the interchange vessels of the placenta (Fig. 1). As in the previous work, nine

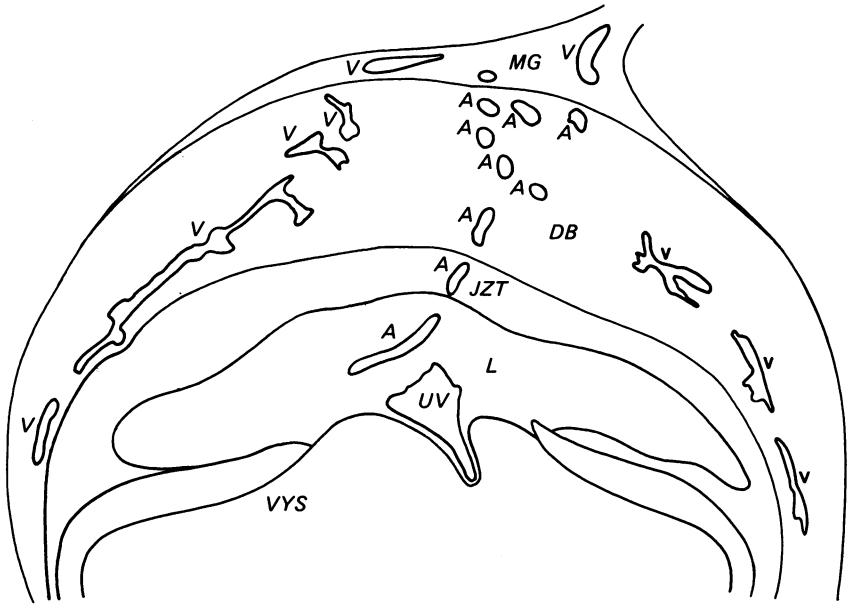
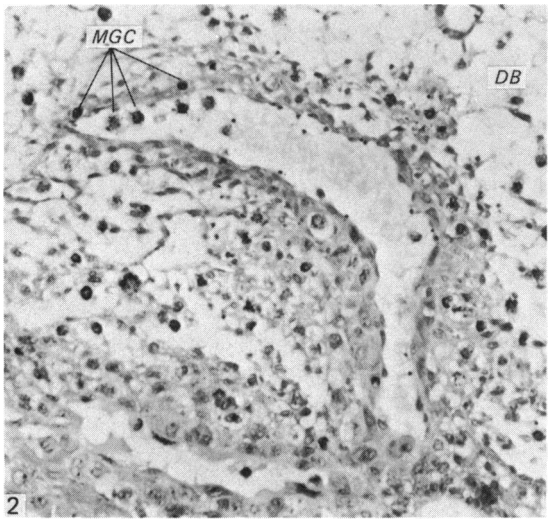


Fig. 1. The supply and drainage vessels of the mouse placenta on the twelfth day of gestation. *A*, arteries; *DB*, decidua basalis; *JZT*, junctional zone trophoblast; *L*, labyrinth; *MG*, metrial gland; *UV*, umbilical vein; *V*, veins; *VYS*, visceral layer of yolk sac.



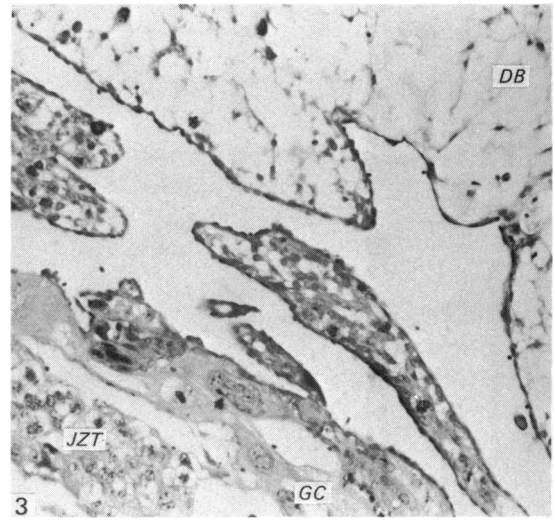


Fig. 2. A placentral supply artery passing through the decidua basalis (*DB*) on the twelfth day of gestation. Metrial gland cells (*MGC*) are seen in both the lumen and the wall. The decidua basalis is vacuolated as a result of loss of metrial gland cells. × 160.

Fig. 3. A uterine vein near the margin of the placenta on the twelfth day of gestation. *DB*, decidua basalis; *GC*, giant cell layer; *JZT*, junctional zone trophoblast. × 160.

PAS/diastase sections, cut perpendicular to the long axis of the uterus and spaced 100 μm apart, were employed for each placenta. The middle section traversed the attachment of the umbilical vessels to the placenta. Three placentae were used for each strain on each day.

Table 1. *The number of metrial gland cells in the maternal placental supply and drainage vessels from the eleventh to the sixteenth day of gestation.* (Each entry refers to one mouse. *MG* = metrial gland.)

	MICE					
	SWISS WEBSTER/ALAS			C57B1/HPB		
	Supply		Drainage	Supply		Drainage
Day	Total	In *MG*		Total	In *MG*	
11	7	0	13	341	0	11
	26	0	2	579	0	15
	13	2	11	351	0	18
12	15	2	9	81	1	7
	17	2	0	129	0	14
	32	6	4	161	3	40
13	21	15	9	63	11	2
	6	4	5	39	4	5
	18	12	9	48	9	10
14	46	32	15	129	118	3
	24	19	4	59	38	7
	65	50	23	16	10	1
15	77	51	6	15	0	0
	33	24	6	46	40	0
	134	127	1	33	30	0
16	64	58	0	5	4	0
	104	90	1	27	21	0
	32	9	1	95	79	2

Metrial gland cells were also counted in the large veins running from the periphery of the placenta to leave the uterus in the mesometrium. These veins drain the uterine wall and decidua as well as the placenta (Holmes & Davies, 1948).

RESULTS

As they pass through the metrial gland and the decidua basalis, the arteries supplying the placenta with maternal blood are identifiable by their peculiar walls (Fig. 2) which often have metrial gland cells in their thickness and, occasionally, apparently in the act of entering the lumen. The main veins are, by contrast, peripheral, large and thin-walled (Fig. 3).

The total number of metrial gland cells found, for each conceptus, in the maternal supply vessels to the placenta between the attachment of the mesometrium to the surface of the uterus and the break-up of these vessels in the labyrinth is recorded in the left column for each strain in Table 1. The number of metrial gland cells found in the main maternal supply vessels within the junctional zone and labyrinth was negligible, possibly indicating rapid passage through that segment, from which blood was also usually absent.

The figures suggest that (*a*) there are more metrial gland cells in the maternal supply vessels to the placenta at the beginning of the period of study in C57B1 than

in Swiss Webster mice, (*b*) there are more metrial gland cells in these vessels in C57B1 mice at the beginning of this period than at the end and (*c*) there are more at the end than at the beginning in Swiss Webster mice. The statistical significance of these and further differences is discussed below.

The second column for each strain of Table 1 lists the number of metrial gland cells, of the total in the left column, that was found in the part of the placental supply vessels lying in the metrial gland. There appear to be more in this situation in the latter part of the period than at the beginning in both strains. Indeed, it seems that, in the latter part of the period, more metrial gland cells are in the maternal supply vessels in the metrial gland than in the decidua basalis. The above noted increase in total number of metrial gland cells in placental supply vessels in Swiss Webster mice is largely due to the presence of the cells within the metrial gland portion of the vessels. Further, were it not for the increase in this situation in C57B1 mice, the apparent decrease noted above from beginning to end of the period would be even larger.

The third column of Table 1 for each strain records the number of metrial gland cells found in the veins draining the placenta and uterus. The numbers noted here are, in general, considerably smaller than those in the supply vessels, which may simply reflect the greater diameter of the veins and/or the fact that, unlike the arteries, they were often empty of blood in the sections. Because of these possible causes of error, statistical comparisons that involved the veins were not made. However, a diminution in the rather small numbers found in this situation at the end of the period does appear to take place in the C57B1 strain.

DISCUSSION

It has been assumed that metrial gland cells found in a maternal placental supply vessel in the metrial gland or decidua basalis are free to proceed in the direction of blood flow. The finding of these cells in the labyrinth, by several workers, makes this assumption more reasonable than an alternative, namely, that when metrial gland cells have entered an artery they remain attached and the blood flows past them. It has also been assumed that the number of metrial gland cells found in a particular vessel at the time of specimen collection is representative of a steady, even flow. There is no direct evidence in favour of this but support for it may be derived from the general similarity in numbers on particular days in one or other strain, though it must be recognised that there are some examples of wide fluctuations within a group pertaining to a particular day. The use of three mice per group tends to reduce the chance of misleading sampling of the population. Further, the results of comparisons between groupings have been interpreted conservatively. The rank correlation method (Hettmansperger, 1975) used previously (Dickson, 1980) was again employed for comparisons. This method takes into consideration only the ranking of the figures within groups, not their magnitude. Because of the likelihood of finding statistically significant differences where none exists when multiple comparisons are made within a set of data, the minimum P value considered to be significant was $0{\cdot}05/7 = 0{\cdot}007$, 7 being the total number of comparisons made within the set of data. All comparisons between or within strains were for the whole period studied, or for the first and/or second halves of it.

The first comparison was between strains and of the number of metrial gland cells in all vessels going to the labyrinth throughout the whole period (left column for

each strain, Table 1). The difference is not significant, as might be expected from the amount of overlap between the figures for each day in these columns.

The number of metrial gland cells in all vessels going to the labyrinth is significantly greater in C57B1 than in Swiss Webster mice in the first half of the period (upper half of left column for each strain, Table 1). It is not significantly different in the second half of the period (lower half of left column for each strain, Table 1).

The number of metrial gland cells in all vessels going to the labyrinth in Swiss Webster mice is significantly greater in the second half of the period than the first (lower versus upper half of Swiss Webster left column, Table 1).

The number of metrial gland cells in all vessels going to the labyrinth in C57B1 mice is significantly greater in the first half of the period than the second (upper versus lower half of C57B1 left column, Table 1).

The number of metrial gland cells in the portion of the placental supply vessels in the metrial gland in Swiss Webster mice is significantly greater in the second half of the period than in the first (lower versus upper half of Swiss Webster second column, Table 1).

The number of metrial gland cells in the portion of the placental supply vessels in the metrial gland in C57B1 mice is significantly greater in the second half of the period than in the first (lower versus upper half of C57B1 second column, Table 1).

The findings that the number of metrial gland cells going to the labyrinth is greater in C57B1 than in Swiss Webster mice in the first half of the period and not significantly different in the second half do not accord well with the observations (Dickson, 1980) that the overall number of cells in the interchange vessels of the labyrinth is greater during the whole period (eleventh to sixteenth day) in Swiss Webster mice ($P < 0{\cdot}0001$) and that the peak number on the fifteenth day is higher (Mann–Whitney, $P = 0{\cdot}05$) in Swiss Webster than in C57B1 mice. One might have expected to find greater numbers migrating in Swiss Webster than in C57B1 mice and more in the second half of the period than in the first. An interpretation of the current findings would be that, in Swiss Webster mice, migration to the labyrinth is at a relatively low, continuous level but, once lodged in the labyrinthine maternal vessels, the cells persist there, whereas, in C57B1 mice, the cells migrate to the labyrinth in a relative flood in the early part of the period studied but do not persist after they have arrived. Previous work (Dickson, 1980) suggests that passage through the labyrinth may not be the major mechanism of the loss in C57B1 mice. If the cells do not pass through the labyrinth and are not found in it, their disintegration on or before reaching the labyrinth would seem probable. In this connection it may be noted that Larkin (1972) described these cells breaking up in the metrial gland with release of their granules.

The number of metrial gland cells in the vessels going to the labyrinth is slightly higher in the latter half of the period than in the earlier half in Swiss Webster mice. It is at about the same level during the latter half of the period in C57B1 as in Swiss Webster mice. Inspection of the data shows that the numbers of metrial gland cells in the portion of the supply vessels lying within the metrial gland comprise, by the 14th day, most of the total in each strain. This may indicate that by this time the metrial gland has become a source of migrating metrial gland cells in both strains. That the decidua basalis was the source earlier is suggested by the observation that, in each strain, and particularly in the C57B1, the number of cells in the metrial gland portion is a small part of the total in the arteries from the 11th to the 13th day of gestation. In other words, it would appear possible that the metrial gland

cells from the decidua basalis and metrial gland function at successive times. Indeed, this is consistent with inspection of the metrial gland cells in the two areas during the first half of the period studied, those in the decidua basalis appearing to be larger and to have more granules than those in the metrial gland.

The finding of metrial gland cells in the veins draining the uterus is consistent with their observation in the lungs (Dickson, 1980). The relative emptiness of the veins in the uterus found here reinforces the suggestion, made then, that investigation of metrial gland cell transport to the lungs might best be done by collection of blood samples from, for example, the inferior vena cava. It is worth mention that no evidence was found indicating whether the metrial gland cells about to leave the uterus in the veins had traversed the labyrinth or had come directly from the decidua basalis or metrial gland.

It would be interesting to know whether the greater number of metrial gland cells going to the labyrinth in C57B1 than in Swiss Webster mice, from the 11th to the 13th day, is associated with differences in depletion of these cells in the decidua basalis or whether differential production rates ensure that no difference can be detected. That study is now being undertaken.

The findings discussed above are consistent with the idea that metrial gland cells are, by means still not fully understood, immunosuppressant. This would account for the greater number in the Swiss Webster labyrinth, the trophoblast in that strain having presumably more paternal antigenicity than in the inbred C57B1 strain. The greater migration of metrial gland cells from the decidua basalis, coupled with non-persistence in the labyrinth in the latter strain, would then be interpretable as dumping of cells that had not encountered significant trophoblastic antigenicity, which, despite much doubt and debate, does seem to exist (Faulk, Sanderson & Temple, 1977; Carter, 1978; Chatterjee-Hasrouni & Lala, 1979).

SUMMARY

The number of metrial gland cells in the maternal placental supply vessels was found to be greater in C57B1 than in Swiss Webster mice from the eleventh to the thirteenth day of gestation. Since it has been found previously that the number of these cells lodged in the labyrinth is greater in Swiss Webster than in C57B1 mice, it appears likely that more disintegrate in the C57B1 than in the Swiss Webster strain. However, some cells in both strains were found in the veins draining the placenta and uterine wall and have been observed previously in lung capillaries. Disintegration is not, therefore, the sole mechanism of loss.

The increase, with time, in the number of metrial gland cells in the metrial gland portion of the placental supply vessels in both strains suggests that, although there is overlap, the decidua basalis is the early source of migrating metrial gland cells, and that the metrial gland later augments the flow.

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