

**GROWTH AND STRUCTURE OF THE COAT IN STRAINS OF
LARGE AND SMALL MICE**

By

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**Thesis submitted to the Faculty of Science of
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Doctor of Philosophy.**

**Institute of Animal Genetics, Edinburgh
July 1958.**



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Introduction

A detailed study of the growth of hair and structure of the coat, with particular reference to the growth of the body was conducted in mice with two main objects in view.

Firstly, very little is known about determinants of growth of hair and the extent to which hair-growth reflects body-growth. The genetic aspect is of interest here as it provides information regarding the extent to which growth of body and hair are controlled by the same genes. This was investigated by a comparison of selected strains because differences between them are genetic and when selection for body size was made, correlated characters too responded. It was important that the strains had a similar origin and that their unselected control, representative of the foundation population, was also included in the comparison. To enhance the value of this study two such comparisons were made with two different stocks of mice.

The second object concerns adaptation to environmental temperature. As heat is lost throughout the body surface the chief function of mammalian hair becomes conservation of body heat. This is clearly exhibited by the thick coats of arctic animals in comparison to the thin coats of tropical ones (Scholander 1955), so that heat loss always balances heat production. But the need for conservation of heat is also influenced by body size. Bergmann (1847) stated that warm blooded species in the colder northern climates tend to be larger in size than do comparable species in the warmer tropical regions. This is supported by the observations of Laurie (1946) in the house mouse living in different habitats. Mice living in cold stores of meat at an average temperature of -10°C were markedly heavier than those under normal environments. Their greater weight was

due to an increase in size, not to excess fat. According to the well-known hypothesis that heat loss $\propto$ weight^{2/3}, a larger animal is expected to lose proportionately less heat than a smaller one. On this assumption small mice ought to have thicker coats than large mice living under similar conditions, and the problem was to find out whether they had adapted themselves to their greater need for conservation of heat in this way. The mouse house was maintained at an average temperature of 20°C that was much lower than the body temperature of 34°C and is likely to encourage loss of heat from the body. Brody (1945) suggests that hair provides the physical aspect of temperature regulation in homeotherms and the chemical aspect is maintained by metabolic changes. Coat characters determine heat tolerance, defined as the ability of an animal to maintain normal physiological processes despite high environmental temperature that has been of great practical value in selecting temperate livestock suited to live in the tropics. Probable differences in heat tolerance between large and small animals are attributed to differences in insulating value of the body and to possible deviations from an exact relationship between heat production and surface area (F.A.O. 1955). An important difference between mice living in separate environments that had a bearing on thermoregulation was detected by Herter (1936) when a mouse had a choice of several temperatures, the one it selects to rest is called the thermotactic optimum. Herter reported that the thermotactic optimum of 37.36°C for wild mice was significantly higher than that of 34.63°C for laboratory albino mice. Later Herter (1938), Herter and Sgonina (1938) found that wild mice had denser fur on the belly and a thinner epidermis than laboratory albino mice. On this evidence Grüneberg (1952) suggests that the thermotactic optimum is determined by the density of fur and thickness of epidermis and is an expression of some factor connected with thermoregulation.

Fraser (1951a) made a similar study to the one presently undertaken, but in much less detail. He compared 4 strains, two being unselected inbreds, one a selected large strain and one a selected small strain of different origin. He found significant differences in some characteristics of their hair, but it was not clear in what way the differences were connected with body size. The present work extends and amplifies that of Fraser.

Though very little is known about factors controlling growth of the coat, the processes of development, histology and morphology have been studied in great detail. A brief review of the literature on the important aspects of hair that follow will help in interpreting the results of this study.

Tissue culture experiments of Hardy (1951) have shown that the skin of mouse embryos as young as 12 days is determined for body hair follicle formation. The cause of initiation of hair follicles is uncertain, for neither the circulating blood nor nervous stimulation was essential for follicle formation. Hair is produced in a cyclic manner and is periodically shed. Growth of hair occurs during Anagen (Dry 1926). Rapid mitotic divisions occur in the cells of the Malpighian layer of epidermis and extend as solid downgrowths into the dermis and adipose layers of the skin to form the hair follicles. The lower end of each cord becomes hollow and encloses dermal cells forming the dermal papilla. Thereafter this remains with the follicle during the subsequent hair generations. The dermal papilla is believed to induce germinal epithelium to produce hair and controls follicle activity at all stages of differentiation and growth. It is continuous at the lower end with the connective tissue sheath surrounding the follicle. The bulb, formed by a continuation of the external sheath surrounding the

dermal papilla portion of the follicle, becomes the site of active mitosis as this cord of epidermal cells representing the follicle grows into the deeper layers of the skin. The matrix, a cap of basal epidermal cells enclosing the upper portion of the dermal papilla, by a high rate of protein synthesis and mitosis, forms an elongated cone called the internal sheath. This pushes its way upwards through the follicular cord, but never extends beyond two thirds the length of the follicle. From outside inwards the internal sheath is composed of Henle's, Huxley's and cuticular layers. It probably serves to support the hair cortex in the lower part of the follicle. At this time a decrease in mitosis and a corresponding accumulation of glycogen occurs in the external sheath. The follicle bulb is deep in the thickened adipose and sometimes even against the panniculus carnosus muscle. In the latter part of Anagen hair proliferation begins. The bulb pushes keratinised cells upwards through the internal sheath to form the hair. The hair gradually breaks through the tip of the internal sheath, then through a part of the original cord and emerges through the follicular orifice, which had formed earlier. The hairs emerge pointing posteriorly because about 3 days after birth the dorsal follicles attain a slope of approximately 30° with the surface (Chase and Montagna 1951; Chase, Rauch, Smith 1951; Chase, Montagna, Malone 1953, Chase 1954). During anagen changes in the relative thickness of the different layers of skin also occur. The epidermis, dermis and adipose layers thicken. The dermis increases about one half due to an increased blood supply and tissue fluid. The adipose increases by about two or three times its original thickness due to great accumulation of fat in its cells. The skin, extending from epidermis to panniculus carnosus muscle layer measures 630μ , the follicle 1116μ and adipose 430μ (Chase, Montagna, Malone (1953); Slee (1954 and 1957)). Anagen lasts for about

17 days during the growth of the first coat (Dry 1926). Glycogen, believed to be a store of energy for active tissues when the circulation is inadequate, was found in the external root sheath of many mature active hair follicles but absent in resting ones (Hardy (1952) and Shipman (1952)). Also a strong alkaline phosphatase reaction in the dermal papilla during the active phase was noticed by Hardy (1952) that was possibly concerned in the transport of organic substances between the papilla and hair matrix.

Catagen is a transitional period of two days for the completion of the hair base and club (Dry 1926). Growth of hair stops by cessation of matrix cell proliferation, the club hair formation occurs and the dormant hair germ is set aside for the next generation. At the base of the hair is formed a keratinised brush like anchoring club which is surrounded by a capsule of partially keratinised cells. The club region shrinks and the hair moves up the follicle until its base lies below the sebaceous gland about 250μ below the surface of the skin. The hair follicle shortens to about one third its previous length and is confined to the dermis and epidermis. (Chase, Montagna (1951); Chase, Rauch, Smith (1951)). The important factor in the ascent of the hair is the reduction in length of the external sheath resulting from the diminution in number and size of its cells (Wolbach 1951). The dermis and adipose too shrink to their resting states. The skin is approximately 101 to 414μ thick and the adipose 315μ at the point of maximum thickness (Slee 1954). No trace of glycogen or alkaline phosphatase was found (Chase 1954).

Telogen is the resting stage (Dry 1926). The hair is anchored only by its club in the capsule just below the duct of the sebaceous gland. The lower end of the external sheath called the 'germ' is in contact with the resting dermal papilla (Chase 1955). The skin is very thin and is

about 195μ of which the adipose is 78μ (Slee 1954). Telogen of the first coat lasts about 10 days.

Hair is composed of a central medulla, outer cortex and a cuticle. The medulla is made up of regularly arranged cells representing cornified epithelial elements. The cortex surrounding the medulla is formed of elongated, fusiform and usually shrunken cells coalesced into a rigid almost homogeneous hyaline mass. The cuticle is the outermost covering of hair composed of thin horny transparent plates of various shapes called cuticular scales. Pigment granules responsible for the colour of the hair are distributed within and among the hair spindles (Hausman 1924). There are 4 main types of hairs in the coat of the mouse called Guard hairs, awls, auchenes and zig-zags. In practice, however, awls and auchenes are seldom distinguished, because they are very much alike. Guard hairs are the longest hairs in the mouse coat and project well above the rest of the coat. They are the least abundant forming only 2% of the coat, but are uniformly distributed and probably sensory in function (Dry 1926). They vary from 0.9 to 1 cm in length of which the tip is more than 0.25 cms. In cross section the broad part of the hair appears circular or oval with a thick cortex and narrow medulla with usually two longitudinal rows of air cells (Dry 1926). Awls are shorter than guard hairs, but are the thickest type of hair in the coat. They are about 0.6 to 0.7 cms long of which the short tip is 0.03 to 0.04 cms. The cortex is thin, but the medulla is broad with about 4 rows of air cells at the broad part (Dry 1926). Auchenes are about the same length as awls, but have a construction at about $2/5$ ths the length of the hair from the apical end. They have only about two rows of air spaces (Dry 1926, Fraser 1951a). Zig-zags are usually shorter than awls or auchenes and have three or four bends along the length

of the hair. Only a single row of air cells are present in the straight parts. At the constriction, the air space is lacking and the hair is solid (Dry 1926, Slee 1954). Sometimes hairs intermediate between the 4 groups occur, but they are infrequent (Dry 1926). Guard hairs are the earliest to start development. Their development commences from the 14th to 17th day of foetal life, awls and achenes from the 17th day until birth, and zig-zags mainly after birth (Falconer, Fraser, King 1951).

The mouse has several cycles of hair during its life. From the second cycle onwards they appear as bilaterally symmetrical waves at different times in different parts of the body. All except guard hair follicles may retain hairs of the previous generation. Zig-zags are about the best retained hairs. Dry (1926) reported that in later hair generations follicular function is capable of being altered to produce a hair different to that of the earlier generation. This occurs mainly in the zig-zag to guard hair order; and so, fewer zig-zags will be produced in later generations probably counterbalancing the number retained. Dry (1926) found that mainly zig-zags conserve body heat by being able to trap a volume of air between its laminations and holding it motionless. Insulating properties in mice also depend upon the length and thickness of hairs, retention of completed hairs by follicles, number of hair follicles, frequency of hair types, frequency of waves of hair growth, and thickness of skin.

The present study deals with the following aspects of hair.

1. The sources of variation within strains in final length of first coat guard hairs.
2. A comparison of strains in respect of
 - (i) Final hair lengths of first and second coats
 - (ii) Growth of hairs of first and second coats

- (iii) Thickness of hairs of first coat
- (iv) Frequency of hair types of first coat
- (v) Periodicity of hair cycles

Evidence from the present study will unravel some important differences in coat characters existing between large and small mice. The extent to which these determine the insulating properties of the mice is only suggestive, because an exact measure of body insulation in mice is not yet available.

Materials and Methods

The two stocks of mice used for this comparative study each consisted of a pair of strains of contrasting body size and differing in body-growth with their unselected control. They were designated as the N stock with a large strain NF, control NC and small strain NS, and the C stock with a large strain CFL, control JC and small strain CFS (Figs. 1, 2, 3 and 4).

The N stock was constituted by a 4 way cross of the inbred strains CBA, RIIL, C57 and A (Falconer 1953, and 1955). The C stock (Falconer and Robertson 1956) was formed by crossing 4 unrelated outbred strains, a crossbred derived from Goodale's and MacArthur's large strain (Falconer and King 1953), a stock selected for high lactation (Bateman 1954), and two other stocks of mutants.

Selection in the N stock was based on body weight at six weeks and in the C stock depended on growth from three to six weeks.

The N stock mice of the large, control and small strains used belonged to about the 41st, 29th and 34th generation respectively. The approximate degree of inbreeding existing within the strains calculated theoretically was 52% for large strain, 40% for the control and 45% for the small strain. All mice of the C stock that were utilized belonged to about the 20th generation of the respective strain. The average degree of inbreeding within strains was 19% for the large, 22% for the control, and 19% for the small.

The mean weight of approximately 12 animals per strain at 6 weeks was:--



FIGURE 1. Large, control and small mice of the N stock.



FIGURE 2. Large, control and small mice of the C stock.

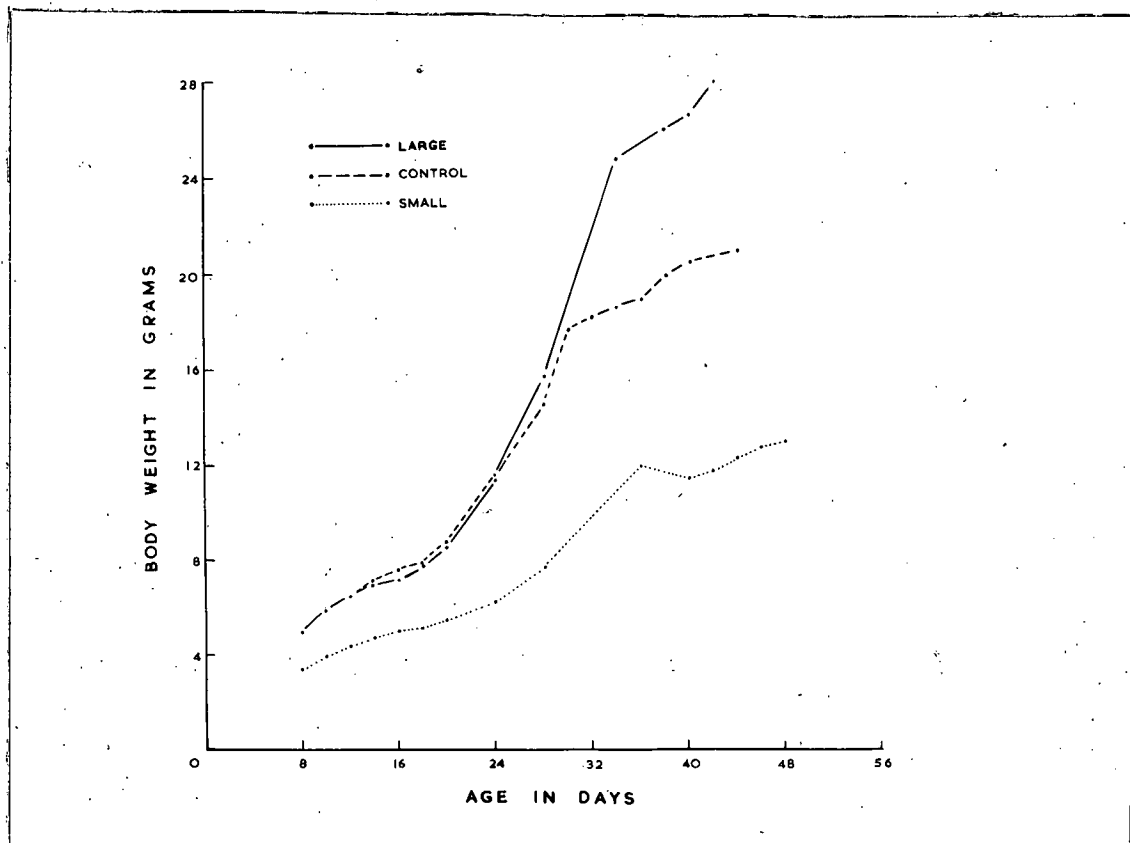


FIGURE 3. Body-growth of large, control and small mice of N stock

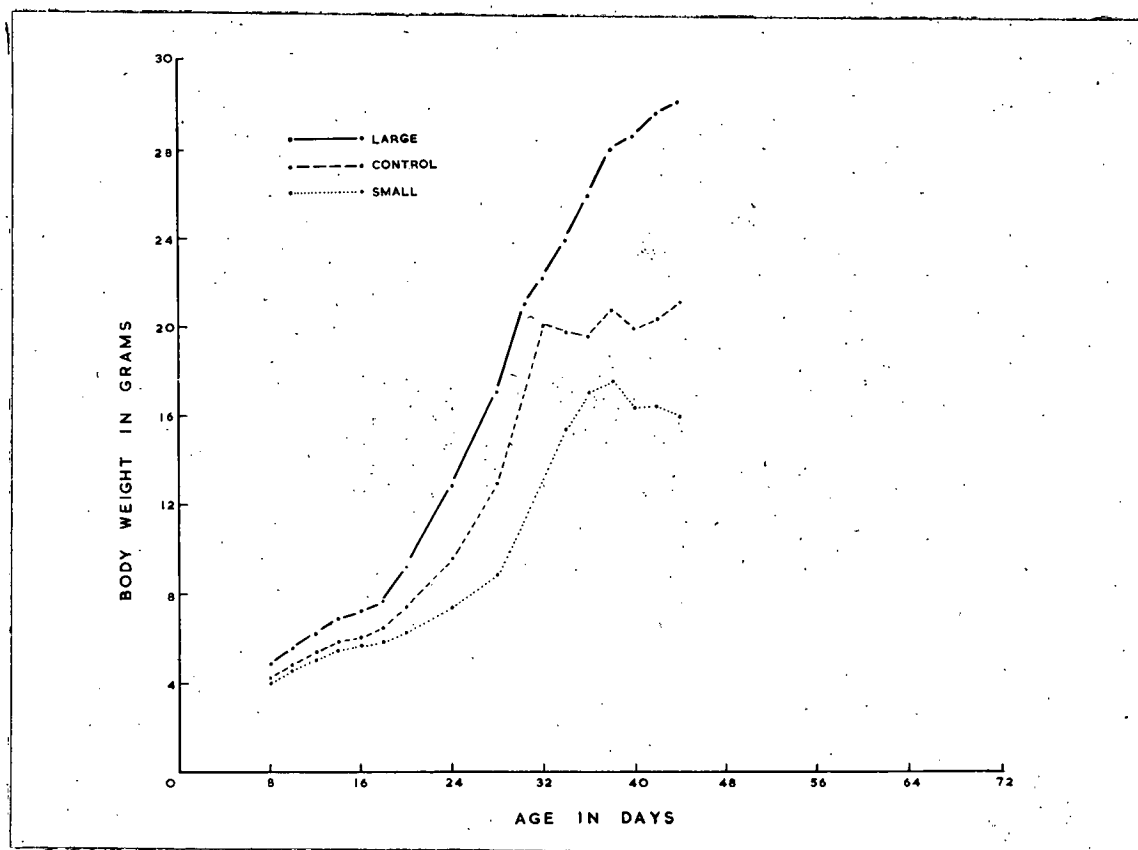


FIGURE 4. Body-growth of large, control and small mice of C stock

NF 28.01 gms.	NC 20.17 gms.	NS 11.81 gms.
CFL 29.93 gms.	JC 20.34 gms.	CFS 16.42 gms.

There is a range of about 15 gms between the large and small strains.

The mice used were drawn from the first or second litter, with only a single litter being used per mating. Usually two mice were chosen from a litter and as many matings were utilized in the generation to include the maximum variability present within the strain. Sometimes animals from the subsequent generation were used to make up the required number. It also happened that a single mouse from a mating was occasionally used due to unavoidable circumstances. In no instance was the litter size standardised. Samples of hair were plucked from the neck region with a pair of forceps at different ages according to the experiment. Details of measurements will be described in the appropriate chapters. Only male mice were used for studies on hair. Whenever it was necessary to distinguish two coats, the existing coat was bleached in coloured mice and dyed in albinos, so that it provided a contrast of colour with the new coat (Figs. 5 and 6). The bleach used was 'Oreal Super Bleach' devoid of ammonia manufactured by Golden Limited, London. The dye was 'Inecto Cream-black' containing 0.1% phenyl diamine w/v manufactured by Rapidol Ltd. These preparations are commonly used by hairdressers. The bleach was mixed with 20 vol. hydrogen peroxide, and the black dye with 30 vol. hydrogen peroxide to a fine paste and then applied on the neck region of mice. The mice were allowed to remain for about half an hour, washed with soap and water and dried with a cloth. In the case of black or darkly coloured mice a better result was produced by a second application

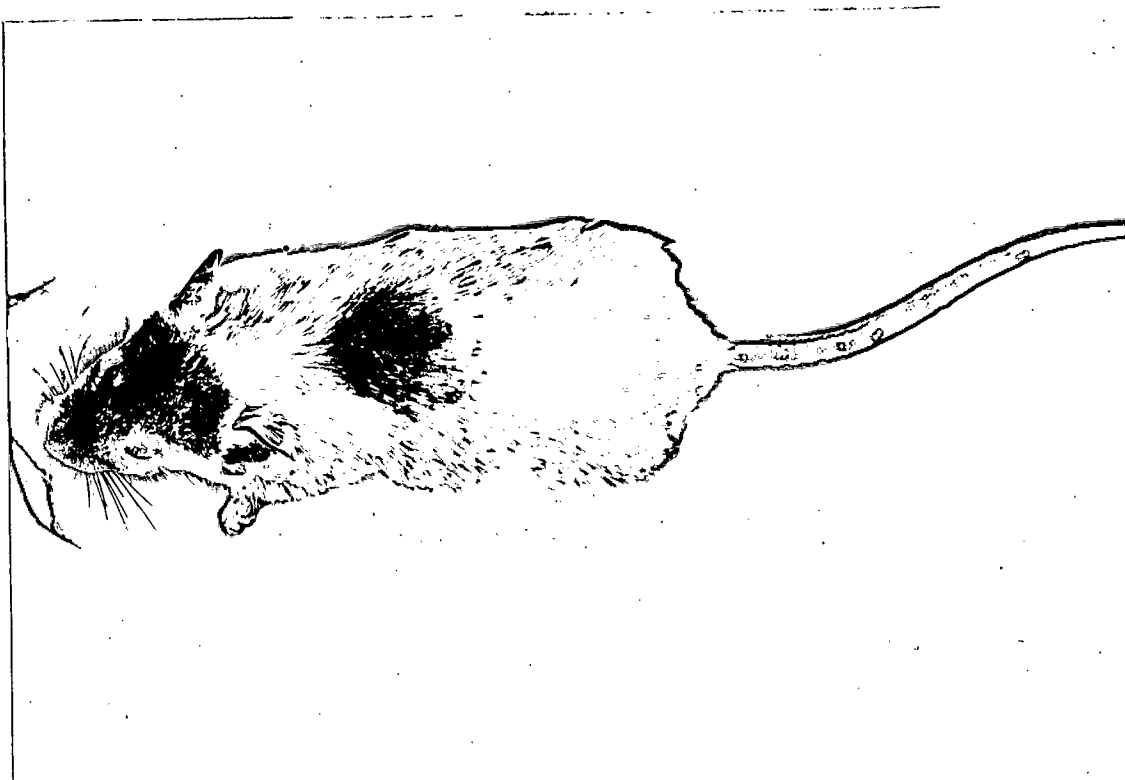


FIGURE 5. A bleached mouse beginning to grow a new coat



FIGURE 6. A dyed mouse with a fully grown new coat in the neck region, beside a normal albino mouse.

11.

of bleach shortly after the first, combined with a prolonged interval for action. Olive oil was applied for a few days subsequent to treatment if the skin appeared dry.

1. HAIR LENGTH

Studies on the length of hair includes the following aspects:-

- (1) Sources of variation occurring within strains affecting the final length of hairs.

Comparison of strains for:-

- (2) Hair-lengths after cessation of growth of the first and second coats.
- (3) Rate of increase in hair-length during growth of the first and second coats.

Method

All these studies including that on hair thickness were conducted on the same hairs obtained by sampling twelve male mice of each strain in the N and C stocks. Hairs from the neck region were plucked with forceps and placed on a drop of glycerine albumen contained on a labelled glass slide. The hairs on the right dorsal side provided the samples for the first coat and those on the left dorsal side for the second coat.

Hair sampling for the first coat was begun on eight day old animals. At every sampling the weight of the mouse was recorded. Samples were taken at two day intervals until the twentieth day. The last two samples of the first coat were taken on the twenty-fourth and twenty-eighth day. After obtaining the latter, the neck region was either bleached in coloured mice or dyed in albinos. The mice were then examined every other day and as soon as the eruption of the second coat was noticed, sampling was begun and continued at the same frequency as for the first coat. 5 guard hairs, 10 awls and 10 zig-zags were chosen at random from each sample under the low-power binocular microscope and stretched on the slide with a smear of glycerine albumen (Figs. 7 and 8). Their lengths were then measured in

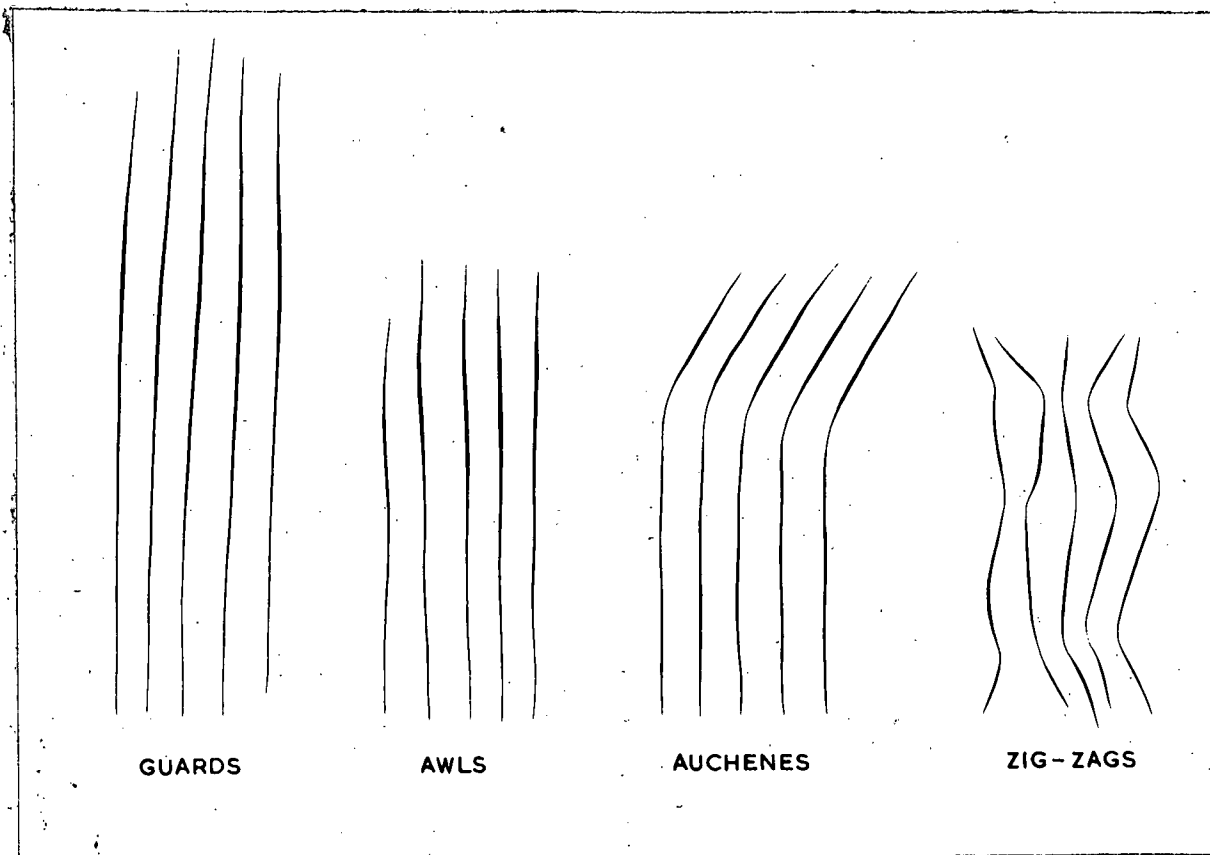


FIGURE 7. The external appearance of the hair types in a mouse coat

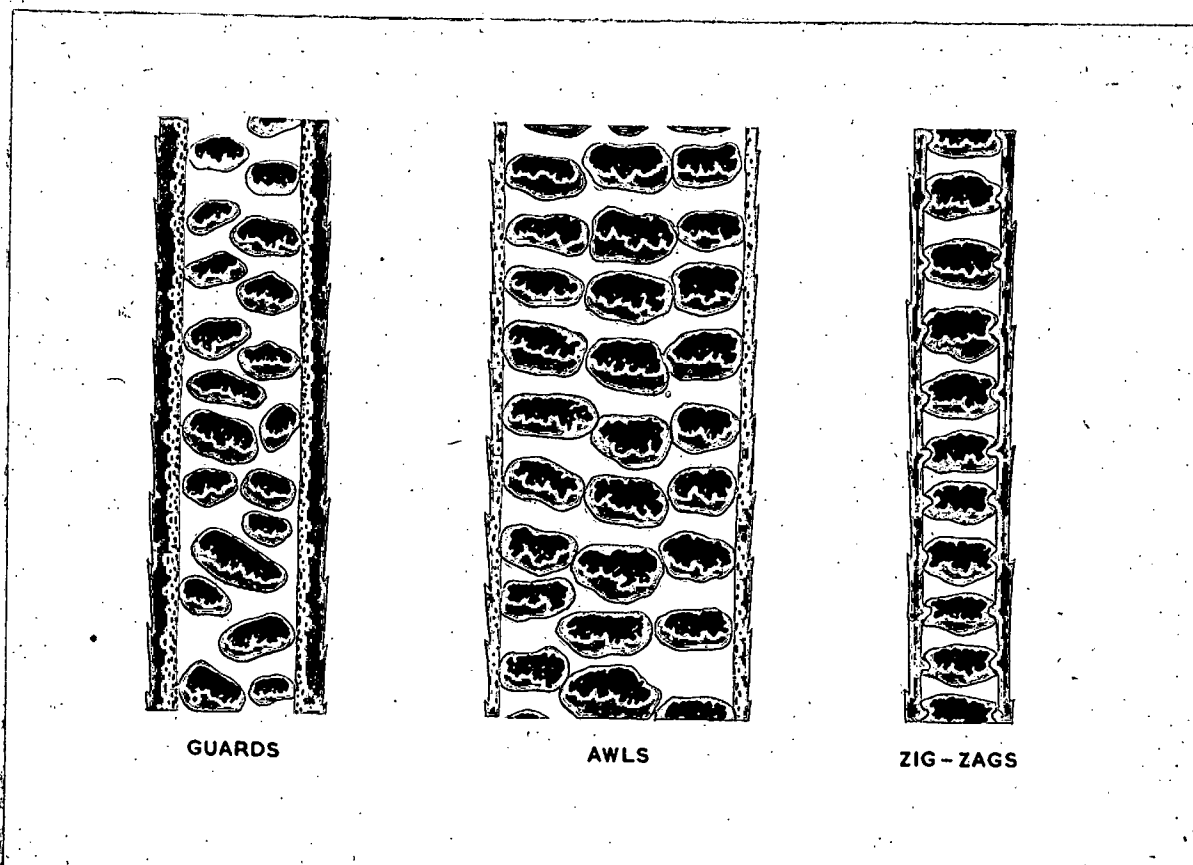


FIGURE 8. The internal appearance of the hair types

units of millimetres at this magnification with a calibrated eye-piece.

A graph of mean length of hair type in mm versus age in days was plotted for each strain separately (Figs. 9 and 10). This was only possible for the first coat as the second coat appeared at variable intervals.

Results.

In all strains growth of all hair types of the first coat was linear from the 8th day of age until about the 16th day (Figs. 9 and 10). Thereafter growth falls rapidly and ceases by about the 18th day. The resting period that follows completes the cycle.

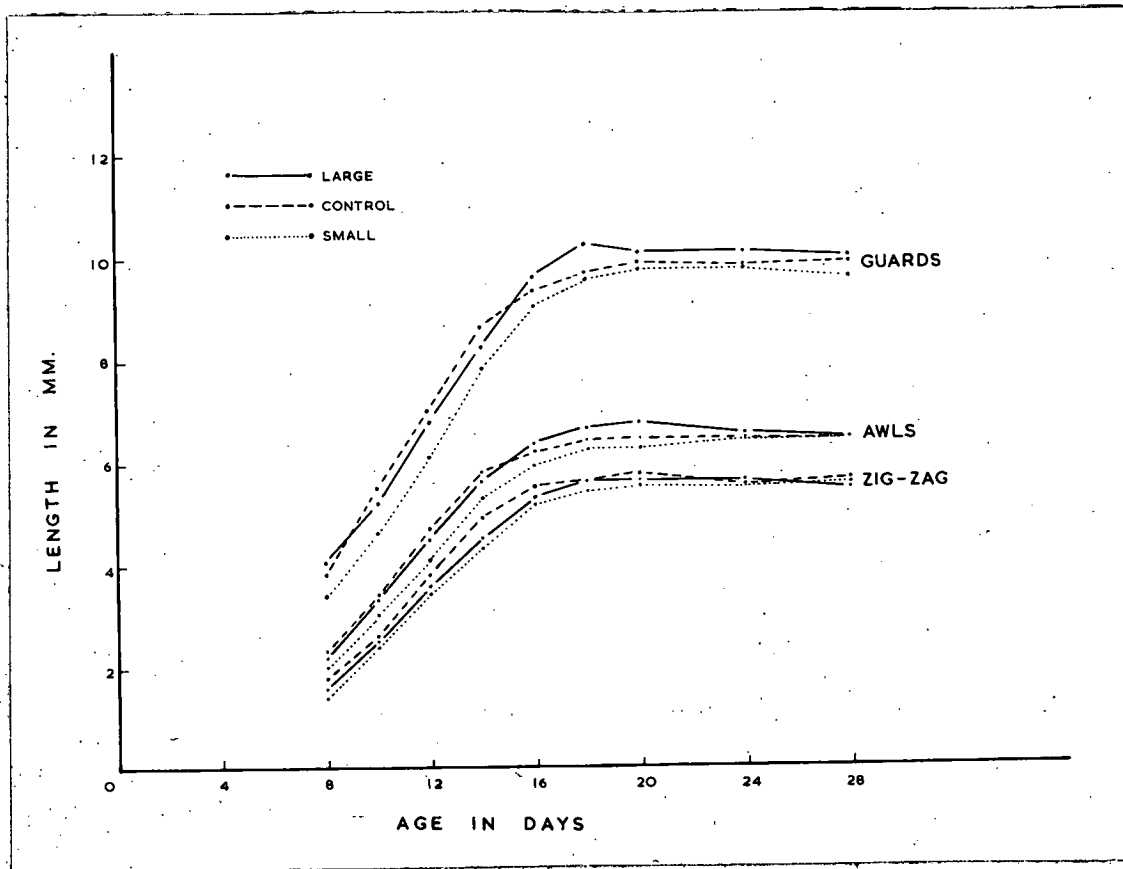


FIGURE 9. Growth of the mouse coat in the N stock

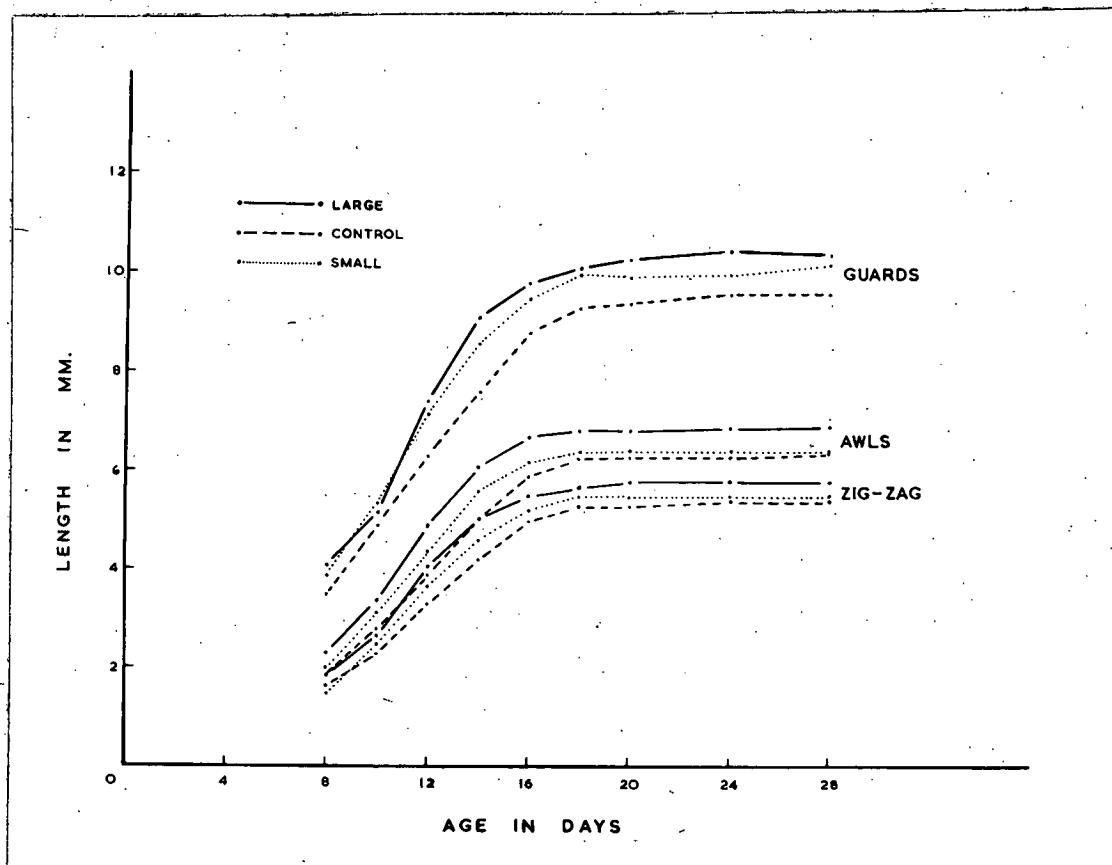


FIGURE 10. Growth of the mouse coat in the C stock

(1) Sources of variation affecting length of hair within strains

The sources of variation causing differences in length of mice hairs within the six strains were investigated. The most important indication of their magnitude will be evidence of differences between animals that may be genetic in origin. The influence of the following sources of variation was investigated.

- (i) Differences between hairs of a single animal
- (ii) Technical differences in taking three samples from an animal
- (iii) Differences between individual mice
- (iv) Differences between families

Method

This study was restricted to only guard hairs drawn from samples obtained on the 20th, 24th and 28th days of age when growth of the first coat was known to have ceased (Figs. 9 and 10). The lengths of 5 guard hairs drawn from a sample were measured in millimetres. In a few instances it was not possible to make up 15 hairs per animal due to lack of sufficient numbers though allowance was made for this in the calculation. All strains of the N and C stock were examined.

An analysis of variance was performed on these measurements and was extended to estimate the components of variance based on the hierarchical classification. The complete analysis of one strain is given in Table 1 to show the method.

TABLE 1/

TABLE 1.

Analysis of Variance for Components in NF strain

Sources of Variation	D.F.	S.S.	M.S.	Composition of Mean Sq.	Components of variance
Between litters	5	59.63	11.93 ^{xx}	$\sigma_W^2 + 4.88\sigma_S^2 + 14.66\sigma_B^2 + 29.32\sigma_L^2$	0.40
Between animals	6	7.85	1.31	$\sigma_W^2 + 4.88\sigma_S^2 + 14.66\sigma_B^2$	0.03
Between samples	24	21.90	0.91	$\sigma_W^2 + 4.88\sigma_S^2$	0.07
Within samples	140	83.64	0.60	σ_W^2	0.60
Total	175	173.02			

All the other strains were analysed in the same way. The results of the analyses are given in Table 2. The total variance in the first column is the sum of all the components and is given in units of mm^2 . The components are given in percentages of the total.

TABLE 2.

Components of Variance of the Six Strains

	Percentages of total variation				
	Total variation	Bet. families	Bet. animals within litters	Bet. samples	Within samples
NF	1.10	36 ^{xx}	3	6	55
NC	1.85	71 ^{xx}	0	4 ^x	25
NE	0.87	3	0	28 ^{xx}	69
CFL	0.95	20 ^x	0	11 ^x	69
JC	2.28	74 ^{xx}	2	2	22
CFS	0.66	18 ^x	0	17 ^{xx}	65

Explanation - 'x' denotes significance of $P < .05$ and 'xx' is $P < .01$

The position of sampling was randomised.

Next the effect of sampling on the 20th, 24th and 28th day was considered within each strain and found to be insignificant ($P > .05$). Hence the variation between samples was used as the error term for testing the significance of the variation between animals belonging to the same litter.

Conclusions.

The results of the six strains were on the whole fairly uniform. They indicate that variation within samples accounts for a large proportion of the total, as hairs in a mouse coat differ widely.

In the majority of strains there are real differences between the three samples obtained from a mouse that can be attributed to a faulty technique and to a possible irregularity of the coat. When hairs are plucked at sampling they may break off at different levels from the skin depending on the force and its point of application. However this does not account for very much of the variation.

The most interesting fact was that there appears to be no real difference between mice of the same litter, suggesting that there is no evidence of genetic variation in the final length of guard hairs. Selection for this character will hence produce little or no effect. This also indicates that there is no environmental variation either between litter mates. However in the next section dealing with a comparative study of hair length between selected strains, there are differences that can only be genetic, but this is very small and unlikely to be detected in individuals of the same strain.

Large significant differences exist between families in most strains that are probably due to environmental effects. These effects were not detected in mice from the same litter, but was marked in animals that were from different mothers being separate families. This suggests that this character is probably maternal in origin, being also influenced by genetic differences present between

mothers. The maternal effects may be pre- or post-natal as guard hairs are initiated from the 14th to 17th day of gestation (Falconer, Fraser, King 1951) and complete growth by about the 18th day of age. This maternal effect can be regarded as a possibility although it seems unlikely as an explanation, because it was not possible to know from the present experiment whether differences in hair length were present in mice drawn from different litters of the same mother.

(2) Final hair-lengths of first and second coats

In the previous study the detection of genetic control of length of hair in individual mice based only on first coat guard hairs was unsuccessful, probably because this effect was small. Hence in the present section an attempt is made to estimate it on a wider basis of differences between strains and including all hairs of the coat.

A comparison of strains for length of hair after cessation of growth of the first and second coats was conducted within stocks. Any evidence of differences between selected strains is regarded as genetic in origin. The length of the coat also provides information about the insulation provided for the animal.

Method.

The final length of the first coat was considered as the mean of the measurements of hairs sampled on the 20th, 24th and 28th day of age (Figs. 9 and 10). Similarly the last three samples of the second coat obtained at the same frequency provided a measure of the second coat. Thus every animal provides 3 samples for each coat. 5 guard hairs, 10 awls and 10 zig-zags were measured from such a sample of hair.

Results.

Differences between strains are small. The mean length of hairs of the six strains were as follows:-

TABLE 3/

TABLE 3.Final length of hairs in mm.

Strains	Guard hairs		Awls		Zig-zags	
	1st Coat	2nd Coat	1st Coat	2nd Coat	1st Coat	2nd Coat
NF	9.9818	9.4311	6.5311	6.5208	5.5240	5.6660
NC	9.8155	9.8472	6.4211	6.7039	5.5936	5.8956
NS	9.6694	8.6317	6.3286	6.1144	5.5260	5.3906
CFL	10.4083	9.8194	6.7990	6.7820	5.8005	5.7589
JC	9.5370	9.2080	6.3290	6.4170	5.3772	5.6194
CFS	10.0367	9.1458	6.4140	6.1700	5.4933	5.3031

Guard hairs are longer than awls, which are in turn longer than zig-zags. The large strains of the N and C stocks have nearly all hair types longer than their respective small strains. The magnitude of these differences expressed in mm are given below in Table 4.

TABLE 4.Differences in length of hairs between selected strains

Explanation - When the length of hair of the large, control and small strains of mice are in the same descending order, positive signs are attached to their differences. If it is in the opposite direction this is indicated by a negative sign. This applies to all subsequent tables.

A single 'x' denotes $P < .05$, double 'xx' is $P < .01$, treble 'xxx' is $P < .001$.

Strain differences	Guards	Awls	Zig-zags	
NF-NS	0.3124 ^{xx}	0.2025 ^{xxx}	-0.0020	- 1st Coat
	0.7994 ^{xxx}	0.4064 ^{xxx}	0.2754 ^{xxx}	- 2nd Coat
CFL-CFS	0.3716 ^{xxx}	0.3850 ^{xxx}	0.3072 ^{xxx}	- 1st Coat
	0.6736 ^{xxx}	0.6120 ^{xxx}	0.4558 ^{xxx}	- 2nd Coat

The differences between the length of second coat hairs of the large and small strains is much greater than for the first coat in both stocks. This has resulted from a correspondingly greater decrease in length of second coat

hairs in the small strains. The differences between the selected strains of the N and C stocks are similar with respect to both coats.

There are hardly any differences between the length of first coat hairs of the N stock and the large and small strains, because the control was intermediate (Table 5). However the second coat hairs of the control are longer than the large strain and more so with the small strain. This

TABLE 5.

Differences in length of hairs between selected and control strains of N stock

Strain differences	Gaurds	Awls	Zig-zags	
NF-NC	0.1663	0.1100 ^x	-0.0696	- 1st Coat
	-0.4161 ^{xxx}	-0.1831 ^{xxx}	-0.2296 ^{xxx}	- 2nd Coat
NC-NS	0.1461	0.0925	0.0676	- 1st Coat
	1.2155 ^{xxx}	0.5895 ^{xxx}	0.5050 ^{xxx}	- 2nd Coat

is a consequence of an increase in length of second coat hairs in the control, with a corresponding decrease in the selected strains.

The C stock control hairs of the first coat are much shorter than the large strain and even slightly less than the small strain (Table 6). However the second coat appears to be intermediate in length to the large and small strains. This has resulted due to similar reasons as for the N stock control when usually a greater length of hair in the second coat of the unselected strain combines with a shorter coat in the selected strains.

TABLE 6/

TABLE 6.

Differences in length of hairs between selected
and control strains of C stock

Strain differences	Guards	Awls	Zig-zags	
CFL-JC	0.8713 ^{xxx}	0.4700 ^{xxx}	0.4233 ^{xxx}	- 1st Coat
	0.6114 ^{xxx}	0.3650 ^{xxx}	0.1395 ^{xxx}	- 2nd Coat
JC-CFS	-0.4997 ^{xxx}	-0.0850	-0.1161 ^x	- 1st Coat
	0.0622	0.2470 ^{xxx}	0.3163 ^{xxx}	- 2nd Coat

The influence of selection for body size on length of hair was approximately estimated by comparing the differences in length of hair to those of body weight resulting in the large and small strains when expressed as proportions to the unselected. This was performed with guard hairs of the first and second coats. The corresponding values of body weight were of the same animals on the 24th and 50th day of age respectively when growth of the coats had ceased.

The length of hair and body weight of the selected strains expressed as proportions of the unselected are given in Table 7.

TABLE 7.

Selected strains expressed as proportions of the unselected
for length of hair and body weight

Proportional Guard Hair length			Proportional Body weight	
	1st Coat	2nd Coat	24 days	50 days
NF	1.017	0.958	0.989	1.359
NS	0.985	0.876	0.540	0.554
CFL	1.091	1.066	1.336	1.644
CFS	1.052	0.993	0.774	0.797

The differences between the large and small strains expressed as proportions of the unselected from above results are given in Table 8.

TABLE 8.

Differences in length of hair and body weight between selected strains expressed as proportions of unselected

Strain differences	Proportional hair length differences	Proportional body weight differences	
NF-NS	0.04	0.45	1st Coat
	0.08	0.81	2nd Coat
CFL-CFS	0.04	0.57	1st Coat
	0.08	0.84	2nd Coat

The proportional differences in length of guard hairs of the first and second coats between large and small strains of mice of both stocks were usually about 10% of their similar differences in body weight. This is only a small portion of the body weight. Hence large differences in body size are only capable of producing very small effects in length of hair.

Finally a comparison of lengths of the first and second coat was made in all strains (Table 9).

TABLE 9.

Differences in hair lengths between first and second coats.

Explanation - A positive sign indicates a longer first coat as compared to the second coat within a strain, and vice versa for a negative sign.

Strains	Guards	Awls	Zig-zags
NF	0.5507 ^{xxx}	0.0103	-0.1420 ^{xxx}
NC	-0.0317	-0.2828 ^{xxx}	-0.3020 ^{xxx}
NS	1.0377 ^{xxx}	0.2142 ^{xxx}	0.1354 ^{xxx}
CFL	0.5889 ^{xxx}	0.0170 ^x	0.0416
JC	0.3290 ^x	-0.0880	-0.2422 ^{xxx}
CFS	0.8909 ^{xxx}	0.2440 ^{xxx}	0.1902 ^{xxx}

Nearly all hairs of the first coat are longer than the second coat in the selected strains, but in the unselected strains the opposite appears to hold. The differences in length seems greatest in the small strains.

Conclusions

Selection for body size in mice that has resulted in large differences in weight has only produced proportionately small alterations in length of hair.

Nearly all hairs of the first and second coats of large mice are significantly longer than small mice in both stocks. These differences between selected strains signify genetic control of length of hair, but are sufficiently small to escape detection in individual mice as seen in the previous section. The maternal effect then suggested, affects only the first coat as weaning occurs at three weeks of age. By the time the second coat erupts the animal is able to express its own genotype, devoid of maternal influences. Accordingly larger differences seen between the second coats of differently selected strains confirms the small genetic control of length of hair suspected in the first coat. The differences between body size are also marked during the growth of the second coat. The maternal influences partially nullify the genetic differences of the first coat. An approximate estimate of it within strains is the magnitude of the differences in lengths of first and second coats. There is a decrease in length of the second coat only in the selected strains and this is appreciably larger in the small strains, suggesting a stronger maternal influence than for the large strains.

The behaviour of the unselected strains is a contrast to the selected strains. The first coat is shorter than the second suggesting

that maternal factors have an inhibitory effect for increased hair length, due to unknown reasons. This behaviour is in agreement with the observations of Dry (1926) in similar unselected mice.

Length of hair does contribute to body insulation, but here greater loss of heat from small animals has not stimulated the production of longer coats. This is in agreement with Bullough's (1949a) conclusions from his studies on the mitotic activity of the ear epidermis of mice, that loss of heat from the body will cause most of the food to be converted into energy to maintain the body temperature, leaving very little available for other physiological processes.

(3) Growth of hairs of first and second coats

In the last section it was shown that the strains differing in body size do also differ in hair length, though not very greatly. The next question for study is therefore, whether these differences in hair length are due to different rates of growth of hairs or due to differences in the duration of growth.

In the present study a comparison of the rates of growth of hairs between strains was made. This was done with both first and second coats. Evidence of differences between selected strains will also provide information about genetic control of growth of hair.

Method

The hair samples taken from the 8th to 14th day at two day intervals were used to study the growth of the first coat. 5 guard hairs, 10 awls and 10 zig-zags were chosen at random from each sample and their lengths were measured. The second coat was similarly sampled as early as possible and treated likewise. As the growth of the first coat was linear from 8 to 14 days (Figs. 9 and 10), its rate for each strain was calculated by linear regression analysis on individual measurements over this period.

For the second coat however, the rate of growth of hair of each strain was estimated by a method of joint regression. As before, linear growth over a period of six days was utilized, but in this instance the rate of growth of each mouse was calculated separately. Thereafter the common rate of growth of a strain was estimated by pooling the individual values.

The rates of growth of two strains were compared by a test of parallelism, and if equal the means of their regressions were tested for

their elevation. When the rates differed, only the lengths of hairs on the 8th day were compared. Differences between strains in elevation of means of regression or length of hairs on the 8th day are considered to indicate differences in times of initiation of hair types.

Finally, the mean ages of eruption of the second coats were calculated approximately for each strain.

The growth of the hairs in the different strains is shown graphically in Figs. 9 and 10 and their rates of growth computed from the regression coefficients are given in Table 10.

Results

TABLE 10.

Regression coefficients of rates of growth of hair in mms. per day

Strains	Guard hairs		Awls		Zig-zags	
	1st Coat	2nd Coat	1st Coat	2nd Coat	1st Coat	2nd Coat
NF	0.6941	0.8663	0.5757	0.6697	0.4895	0.5860
NC	0.7940	0.8734	0.5813	0.6186	0.5180	0.5569
NS	0.7322	0.7953	0.5540	0.6225	0.4822	0.5539
CFL	0.8583	0.9490	0.6339	0.6860	0.5430	0.6257
JC	0.6960	0.8437	0.5243	0.6210	0.4382	0.5521
CFS	0.8009	0.8570	0.6026	0.5937	0.5259	0.5426

Firstly a comparison of the rates of growth of hairs between strains was conducted. In all instances guard hairs grow faster than awls and awls faster than zig-zigs.

During the growth of the first coat there were no differences between the selected strains of the N stock but in the C stock there was evidence suggestive of small differences. (Table 11).

TABLE 11.Differences in rates of growth of hairs between selected strains

Explanation - When the rates of hair growth of the large, control and small strains are in the same descending order, positive signs are attached to their differences. If it was in the opposite direction this was indicated by a negative sign. This applies to all other instances that will follow.

A single 'x' denotes $P < .05$; 'xx' is $P < .01$; 'xxx' is $P < .001$ when attached to differences in rates of growth between strains.

Strain differences	Guards	Awls	Zig-zags	
NF-NS	-0.0381	0.0217	0.0073	- 1st Coat
	0.0710 ^{xx}	0.0472 ^{xxx}	0.0321 ^{xxx}	- 2nd Coat
CFL-CFS	0.0574 ^x	0.0313 ^x	0.0171	- 1st Coat
	0.0920 ^{xx}	0.0923 ^{xxx}	0.0831 ^{xxx}	- 2nd Coat

In contrast the second coat showed much greater differences between the large and small strains of both stocks, more so in the C stock. The N stock control appears to grow its first coat slightly faster than its selected strains, but during the growth of the second coat it was slower than the large strain and closer to the small strain (Table 12).

TABLE 12.Differences in rates of growth of hairs between selected and control strains in N stock

Strain differences	Guards	Awls	Zig-zags	
NF-NC	-0.0999 ^{xx}	-0.0056	-0.0285 ^x	- 1st Coat
	-0.0071	0.0511 ^{xxx}	0.0291 ^{xx}	- 2nd Coat
NC-NS	0.0618	0.0273	0.0358 ^{xx}	- 1st Coat
	0.0781 ^{xx}	-0.0039	0.0030	- 2nd Coat

During the growth of the first coat the C stock control was not only much slower than the large strain, but also slower than the small strain (Table 13).

TABLE 13.

Differences in rates of growth of hairs between selected and control strains in C stock

Strain differences	Guards	Awls	Zig-zags	
CFL-JC	0.1623 ^{xxx}	0.1096 ^{xxx}	0.1048 ^{xxx}	- 1st Coat
	0.1053 ^{xxx}	0.0650 ^{xxx}	0.0736 ^{xxx}	- 2nd Coat
JC-CFS	-0.1049 ^{xx}	-0.0783 ^{xxx}	-0.0877 ^{xxx}	- 1st Coat
	-0.0133	0.0273 ^x	0.0095	- 2nd Coat

During the growth of the second coat it still remained lower than the large strain, but had closed the gap with the small strain. Finally a comparison of rates of growth of the first and second coats within strains was made and the results follow (Table 14).

TABLE 14.

Differences in rates of growth of hairs between first and second coats

Explanation - A positive sign indicates a higher rate of growth of the second coat in comparison to the first coat.

Strains	Guards	Awls	Zig-zags
NF	0.1722 ^{xxx}	0.0940 ^{xxx}	0.0965 ^{xxx}
NC	0.0794 ^x	0.0373 ^x	0.0389 ^{xx}
NS	0.0631 ^x	0.0685 ^{xxx}	0.0717 ^{xxx}
CFL	0.0907 ^{xx}	0.0521 ^{xxx}	0.0827 ^{xxx}
JC	0.1477 ^{xxx}	0.0967 ^{xxx}	0.1139 ^{xxx}
CFS	0.0561	-0.0089	0.0167

It is noteworthy that in all strains except the small strain of the C stock, the second coat hairs grow faster than the first coat. In this strain there was no difference between the rates of growth of the two coats.

The large strain of the C stock had the highest rates of growth for

all hairs of both coats in the six strains.

Next the differences in length of hairs between strains at the beginning of sampling was considered (Table 15).

TABLE 15.

Initial length of hairs in mms.

	Guard hairs		Awls		Zig-zags	
	8th day	Regression means	8th day	Regression means	8th day	Regression means
NF	4.0559	6.0035		3.9002	1.6225	3.0733
NC	3.8456	6.2821		4.0617	1.8300	
NS		5.4293		3.5648	1.4542	2.9000
CFL	4.0930		2.3308		1.8608	
JC	3.5000		1.9150		1.5683	
CFS	3.8776		2.0380		1.5458	

There are significant differences between regression means of the selected strains in the N stock indicating earlier growth in the large strain.

<u>Strain differences</u>	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
---------------------------	---------------	-------------	-----------------

NF-NS	0.5742 ^{xxx}	0.3354 ^{xxx}	0.3733 ^{xxx}
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The notation of symbols is similar to that of growth of hair.

Similarly in the C stock significant differences between length of hairs on the 8th day are present in the selected strains indicating:

<u>Strain differences</u>	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
---------------------------	---------------	-------------	-----------------

CFL-CFS	0.2154 ^x	0.2928 ^{xxx}	0.3150 ^{xxx}
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earlier growth in the large strain.

Most hairs of the N stock control are longer than the large strains at initiation.

<u>Strain differences</u>	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
---------------------------	---------------	-------------	-----------------

NF-NC	0.2103	-0.1615 ^{xxx}	-0.2075 ^{xxx}
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They are markedly longer than the small strain at initiation.

<u>Strain differences</u>	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
NC-NS	0.8528 ^{xxx}	0.4969 ^{xxx}	0.3758 ^{xxx}

The C stock control hairs are much shorter than the large and even slightly less than the small strain at initiation.

<u>Strain differences</u>	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
CFL-JC	0.5930 ^{xxx}	0.4158 ^{xxx}	0.2925 ^{xxx}
JC-CFS	-0.3776 ^{xx}	-0.1230 ^{xx}	0.0225

Finally the mean ages of eruption of the second coats within the six strains were calculated approximately and given in Table 16.

TABLE 16.

Mean age of eruption of 2nd coat

NF = 35.67 days	CFL = 34.50 days
NC = 32.00 days	JC = 35.67 days
NS = 38.83 days	CFS = 43.83 days

The ages of eruption of the second coats are comparable in the corresponding strains of the N and C stock.

The large strains quite definitely began earlier growth of the second coat in comparison to their small strains.

Strain differences

NF-NS	3.16 days
CFL-CFS	9.33 days

The N stock control began slightly earlier growth than the large strain, but was marked with respect to the small strain.

Strain differences

NF-NC	-3.67 days
NC-NS	6.83 days

The C stock control though intermediate to the large and small strains, distinctly began growth of the 2nd coat earlier than the small strain.

Strain differences

CFL-JC	1.17 days
JC-CFS	8.16 days

Since the difference between the large and control strains is small it cannot be considered seriously.

Conclusions

Genetic control of growth of hair is clearly evident by the marked differences present between selected strains during growth of their second coat. Selection for body size has produced large strains with longer coats and higher rates of hair growth than their respective small strains. Probably maternal influences masked these differences in growth between strains for the first coat when the animal was still suckling.

Fraser (1951a) conducted a comparable study of only the first coat in a large, two controls and a small strain of mice and his results were in agreement with the present observations. He reported that there were no differences in rates of growth between strains for the same type of hair, though he considered growth from 10 to 20 days as linear and based his results on this period. The inclusion of this long period irrespective of the fading of growth before cessation, may probably account for the lower values of the rates of growth in comparison to the present results. Fraser's

technique was tedious and liable to slight errors during conversion of measurements from one system to another. It also suffered from the disadvantage of killing an animal for a single measurement and being unable to follow the growth of hair uninterruptedly in a mouse.

Since there were hardly any differences in rates of growth of first coat hairs between differently selected strains, it was unlikely to be the cause for differences in hair length seen in the previous section. Next an examination of the duration of growth of hairs (Figs. 9 and 10) also shows hardly any differences in time of cessation between the selected strains that can account for differences in length of hairs. On the whole there appears to be a great similarity in the patterns of growth and cessation in the selected strains.

The only remaining aspect was an examination of the length of hairs at the beginning of growth. All hairs of the large strains were estimated to be longer than their respective small strains at initiation of growth in both stocks. It is probable that the large strains with longer hairs at initiation began growth earlier than their small strains, because if the graphs of the large strains were shifted a little to the right they overlap to a great degree with those of their small strains.

A measure of the shift provides an approximate estimate of the differences in time of initiation. In both stocks the large strains have begun growth of their first coat about half a day earlier than their small strains. Fraser (1951a) observed similar small but significant differences in means of regressions and he concluded that each type of fibre was probably initiated at different times in different strains. He however does not indicate whether this meant that the large strain began earlier growth than the small strain.

Nothing definite can be said about growth of hair from birth until the 8th day of age to make an exact determination of the differences in times of initiation between the selected strains. Fraser (1951a) extrapolated his linear growth rates to estimate the ages at which the different hair types were formed, though he admits that they are not likely to grow lineally throughout this period of formation. If the present growth rates too were extrapolated they will fall within this range where none of the hairs begin growth before birth. This will be directly contradictory to the ages of initiation reported by Falconer, Fraser and King (1951). Thus growth prior to the 8th day is likely to be non-linear. This appears to be indicated also by the shape of the graphs.

It was not possible to indicate this effect graphically for the second coat, because mice began growth of their coat at variable intervals. However large mice maintained their earlier growth similarly for the 2nd coat with respect to small mice. Their differences in times of initiation are now much more than for their first coats. This will be discussed in detail in the study of the cyclic changes in the mouse coat.

In nearly all strains the second coats grow faster than the first coats. Fraser (1951b) suggested the possibility of competition occurring between adjacent follicles for a limited amount of fibre substrate causing denser fleeces to be finer and shorter in sheep. On this hypothesis mice having a marked increase in body area occurring after birth decreases follicle density leading to a reduction in intensity of competition. Since the follicle number remains constant, follicles of the second coat have a greater abundance of fibre substrate, especially so in the large strains. This can explain the faster growth of the second coat as compared to the

first, and account for a part of the superiority of the rate of growth of the large strains over their small strains. However, as Rae (1956) points out, much more information is required before Fraser's theory can be accepted.

II. THICKNESS OF HAIRS OF FIRST COAT

A comparison of thickness of hairs of the first coat between strains was undertaken. Large mice were known to have longer hairs than small mice, though these differences were small in proportion to differences in their body weight. The next question that follows is whether there are also significant differences in thickness of hairs between the selected strains. Another interesting aspect of the problem is whether thicker hairs are produced by larger follicles in the large strains of mice as compared to small strains. Since body organs of large mice can be considered to be larger than those of small mice, it is reasonable to suppose that their follicles may also be larger.

Only Slee (1954) has mentioned a technique for measurement of hair thickness. Hairs were mounted on slides and measured under the microscope at the point of maximum thickness with a calibrated ocular micrometer.

Dry (1926) reported his measurements on thickness of first coat hairs from the mid-dorsum. Guard hairs were 26μ thick, awls 38μ , auchenes $30-34\mu$ and zig-zags 15μ in segments II, III or IV. Slee (1954) studied hairs from the neck, but made no mention of the pelage from which the samples were derived. His results indicated the hairs to be thicker than those observed by Dry. Guard hairs were 39.2μ thick, awls 48μ and zig-zags 24.8μ . Slee (personal communication) sampled the mice at approximately six weeks of age and it is probable that his results apply mainly to hairs of the second coat. In all instances awls were the thickest hairs, guard hairs intermediate and zig-zags the thinnest.

Guard hairs, awls and zig-zags were used for this study. They

were distinguished on the basis of their internal and external structure (Figs. 7 and 8). These are described in detail in the introduction.

The hairs sampled on the 28th day, and used for the study of length, were utilized for comparison of thickness.

Method

Hairs were mounted on a slide with Canada balsam and 5 hairs of each of the 3 types were measured in each animal with a calibrated eyepiece under the oil immersion lens at a magnification $\times 630$. Thus a total of 15 hairs were measured in an animal.

The measurement was made at the point of maximum thickness, which was usually around the middle of the hair, and expressed in units of μ .

The results are given in Table 17.

Results

TABLE 17.

Thickness of Hairs in μ

	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
NF	32.22	39.10	17.06
NC	30.48	41.64	16.67
NS	29.84	36.88	15.74
CFL	31.40	38.25	16.93
JO	28.33	35.66	15.92
CFS	28.57	36.01	15.37

Guard hairs, awls and zig-zags of the large strains are significantly

	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
NF-NS	2.38 ^{xxx}	2.22 ^{xxx}	1.32 ^{xxx}
CFL-CFS	2.83 ^{xxx}	2.24 ^x	1.56 ^{xxx}

thicker than their respective small strains to about the same extent in both stocks of mice.

The N stock control hairs are generally thicker than the small strain, but not much different from the large strain. The thickness

	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
NF-NC	1.74 ^x	-2.54 ^{xxx}	0.39
NC-NS	0.64	4.76 ^{xxx}	0.93 ^{xxx}

of the control awls is anomalous.

The C stock control hairs are of about the same thickness as the small strain, but much thinner than the large strain.

	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
CFL-JC	3.07 ^{xxx}	2.59 ^{xx}	1.01 ^{xxx}
JC-CFS	-0.24	-0.35	0.55 ^x

As for hair length, the proportional differences in thickness of guard hairs between the large and small strains were compared with their similar differences in body weight. The results are given in Table 18.

TABLE 18.

Selected strains expressed as proportions of unselected for hair thickness and body weight

<u>Proportional guard hair thickness</u>		<u>Proportional body weight</u>
NF	1.0571	1.0755
NS	0.9790	0.5262
CFL	1.1084	1.3146
CFS	1.0085	0.6836

The differences between these large and small strains expressed as proportions of the unselected are as follows:-

	<u>Proportional hair thickness difference</u>	<u>Proportional body weight difference</u>
NF-NS	0.0781	0.5493
CFL-CFS	0.0999	0.6310

The proportional difference in hair thickness between the large and small mice was usually 15% of their differences in body weight.

Conclusions

Selection for body size in mice that produced large differences in weight has only produced small differences in thickness of hairs.

Though there is no evidence available about the relationship between the size of the follicle and the thickness of the hair it produces, it is reasonable to suppose that such an association exists.

The large strains can be considered to have bigger organs, such as follicles, than the small strains. These presumably larger follicles have produced thicker hairs.

This also indicates genetic control of hair thickness.

The measurements of the three types of hairs are in close agreement with the findings of Dry (1926).

III. FREQUENCY OF HAIR TYPES OF FIRST COAT

A comparison of frequencies of hair types in the different strains was made.

It has been seen earlier that there are differences in the periods of initiation of coats in the selected strains. The time of initiation may probably influence another character of the coat, the frequencies of hair types, because Falconer, Fraser and King (1951) found that the three types of hairs of the first mouse coat were initiated at different times. Guard hairs are formed from the 14th to the 17th day of foetal life, awls and auchenes from the 17th day until birth, and zig-zags mainly after birth. Dry (1926) and Gibbs (1941) reported the initiation of zig-zag follicles until about the 7th or 8th day after birth. Therefore it is interesting to know whether such differences in times of initiation of coats in mice derived from contrasting strains will influence the production of any hair type. Since the precise periods of initiation of the three types of hairs of the first coat are known, this study was restricted to the first coat.

Dry (1926) reported a frequency of 2% guard hairs, 14-15% awls and auchenes, and 83% zig-zags for the first coat. The hairs were drawn from the mid dorsum. Fraser (1951a) observed 2% guard hairs, 26% awls and auchenes and 71.5% zig-zags. Slee's (1954) results were in agreement with Fraser, but these values probably apply to the second coat, because the mice were sampled at six weeks of age (personal communication). Dry (1926) too reported a similar frequency of hair types for the second coat caused by an alteration in function of follicles. Dry found that follicles are capable of producing hair types different to that of the earlier pelage. The new type of hair produced is in the ascending order from zig-zags to guard hairs, but only rarely does the opposite process occur. He studied

second coat hairs on the mid dorsum and found that guard hairs increased by about 0.75%, awls and auchenes by 8.8%, while zig-zags decreased by a corresponding figure of 9.55%.

Dry (1926) and Chase (1954) also found that hairs of the earlier pelages are often retained in the follicle. Only guard hairs were entirely shed during the growth of new hairs of the succeeding generation. All other hair types may be retained. Auchenes are retained longer than awls, and zig-zags longer than auchenes. A maximum of four zig-zags have been observed to be present in a single follicle.

Alteration of follicular function and retention of hairs of previous generations complicate the picture if the hair type frequency of any coat other than the first coat were studied.

Method

Samples of hair were plucked with forceps from the neck, in the mid dorsal line at about the interscapular region from mice four weeks of age. Twelve male mice were sampled from each strain. None of these animals had been used in previous experiments.

A batch of hairs drawn from such a sample was estimated for its guard hairs, awls and auchenes, and zig-zags on a black velvet cloth under a low power binocular microscope. An average of about 400 hairs was counted from each sample.

The estimated number of hairs of the corresponding types from the twelve mice were pooled together to determine the common frequency of a strain.

Then the corresponding hair type proportions of the strains were compared by a test of χ^2 .

The numbers of hairs of the 3 types in the N stock are given in Table 19.

Results

TABLE 19.

Frequency of hair types in N stock

	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
NF	58	667	3343
NC	84	1078	3997
NS	91	1201	3772

$$\chi^2_{df4} = 78.10$$

There are significant differences ($P < .001$) in corresponding frequencies of hair types between strains of the N stock. When expressed in percentages as given in Table 20 these proportions are better appreciated.

TABLE 20

Percentages of hair types in N stock

	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
NF	1.43	16.40	82.18
NC	1.63	20.90	77.48
NS	1.80	23.73	74.49
Overall	1.62	20.34	78.05

The significance of these differences between hair types of the N stock strains were estimated on the basis of individual percentages of the mice. The mice of the large strain have more zig-zags, but less awls than

	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
NF-NS	-0.37	-7.33 ^{xxx}	7.69 ^{xxx}

the small strain..

The control strain is intermediate between the selected strains

	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
NF-NC	-0.20	-4.50 ^{xx}	4.70 ^{xx}
NC-NS	-0.17	-2.83 ^{xx}	2.99 ^x

It has a higher frequency of awls and a lower frequency of zig-zags than the large strain; and a lower frequency of awls and a higher frequency of zig-zags than the small strain. In the C stock there are no differences in frequencies of hair types between strains ($P > .05$).

TABLE 21.

Frequency of hair types in C stock

	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
CFL	90	859	4021
JC	107	1116	5041
CFS	97	1001	4424

$$\chi^2_{df4} = 1.44$$

These proportions are seen in Table 21. They are expressed as percentages in Table 22 for convenience in comparison.

TABLE 22.

Percentages of hair types in C stock

	<u>Guards</u>	<u>Awls</u>	<u>Zig-zags</u>
CFL	1.81	17.28	80.90
JC	1.71	17.82	80.48
CFS	1.76	18.13	80.12
Overall	1.76	17.76	80.48

The overall hair type frequencies of both stocks are very similar.

Conclusion

It is reasonable to suspect that the differences within the N stock may result from a low frequency of zig-zags in the small strain. A comparison

of the zig-zag frequencies in strains appear in Table 23.

TABLE 23.

Percentage of zig-zags

		<u>Large</u>	<u>Unselected</u>	<u>Small</u>
Present study	N stock	82.2	77.5	74.5
	C stock	80.9	80.5	80.1
Fraser		72.2	69	74.4
			70.5	

The zig-zag hair follicles are the last to be produced in the mouse coat and their formation ceases after a definite age (Dry 1926; Gibbs 1941). The delay in initiation of guard hairs in the small strain probably produces equal sequential shifts in all other hair types. Ultimately a part of the formation period of zig-zags may be moved beyond its limit into an inactive stage, resulting in probably fewer zig-zags.

This is however not borne out in C stock where there was no difference between the selected strains. The two stocks are known to have different origins and methods of selection.

Fraser's (1951a) results on a similar study are in contrast to those of the N stock. It will be recalled that the selected strains used by Fraser had totally different origins.

Falconer, Fraser and King (1951) reported an extreme instance where a total absence of guard hairs and zig-zags occurred in 'Crinkled' mice, but the mechanism of suppression of follicle formation and its underlying cause was unknown.

IV. PERIODICITY OF HAIR CYCLES

Differences in the time of initiation of the first and second coats in the differently selected strains were mentioned in the previous study of growth of hair. Whether these differences in times of initiation were maintained in the subsequent coats is the next question that will now be investigated using male mice as usual. This study was pursued until the seventh coat extending, over a period of about ten months. A review of the previous work done on the coats of animals will facilitate the interpretation of the conclusions drawn from this study. No comparative study of this nature between strains selected for body size has been reported earlier.

The following techniques were used to detect the new coats. Dry (1926) used dissections and histological methods for the study of hair cycles that necessitated killing of the animal and hence did not permit a sequential study of coats on the same animal.

Iljen (1945) used Thallium for the same purpose causing growing fibres of long haired animals, particularly of Angora rabbits, to be shed. But he found that it did not affect short haired animals with short periods of hair growth as mice and this was later confirmed by Fraser (1951a).

Nay and Fraser (1954) on the same principle used a mutant gene 'Naked' that causes hairs which have nearly completed their growth to break off near the skin leaving the area naked. Subsequently Fraser and Nay (1955) compared the growth of coats in Naked and normal mice by clipping the latter and recording the eruption of the new coat as in 'Naked' mice.

Hadow and Rudall (1945) injected alloxazines into albino rats and produced an artificial yellow pigmentation of the cortex of the hair that

was helpful in determining the time of eruption of the new coat by providing a contrast of colour. Unfortunately this substance does not affect mice (Haddow, Elson, Roe, Rudall, Timmis (1945); Fraser (1951a)). Borum (1954) adopted a very convenient technique of dyeing albino mice black to produce the same result as the alloxazines did in rats. The same method was employed in the present study for albino mice and the principle was extended to coloured mice by bleaching them instead. Borum was satisfied with a single treatment for judging two coats, but in this study mice were treated after each new coat. Whenever damage to the skin occurred the animals were discarded, because some chemicals were found to produce epilation and initiated hair regeneration when applied during the resting stage (Rauch 1952; Chase 1954).

Nearly all the previous studies on coat initiation were limited to a few earlier coats. Reports of their dates of eruption were as follows. The first coat appeared on the skin at the age of 2 to 3 days (Borum 1954) and growth was completed usually by about the 18th to 20th day according to Dry (1926), Fraser (1951a) and Fraser and Nay (1955); but Grüneberg (1952), Andreassen (1953) and Borum (1954) are of the opinion that it ceases at an early age of about 10 to 12 days. The first coat commenced growth simultaneously all over the body, but the subsequent coats occurred as several bilaterally symmetrical waves independent of each other on different parts of the body at variable intervals. The growth phases of hair generations lasted about 10 days while the remaining longer periods of the cycles were the resting stages (Andreassen 1953).

The second coat usually appeared from about the 28th to 36th day of age and was completed by about the 40th to 50th day (Woolbach 1951; Andreassen 1953; Borum 1954; Fraser and Nay 1955.) However Dry (1926)

thought it began growth as early as the 18th day.

The third coat began growth from about the 45th to 85th day and was complete by about the 100th day (Dry 1926; Andreassen 1953; Borum 1954; Fraser and Nay 1955).

Only Borum (1954) has any information about the subsequent cycles. The fourth coat began growth on about the 119th day of age, the fifth coat on the 175th day, the sixth coat on the 240th day and the seventh coat on the 284th day.

Some late hair cycles set in before the preceding or even earlier pelages had been completed in other parts of the body. Thus it was possible for the same mouse to possess two or three hair cycles of different generations. Borum (1954) found that mice of the same litter resembled each other more closely than those from unrelated litters.

Method

The ages of initiation of the second to the seventh hair cycles were studied in mice belonging to the six strains. 13 male mice were selected from each strain. Coloured mice were bleached and albinos dyed when they were 4 weeks old. Only the region of the neck, about the anterior one third of the dorsal surface of the animal, was treated. Thereafter they were examined every other day until the eruption of the new coat (Figs. 5 and 6). When the new coat appeared the age of the animal was noted.

Twelve days later after the new coat had ceased growth the animal was treated again and similarly examined. This procedure was repeated until the seventh coat.

Only very few animals died or had any skin reaction. These were all very weak and emaciated at the time of selection. Death usually

resulted after bathing. Only five mice were lost and these were replaced soon afterwards.

Before dyeing and bleaching was practised it was shown that they did not induce new growth of hair. Only one longitudinal half of an animal was treated and the appearance of the new coat was observed. The normal bilaterally symmetrical hair cycle still occurred simultaneously in the treated and untreated areas showing that the treatment made no difference whatever. Sometimes animals had a tendency to savage their cage mates. This usually occurred with advancing age. Two animals were lost by this means, but many more were saved in time.

Results

A graph of age in days against number of the coat was plotted for each stock (Figs. 11 and 12). This clearly indicated a linear appearance of hair cycles in all strains because the points were very close to their linear regression lines. Only in the small strain of the C stock was there a little variability. A steep linear regression line for a strain indicates a delay in development of hair cycles than a strain with a lesser incline. Large regression coefficients hence express a slower rhythm of hair cycles to denote a longer periodicity.

Next the rates of eruption of hair cycles in the different strains were calculated by linear regression analyses on individual values. The results are given in Table 24.

TABLE 24./

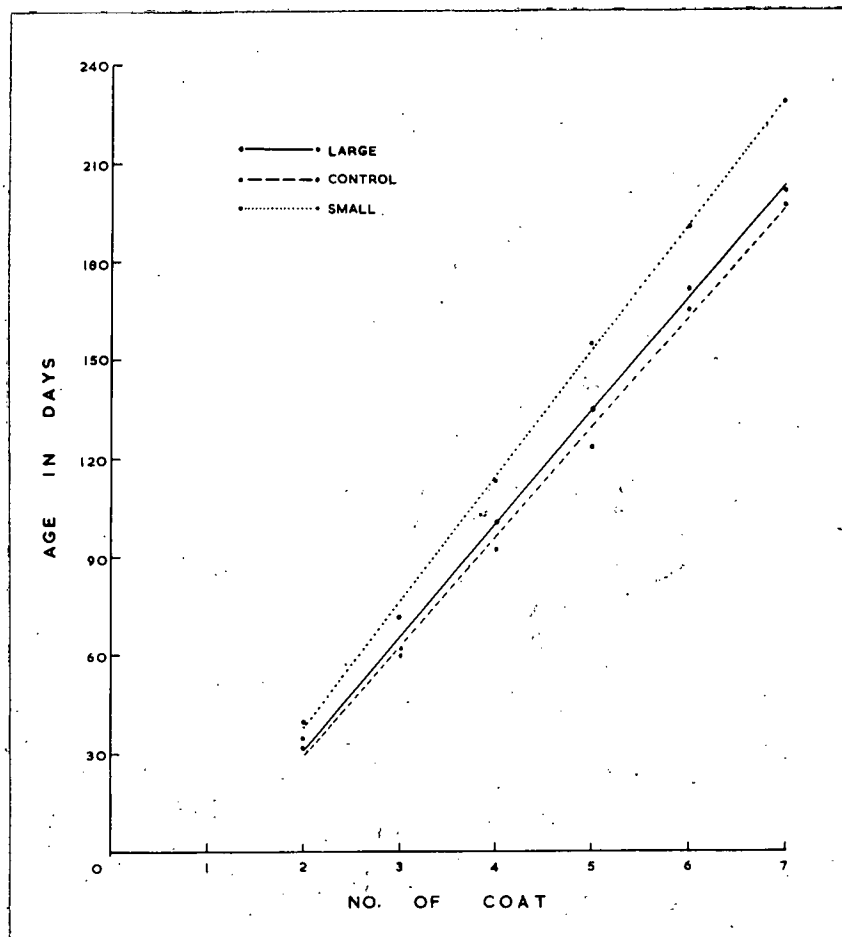


FIGURE 11. Periodicity of hair cycles in the N stock

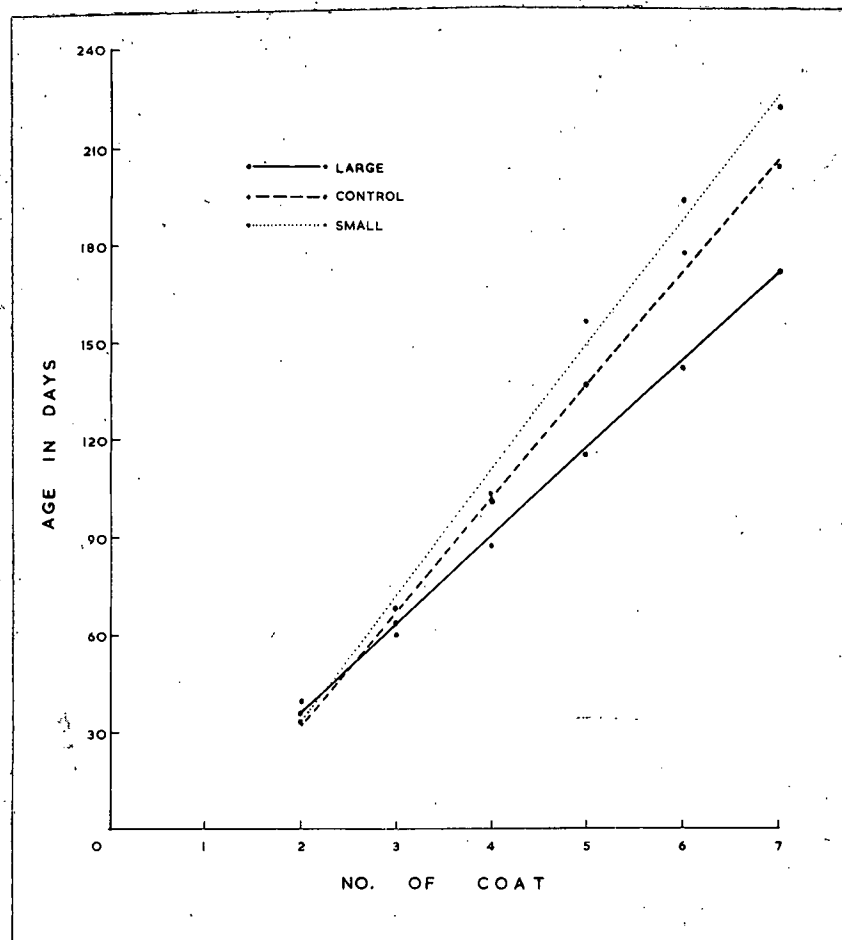


FIGURE 12. Periodicity of hair cycles in the G stock

TABLE 24.

Regression coefficients of rate of eruption of hair cycles in days per coat

NF	34.92	CFL	27.54
NC	33.50	JC	35.37
NS	38.62	CFS	39.04

In both stocks the large strains had a faster rate of appearance of hair cycles than their respective small strains, as indicated by a shorter period. Their differences in the rates of eruption follow.

Strain differences

$$NF-NS \quad -3.70^{XX}$$

$$CFL-CFS \quad -11.50^{XXX}$$

The cycles also began earlier in the large strains (Figs. 11 and 12). The N stock control was not different from the large strain in its rate of coat eruption and hence the elevations of the two regressions were

$$NF-NC = 1.42$$

compared. There was neither any difference in the times of initiation ($P > .05$). Hence it behaved as the large strain (Fig. 11). In comparison, the control had a faster rate of coat eruption than the small strain and

$$NC-NS = -5.12^{XXX}$$

the cycles appeared earlier. The C stock control was intermediate in its rate of coat eruption, though it did not significantly differ from the small

$$CFL-JC = -7.83^{XX}$$

$$JC-CFS = -3.67$$

strain. It was less than the large strain. The ages of appearance of the cycles were also intermediate (Fig. 12). This was statistically confirmed with respect to the small strain ($P < .025$).

The large strain of the C stock had the fastest rate of hair cycles. As in the case of final length of hairs, the effect of selection in opposite directions for body size was approximately estimated by comparing the differences in rates of coat eruption to those of body weight in the large and small strains when expressed as proportions of the unselected. The corresponding values of body weight were obtained on the 50th day when growth of the body had ceased in animals used previously for studies on hair length. The rate of eruption of coats and body weight of the selected strains expressed as proportions of the unselected are in Table 25.

TABLE 25.

Selected strains expressed as proportions of unselected for rate of eruption of coats and body weight

<u>Proportional rate of coat eruption</u>		<u>Proportional body weight</u>
NF	1.0424	1.359
NS	1.1528	0.554
CFL	0.7786	1.644
CFS	1.1038	0.797

The differences between the large and small strains expressed as proportions of the unselected from the above results are as follows.

<u>Proportional rate of coat eruption differences</u>		<u>Proportional body weight differences</u>
NF-NS	-0.1104	0.81
CFL-CFS	-0.3252	0.84

Hence the proportional difference in rate of coat eruption between large and small mice in the N stock is usually about 14% of similar differences in body weight.

In the C stock the proportional difference in rate of coat eruption between large and small mice is usually about 39% of similar differences in

body weight. This is much larger than for the N stock.

Conclusions

Selection for large and small body size in mice that has resulted in great differences in weight have also produced proportionately recognisable differences in rates of coat eruption. This is by far the greatest difference produced in a coat character until now and is much more marked in the C stock. The fact that the property for initiating coats earlier in large mice, as compared to small mice, has been maintained long after body growth has ceased leads to a reasonable supposition, that there is a permanent physiological process associated with large mice that does not cease with body growth. The nature of this process will be discussed later after a review of the properties of waves of hair growth.

The results of this study support the findings of the previous section. The large strains that began growth of hair earlier than the small strains from birth, maintained this superiority throughout the subsequent cycles. The turnover of the cycles was also faster in the large strains. The greater frequency and early appearance of cycles of hair in the large strains is best understood in the light of the causative factors which are still a matter of speculation.

Durward and Rudall (1949) found that if a piece of skin was rotated through 180° in a rat, leaving the blood supply intact, the wave of hair growth proceeded normally as it were in its original position, independent of that on the main areas. Hence it was inferred that firstly the direction of the wave of hair growth was inherent in the skin. Later they found that denervation of segmental nerves, composed of the somatic and sympathetic post ganglionic fibres, did not alter the pattern of growth of hair, because it was

independant of the innervation of the skin.

Haddow, Elson, Roe, Rudall, Timmis (1945) and Haddow and Rudall (1945) suspected another factor. They injected chlorozoll sky blue FFS into the blood and examined the undersurface of the skin after some time. The greatest density of capillaries occurred at the advancing edge of the growing wave of hair with a sharp decrease at the receding edge.. They suggested that the constantly moving patterns of hair-growth appeared in response to the rhythmic alterations in the distribution of blood to the hair follicle. Chase (1954) found that when the food intake is reduced in mice to about half the normal diet, new cycles of hair did not appear. Even the plucking stimulus failed to induce growth of new hair in such mice.

The most likely factors governing growth of hair cycles seemed to be hormones. Fraser (1953) found that oestrogen retarded the growth of hair cycles. In ovariectomised mice the hair bands were observed to move faster than in the normals, probably because of the low level of oestrogen. In pregnant females growth of hair ceased towards the end of pregnancy corresponding with a high level of oestrogen at this period. Emmens (1942) also observed similar effects.

Baker (1951) reported that if rats had been previously adrenal-ectomised oestrogen had no effect. The adrenal cortex when functioning normally inhibits growth of hair.

In contrast, the thyroid and hypophysis encourages growth of hair (Baker 1951). Administration of thyroxine to thyroidectomised rats restored normal growth of hair. Hypophysectomy of a rat causes a decrease in the rate of growth of hair and a greater time lag in the successive cycles.



Baker's (1951) observations on the influence of the hypophysis on hair growth can be extended to interpret the differences in rates of coat eruption between selected strains. Edwards (1957) concludes that mice of the small strain appear to be deficient in growth hormone, follicle stimulating hormone, luteinising hormone and probably luteotrophin, which are produced by the anterior pituitary, while the large strain mice may have increased amounts of them. These two observations of Baker and Edwards, therefore suggest that the differences in the cycles of hair regeneration may well be connected with differences of pituitary function.

The ages of initiation of coats are reasonably in agreement with Dry (1926), Andreassen (1953), Borum (1954), and Fraser and Nay (1955). It is interesting to note the marked linearity of the appearance of hair cycles in the neck region of all strains of mice. This may be true of other regions of the body too. Similar results were obtained by Fraser and Nay (1955) in Naked mice that showed regular cycles of hair growth, but the authors were of the opinion that this was due to nakedness, caused by shedding of completed hairs, placing a stress on the metabolic system.

Bullough (1949a & b) however showed that low temperatures did not alter the mitotic activity in the epidermis of the mouse ear. On the contrary, a reduction in mitotic activity occurred in mice kept at a low environmental temperature, probably due to utilization of sugar reserves to maintain the body temperature. The processes found in the ear epidermis may be considered to be occurring in other regions of the body producing hair and the mitotic activity may be indicative of follicle activity. The fact that mice used in the present study possessed their

normal coat of hair also suggests that nakedness was unlikely to have induced regular cycles of hair as suggested by Fraser and May (1955).

An interesting analogy can be drawn between growth of hair and eruption of coats. Both processes are linear and the general relationships between strains appears to hold true. The large strains have higher rates than small strains and the C stock control is more intermediate than the N stock control.

Discussion

Before drawing any conclusions about body size and characters of hair, the possible effects of inbreeding needs attention. The N stock was much more inbred than the C stock and hence the differences between the corresponding strains of the two stocks might be attributed to inbreeding rather than to the method of selection and genotype of the foundation populations. Differences within stocks are not due to inbreeding, because the levels of it in the selected strains were about the same.

The corresponding strains of the two stocks were compared for the characters studied and the results are given in Table 26. The results of the large strains are very consistent. The large strain of the C stock had the highest rate of hair growth, the longest coats and fastest regeneration of coats than all other strains.

Inbreeding has probably reduced the rate of growth and length of hair, increased the thickness, and delayed the regeneration of hair cycles. The frequencies of hair types do not show any evidence of being influenced by inbreeding.

The next part deals with the extent to which hair growth reflects body growth. Differences in the length, thickness and period of regeneration of hair cycles between large and small mice were always less than their proportional differences in body weight. This indicated that the genetic relationship between body weight and properties of hair were small.

It was not possible to study the connection between growth of body and hair because there were hardly any differences between strains in either the growth of first coat hairs or body weight at this period when

maternal effects were predominant. When the animals were able to exert their genotype there were marked differences in hair-growth, but the maximum differences in body growth had elapsed and body growth had ceased in small mice. There was however reasonable evidence to suppose that growth of the body does not affect growth of the hair, because the differences in the rate of regeneration of the coats, which was the greatest difference between the large and small strains, persisted long after body growth had ceased. This suggested that growth of hair depended on another factor not concerned with the rate of body-growth at the time.

On the evidence of Baker (1951) and Edwards (1957) this factor can be suspected to be hormones of the pituitary. Baker observed that hypophysectomy in rats caused a decrease in rate of growth of hair and a greater time lag in the successive cycles; and Edwards concluded that the small strain, as compared to the large strain, had a lower level of pituitary hormones. This decrease in hormones may be responsible for the similar, but much less pronounced, changes in the coat seen after hypophysectomy. The pituitary probably exerts its influence via the growth hormone affecting the carbohydrate metabolism to stimulate new sugar formation and raising the blood sugar level. Bullough (1949b) observed that in normal mice the mitotic activity of the ear epidermis is high and blood sugar level is low during sleep, while the mitotic activity is low and blood sugar level is high during hours of waking. He was therefore of the opinion that the critical factor in the control of these diurnal cycles is the concentration of sugar or glycogen within the tissues themselves. Thus sugar may be deposited in the skin, as it is known to occur in the liver, so giving rise to a simultaneous fall in the level of blood

sugar and a rise in the mitosis rate of the epidermis. Glycogen was reported to be present in the external root sheath of many mature active hair follicles by Hardy (1952) and Shipman (1952), but absent in resting ones. Glycogen present in the follicle provides the energy for epidermal mitoses and probably determines the rate of growth of hair, depending on the functional capacity of the follicle. On this theory a greater secretion of growth hormone by large mice will stimulate greater carbohydrate metabolism resulting in larger amounts of glycogen being available to the follicles to produce a higher rate of hair growth than the small strain. Large mice may be considered to possess larger hair follicles than small mice since the hairs are thicker and because all organs of their body can be expected to be bigger. It is possible that a large follicle will also help in producing a superior functional capacity.

There was no sign of thermoregulation for adaptation to environmental temperature by small mice. Small mice had fewer zig-zags and shorter hairs making the coat less insulating than large mice. It may be that the thermal stress was insufficient to produce adaptation of this sort.

There are also some remaining aspects, such as density of hair and skin thickness, to be studied at a later date before this investigation about adaptation to environmental temperature is complete.

Some facts of general interest to the study of growth of hair became apparent in the course of this investigation. Large environmental factors were found to influence the length of hair. It is hoped that these will be identified in the future. Another interesting fact was the linearity in the age of regeneration of coats. It is possible

that this regularity exists in other regions of the body apart from the neck, but it will be worth while to know what follows in regions when there is an alteration of the patterns of hair cycles causing overlapping.

In nearly all instances the second coat grew faster than the first coat. Fraser (1951b) suggested that this resulted from a decrease in intensity of competition for a limited amount of fibre substrate between adjacent follicles. To confirm this it would be interesting to know whether the rates of growth of the subsequent coats were similar to the second coat, since growth of the skin had ceased and the density of the follicles remained constant.

Nearly all second coat hairs of the selected strains are shorter than those of the first coat but in the unselected strains the opposite is true due to unknown reasons. A similar comparison for thickness of first and second coats to find any relationship between length and thickness would provide interesting information.

TABLE 26.Comparison of the two stocks in respect to various hair properties

Ratio of C-stock to N-stock; large strain in left hand column;
small strains in right hand column. G, guard hairs; A, awls;
Z, zig-zags.

	<u>CFL/NF</u>	<u>CFS/NS</u>
<u>Length</u>		
1st coat	G 1.04 A 1.04 Z 1.05	G 1.04 A 1.01 Z 0.99
2nd coat	G 1.04 A 1.04 Z 1.02	G 1.06 A 1.01 Z 0.98
<u>Growth</u>		
1st coat	G 1.24 A 1.10 Z 1.11	G 1.09 A 1.09 Z 1.09
2nd coat	G 1.10 A 1.02 Z 1.07	G 1.08 A 0.95 Z 0.98
<u>Thickness</u>		
1st coat	G 0.97 A 0.98 Z 0.99	G 0.96 A 0.98 Z 0.98
<u>Coat Regeneration</u>		
	0.79	1.01
<u>Frequency</u>		
1st coat	G 1.26 A 1.05 Z 0.98	G 0.98 A 0.76 Z 1.08

Summary

1. A study of the growth and structure of the hairs of the coat was conducted in large and small mice. The object was to see in what ways growth of hair was related to growth of body, and whether there was any adaptation to environmental temperature.
2. Two large and two small strains of mice were used. They belonged to stocks selected over about 20 and 30 generations respectively, hence causing differences in the level of inbreeding. Selection within stocks was for large and small body size. The unselected control strain for each pair of selected strains was also studied.
3. An investigation of the factors affecting final length of hair was made first and it showed only environmental effects, probably maternal in origin. But in the subsequent comparison of large and small strains for final hair length there was evidence of slight genetic control of this character.
4. Selection for body size, that had produced large differences in body weight between large and small strains, brought about proportionately small alterations in hair characters such as length and thickness, but considerably larger changes in the rate of coat eruption. This suggests that there is only a small relationship between genes governing body and hair growth. The differences in coat characters became marked after weaning, when animals were able to express their own genotype.
5. The effect of inbreeding was judged on the basis of differences between corresponding strains of the two stocks. This indicated that inbreeding has probably had a detrimental effect on the growth of the mouse coat.
6. The mice of one control strain were always superior to the corresponding

small strain and usually not different from the large strain in most hair characters. In contrast the other control mice were usually intermediate or similar to the corresponding small mice.

7. Mice belonging to the large strains had thicker and longer hairs in the first coat than mice from their respective small strains. The differences in length became more marked in the second coat.
8. Usually no differences were present between large and small mice in the growth of the first coat, but during the growth of the second coat the large mice had an appreciably higher rate than the small mice.
9. There was a delay in initiation of the first coat in small mice as compared to large mice. The delay in initiation of the coat may have produced a sequential shift of the hair types causing a part of the zig-zag formation period to be forced into an inactive stage resulting in fewer zig-zags in the small mice.
10. The delay in the appearance of the coat in small mice was maintained throughout the subsequent hair cycles. The large strains consequently had a faster rate of regeneration of coats. This was by far the largest difference in coat characters between large and small mice. The fact that these differences were maintained after body growth had ceased suggested the existence of a permanent physiological process, probably the growth hormone of the anterior pituitary, influencing growth of hair. There also appeared to be a constant interval between the cyclic appearance of coats within strains.
11. No evidence of adaptation to environmental temperature was detected in coat structure of length, thickness and frequency of zig-zags as expected of small mice. A study of hair density and skin thickness remains to be done to support these findings. It may be that the thermal stress was insufficient to evoke any response.

Acknowledgements

I am very grateful to Dr. D.S. Falconer for his kind advice and guidance given throughout the period of research, and to Professor C.H. Waddington F.R.S. for his interest and support given during this work in his department.

I appreciate the kind advice I received from Mr. B. Latter and Dr. J. Slee.

I must thank Mr. J. Isaacson and his staff for their help with mice, Mr. D. Roberts for his assistance with graphs, and Mr. D. Pinkney and his staff for their photography.

Finally I wish to express my gratitude to the United Kingdom Government for the fellowship under the Technical Co-operation Scheme of the Colombo Plan that enabled me to conduct this work.

References

- ANDREASEN, E. 1953. Cyclic changes in the skin of mouse. *Acta path. microbiol. scand.* 32, 157-164.
- BAKER, B.L. 1951. Relationship of the adrenal, thyroid and pituitary to the growth of hair. *Ann. N.Y. Acad. Sci.*, 53, 690-706.
- BATEMAN, N. 1954. The measurement of milk production of mice through preweaning growth of suckling young. *Physiol. Zool.*, 27, 163-173.
- BERGMANN, C. 1847. Ueber die Verhältnisse der Wärmeökonomie der Thiere zu ihrer Grösse. *Göttinger Studien*, pt. 1, 595-708.
- BORUM, K. 1954. Hair pattern and hair succession in the albino mouse. *Acta path. microbiol. scand.*, 34, 521-541.
- BRODY, S. 1945. *Bioenergetics and growth*. New York. Reinhold Publishing Corporation.
- BULLOUGH, W.S. 1949a. The effects of high and low temperatures on the epidermal mitotic activity of the adult male mouse, *Mus musculus* L. *J. exp. Biol.*, 26, 76-82.
- _____ 1949b. The relation between epidermal mitotic activity and the blood sugar level in the adult male mouse, *Mus musculus* L. *J. exp. Biol.*, 26, 83-99.
- BUTCHER, E.O. 1934. Hair cycles in the albino rat. *Anat. Rec.*, 61, 5-19.
- _____ 1936. Hair growth on skin transplants in the immature albino rat. *Anat. Rec.*, 64, 161-171.
- _____ 1951. Development of the pilary system and the replacement of hair in mammals. *Ann. N.Y. Acad. Sci.*, 53, 508-516.
- CHASE, H.B. 1954. Growth of hair. *Physiol. Rev.* 34, 113-126.
- _____ 1955. The physiology and histochemistry of hair growth. *J. Soc. cosmet. Chem.*, 6, 9-14.
- CHASE, H.B., MONTAGNA, W. 1951. Relation of hair proliferation to damage induced in the mouse skin. *Proc. Soc. exp. Biol. Med.*, 76, 35-37.
- CHASE, H.B., MONTAGNA, W., MALONE, J.D. 1953. Changes in the skin in relation to the hair growth cycle. *Anat. Rec.*, 116, 75-81.
- CHASE, H.B., RAUCH, H., SMITH, V.W. 1951. Critical stages of hair development and pigmentation in the mouse. *Physiol. Zool.*, 24, 1-8.

- DAVID, L.T. 1934. Studies on the expression of genetic hairlessness in the house mouse (*Mus musculus*). J. exp. Zool., 68, 501-518.
- DOWLING, D.F. 1955. The thickness of cattle skin. Austr. J. agric. Res., 6, 776-785.
- DRY, F.W. 1926. The coat of the mouse (*Mus musculus*). J. Genet., 16, 287-340.
- DURWARD, A., RUDALL, K.M. 1949. Studies on hair growth in the rat. J. Anat., 83, 325-335.
- EDWARDS, R. 1957. Studies on the physiology of mice selected for large or small body size. Thesis, University of Edinburgh.
- EMMENS, C.W. 1942. The endocrine system and hair growth in the rat. J. Endocrin., 3, 64-78.
- FALCONER, D.S. 1948. Selection for size in mice. Heredity, 2, 403. (Abstr.)
- _____ 1953. Selection for large and small size in mice. J. Genet., 51, 470-501.
- _____ 1955. Patterns of response in selection experiments with mice. Cold Spr. Harb. Symp. quant. Biol., 20, 178-196.
- FALCONER, D.S., FRASER, A.S., KING, J.W.B., 1951. The genetics and development of 'Crinkled' a new mutant in the house mouse. J. Genet., 50, 324-344.
- FALCONER, D.S., KING, J.W.B., 1953. A study of selection limits in the mouse. J. Genet., 51, 561-581.
- FALCONER, D.S., LATYSZEWSKI, M. 1952. The environment in relation to selection for size in mice. J. Genet., 51, 67-80.
- FALCONER, D.S., ROBERTSON, A. 1956. Selection for environmental variability of body size in mice. Z. indukt. abstamm. u. Vererblehre, 87, 385-391.
- F.A.O. 1955. Meeting on livestock production under tropical and sub-tropical conditions. Meeting report No. 1955/19.
- FERGUSON, K.A., CARTER, H.B., HARDY, M.H., 1949. Studies on Comparative fleece growth in sheep. Aust. J. sci. Res., B, 42-81.
- FRASER, A.S. 1951a. Growth of the Mouse Coats. J. exp. Zool. 117, 15-30.
- _____ 1951b. Competition between skin follicles in sheep. Nature, 167, 202-203.
- FRASER, A.S., NAY, T. 1953. Growth of the Mouse Coat. II. Effect of sex and pregnancy. Aust. J. biol. Sci., 6, 645-656.

- FRASER, A.S., NAY, T. 1955. Growth of the Mouse coat. IV. Comparison of Naked and Normal mice. Aust. J. biol. Sci., 8, 420-427.
- GIBBS, H.F. 1941. A study of the post natal development of the skin and hair of the mouse (*Mus musculus*). Anat. Rec. 80, 61-81.
- GIJECKSOHN-WAELSCH, S. 1951. Physiological genetics of the mouse. Advanc. Genet., 4, 1-49.
- GRUNEERBERG, H. 1952. The genetics of the mouse. 2nd Ed. The Hague: Nyhoff.
- HADDOW, A., ELSON, L.A., ROE, E.M.F., RUDALL, K.M., TIMMIS, G.M., 1945. Artificial production of coat colour in the albino rat. Nature, 155, 379-386.
- HADDOW, A., RUDALL, K.M., 1945. Artificial coat colouration and the growth of hair. Endeavour, 4, 141-147.
- HARDY, M.H. 1951. The development of the pelage hairs and vibrissae from skin in tissue culture. Ann. N.Y. Acad. Sci., 53, 546-561.
- _____ 1952. The histochemistry of hair follicles in the Mouse. Amer. J. Anat., 90, 285-338.
- HAUSMAN, L.A. 1924. Further studies on the relationships of the structural characters of Mammalian hair. Amer. Nat., 58, 544-558.
- HERINGTON, L.P. 1951. The role of the pilary system in mammals and its relation to the thermal environment. Ann. N.Y. Acad. Sci., 53, 600-607.
- HERTER, K. 1936. Das thermotaktische Optimum bei Nagetieren, ein mendeles Art- und Rassenmerkmal. Z. vergl. Physiol. 23, 605-650.
- _____ 1938. Die Beziehungen zwischen Vorzugstemperatur und Hautbeschaffenheit bei Mäusen Zool. Anz. Suppl. Bd., 11, 48-55.
- HERTER, K., SCONINA, K., 1938. Vorzugstemperatur und Hautbeschaffenheit bei Mäusen. Z. vergl. Physiol., 26, 366-415.
- ILJIN, N.A. 1945. The role of heredity in response to a drug as demonstrated by the experimental molt of rabbits induced by toxic thallium compounds. J. Hered., 36, 85-91.
- LAURIE, E.M.O. 1946. The reproduction of the house mouse (*Mus musculus*) living in different environments. Proc. Roy. Soc. B. 133, 248-281.

- LEBLOND, C.P. 1951. Histological structure of hair with a brief comparison to other epidermal appendages and epidermis itself. *Ann. N.Y. Acad. Sci.*, 53, 464-475.
- MONTAGNA, W., CHASE, H.B., MALONE, J.D., MELARAGNO, H.P. 1952. Cyclic changes in polysaccharides of the papilla of the hair follicle. *Quart. J. micr. Sci.*, 93, 241-245.
- NAY, T., FRASER, A.S. 1954. Growth of the Mouse coat. III. Patterns of hair growth. *Aust. J. biol. Sci.*, 7, 361-367.
- _____ 1955. Growth of the Mouse coat. V. Effects of pregnancy and lactation. *Aust. J. biol. Sci.*, 8, 428-433.
- PARNELL, J.P. 1949. Post natal development and functional histology of the sebaceous glands in the rat. *Amer. J. Anat.* 85, 41-71.
- RAE, A.L. 1956. Genetics of the sheep. *Advances in Genetics*, 8, 190-253 New York: Academic Press Inc.
- RAUCH, H. 1952. The effect of topical applications of chemical agents on hair development. *Physiol. Zool.*, 25, 268-272.
- SCHOLANDER, P.F. 1955. Evolution of climate adaptation in homeotherms. *Evolution*, 9, 15-26.
- SCHOLANDER, P.F., WAITERS, V., HOCK, R., IRVING, L. 1950. Body insulation of some arctic and tropical mammals and birds. *Biol. Bull, Woods Hole*, 99, 225-236.
- SHIPMAN, M. 1952. A study of glycogen in the skin of the mouse in relation to the hair growth cycle. Thesis, Brown University.
- SLEE, J. 1954. The morphology and development of 'Ragged', a mutant affecting the skin and hair of the house mouse. Thesis, University of Edinburgh.
- _____ 1957. The morphology and development of 'Ragged', a mutant affecting the skin and hair of the house mouse. *J. Genet.*, 55, 100-121.
- SNEDECOR, G. 1956. *Statistical Methods*, 5th Ed. Iowa: Iowa State College Press.
- STEINBERG, A.G., FRASER, F.C. 1946. The expression and interaction of hereditary factors affecting hair growth in mice. *Canad. J. Res.*, 24, 1-9.
- STOREY, W.F., LEBLOND, C.P. 1951. Measurement of the rate of proliferation of epidermis and associated structures. *Ann. N.Y. Acad. Sci.*, 53, 537-545.

- WOLBACH, S.B. 1951. The hair cycle of the mouse and its importance in the study of sequences of experimental carcinogenesis. Ann. N.Y. Acad. Sci., 53, 517-536.
- WRIGHT, N.C. 1954. The ecology of domesticated animals. Progress in the physiology of farm animals. 1, 191-251. London: Butterworths Scientific Publications.

ABSTRACT OF THESIS

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Name of Candidate W.V.S. WIJERATNE.
Degree..... Ph.D. Date..... 20th July, 1958.
Title of Thesis..... GROWTH AND STRUCTURE OF THE COAT IN STRAINS OF LARGE AND SMALL MICE

A study of the growth and structure of the hairs of the coat was conducted in large and small mice. The object was to see in what ways growth of hair was related to growth of body.

The study was made by comparisons between strains that had been selected for large and for small body size. Selection for body size, that had produced large differences in body weight between large and small strains, brought about proportionately small alterations in hair characters such as length and thickness, but considerably larger changes in the rate of coat eruption. This suggested that there was only a small relationship between genes governing body and hair growth. The differences in coat characters became marked after weaning, when animals were able to express their own genotype.

Mice belonging to the large strains had thicker and longer hairs in the first coat than mice from their respective small strains. The differences in length became more marked in the second coat. Usually no differences were present between large and small mice in the growth of the first coat, but during the growth of the second coat the large mice had an appreciably higher rate than the small mice.

The most striking difference found between the large and small strains was in the rate of replacement of hairs by the successive cycles of hair regeneration. The mice of the small strains were considerably slower in their cycles. The fact that these differences were maintained after body growth had ceased suggested the existence of a permanent physiological process, probably the growth hormone of the anterior pituitary, influencing the growth of hair. There also appeared to be a constant interval between the cyclic appearance of coats within strains.

