THE DEVELOPMENT AND GROWTH OF VIBRISSAE IN THE HOUSE MOUSE WITH PARTICULAR REFERENCE TO THE TIME OF ACTION OF THE TABBY (*Ta*) AND RAGGED (*Ra*) GENES

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Summary

The order of development of certain vibrissae, found on the head and fore limbs of the mouse, has been determined using observations on the developmental stage and relative length of each follicle at 11, 12, 13, and 14 days foetal age. The length of vibrissal fibres at birth was also utilized.

In homozygous ragged (*RaRa*) mice, no vibrissa follicle commencing development after approximately 12 days foetal age produces a functional fibre. This is in contrast to the tabby genotypes where there is no precisely timed gene action, but within any group of vibrissae the incidence follows the order of follicle initiation.

I. Introduction

Only three of the genes known in the mouse which affect the development of the skin and hair influence the production of specific types of hair. The genes which fall into this classification are crinkled (*cr*) (Falconer, Fraser, and King 1951), tabby (*Ta*) (Falconer 1953), a sex-linked mimic of crinkled, and ragged (*Ra*) (Carter and Phillips 1954). Because of their specific effects, they furnish favourable material for detecting the onset of gene action, provided the times at which each type of follicle commences development are known.

Dry (1926) classified the coat of the mouse into the following hair types:

(1) Tactile hairs or vibrissae

(2) Hairs of the coat proper
   (*a*) Guard hairs
   (*b*) Awls
   (*c*) Auchenes
   (*d*) Zig-zags

Considering the vibrissae first, Figure 1 shows the distribution of the more prominent vibrissae of the mouse.

Certain mystacial vibrissae are the first follicles to commence growth. Grüneberg (1943*a*) states that, in the 12½-day embryo, three rows of mystacial follicles were present and that the full complement of rows was not seen until 13½ days. Davidson and Hardy (1952) examined the stages in the development of vibrissae using one or more of the most posterior mystacials which were observed to commence growth at 12 days. Because of the difficulty in orientating the mystacial

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follicles, no information is available comparing the time of initiation of individual vibrissae.

More information is available comparing the development of certain members of the minor groups of vibrissae. Grüneberg (1943*a*) says that in the 12½-day mouse

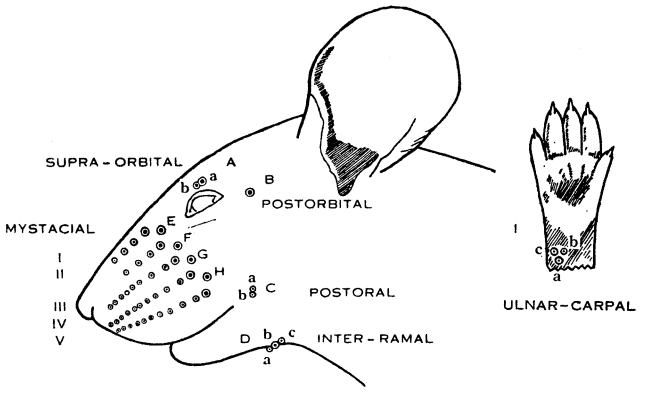

Fig. 1.—Head and distal part of the right fore limb of the mouse showing distribution of vibrissae.

embryo, one supra-orbital follicle is always present and that the postorbital follicle is sometimes visible. At 13½ days, the supra-orbitals, postorbital, and postoral vibrissae were all observed. No other sites were examined.

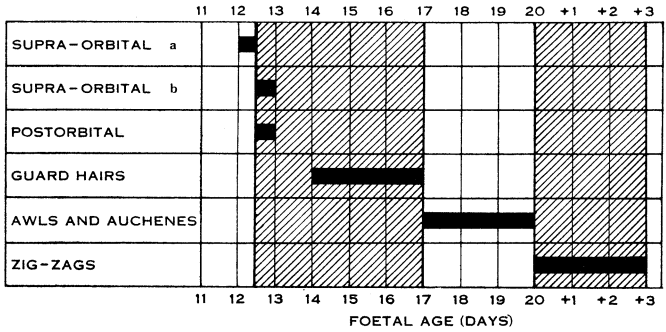

Fig. 2.—Action of the crinkled gene related to the time of initiation of vibrissae and pelage-hair types in the mouse (after Falconer, Fraser, and King (1951).

Falconer, Fraser, and King (1951) examined the supra-orbital and postorbital sites in their analysis of the crinkled gene. At 12½ days, one supra-orbital follicle was well developed and by 13½ days the second follicle was present. The postorbital vibrissa had just commenced development in the 12½-day foetus and was well developed by 13½ days. The postoral follicles were present at 13½ days but it was impossible to distinguish any details of follicle morphology. These authors found the remaining vibrissae too difficult to examine in their material.

With regard to the coat hairs, Falconer, Fraser, and King (1951), after examining sagittal sections of skin from the mid-dorsum of the body, suggested that the type of fibre was related to the age at which the follicles were formed. The order of development would be guard hairs first, then awls and auchenes, and lastly the zig-zags. They proposed a model for the action of the crinkled gene which is illustrated in Figure 2. The black bands show the periods during which the follicles of each type are commencing development, while the cross-hatched areas indicate the periods when the initiation of follicles is stopped by the crinkled gene. Thus the coat of the crinkled mouse lacks certain vibrissae and all guard hairs and

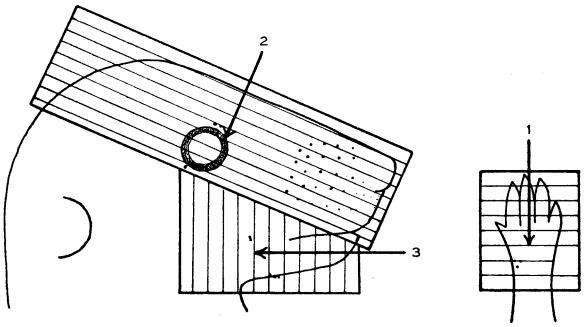

Fig. 3.—Sectioning planes for examining the development of specific vibrissa follicles.

zig-zag fibres. Falconer, Fraser, and King (1951) showed that the coat of the crinkled mouse possessed one type of fibre, the follicles of which had commenced growth between 17 and 20 days gestation. In length these fibres resembled awls but their internal structure was not characteristic.

One of the main difficulties with this model is that there is insufficient knowledge of the development of individual vibrissa follicles. If the development of all follicles which are normally initiated between $12\frac{1}{2}$ and 17 days is inhibited by the crinkled gene, it is difficult to understand why some mystacial vibrissae are not affected. As this seemed to be a crucial point in the theory, it was decided to examine the time of initiation of many vibrissae and relate this information to the vibrissae grown by tabby mice. The sex-linked tabby was used in preference to its autosomal mimic crinkled, as tabby is the gene being used in a selection experiment which is being conducted at this Laboratory (Dun and Fraser 1958). Observations were also made on the vibrissae of ragged mice to see if there was any similarity with the tabby–crinkled syndrome.

II. Materials and Methods

Foetuses of known ages were obtained by recording the date at which vaginal plugs were observed in a mating between inbred lines (CBA males × Aw101 females). Litters were obtained at $11\frac{1}{2}$, $12\frac{1}{2}$, $13\frac{1}{2}$, and $14\frac{1}{2}$ days gestation and the calculated ages were checked by examining the external features of the embryos (Grüneberg 1943*b*).

TABLE 1

PERCENTAGE INCIDENCE OF VIBRISSAE IN THE MINOR GROUPS OF MICE WITH TABBY AND NORMAL GENOTYPES

Vibrissae scored on both sides of the head

Genotype	Number of Mice	Supra-orbital		Post-orbital	Postoral		Inter-ramal			Ulnar–Carpal		
		a	*b*		*a*	*b*	*a*	*b*	*c*	*a*	*b*	*c*
+·	224	100·0	99·6	100·0	100·0	100·0	95·5	100·0	95·5	100·0	99·6	100·0
++	230	100·0	100·0	100·0	100·0	99·6	95·2	100·0	95·2	100·0	99·6	100·0
Ta+	227	100·0	96·5	92·7	99·3	15·0	34·6	100·0	34·6	100·0	72·2	98·5
Ta·	256	100·0	56·8	1·6	75·4	0	8·2	100·0	8·2	100·0	2·7	45·9

Two litters of five mice each were obtained at the different ages and fixed in Bouin's fluid. After embedding the foetuses in paraffin wax, serial sections (8 μ thick) were stained with haematoxylin and eosin. Serial sections were made of the head and fore legs (Fig. 3) to allow histological examination of the vibrissae.

TABLE 2

NUMBER OF VIBRISSAE IN THE ROWS OF THE MYSTACIAL GROUPS OF MICE WITH TABBY AND NORMAL GENOTYPES

Genotype	Number of Mice	Row E–F–G–H	Row I	Row II	Row III	Row IV	Row V
+·	84	4·00	3·98	4·00	9·75	10·63	11·67
++	84	4·00	4·00	3·99	9·72	10·70	11·57
Ta+	96	4·00	3·94	3·83	9·48	10·73	11·38
Ta·	110	4·00	3·92	3·90	9·25	10·84	11·22

During microscopic examination of the serial sections, scale drawings of each vibrissae follicle were made using a measuring eyepiece. The stage of growth of each follicle was recorded using the numerical scores of Davidson and Hardy (1952).

TABLE 3

DIFFERENCES BETWEEN TABBY GENOTYPES IN THE NUMBER OF VIBRISSAE IN MYSTACIAL ROWS III, IV, AND V

Genotypes	Row III		Row IV		Row V	
	Difference	*t*	Difference	*t*	Difference	*t*
++ minus *Ta*+	+0·24	2·35*	−0·03	0·26	+0·19	1·98*
+· minus *Ta*·	+0·50	4·67**	−0·21	1·78	+0·45	3·85**
Ta+ minus *Ta*·	+0·23	2·32*	−0·11	0·96	+0·16	1·50

*$P < 0{\cdot}05$. **$P < 0{\cdot}01$.

With the 13½- and 14½-day foetuses, it was not possible to examine mystacial rows I and II in this way as the follicles had been sectioned obliquely. When examining the sectioned material, difficulty was encountered in that, of 10 foetuses prepared at each age, very few were found to be suitable for microscopy. In many cases follicles could not be measured with certainty because of oblique sections or imperfect preparation. This meant that no estimates of the variation between individuals

TABLE 4

PERCENTAGE INCIDENCE OF VIBRISSAE IN THE MINOR GROUPS OF MICE WITH RAGGED AND NORMAL GENOTYPES

Genotype	Number of Mice	Supra-orbital		Post-orbital	Postoral		Inter-ramal			Ulnar–Carpal		
		a	*b*		*a*	*b*	*a*	*b*	*c*	*a*	*b*	*c*
++	35	100·0	100·0	100·0	100·0	100·0	88·3	100·0	88·3	100·0	100·0	100·0
Ra+	60	100·0	100·0	100·0	100·0	100·0	91·5	100·0	91·5	100·0	100·0	100·0
RaRa	32	90·6	0	75·0	0	0	0	0	0	0	0	0

could be made. The values quoted refer only to means of the two or three foetuses of each age which could be adequately measured.

The presence of the minor groups of vibrissae on living mice was scored by naked eye using a desk lamp. Two scores were made, the first at 5 days and a check score 10 days after birth. Vibrissae were scored on both sides of the head. The vibrissae in the mystacial rows were counted in new-born mice using a dissection microscope. In the case of the homozygous ragged mice, the mystacial vibrissae

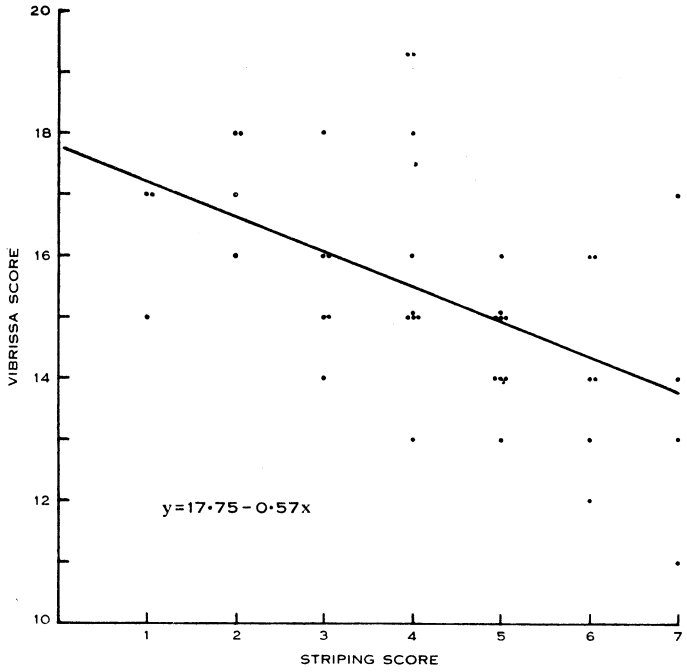

Fig. 4.—Influence of the degree of striping of the coat on vibrissa number in heterozygous tabby female mice.

were scored at 10 days of age but, if death occurred prior to this time, the vibrissae were still readily counted in mice more than 5 days old. The mice of the various tabby and ragged genotypes examined were the F_2 of CBA-based stocks mated to Aw101.

The vibrissae of tabby females (*Ta*+) were examined and their coats were seen to vary from near normality through various intensities of striping to a type which was almost indistinguishable from that of the tabby hemizygous male (*Ta*·). The tabby females were scored for degree of striping at 45 days of age using a series of six end-point photographs. Thus scores ranged from 1 to 7, 1 being for the least degree of striping.

In order to measure the effect of the tabby gene on the growth of vibrissae, matings were arranged between normal males (+·) and tabby females (*Ta*+). The litters were examined at birth and only those which contained a member of each of the four genotypes (+·, *Ta*·, ++, and *Ta*+) were included in

the experiment. The litters were standardized to four mice as above and the lengths of vibrissae were measured at day 1, 5, 9, and 21. Five litters remained intact until the final measurement and provided the data for the estimation of growth rates. Only the supra-orbital, postorbital, postoral, and inter-ramal groups were measured throughout but, at day 1, the ulnar–carpal group and vibrissa G and row IV mystacials were measured in the normal mice.

III. Results

The incidence of the vibrissae in the minor groups of tabby females, tabby males, and wild-type mice are shown in Table 1. The vibrissae which were missing from the inter-ramal group were presumed to be equal numbers of either *a* or *c*. With the exception of the inter-ramals, all vibrissae are almost invariably present in wild-type mice. Many vibrissae are missing in tabby mice, the effect being more marked in the hemizygous male than in the heterozygous female.

Table 5

NUMBER OF VIBRISSAE IN THE ROWS OF THE MYSTACIAL GROUP IN MICE WITH RAGGED AND NORMAL GENOTYPES

Genotype	Row E–F–G–H	Row I	Row II	Row III	Row IV	Row V
++	4·00	4·00	4·00	9·70	10·68	11·72
Ra+	4·00	4·00	4·00	9·69	10·60	11·72
RaRa	4·00	0·94	0·97	1·28	0·97	0·50

The relationship between the total number of vibrissae present in the minor groups and the degree of striping on the coats of tabby females, is shown in Figure 4. There was a highly significant negative correlation of −0·53 between striping score and vibrissae number. The repeatability of the striping score was 0·87.

Table 2 shows the number of vibrissae in the single vertical and the five horizontal rows which comprise the mystacial group. The significance of the differences between horizontal rows III, IV, and V for the different genotypes are shown in Table 3.

The vertical row E–F–G–H and mystacial rows I and II normally have four vibrissae each. This arrangement is hardly affected by the tabby gene although there tends to be slightly more mice with *d*, the most anterior vibrissa, missing from rows I and II. Rows III, IV, and V have much more variable counts in normal mice. Tables 2 and 3 show that rows III and V have slightly but significantly less numbers of vibrissae in tabby mice. Row IV shows no significant differences. The actual vibrissae which may be missing in rows III and V of tabby mice could not be identified as there was a continuous gradation in length of vibrissae down the rows and there were no large gaps between vibrissae. Thus, the tabby gene has little effect on the number of mystacial vibrissae.

TABLE 6

GROWTH OF CERTAIN VIBRISSAE IN TABBY AND NORMAL MICE FROM DAY 1 TO 21 DAYS OF AGE

Genotype	Vibrissa	Day 1		Day 5		Day 9		Day 21	
		Length (mm)	Variance	Length (mm)	Variance	Length (mm)	Variance	Length (mm)	Variance
+·	Supra-orbital *a*	1·53	0·712	3·84	3·004	6·66	6·360	13·00	3·333
	Postorbital	1·07	0·201	2·95	1·250	5·74	4·471	13·00	4·444
	Postoral *a*	0·46	0·160	1·64	0·404	3·57	0·779	6·50	1·667
	Inter-ramal *b*	0·34	0·130	1·26	0·330	2·70	0·650	6·40	1·750
++	Supra-orbital *a*	1·59	0·277	3·97	1·690	6·77	1·401	12·70	1·778
	Postorbital	1·07	0·246	3·09	0·699	5·82	0·996	13·15	5·580
	Postoral *a*	0·52	0·151	1·67	0·246	3·88	0·751	6·60	1·556
	Inter-ramal *b*	0·36	0·030	1·40	0·100	2·76	1·030	6·60	4·250
Ta+	Supra-orbital *a*	1·33	0·312	3·44	1·004	6·19	3·299	11·55	4·694
	Postorbital	0·85	0·049	2·69	1·677	5·06	1·782	11·75	0·694
	Postoral *a*	0·28	0·317	1·10	0·054	2·71	0·432	5·50	1·667
	Inter-ramal *b*	0·33	0·018	1·16	1·180	2·52	1·070	5·70	0·750
Ta·	Supra-orbital *a*	1·18	0·996	3·10	2·400	5·98	7·440	10·25	9·583
	Postorbital	—	—	0·52	0·084	1·56	1·027	3·70	1·778
	Postoral *a*	0·18	0·062	0·86	0·360	2·08	0·262	4·77	4·068
	Inter-ramal *b*	0·24	0·040	1·10	0·300	2·32	0·870	6·20	5·750

TABLE 7

LINEAR REGRESSION EQUATIONS DESCRIBING THE GROWTH OF CERTAIN VIBRISSAE IN MICE WITH TABBY AND NORMAL GENOYTPES

x = age in days; y = length of vibrissae (mm)

Vibrissa	+·		++		*Ta*+		*Ta*·	
	Regression Equation	Fiducial Limits of Constant	Regression Equation	Fiducial Limits of Constant	Regression Equation	Fiducial Limits of Constant	Regression Equation	Fiducial Limits of Constant
Supra-orbital *a*	$y = 0{\cdot}573x + 1{\cdot}101$	$\pm 0{\cdot}026$	$y = 0{\cdot}553x + 1{\cdot}281$	$\pm 0{\cdot}020$	$y = 0{\cdot}510x + 1{\cdot}038$	$\pm 0{\cdot}024$	$y = 0{\cdot}452x + 1{\cdot}062$	$\pm 0{\cdot}036$
Postorbital	$y = 0{\cdot}606x + 0{\cdot}236$	$\pm 0{\cdot}024$	$y = 0{\cdot}611x + 0{\cdot}284$	$\pm 0{\cdot}020$	$y = 0{\cdot}551x + 0{\cdot}129$	$\pm 0{\cdot}014$	$y = 0{\cdot}194x - 0{\cdot}337$	$\pm 0{\cdot}018$
Postoral *a*	$y = 0{\cdot}303x + 0{\cdot}316$	$\pm 0{\cdot}018$	$y = 0{\cdot}305x + 0{\cdot}348$	$\pm 0{\cdot}016$	$y = 0{\cdot}265x + 0{\cdot}015$	$\pm 0{\cdot}012$	$y = 0{\cdot}234x - 0{\cdot}133$	$\pm 0{\cdot}014$
Inter-ramal *b*	$y = 0{\cdot}308x - 0{\cdot}097$	$\pm 0{\cdot}024$	$y = 0{\cdot}316x - 0{\cdot}064$	$\pm 0{\cdot}022$	$y = 0{\cdot}274x - 0{\cdot}046$	$\pm 0{\cdot}014$	$y = 0{\cdot}304x - 0{\cdot}271$	$\pm 0{\cdot}026$

Tables 4 and 5 show the vibrissae which are present in mice with different ragged genotypes. The heterozygous ragged mice (*Ra*+) had a complement of vibrissae which was indistinguishable in number from that of wild-type, but when mice were homozygous the only vibrissa follicles which produced fibres were the

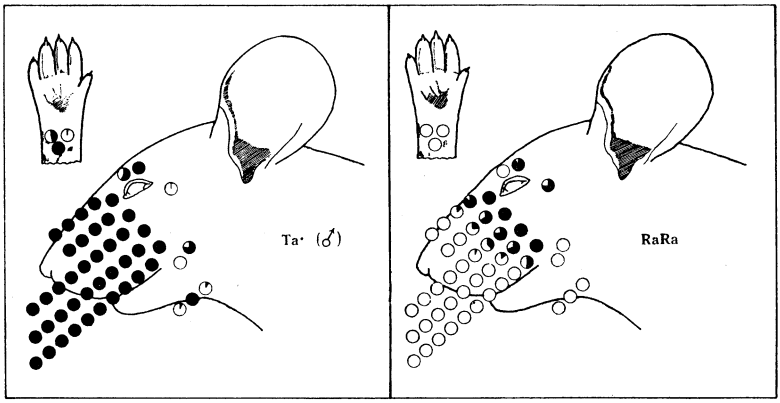

Fig. 5.—Incidence of vibrissae in tabby males and homozygous ragged mice. The percentage incidence of each vibrissa is shown as the proportion (black shading) of a circle (indicating a vibrissal site).

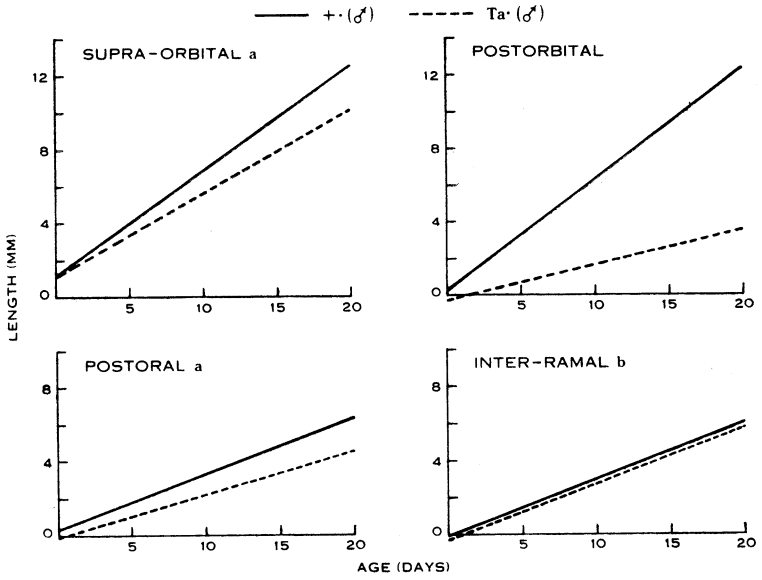

Fig. 6.—Comparisons in growth rate between vibrissae of normal male and tabby male mice.

most posterior mystacials and the two largest vibrissae in the minor groups. Follicle growth was observed at the sites of certain other vibrissae but in no case did a fibre emerge. The comparison between tabby hemizygous males and homozygous ragged mice is illustrated in Figure 5.

The growth in fibre length of certain vibrissae was examined in mice with normal and tabby genotypes. These results are shown in Tables 6 and 7. In general, the tabby gene exerts a depressant effect on the length of vibrissae at birth and on the subsequent growth rate. As with other characteristics, the tabby female tends to be intermediate between the wild type and the tabby male. Figure 6 demonstrates that the reduction in the growth rate of vibrissae is much more marked at certain sites, e.g. postorbital than at others, e.g. inter-ramal *b*.

Table 1 shows that a typical postorbital vibrissa is rarely recorded in tabby males. However, a fibre which cannot be demonstrated at birth is invariably seen at the postorbital site at 5 days of age. This fibre shows slow growth as shown in Tables 6 and 7 and Figure 6 but it is atypical in that it reaches a length about a third that of the normal and it tends to curl into and be hidden by the hairs of the coat.

TABLE 8

AVERAGE LENGTH OF VIBRISSAE AT BIRTH IN NORMAL MICE

Measurements are means for 10 mice

Vibrissa	Length (mm)	Vibrissa	Length (mm)
Supra-orbital *a*	1·56	Mystacial G	2·18
Supra-orbital *b*	0·75	Row IV *a*	1·71
Postorbital	1·07	,, *b*	1·33
Postoral *a*	0·49	,, *c*	0·96
Postoral *b*	0·38	,, *d*	0·73
Inter-ramal *a*	0·24	,, *e*	0·45
Inter-ramal *b*	0·35	,, *f*	0·32
Inter-ramal *c*	0·22	,, *g*	0·21
Ulnar–carpal *a*	0·18	,, *h*	0·20
Ulnar–carpal *b*	0·05	,, *i*	0·20
Ulnar–carpal *c*	0·14	,, *j*	0·19

"Vestigial vibrissae" were suspected of being present at certain other sites in tabby males, e.g. supra-orbital *b* and postoral *b*. Many such cases were recorded at 5 days but the fibres could not be distinguished when making subsequent measurements.

Table 8 shows the average length of the vibrissae which were measured at day 1 in normal mice. Tables 9 and 10 and Figures 7 and 8 show the stages of development and lengths of vibrissae follicles in $12\frac{1}{2}$-, $13\frac{1}{2}$-, and $14\frac{1}{2}$-day normal embryos. There was no sign of follicle development in the $11\frac{1}{2}$-day foetuses. With the mystacial vibrissae, the only results listed are for vibrissa *G* and row IV as longitudinal sections of these follicles were obtained at all ages.

The stages of development reached by all follicles at $12\frac{1}{2}$ days foetal age are shown in Figure 9. In this case it was possible to examine approximately longitudinal sections of all mystacial vibrissae because the largest follicle was only at the prepapilla stage.

TABLE 9

STAGES OF DEVELOPMENT AND LENGTHS OF FOLLICLES FOR THE MINOR GROUPS OF VIBRISSAE IN 12-, 13-, AND 14-DAY NORMAL FOETUSES

Vibrissa	12½-day Foetus*		13½-day Foetus†		14½-day Foetus†	
	Developmental Stage	Length of Follicle (mm)	Developmental Stage	Length of Follicle (mm)	Developmental Stage	Length of Follicle (mm)
Supra-orbital *a*	1	0·052	3*b*	0·256	5	0·500
Supra-orbital *b*	1	0·024	2	0·100	3*c*	0·260
Postorbital	1	0·040	3*a*	0·172	4	0·328
Postoral *a*	—	—	2	0·080	3*b*	0·220
Postoral *b*	—	—	2	0·088	3*b*	0·220
Inter-ramal *a*	—	—	M.P.‡	—	2	0·104
Inter-ramal *b*	—	—	M.P.	—	3*a*	0·132
Inter-ramal *c*	—	—	M.P.	—	2	0·116
Ulnar–carpal *a*	—	—	M.P.	—	2	0·112
Ulnar–carpal *b*	—	—	M.P.	—	1	0·052
Ulnar–carpal *c*	—	—	M.P.	—	1	0·068

* Three foetuses from one litter measured.

† Two foetuses from one litter measured.

‡ Mesodermal proliferation.

TABLE 10

STAGES OF DEVELOPMENT AND LENGTH OF FOLLICLES FOR CERTAIN MYSTACIAL VIBRISSAE IN 12-, 13-, AND 14-DAY NORMAL FOETUSES

Vibrissa	12½-day Foetus*		13½-day Foetus†		14½-day Foetus†	
	Developmental Stage	Length of Follicle (mm)	Developmental Stage	Length of Follicle (mm)	Developmental Stage	Length of Follicle (mm)
Mystacial G	2	0·088	4	0·360	5	0·664
Row IV *a*	1	0·056	3*c*	0·300	5	0·568
,, *b*	1	0·036	3*b*	0·220	5	0·468
,, *c*	1	0·028	3*a*	0·172	4	0·392
,, *d*	—	—	3*a*	0·116	4	0·332
,, *e*	—	—	2	0·076	3*c*	0·264
,, *f*	—	—	1	0·048	3*b*	0·192
,, *g*	—	—	1	0·036	3*a*	0·140
,, *h*	—	—	—	—	2	0·092
,, *i*	—	—	—	—	2	0·072
,, *j*	—	—	—	—	1	0·056
,, *k*	—	—	—	—	1	0·044
,, *l*	—	—	—	—	1	0·032

* Three foetuses from one litter measured.

† Two foetuses from one litter measured.

Although the present data is insufficient to allot an accurate developmental time to each vibrissa follicle, it is possible to arrange the vibrissae in the order in which they commence development. It has been assumed that the size and stage of development of a follicle were indications of its age. Use was also made of the

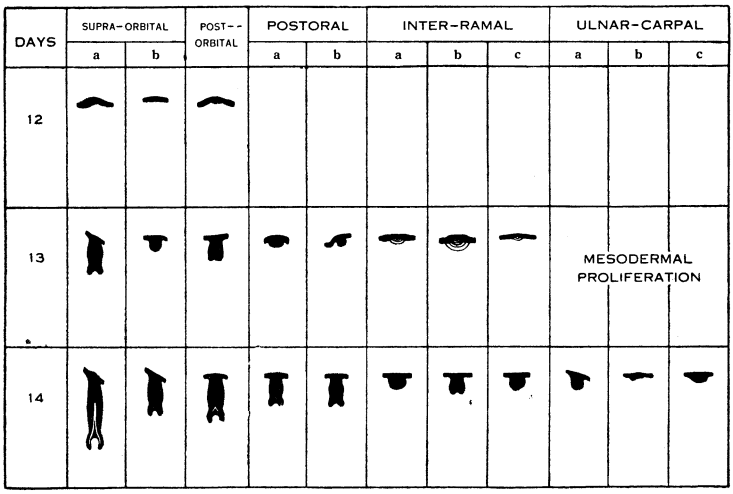

Fig. 7.—Longitudinal sections of the developing follicles in the minor groups of vibrissae at $12\frac{1}{2}$, $13\frac{1}{2}$, and $14\frac{1}{2}$ days foetal age in normal mice.

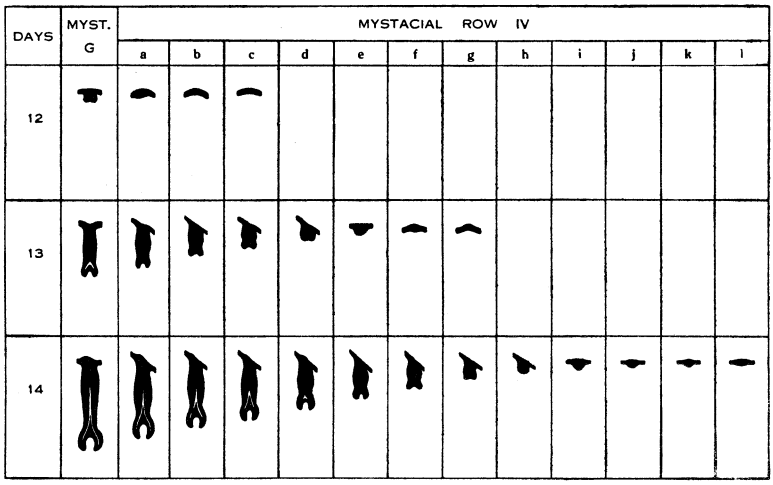

Fig. 8.—Longitudinal sections of the developing follicles of certain mystacial vibrissae at $12\frac{1}{2}$, $13\frac{1}{2}$, and $14\frac{1}{2}$ days foetal age in normal mice.

relationship between follicle length at $14\frac{1}{2}$ days and the length of the tactile hairs at birth ($r = 0{\cdot}96$) when deciding between members of a group which commence development almost simultaneously. For example, postoral *a* and *b* could not be differentiated on histological examination but length measurements at birth showed

that the dorsal member of the pair, postoral *a*, was slightly but consistently longer than *b*. This indicated that *a* preceded *b* very slightly in time of initiation. Table 11 therefore shows the order of initiation of the vibrissae, the measurements used to form the list, and the percentage incidence of each vibrissa in tabby males and homozygous ragged mice.

TABLE 11

CERTAIN VIBRISSAE OF THE MOUSE ARRANGED IN THE ORDER IN WHICH THEY COMMENCE DEVELOPMENT

Some results from Tables 1, 2, 4, 9, and 10 are included to illustrate why this sequence was chosen and to show the incidence of each vibrissa in tabby male and homozygous ragged mice

Vibrissa	Length (mm) of Follicles at:				Percentage Incidence of Vibrissae in:	
	12 Days	13 Days	14 Days	Birth	Tabby Males	Homozygous Ragged Mice
1. Mystacial G	0·088	0·360	0·664	2·18	100·0	100·0
2. Mystacial row IV *a*	0·056	0·300	0·568	1·71	100·0	93·7
3. Supra-orbital *a*	0·052	0·256	0·500	1·56	100·0	91·0
4. Postorbital	0·040	0·172	0·328	1·07	1·6	75·0
5. Mystacial row IV *b*	0·036	0·220	0·468	1·33	100·0	3·1
6. Mystacial row IV *c*	0·028	0·172	0·392	0·96	100·0	0
7. Supra-orbital *b*	0·020	0·100	0·260	0·75	56·8	0
8. Mystacial row IV *d*	—	0·116	0·332	0·73	100·0	0
9. Postoral *a*	—	0·080	0·220	0·49	75·4	0
10. Mystacial row IV *e*	—	0·076	0·264	0·45	100·0	0
11. Postoral *b*	—	0·088	0·220	0·38	0	0
12. Mystacial row IV *f*	—	0·048	0·192	0·32	100·0	0
13. Mystacial row IV *g*	—	0·036	0·140	0·21	100·0	0
14. Inter-ramal *b*	—	—	0·132	0·35	100·0	0
15, 16. Inter-ramals *a* and *c*	—	—	0·112	0·23	8·2	0
17. Ulnar–carpal	—	—	0·112	0·18	100·0	0
18. Mystacial row IV *h*	—	—	0·092	0·20	100·0	0
19. Mystacial row IV *i*	—	—	0·072	0·20	100·0	0
20. Ulnar–carpal *c*	—	—	0·068	0·14	45·9	0
21. Mystacial row IV *j*	—	—	0·056	0·19	100·0	0
22. Ulnar–carpal *b*	—	—	0·052	0·05	2·7	0
23. Mystacial row IV *k*	—	—	0·044	0·19	100·0	0
24. Mystacial row IV *l*	—	—	0·032	0·19	100·0	0

IV. DISCUSSION

The difference in the times of action of the two genes is very striking. In the case of the homozygous ragged mouse, no follicle commencing after $12\frac{1}{2}$ days foetal age produces a functional fibre with the result that the body is almost completely naked, possessing only those fibres produced by the $12\frac{1}{2}$-day vibrissae (note the almost perfect analogy between the incidence of vibrissae in the *RaRa* mouse (Fig. 5) and the follicles of the $12\frac{1}{2}$-day normal foetus (Fig. 9)). Slee (1957) has

shown that the skin of homozygous ragged mice has a lowered density of follicles which rarely carry hairs. Our results show that hair eruption occurs only in those follicles which commence growth before $12\frac{1}{2}$ days foetal age.

On the other hand, tabby does not have a precisely timed gene action. The two most outstanding illustrations of this fact are listed below:

(1) The mystacial vibrissae which are initiated in continuous sequence between 12 and $14\frac{1}{2}$ days foetal age are hardly influenced by the tabby gene.

(2) The postorbital vibrissa, which is the fourth earliest in the time sequence, is almost invariably influenced by the tabby gene, whereas ulnar-carpal *a*, the sixteenth in the series, is almost invariably present.

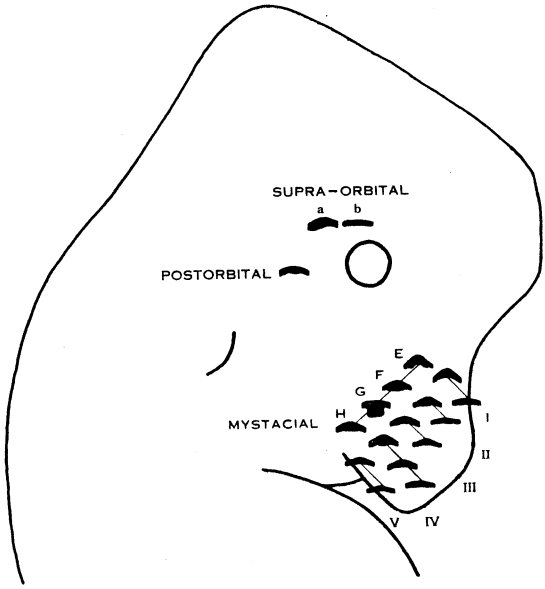

Fig. 9.—The vibrissa follicles which are present in a $12\frac{1}{2}$-day normal foetus.

Thus these data give no support to the Falconer, Fraser, and King (1951) theory of action of the tabby gene (Fig. 2). The data rather indicates a localized action, a theory which is further supported by the phenotype of the tabby female. In these mice, the coat is a mosaic of normal and dark areas, the latter areas showing a fibre array similar to the whole coat of the hemizygous male (Falconer, Fraser, and King 1951). In this case normal skin and "tabby skin" are alongside each other, no doubt due to a threshold for normality being reached in some areas, not in others. Adjoining areas of skin thus demonstrate an independence in their reaction to the tabby gene, similar to that shown by the different groups of vibrissae. The correlation between heavy striping and greater loss of vibrissae in tabby females could simply mean that, in heavily striped mice, a band of tabby

skin is more likely to include a vibrissal site than in mice where striping is of low intensity.

An examination of the tabby male phenotype (Fig. 5) reveals that, although there is no time-relationship between groups of vibrissae, time of initiation of follicles is important within groups. The pertinent observations are set out in Table 12. It can be readily seen that within any group of vibrissae affected by the tabby gene, the incidence of vibrissae follows the order of initiation of the follicles.

TABLE 12

ORDER OF FOLLICLE INITIATION WITHIN VIBRISSAL GROUPS IN THE TABBY MALE PHENOTYPE

Group	Order of Development	Percentage Incidence in Tabby Males
Supra-orbital	1. Supra-orbital *a*	100·0
	2. Supra-orbital *b*	56·8
Postoral	1. Postoral *a*	75·4
	2. Postoral *b*	0
Inter-ramal	1. Inter-ramal *b*	100·0
	2. Inter-ramal *a* and *c*	8·2
Ulnar–carpal	1. Ulnar–carpal *a*	100·0
	2. Ulnar–carpal *c*	45·9
	3. Ulnar–carpal *b*	2·7
Mystacial	1. Row I *a*	100·0
	2. Row I *b*	100·0
	3. Row I *c*	100·0
	4. Row I *d*	92·0
	1. Row II *a*	100·0
	2. Row II *b*	100·0
	3. Row II *c*	100·0
	4. Row II *d*	90·0

Another observation from Figure 5 is that there is an apparent gradient of action, from anterior to posterior, anterior mystacials being least affected while the posterior groups (postorbital and postoral) are severely depleted. Further evidence of an anterior–posterior gradient comes from the greater reduction of the growth rate of the vibrissal hairs at the postorbital and postoral sites.

The following model is therefore suggested for the action of the tabby gene and its mimic gene, crinkled. In the homozygous or hemizygous genotypes (*Ta*·, *TaTa*, *crcr*) a substance needed for both initiation and growth of follicles is produced at a slower rate than normal. This substance has a threshold level which must be present for initiation of follicles. The supply is depleted by follicle growth and, as it is produced locally in the skin, the earliest developing follicles of a group

have an advantage. At 12 days, when follicles commence growth, this substance has a gradient of concentration—high anterior to low posterior.

The result is that in the period 12–17 days, certain vibrissae are the only follicles to grow. The most anterior group (mystacial) is untouched (the most posterior (postorbital) is almost invariably affected) while groups of vibrissae in intermediate locations show a variable amount of loss. In these cases, incidence within a group is closely related to the time at which each member follicle commences development.

By 17 days foetal age, sufficient of the substance has been produced over the body region so that a wave of follicle growth commences and new follicles are initiated until 20 days when the supply of the substance again falls below a critical level. It is interesting to note that the postorbital follicle, which is initially depressed, appears to make a belated effort to produce a vibrissa during this second wave of follicle growth. In the same way many of the hairs in the coat of the hemizygous tabby male may be aberrant guard hairs with a retarded time of development. This may explain Falconer's (1953) observation that the internal structure of the coat hairs of the tabby males is not typical of the awl–auchene group.

One of the most interesting features of these results is that in one case ragged is a timed gene, i.e. it blocks the development of all vibrissae which commence to grow later than 12½ days foetal age. In the other case, each group of vibrissae reacts to the presence of the tabby gene in a manner independent of time, but possibly associated with chemical or physical forces related to the position of each group.

Dun (1958) and Dun and Fraser (1959) have shown that the polygenic system, which controls the number of vibrissae in normal mice, does not affect each group of vibrissae uniformly. The evidence, from selection experiments on the number of vibrissae in individual groups, suggests that there is a separate set of genes governing the development of each group of vibrissae. This situation, although surprising, is understandable when considered in relation to the developmental study. Regional forces are such that genes affecting one group of vibrissae need not necessarily influence any other group. The data from the ragged mice suggests that groups are not completely independent and one would therefore expect some degree of overlap between genetic systems. The accumulation of further data may enable such an overlap to be demonstrated.

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