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The initiation and development of the hair follicle population in tabby mice

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1. INTRODUCTION

The phenotypic effects of the sex-linked mutant gene tabby (*Ta*) were first reported by Falconer (1952) and subsequently described in more detail by the same author (Falconer, 1953). The remarkable similarity between the tabby phenotype and that of mice homozygous for the autosomal gene crinkled (*cr*), led Falconer (1953) to suggest that both genes may be responsible for the same primary defect of development. In crinkled mice this defect was traced initially to a failure of hair follicle formation in embryos aged between $12\frac{1}{2}$ and 17 days and in young mice immediately after birth (Falconer *et al.*, 1951).

There is now, however, some doubt whether the absence of guard hairs and many zig-zag fibres from the tabby and crinkled coats is due simply to the suppression of follicles normally producing these fibres; the observations of Claxton (1966) suggest rather that the *cr* and *Ta* mutants do not modify the normal sequence of follicle initiation without also influencing the normal relationship between the age of a follicle and the type of fibre it grows.

In addition to its abnormal texture, Falconer and his colleagues (1951) noted that the crinkled coat appeared to be thinner than in normal mice but no detailed examination of the numbers and arrangement of follicles in the skin of *cr* mutants was made; the influence the *Ta* gene may have on these features of the follicle population has, likewise, not been investigated. The work reported here bears on this latter aspect and has relevance to the primary action of the *Ta* gene. Observations were focused mainly on two lines of tabby mice, one selected for high and the other for low numbers of secondary vibrissae; to a lesser extent, the follicle populations of unselected tabby mice were also examined.

2. MATERIALS AND METHODS

Tabby mice were obtained from the Animal Genetics Section of C.S.I.R.O., Sydney. The unselected tabby mutants originated from the TA stock and were maintained subsequently with random breeding. Two lines that had been selected over twenty-six generations, one for high (HST), and the other for low (LST), numbers of secondary vibrissae, were developed initially by intercrossing the TA

stock and two lines derived from it with CBA and 101 inbred mice. A full account of the composition of the stocks and selection lines together with selection procedures was given by Dun & Fraser (1959).

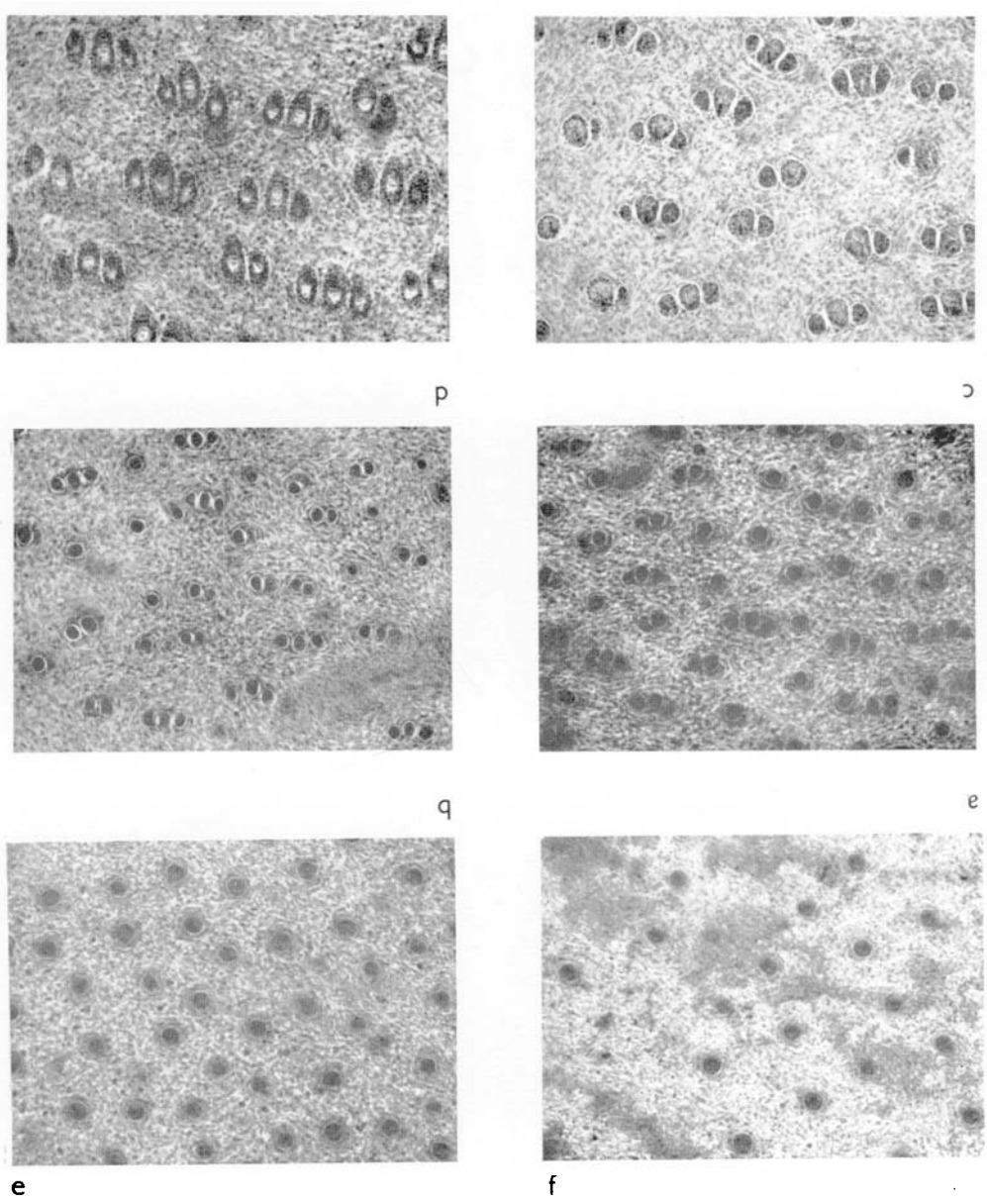
A series of embryos and young mice was sampled from each selection line at daily intervals from the 17th to the 22nd days and also at the 24th day after mating. These ages were determined by mating pairs of mice in separate cages and examining the females twice daily, at 9 a.m. and 5 p.m., for the presence of vaginal plugs. This evidence of union provided the base for calculating the ages of progeny, although it is probable these may be underestimated by about one-fourth day in view of the fact that the onset of estrus in mice is usually between 10 p.m. and 1 a.m. (Snell, 1941).

The tissues of whole mice were fixed in formol phosphate buffered at neutral pH; in the older animals the fixing process was facilitated by making a small slit in the ventral surface of the abdomen. Following fixation, a small sample of skin was removed from the dorsal neck region of each embryo or young mouse, the sampling site being located immediately posterior to an imaginary line connecting the bases of the ears (c.f. Claxton, 1966). Sections of skin, 10–12 microns in thickness, were cut with a freezing microtome, stained with methylene blue, and mounted in glycerol.

The extent to which the histological treatment may have caused shrinkage in the mounted skin sections was not examined, although a study of this problem in normal mice (Claxton, 1966), where an identical histological procedure was adopted, suggested that quantitative measurements such as follicle density would not be seriously biased if shrinkage was ignored.

The initial quantitative observations on the follicle population were made in the skin of brother-sister pairs of tabby mice, each pair being drawn at random from a different litter. Skin samples were removed from the dorso-lumbar region about 3 weeks after birth (at the time of weaning), but here, in so far as the collection of skin preceded its fixation, estimates of follicle density, for example, may be biased if shrinkage occurred during fixation. Therefore, although the ratios of the numbers of different follicle types are still valid, the values of follicle density in this material may have restricted significance.

The spatial relationships among the earliest follicles to be initiated were investigated by calculating values for a parameter, R, defined as twice the product of the mean distance from follicles to their nearest neighbours, and the square root of follicle density (cf. Clark & Evans, 1954). R, which takes values within the theoretical limits $0 \leqslant R \leqslant 2{\cdot}1491$, and whose departure from unity, either toward the lower bound of zero or the upper bound of 2·1491, reflects shifts from random spacing toward aggregation or uniformity respectively, was supplemented with estimates of the coefficient of variation of nearest neighbour distances. The application of these measures of spatial relationships has been illustrated and discussed in previous publications (e.g. Claxton, 1964).



Photomicrographs of transverse sections of skin taken from the dorsal neck region of embryos and young tabby mice. Each figure is orientated so that the length of the page corresponds with the median long axis of the body and anterior and posterior correspond with the bottom and top of the page respectively. The sections, 7–8 microns in thickness, were cut with a freezing microtome, stained with Ehrlich's haematoxylin, dehydrated, and mounted in Euparal. Magnification, × 85.

Figures ab . . . f represent in sequence, the initiation and development of the follicle population in 17-, 18-, 19-, 20-, 23- and about 40-day-old embryos and young mice. The even spacing between the central primary follicles together with the regular structure and orientation of the follicle groups are clearly evident. Figure f illustrates particularly, the ease with which the individual groups may still be identified about 3 weeks after birth.

3. RESULTS

(i) *Development of the follicle group*

The development of the follicle population in tabby mutants was examined in embryos and young mice during the period of follicle initiation. On the dorsal neck region, the earliest follicles appeared when the embryos were about 17 days old; although the density of new follicles varied in different embryos, anlagen were visible in most, but not all, skin sections of this age. On those 17-day-old embryos where development was most advanced, anlagen were spaced at fairly regular intervals in the skin, and in this respect the spatial pattern resembled that of the earliest appearing follicles in normal mice (Claxton, 1966).

The even spacing between follicles was also a feature of the follicle population at the 18th day although it was apparent that some of the newest anlagen at this age were beginning to develop near the older-established follicles. By the 19th day (about the time of birth) many follicles were arranged in groups, each of which contained one of the evenly spaced follicles and either one or two new anlagen located nearby. At this stage, therefore, the follicle population was a composite of trio and couplet groups as well as solitary follicles with which new anlagen had not become associated. At the 24th day and 2–3 weeks later at the time of weaning, this pattern of follicles did not change markedly, and it appeared that most follicles were established in the skin at the time of birth.

The foundation member of each trio follicle group occupied a more or less central position between the other two members, and the resulting row of three follicles was approximately parallel to other rows of three, and, on the dorsal neck region, was directed at right angles to the median long axis of the body. The lines connecting the follicles of each couplet group also conformed with this regularity of orientation.

According to the terminology proposed by Wildman & Carter (1939), the follicle population in tabby mice consists of central and lateral primary follicles, the former preceding the latter in the sequence of follicle initiation, thereby establishing the foundations for the subsequent regular development of follicle groups.

The foregoing description of the initiation and development of the follicle population is illustrated by the series of photomicrographs presented in Plate I.

(ii) *Size and composition of the follicle groups*

Quantitative aspects of the follicle population which were examined initially in tabby mice (homozygous tabby females and hemizygous tabby males of weaning age) included measurements of follicle density and of the relative proportions of lateral primary (PL) and central primary (PC) follicles. However, body weights of animals sampled from the unselected tabby population were not available, and no critical information was provided by the corresponding values of follicle density.

Follicles not grouped and those that occupied the central position of each trio group, were, by virtue of their relative spatial locations, classified as central primaries. It was not always possible, however, to decide which member of a couplet group was the central and which was the lateral primary, but measurements

of follicle density and of the PL/PC ratios were not dependent on specific identification being made in these cases; the couplet groups were themselves easily recognizable, and on the basis of the previous observations during initiation, they were assumed to contain one of each primary follicle type. Mean values of follicle density and of the ratio PL/PC are given in Table 1.

Table 1. *Mean values (and their standard errors) of central primary (PC) and lateral primary (PL) follicle density (follicles/mm.²), and the relative proportions of these follicle types in pairs of full sibs from the HST and LST lines, and also from an unselected line of tabby mice*

	Sex	Number of mice	Body weight (gm.)	Density P_C	Density P_L	P_L/P_C
HST	♂	12	7·11 ± 0·33	64·2 ± 3·3	85·4 ± 4·4	1·333 ± 0·033
	♀	12	7·23 ± 0·31	67·3 ± 2·4	79·8 ± 3·2	1·192 ± 0·038
LST	♂	12	6·90 ± 0·27	66·3 ± 3·9	61·4 ± 5·9	0·919 ± 0·051
	♀	12	6·50 ± 0·15	69·2 ± 2·3	49·3 ± 5·1	0·703 ± 0·062
Unselected tabby mice	♂	10	—	61·9 ± 3·2	56·3 ± 4·0	0·927 ± 0·069
	♀	10	—	53·4 ± 2·8	44·0 ± 4·3	0·818 ± 0·054

Statistical comparisons of follicle density were restricted to the two selection lines, and here, covariance analysis techniques were adopted to reduce density variation due to differences in body weight. With this procedure, the remaining central primary density differences between selection lines ($F < 1·0$; d.f. 1, 21; $p > 0·05$) and sexes ($F = 1·3$; d.f. = 1, 21; $p > 0·05$) were not statistically significant. For the density of lateral primary follicles the differences corresponding with these classifications were significant ($F = 41·9$; d.f. = 1, 21; $p < 0·01$; and $F = 5·7$; d.f. = 1, 21; $p < 0·05$; for selection lines and sexes respectively). Both these results were consistent with the outcome of a variance analysis of PL/PC ratio values which, for the two selection lines alone, indicated significant selection line ($F = 59·2$; d.f. = 1, 22; $p < 0·01$) and sex ($F = 25·0$; d.f. = 1, 22; $p < 0·01$) differences.

A variance analysis of the PL/PC ratios for HST, LST, and unselected tabby mice showed that the differences between these groups ($F = 30·7$; d.f. = 2, 31; $p < 0·01$) and between sexes ($F = 26·1$; d.f. = 1, 31; $p < 0·01$) were both highly significant. There was no significant interaction between groups and sexes however, so it is unlikely that the sex difference in PL/PC ratio was brought about by, or altered during, the course of selection.

(iii) *Growth and development of the follicle population*

Measurements of follicle density and of the ratio PL/PC were also made during and immediately after the period of follicle initiation in skin sampled from the dorsal neck region. Embryos and young tabby mice were obtained from parental matings between hemizygous tabby males and heterozygous tabby females which produced two main genotypic (and phenotypic) classes of progeny within each sex. Only

hemizygous tabby males and homozygous tabby female offspring were studied so it was not practicable to ensure that equal or even proportionate numbers of males and females contributed to the mean results for each selection line and age; nor were these sub-class means based on the same numbers of animals. Thus because of the earlier evidence that the ratio PL/PC is sex dependent, it was theoretically invalid to pool unweighted male and female data when comparing the two selection lines. Nevertheless, this procedure was adopted because of the relatively small numbers of male and female mice within each selection line and age, and also because the PL/PC difference between sexes appeared small in relation to the difference between selection lines. Although the subsequent discussion ignores this possible source of error, the conclusions which arose from the data in these circumstances were carefully viewed in relation to the separate sets of data for each sex; no inconsistencies were noticed.

Table 2. *Mean values of central primary (PC) and total follicle density (follicles/mm.^{2}), and the ratio (PL/PC) of lateral and central primary follicle numbers in the two selection lines of tabby mice. The numbers of mice observed and their average body weights (gm.) are also tabulated. The standard errors of the mean values include between-sex and between-litter components of variance*

Age	Selection line	Number of mice	Body weight	Density		P_L/P_C
				P_C	Total	
17 days	HST	24	$0{\cdot}74 \pm 0{\cdot}03$	36	36	0·0
	LST	17	$0{\cdot}74 \pm 0{\cdot}02$	38	38	0·0
18 days	HST	8	$1{\cdot}06 \pm 0{\cdot}04$	133 ± 6	133 ± 6	0·0
	LST	14	$0{\cdot}92 \pm 0{\cdot}04$	123 ± 6	123 ± 6	0·0
19 days	HST	8	$1{\cdot}22 \pm 0{\cdot}02$	83 ± 9	147 ± 7	$0{\cdot}86 \pm 0{\cdot}13$
	LST	13	$1{\cdot}30 \pm 0{\cdot}02$	89 ± 5	154 ± 8	$0{\cdot}79 \pm 0{\cdot}12$
20 days	HST	7	$1{\cdot}56 \pm 0{\cdot}08$	81 ± 10	175 ± 17	$1{\cdot}20 \pm 0{\cdot}07$
	LST	15	$1{\cdot}43 \pm 0{\cdot}03$	82 ± 4	160 ± 8	$0{\cdot}97 \pm 0{\cdot}05$
21 days	HST	10	$1{\cdot}59 \pm 0{\cdot}05$	70 ± 5	177 ± 10	$1{\cdot}53 \pm 0{\cdot}06$
	LST	10	$1{\cdot}48 \pm 0{\cdot}04$	78 ± 7	151 ± 14	$0{\cdot}93 \pm 0{\cdot}04$
22 days	HST	9	$2{\cdot}44 \pm 0{\cdot}07$	66 ± 3	157 ± 9	$1{\cdot}40 \pm 0{\cdot}09$
	LST	12	$2{\cdot}02 \pm 0{\cdot}15$	66 ± 4	132 ± 7	$1{\cdot}03 \pm 0{\cdot}07$
24 days	HST	9	$2{\cdot}53 \pm 0{\cdot}06$	56 ± 3	139 ± 10	$1{\cdot}46 \pm 0{\cdot}05$
	LST	8	$2{\cdot}59 \pm 0{\cdot}08$	57 ± 5	121 ± 6	$1{\cdot}16 \pm 0{\cdot}11$

The mean values of central primary and total primary follicle density, of the PL/PC ratio, and of body weight, are given for both selection lines at daily intervals between the 17th and 22nd days and also at the 24th day, in Table 2. Because the follicle population in the skin of tabby mice (at least on the two body regions examined) consisted only of primary types, the mean density of lateral primaries for either selection line at any age is simply the difference between the corresponding figures for total and for central primary density in Table 2. The changes with age in central primary and total primary densities are represented graphically in Fig. 1.

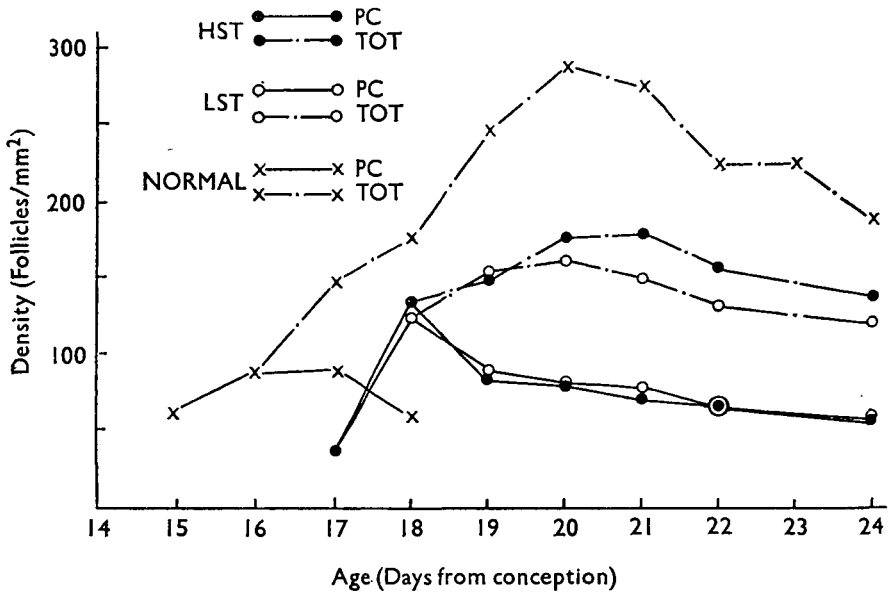


Fig. 1. The changes in central primary (PC) and total (TOT) follicle density with age in the two selection lines of tabby mice. For comparative purposes the corresponding density changes in normal mice (Claxton, 1966) are also represented.

(iv) *Spatial relationships between follicles*

Values of mean distance to nearest neighbour ($\bar{r}$), of the coefficient of variation of nearest neighbour distances (c.v.$_r$), and of R, were estimated during the period of follicle initiation in skin sampled from the dorsal neck region. The results for the 17th and 18th days are presented in Table 3.

Table 3. *Mean values of* R, *of mean distance to nearest neighbour* ($\bar{r}$*mm.*), *and of the coefficient of variation of nearest neighbour distances* (c.v.$_r$%), *in* 17- *and* 18-*day-old tabby mice. The standard errors of the mean values include between-sex and between-litter components of variance*

Age	Selection line	Number of mice	R	$\bar{r}$	c.v.$_r$
17 days	HST	4	1·72 ± 0·01	0·075 ± 0·002	12·7 ± 0·5
	LST	2	1·64 ± 0·03	0·076 ± 0·003	10·1 ± 1·8
18 days	HST	8	1·67 ± 0·02	0·073 ± 0·002	12·0 ± 0·4
	LST	14	1·70 ± 0·01	0·078 ± 0·002	11·9 ± 0·7

The data at 17 days only includes that from the skin samples in which follicle initiation was most advanced and where follicle density exceeded a figure of 100 follicles/mm.^{2}. Although a small number of lateral primary follicle anlagen were observed at the 18th day in the general body region under examination, none were recorded in the sub-region of each skin section where measurements were made. Therefore the data of Table 3 pertain only to the central primary follicle population.

Values of R and c.v.$_r$ were also obtained at later stages in the sequence of follicle initiation and development, but these results, especially for example, when drawing comparisons between tabby and wild-type, were difficult to interpret clearly because of the increasing spatial complexity within the follicle populations. They did suggest, however, that the groups of primary follicles were more compact in tabby than in normal mice, and this possibility was examined more closely by calculating in the 19-day-old tabby material, ratios of the mean nearest neighbour distances between central and lateral primary follicles in the same follicle group, and the mean nearest neighbour distances between central primary follicles. Distances between central and lateral primaries were measured directly but those between the central primary follicles at 19 days were obtained from the formula, $\bar{r} = \frac{1}{2}.R.n^{-\frac{1}{2}}$, by substituting the appropriate direct estimates of follicle density (Table 2) and a value of $R = 1{\cdot}69$, the latter being the average of individual R values for the central primary follicle population in 17- and 18-day-old tabby mice.

Table 4. *Ratios* ($\bar{r}_1/\bar{r}_2$) *of the mean nearest neighbour distances between central and lateral primary follicles* ($\bar{r}_1$), *and between central primary follicles* ($\bar{r}_2$), *in* 19*-day-old tabby mice, together with comparable figures for* 17*-day-old normal mice* (*Claxton, unpublished*)

	HST	LST	Normal
	0·33	0·31	0·55
	0·29	0·36	0·53
	0·28	0·33	0·42
	0·32	0·32	0·53
	0·32	0·37	0·51
	0·31	0·34	0·57
	0·28	0·36	0·45
		0·30	0·55
		0·36	0·48
		0·35	
		0·33	
		0·27	
Means and standard errors	$0{\cdot}304 \pm 0{\cdot}007$	$0{\cdot}332 \pm 0{\cdot}009$	$0{\cdot}512 \pm 0{\cdot}017$

The ratios of these different mean nearest neighbour distances are given in Table 4 which includes ratio values for a number of 17-day-old normal mice. In so far as lateral primary follicle initiation had been in progress for about 24 hours at these ages (cf. Claxton, 1966), the results for the mutant and normal follicle populations are reasonably comparable.

A variance analysis of the Table 4 data revealed very highly significant differences between HST, LST and normal mice ($F = 110{\cdot}6$; d.f. $= 2, 25$; $p < 0{\cdot}01$). The application of Duncan's (1955) multiple range test to these differences showed the statistical significance to stem entirely from the contrast between mutant and normal.

4. DISCUSSION

The histological examination made of skin samples from both selection lines of tabby mice indicated that follicle initiation begins at or very near the 17th embryonic day. This observation agrees with those of Falconer *et al.* (1951) in crinkled mice, and of Falconer (1953) in tabby mice. However, the state of follicle development varied in different 17-day-old embryos, and whereas in some the density of anlagen was greater than 100 follicles/mm.^{2}, in others initiation either had not commenced or, more commonly, was apparent only from the presence of a few scattered cell aggregations. For the reason that no negative weighting could be given to the zero density values at 17 days, the mean for this age is in some ways misleading; with respect to the beginning of follicle initiation, for example, little significance can be attached to the fact that the extrapolated density curves (Fig. 1) intercept the age axis between the 16th and 17th days.

In both selection lines central primary follicle density increased between the 17th and 18th days but subsequently decreased continuously, although relatively

Table 5. *Follicle density (follicles/mm.^{2}) on five body positions of adult normal and tabby mice*

	Number of mice	Average weight gm.	Density					
			Neck	Shoulder	Back	Midside	Britch	Average
Tabby	2	24·3	56·6	51·9	48·1	60·8	53·2	54·1
Normal	2	24·2	73·8	69·6	63·2	59·6	61·5	65·6

slowly, from the 19th to the 24th day. The fact that density was highest at the 18th day suggests that most central primaries are established in the skin at about this time. There appears to be little doubt, therefore, that the period in which most central primary follicles are initiated is of shorter duration in tabby than it is in normal mice where initiation occupies about 3 days (Claxton, 1966). The comparison drawn in Fig. 1 shows equally clearly that the desnity of central primary follicles reaches a higher maximum value in tabby than in normal mice, and evidently the central primaries are laid down at a more rapid rate in the mutants.

Whether or not tabby mice ultimately possess greater than normal total numbers of central primary follicles, depends on differences in body surface area as well as on differences in follicle density. The 18-day-old tabby embryos, for example, were about 16% lighter in body weight than comparably aged normal embryos studied previously (Claxton, 1966), but even allowing for the expected accompanying differences in surface area (determined by assuming surface area to be proportional to the $\frac{2}{3}$ power of body weight), the central primary follicles appeared to be more numerous in the mutants. Additional evidence on this point was obtained from measurements of follicle density in pairs of tabby and normal adult mice of similar weights. When the average density values (Table 5) were partitioned according to the estimated fractions of central primaries in the total follicle populations (Table 1

and Claxton, 1966), the tabbies were found to have about 70% more central primary follicles than normal mice.

During the period of initiation in tabby, the rate of increase in total follicle density became smaller with increasing age, and the resulting curvilinear density-age relationship contrasts with this aspect of the normal sequence of follicle initiation where the increases in density were approximately linear (Fig. 1). The fact that total follicle density reached its highest values at the 20th day in LST and at the 21st day in HST, suggests that follicle initiation continues for one, and possibly two days after birth. This conclusion is also supported by the age changes in the ratio PL/PC; the value of the ratio increased continuously from the 18th until the 20th day in LST and until the 21st day in HST (Table 2). Although these results are not consistent with those of Falconer *et al.* (1951) showing that follicle initiation is complete at birth in crinkled mice, no completely satisfactory explanation can be given for the discrepancy.

Because of the absence of secondary follicles in the skin of tabbies, the spatial structure of the follicle population does not attain the same complexity as it does in normal mice (cf. Claxton, 1966). In spite of this and of differences in the absolute and relative timing of events, there are nevertheless basic similarities in development. The even spacing of the first-formed central primary follicles, the appearance of lateral primary follicles in association with these, and the regular orientation of the resulting follicle groups (both with respect to each other and to the long axis of the body), are features sufficient to establish a common constructional plan unfolding during follicle initiation.

The general observation that the central primary follicle population is characterized by a marked degree of regularity in the size of the spacing intervals between follicles was confirmed quantitatively by estimating values for the parameter R. These were very much larger than unity, and the average value $R = 1{\cdot}685$ obtained by combining the results for both selection lines at 17 and 18 days (Table 3) was remarkably similar to a comparable estimate for the central primary follicle population of 15-day-old normal embryos ($R = 1{\cdot}689$, Claxton, unpublished). The corresponding mean values of c.v.$_r$ (11·9% and 11·3% for tabby and normal embryos respectively) were also similar, and it is concluded that the relative spacing of the central primary follicles is not influenced by the *Ta* gene. On the other hand, although the lateral primary follicles in tabby mice are typically located near and on opposite sides of each central primary, the association of these follicles is relatively closer and the groups of primary follicles are more compact in the mutants.

While there is no doubt that follicle initiation is delayed in tabbies, the relationships between follicle density and age (Fig. 1) do not suggest that initiation ceases markedly, if at all, earlier than in normal mice. This and other evidence (Claxton, 1966) disagrees with the suggestion of Falconer and his colleagues (1951) that the absence of guard hairs and zig-zag fibres in the crinkled coat is due simply to the absence of follicles normally producing these fibres. In other words, if guard hairs, awls, auchenes, and zig-zags, grow from follicles initiated in this order—as suggested by the reports of Dry (1926), Falconer *et al.* (1951), and Mann (1962)—then the

fibre type anomaly of the tabby and crinkled coats is not simply the result of restricting initiation to an intermediate period of the normal sequence when follicles only with the potential for producing mainly awls and auchenes would be established. Nor can it be assumed that a normal succession of fibre types automatically results from a normal-length sequence of initiation, irrespective of the time when the sequence unfolds; for although follicle initiation occupies a shorter time interval in tabby mice, and while the absence of many zig-zag fibres may be accommodated in this way, one would expect, contrary to observation, the presence of guard hairs in the mutant coats. Finally, Claxton (1966) dismissed the possibility of any specific, or even close, relationship between follicle and fibre types in normal mice, so the failure of secondary follicle initiation in tabbies is not, in itself, a reason for the fibre type peculiarities of the coat. Therefore, these peculiarities are apparently not the result of any simple modification imposed by the *Ta* and *cr* genes.

With respect to the nature of the correlated effects in the maincoat arising from selection for high and low numbers of secondary vibrissae, it is noteworthy that the initial quantitative comparisons (Table 1) placed the values of the ratio PL/PC for unselected tabbies intermediate between those corresponding with the two selection lines. This result of selection is precisely that which would be expected if it extends in the case of HST, and curtails in the case of LST, the usual period of follicle initiation in tabby mice; a lengthening or shortening of the final stages of initiation could increase or decrease respectively, the relative numbers of the last-formed follicles, the lateral primaries. On the other hand, selection does not appear to alter the age when initiation begins in tabbies—the density-age relationships for the HST and LST central primary follicle populations are very similar, both in shape and in location (Fig. 1). Therefore, it seems unlikely that the manifestations of selection are primarily achieved in the same way as those of the *Ta* gene. It is possible that the basis for this conclusion may be closely related to the evidence from which Kindred (1967) argues, '... there may be two aspects to the action of the Tabby mutant, only one of which has been influenced by selection.'

SUMMARY

Hair follicle initiation and development was examined in tabby mutants and compared with a previous study of this sequence in normal mice. Initiation commenced at about the 17th embryonic day and continued for 1 and possibly 2 days after birth. Although central primary follicle initiation was of shorter than normal duration, it was more rapid, with the result that the central primaries achieved a greater maximum density, and their total numbers were greater in tabby than in normal mice.

In general structural terms, follicle group development proceeded normally except that no secondary follicles appeared, and for this reason, the mature grouping pattern of follicles was comparatively simple. Central primary follicles, the first to be initiated, were evenly spaced in the skin but the later association of lateral primaries with them was unusually close, and the resulting groups of primary

follicles were relatively more compact in the mutants than they were in normal mice.

No simple explanation in terms of the altered timing of follicle initiation or the reduced complexity of the follicle group could be given for the abnormalities of the tabby coat.

Selection for high and low numbers of secondary vibrissae in tabby mice produced some correlated changes in the maincoat follicle population, but there was no apparent alteration to the time of onset of initiation. Evidently selection did not simply modify the effects of the *Ta* gene.

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