INHERITANCE IN THE HOUSE MOUSE, THE LINKAGE RELATIONS OF SHORT-EAR, HAIRLESS, AND NAKED[1]

GEORGE D. SNELL

Bussey Institution, Harvard University, Boston, Massachusetts

Received January 6, 1930

TABLE OF CONTENTS

[1] Based on a thesis for the degree of Sc. D.

INTRODUCTION

In the years 1926, and 1927, two new unit characters of mice were reported, one a recessive, the other a dominant, both causing absence of hair. The first of these, the recessive Mendelian character, "hairless," was described by BROOKE (1926), being derived from a hairless male and female captured in London. The second, "naked," an incomplete dominant, appeared as a mutation in the mouse stocks of the UNIVERSITY OF LATVIA in Riga and was described and shown to be a Mendelian character by LEBEDINSKY and DAUVART (1927). Through the efforts of Doctor CASTLE mice of these two types were received at the BUSSEY INSTITUTION in the spring of 1928, and during the past year and a half tests have been in progress to detect possible linkage with the other known characters of mice. This paper presents data proving a linkage of the recessive hairless with piebald, and showing the absence of linkage between naked and all of the other well established characters.

New data are also presented on the linkage of short-ear and dilution, together with a study of the multiple effects of the gene causing short-ear, particularly in regard to alterations in the shape of the skull.

The first section of the paper is devoted to a description of the Mendelian or apparently Mendelian characters which have been reported in the house mouse. Known facts concerning linkages are also presented, but, owing to the very complete review of linkage data given by GATES (1926a), less emphasis is put on this than on the discussion of the nature and history of the unit factors. The second section of the paper presents new data gathered by the author. For a more complete bibliography than is here given the reader should consult CUÉNOT'S article (1928).

THE UNIT CHARACTERS OF THE HOUSE MOUSE

Agouti and its allelomorphs

Non-agouti

Non-agouti is the lowest member of the agouti series of allelomorphs, all others being dominant to it. Whereas its allelomorphs suppress the development of pigment in some part or other of the coat, the non-agouti gene permits the maximum development of pigment throughout the length of each hair. Hence when non-agouti is substituted for agouti in a mouse otherwise of the wild gray type the pelage, instead of being gray, is uniform black in color.

Black-and-tan

Black-and-tan mice are similar in appearance to non-agoutis except that the belly is whitish, cream, or bright yellow, with occasionally a

patch of reddish-brown hair between the front legs. As manifested in the light belly, this gene is dominant to all other members of the agouti series, but as manifested in the black back it is recessive to agouti, white-bellied agouti and yellow.

The name was first applied to the darker forms of sable mice which are genetically modified yellows, black-and-tan (as it is now known) not being reported till DUNN (1928) obtained some mice of this type from an English fancier and established the character as an allelomorph in the agouti series.

Black-and-tan has occurred at least once as a mutation in a laboratory stock, PINCUS (1929) having obtained a single black-and-tan mouse in the ninth inbred generation of a non-agouti stock. I have recently found what appear to be four similar mutants in my own crosses. These will be discussed in more detail in a later section of the paper.

Agouti

The agouti gene causes the development of a sub-apical yellow band on each hair, the black and brown pigments being suppressed in this region and only the yellow showing. The result is to make an otherwise black coat into the grayish-brown coat characteristic of the wild house mouse and many other rodents.

White-bellied agouti

White-bellied agouti mice have a typical gray or agouti dorsum, but the belly is whitish or yellow like that of the black-and-tan. They are indistinguishable in appearance from mice heterozygous for black-and-tan and agouti.

LITTLE (1916) has reported four mutations to white-bellied agouti, but unfortunately the nature of the crosses in which they appeared make it impossible to tell whether the mutations were from agouti or from non-agouti.

Owing to the fact that the light belly of white-bellied agouti appears phenotypically as a distinct character rather than as an intermediate form between agouti and yellow, MORGAN (1914) suggested that it is due to a gene different from but closely linked with the agouti gene. However, in a backcross generation of 180 individuals raised to test this hypothesis he failed to obtain a crossover.

Yellow

The yellow factor in the heterozygous condition causes a reduction of black and brown pigment, thus leaving the hair a bright yellow. In the

presence of certain modifying genes, however, yellow mice are changed into "sables" or "black-backed yellows," in which the back is considerably darkened, the most extreme individuals being similar in appearance to black-and-tans. The eyes are always dark pigmented. The gene for yellow also induces a marked accumulation of fat accompanied by a tendency to sterility. In the homozygous condition it is lethal, causing the death of the embryo at or shortly after implantation.

Albinism and its allelomorphs

Albinism

CUÉNOT (1902), CASTLE and ALLEN (1903, ALLEN 1904) showed albinism to be inherited as a Mendelian factor.

It is linked with pink-eye and shaker.

Extreme dilution

Mice homozygous for the extreme dilution factor are practically white in the first pelage, but later acquire a brownish shade on the dorsum. The eyes are only a trifle lighter than those of full colored mice and the ears and scrotum show distinct dark pigmentation. Extreme dilution is incompletely dominant to albinism.

Chinchilla

The chinchilla gene causes a slight dilution of the coat pigments, especially the yellow, and is therefore more conspicuous in agouti than in non-agouti animals as these normally show the most yellow. It is incompletely dominant to extreme dilution and to albinism.

Color

Full color is normally completely dominant to all lower members of the albino series, but under certain conditions the dominance is incomplete. Thus CUÉNOT (1928) states that pink-eyed mice heterozgous for color and albinism or even for color and chinchilla are appreciably lighter than those homozygous for full color, and PLATE (1910) and RABAUD (1919) have reported mice heterozygous for color and albinism (and also for brown and perhaps other factors in the case of PLATE'S mice) which developed large patches of white or silvered hair as they grew older. A further demonstration of the incomplete dominance of color has been furnished by HANCE (1927, 1928) who finds that mice carrying albinism, when treated at ten to fourteen days of age with just sufficient X-rays to produce hair falling, regenerate a semi-white coat.

Brown

In brown mice all black pigment is absent, the remaining pigmentation, according to WRIGHT (1917), being "really intermediate between black and yellow, uniformly throughout skin, coat and eye." The result is cinnamon or chocolate colored mice according as the brown factor is combined with agouti or non-agouti.

Brown is usually entirely recessive to its allelomorph, black, but in at least two cases the dominance is partially reversed. Pink-eyed non-agouti mice carrying brown in the heterozygous condition are distinguishable from those homozygous for black by their lighter shade. A more striking lack of dominance is found in combination with silver. When silver mice carry the brown factor in the heterozygous condition the silvering is greatly intensified, the underfur being practically white and the general shade of the pelage little if any darker than that produced by extreme dilution. The eye is black. Chocolate silvers, despite the double dose of the brown factor, are often darker than these heterozygous black mice, though the unsilvered hairs are brown rather than black.

LITTLE (1916) has reported one case of a mutation from black to brown, cinnamon mice appearing in a strain of grays inbred brother with sister for five generations and by other matings for several generations before that.

Pink-eye

The eye of pink-eyed mice, as the name implies, is very light, closely resembling that of albinos; but according to Miss DURHAM (1911) traces of pigment are present in both retina and iris. The color of the skin and coat is also considerably lightened, the pigmentation as reported by WRIGHT (1917) being more or less intermediate between black and yellow.

LITTLE (1916) has reported one case of mutation to pink-eye, mice of this type appearing in a strain previously tested for the absence of the character.

Pink-eye is linked with albinism and shaker.

Dilution

The recessive factor, dilution, produces a general lightening of the coat color, not by a reduction in the number of pigment granules but by causing them to be clumped together. It is ordinarily entirely recessive but in two or perhaps three mice described in detail in a later section of this paper I have obtained what appears to be a temporary reversal of dominance.

Dilution, as first discovered by GATES (1927, 1928a), is very closely linked with short-ear.

Piebald

Piebald is an imperfectly recessive character consisting of white spotting. Most commonly there is one white patch in the belly and one or more white patches on the back and forehead, but according to DUNN (1920) the homozygous piebald genotype "may vary somatically from solid colored to all white with dark eyes."

Mice heterozygous for piebald often show a small white area on the belly. When in addition the gene from black-eyed white is also present in the heterozygous condition, the result is the so-called "variegated" or "Type A" spotting, a type with much more white than that caused by either gene acting alone. Piebald cannot therefore be classified as entirely recessive.

Data presented in a later section of this paper show piebald to be linked with hairless.

Black-eyed white

In the heterozygous condition the gene for black-eyed white produces a low grade of spotting, while in the homozygous condition it is lethal, causing death from anemia shortly before or after birth. According to So and IMAI (1920) it can be distinguished somatically from piebald by the lack of a sharp line of demarcation between the light and dark areas, the white patches overlapping the dark as "silvering" or occasional white hairs. The name is derived from the fact that when combined with piebald in the homozygous condition it may produce all white mice with black eyes, the so-called "black-eyed white" mice. The black-eyed white gene acting alone produces only small areas of white.

Spotting modifiers

Both types of spotting, but especially piebald, are subject to wide variation with respect to the extent and location of the white areas. CUÉNOT (1928) states it as probable "that spotting is conditioned by multiple or allelomorphic factors for extension whose effect is algebraically additive." He finds that the lower degrees of spotting are dominant over the higher. DUNN (1920) also reports spotting modifiers "which appear to increase the general amount of color forming substance" so that in their presence both black-eyed white and pieblad genes produce relatively less than the normal amount of white spotting.

The first and only successful isolation of pattern varieties was accomplished by DUNN and DURHAM (1925), who, by inbreeding two strains of

piebald, one with a white face and the other a white-belted variety, and then crossing, obtained clear segregation in the F_2. The gene causing white face was shown to be dominant as it appeared in practically all F_1 individuals and in three-fourths of the F_2's. The belted pattern, on the contrary, was recessive.

CUÉNOT (1904) and DUNN and DURHAM (1925) both reach the conclusion that the finest details of piebald spotting are not represented in the germ plasm, but are rather due to variations in the environment.

Silver

Silver is a multiple factor character, though probably with one principal recessive gene involved. It consists of the presence of white hairs scattered throughout the coat, but the number of such hairs and hence the intensity of the silvering may vary through a wide range. In black mice heterozygous for brown it is greatly intensified, the whole underfur being practically white.

Data recently published by KEELER (1930) indicate that the principal gene for silver lies on the same chromosome as the gene for rodless.

Hairless

Hairless is a recently studied recessive character causing reduced viability, partial sterility especially in the females, and practically complete loss of hair after the second week of life (figure 1). The homozygous hairless young are indistinguishable from their normal sibs until about fourteen days of age when, at just about the same time that the eyes open, they can be recognized by loss of hair on the upper eyelid. At the same time, shedding begins on the under jaw and on all four feet just above the toes, and slightly later at the base of the tail. During the course of the next week a wave of shedding spreads from these centers, especially that around the eye, until it has passed over the entire body, leaving the animal completely naked except for a few scattered hairs. The vibrissæ may or may not be present. Sometimes they remain indefinitely, sometimes they are lost as early as the fifteenth day, but they always reappear eventually for in old individuals at least a few are invariably present. At about six weeks of age some slight regeneration of the whole coat occurs, but it is usually so slight as easily to escape notice. One piebald male in my stocks, however, developed sufficient re-growth so that the piebald pattern was distinctly visible. The skin, when naked, is often slightly moist, but usually comparatively smooth, though old animals may show a few criss-cross wrinkles on the head.

The majority of hairless females are entirely sterile, but occasionally one gives birth to a litter. Of the four litters, however, which have been born to hairless females in my stocks, all have been dead when found except for a single individual which was given to a foster mother but died

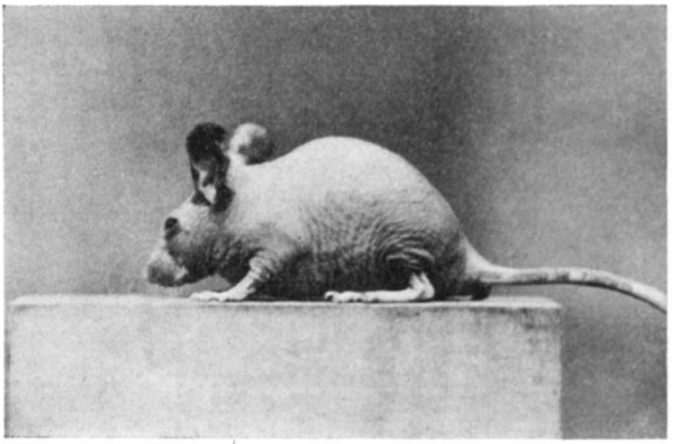


FIGURE 1.—Male homozygous for hairless ($h^r h^r$).

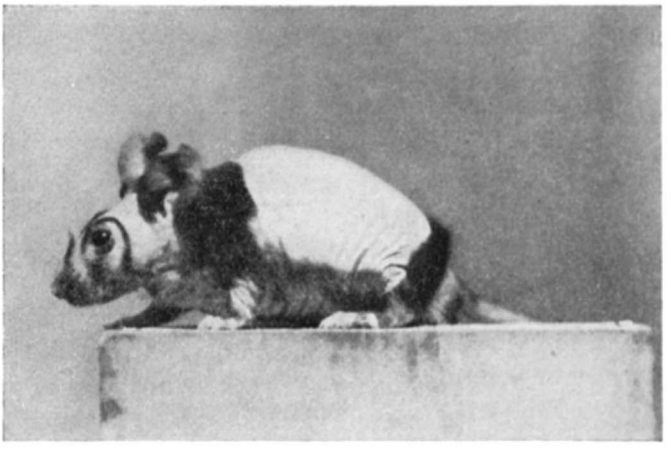


FIGURE 2.—Male heterozygous for both hairless and naked ($H^r h^r N_n$), showing the goggle-like rings of hair around the eyes characteristic of individuals of this genetic constitution.

soon after. In all cases except this one, death apparently occurred at or very shortly after birth. The males are also considerably reduced in fertility.

The character is entirely recessive except when present in mice heterozygous for dominant hairless or naked. These doubly heterozygous

animals are distinguishable by the increased hairlessness and by the unusual patterns which the hair assumes, especially conspicuous being the goggle-like ring of hair around the eyes (figure 2) often seen in them but never in mice carrying only the gene for naked.

The only reference in the literature to hairless mice which can be stated with complete assurance as applying to mice of the type described above is that of BROOKE (1926) who reports a pair captured in an aviary in London. The hairless mice used by the present author for linkage tests are descended from this pair. Earlier descriptions of hairless mice probably also of this type are given by GASKOIN (1856), MARSHALL (1887), BATESON (1894), ALLEN (1904), POCOCK (1904), and CAMPBELL (1907).[2] All these authors describe the hairless animals as having a skin deeply folded and wrinkled, a characteristic which caused the name "rhinocerous mice" to be applied to them. CAMPBELL gives some data, unfortunately very incomplete, indicating linkage of his "corrugated hairless" with piebald. Were it not for this indication of linkage with piebald, the same linkage as that which I have found, I would suspect from the unusual folding and creasing of the skin reported by all these earlier writers, but not appearing in my own mice, that I was dealing with a different type of hairlessness. It is probable, however, in view of the linkage, that this folded skin is the product merely of environmental conditions or modifying factors, or at most an allelomorph of hairless, but it will certainly be of interest to make a genetic study of hairless mice from new sources on the possibility that other types of hairlessness can be found.

The linkage of hairless with piebald has already been noted, and will be discussed in more detail later.

Naked

Naked is a partially dominant mutation of recent origin. Mice carrying the gene in double dose are completely naked from birth with the exception of occasional hairs hardly visible to the naked eye, even the vibrissæ being absent. They are almost without exception sterile, though young can occasionally be reared from matings of naked males with fully haired females. They seldom attain as much as three-fourths normal size; the body is shrunken, the skin somewhat wrinkled, and the vitality in all respects greatly reduced.

Mice carrying the gene in single dose resemble those homozygous for the recessive hairless character in that the shedding starts in the neighbor-

[2] Another reference to hairless mice is that of BREE, appearing in *Field* for October 5, 1872. p. 328. I have been unable to obtain this reference, and so omit it from the above discussion,

hood of the eyes simultaneously with its opening on about the fourteenth day after birth, and in the course of the following week progresses backwards over the length of the body. Here, however, the similarity ends. In the histological abnormalities of the skin and in the general manner of shedding, there are marked differences between the two types. Unlike mice carrying genes for hairless, those heterozygous for naked can usually be identified prior to the fourteenth day by the shortness and lack of luster of their coat. Unlike them, again, the feet and tail are not centers of shedding; on the contrary, the tail, the fore feet to the elbow, and the hind feet as far as the heel are almost normally haired throughout life. Ears and tip of nose may also maintain a certain amount of covering. Again,

FIGURE 3.—Female heterozygous for naked (N_n).

the shedding in naked mice, instead of consisting of an actual falling of the hair, is the result of the breaking off of the hairs at the surface of the skin, the root remaining for some time. Moreover, the line of demarcation between the naked and haired regions is not so sharp. The most striking difference, however, is the repeated successions of regeneration and shedding exhibited by the heterozygous naked mice. At about one month of age, shortly after the first moult is complete, a new coat begins to appear on the head, the new growth progressing posteriorly over the body, only to be followed by another wave of shedding. This process is repeated throughout the life of the individual at intervals of roughly one month, two or three successive waves sometimes being in evidence at one time as isolated bands of hair across the body (figure 3). The rate of shedding, however, and the resulting coat patterns, vary considerably

from one individual to another. The vibrissae are usually present though they may be of less than normal length and are occasionally absent altogether.

The naked character arose as a mutation in the mouse stocks of the UNIVERSITY of LATVIA in Riga, and was described and shown to be a simple Mendelian dominant by LEBEDINSKY and DAUVART (1927). The only other reference in the literature which clearly applies to mice of this type is GORDON'S (1850) description of three hairless mice sent to him from Elgin. He says of them, "The whole bodies of these three little creatures were completely naked,—as destitute of hair and as fair and smooth as a child's cheek. There was nothing peculiar about the snout, whiskers, ears, lower half of the legs and tail; all of which had hair of the usual length and colour." The presence of hair on the snout, legs, ears, and tail and its absence elsewhere clearly brands these mice as being heterozygous for naked, and probably about one month old.

Short-ear

Short-ear is a recessive character whose primary effect in the homozygous condition is a reduction of the ear to less than one half normal length, but which also causes kinkyness of the tail, changes in shape of the skull, and a slight decrease in size and vigor. The kinky-tail associated with short-ear is easily distinguished from the flexed-tail described by PLATE (1910), and HUNT and PUMAR (1928), by the fact that it is not due to fusion of the vertebrae but rather is purely muscular, disappearing when the animal is etherized. Both GATES (1926a) and KEELER (1927) report rather frequent crossovers between short-ear and kinky-tail,and therefore conclude that the two are due to distinct but linked genes. In extended crosses, however, I have found no evidence that the two can be separated and hence believe them to be expressions of the same gene.

As discovered by GATES (1927), short-ear is very closely linked with dilution, the first crossover to occur having been obtained by the present author (1928). New data on this linkage and on the various effects of the gene for short-ear are given in a later section of this paper.

Rodless

Rodless is a recessive Mendelian character consisting of complete absence of rods and external molecular layer from the eye, and reduction of the external nuclear layer. Usually only one row of nuclei is present, but occasionally three or six rows are found to occur. Rodless mice are totally blind.

KEELER (1930) has reported data indicating linkage of rodless with silver.

Waltzing

Mice homozygous for the waltzing gene are totally deaf and seriously defective in their sense of balance, this inability to orient themselves causing the whirling or waltzing movements for which they are famous. They also show reduced size and viability.

GATES (1926a) has demonstrated that the pure-bred Japanese waltzing mice are descended from *Mus wagneri* rather than *Mus musculus*. GATES (1926b) has also demonstrated in a cross of waltzing and normal mice the first and only case of non-disjunction in mice, the genetic evidence which he presents proving the absence of part of one of the chromosomes carrying the waltzing gene in an F_1 female and half of her offspring. Cytological confirmation of this has been furnished by PAINTER (1927).

Shaker

GATES (1928b) has recently found a new recessive Mendelian character in mice, "shaker," which manifests itself as rapid and continuous up and down movements of the head. The same type of motion is sometimes observed in waltzers but the two factors are entirely distinct. LORD and GATES (1929) find that young shakers are normal in hearing, but that they become deaf at ages ranging from 22 to 29 days. Mice heterozygous for shaker ordinarily possess unimpaired hearing, at least up to 1 year of age, but when waltzing is also present in the heterozygous condition they usually go deaf when from 3 to 6 months old. Shaker is thus incompletely recessive when combined with one dose of waltzing.

Shaker is quite closely linked with albinism, and hence with pink-eye, the meagre data at present available indicating that albinism will lie between shaker and pink-eye on the chromosome map.

Tailless

Tailless is a dominant mutation manifesting itself as a marked reduction or even complete absence of the tail. The homozygous tailless form has never been obtained indicating that it, like yellow and black-eyed white cannot develop to maturity, though embryological evidence of its prenatal death is altogether wanting. In experiments made to test the nature of its inheritance, NÄGELI and LANG (LANG 1912) obtained the expected 1:1 ratio (199 normal to 180 tailless) in a backcross, but a 1:1 rather than a 2:1 ratio in the F_2; and DUBOSCQ (1922) found the charater sometimes

dominant and sometimes recessive. Only DOBROVOLSKAIA-ZAVADSKAIA (1927) obtained the expected Mendelian ratios in all crosses.

No linkage relationships have been determined.

Flexed-tail

Flexed-tail is an imperfect Mendelian character consisting in well marked cases of numerous sharp kinks in the tail due to displacement and partial fusion of successive vertebrae. Several recessive genes are probably involved. It was first reported by PLATE (1910) and BLANK (1916), and what is probably the same character has more recently been reported in this country by HUNT and PUMAR (1928). HUNT finds it to breed true and to give the expected 1:1 ratio in a backcross, though the F_2 ratio is nearer 7:1 than 3:1. PLATE and BLANK obtained even more abnormal results, the character in some cases appearing to behave as a dominant.

Linkage relations have not been determined, but GATES (1926a) believes PLATE'S data to indicate a linkage with pink-eye.

Ectromelus ("Souris Luxees")

An imperfect Mendelian character, ectromelus ("luxee"), consisting of the absence of the tibia from the hind legs and certain malformations of the fibula, was reported by RABAUD (1914). CUÉNOT (1928) interprets the character as probably a simple recessive showing, however, a considerable number of normal overlaps. No linkage tests have been made.

Polydactylism ("hyperdactylie")

RABAUD'S ectromelus mice gave birth to some young showing polydactylism (19 out of 240), one or both hind feet having six or seven toes (RABAUD 1919). Polydactylism, by appropriate crosses, may be separated from the ectromelus form, but the manner of its inheritance is in doubt.

Haemoragic head

Haemoragic head is a semi-lethal recessive abnormality found by LITTLE and BAGG (1924) among the descendants of two different pairs of X-rayed mice. It is highly variable in its expression, consisting in widely varying degrees of malformation of eyes, feet, kidneys, and occasionally other internal organs. In mild cases the eyes may show slight clouding or distortion, or one kidney may be reduced in size; in extreme cases both eyes may be sightless or even lacking and both kidneys entirely absent, this condition causing death about twenty-four hours after birth. Cases

of syndactylism, polydactylism, and especially club feet are occasionally present as expressions of the character, and BAGG (1929) finds that their incidence can be greatly increased by selection. Embryological studies have shown all these defects to be associated with blood extravasations. While the inheritance of haemoragic head is not strictly Mendelian, an excess of normals appearing in all crosses, it is probably the effect of a single recessive gene. BAGG (1925) reports 17 normal overlaps among 179 offspring from matings of affected (hence homozygous) individuals, while F_2 and backcross generations (BAGG and HALTER 1927) gave ratios of normals to abnormals of 1082:282 and 333:240 respectively.

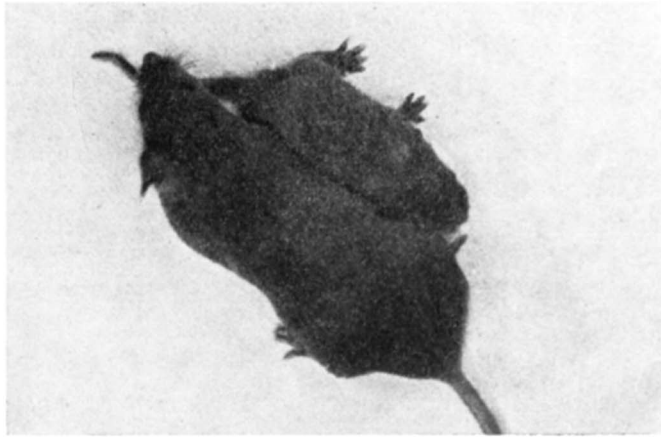


FIGURE 4.—Dwarf mouse and normal sib two months old.

Another type of deformity appearing among offspring of both X-rayed and control mice and named by LITTLE and BAGG (1924) the "Lethal head and jaw abnormality" is now regarded by BAGG as a manifestation of the same gene that causes haemoragic head.

No tests for linkage of haemoragic head with other characters have been reported.

Dwarf

Dwarf is a recessive Mendelian character causing a great reduction in growth rate after the fourteenth day, with the result that mature dwarf mice are scarcely more than one-fourth normal size (figure 4). Up to the fourteenth day growth is practically normal though affected individuals can be identified on about the twelfth day by their shorter noses and tails. The dwarfs are sterile and somewhat reduced in vigor, showing little tendency to jump or run and a marked thinning of the hairs as they get old,

but in other respects their health and viability are good. They were first reported by the author (1929). Linkage tests are now in progress.

Sex-linked lethals

Possible sex-linked lethals have been reported by two investigators. MORGAN (1914) found a ratio of 76 females to 26 males in the offspring of a certain cross, and believes this to indicate a probable sex-linked lethal. LITTLE (1920) obtained a similar excess of females (100 to 53) in a line of Japanese waltzers and attributes it to the same cause. In neither case was it shown that the lethal was transmitted to half the daughters of an affected female, the other half being normal, as should be the case with a sex-linked lethal, and in other respects the data are rather incomplete. It is, of course, impossible to tell whether or not the same gene was involved in the two cases.

Hyperglycaemia

CAMMIDGE and HOWARD (1926) have reported a recessive Mendelian character in mice consisting of an excess concentration of sugar in the blood. Their ratios are very close to the expected. It remains to test this character, hyperglycaemia, for linkage with most of the other known factors, but absence of linkage with albinism is clearly shown by their crosses.

Angora

COCKS (1852) described a long-haired or angora mouse caught in England, but this mutation does not seem to have reappeared.

Congenital eye anomaly

PEARSON (1924) has reported an eye defect, probably congenital, consisting of opacity of the lenses and occasionally reduction in size of the eye, which appeared in about 1.5 percent of a strain of albino mice. The manner of inheritance is in doubt.

Twisted nose

The occurrence of a twisted or stunted nose due to a shortening of one or both of the nasal bones has been reported by KEELER (1929) in four closely related mice. The manner of inheritance suggests a "dominant unit character with normal overlaps," but this must be regarded as uncertain due to the small amount of data.

DISCUSSION OF THE KNOWN UNIT CHARACTERS OF THE HOUSE MOUSE

A comparison of the dates of discovery of the known unit characters in mice shows that those first discovered were nearly all concerned with

coat color, whereas those more recently described are principally anatomical or physiological abnormalities. Of the eight sets of allelomorphs affecting the coat pigmentation, all were known prior to 1900 except silver (a multiple factor character and hence probably the result of long selection), the black-and-tan allelomorph of the agouti series, and extreme dilution and chinchilla in the albino series. While a more intensive search than ever before has been maintained since 1900 for new genes and the total number more than doubled, few of the new characters are concerned with pigmentation. It would therefore seem probable that all or practically all the discoverable factors of this type are now known, and that future search will reveal principally mutations which, like rodless, tailless, or hyperglycaemia, are concerned with function or internal structure.

MORGAN, BRIDGES, and STURTEVANT (1925) point out that "most of the dominant mutations in Drosophila are lethal when homozygous." The same generalization holds in the case of mice, three of the five dominant mutations (yellow, black-eyed white, and tailless) having a recessive lethal effect, while naked is a semi-lethal and only light-belly is without damaging consequences in the homozygous condition. MULLER remarks that this is probably not a peculiarity of dominant genes as contrasted with recessive ones, but because lethal mutations are themselves more common than other kinds and may well be expected to manifest themselves in certain cases in the heterozygote as a visible character.

Whereas mice are like Drosophila in the presence of dominant factors causing death in the homozygous condition, they differ markedly from Drosophila in the almost complete absence of lethals which are apparent only by their lethal effect. MULLER (1928) and others have stated that in Drosophila lethal genes are the most common type. In mice, on the other hand, only two pure lethals (the sex-linked lethals of MORGAN and LITTLE) have been reported, and these are not confirmed by embryological evidence or even well established genetically. It may perhaps be that this is due to lethals being actually less frequent in mice, but it seems more probable that it is the result of the relatively small number of offspring ordinarily raised from a single mating in the case of mice, this making it often impossible to establish the statistically significant difference between 3:1 and 2:1, 1:1 and 2:1, or even 3:1 and 3:0 ratios, necessary to prove the existence of a lethal. That ratios often do show undue departures from the expected is easily seen even by a casual examination of the literature, and I suspect that in some cases at least these departures are due to the action of lethal factors, but to prove this in

TABLE 1

Unit characters of the house mouse with their symbols and linkages.

CHROMOSOME	GENE	SYMBOL	NAME	CROSSOVER PERCENT
1	1	P	Dark-eye	
		p	Pink-eye	
				19.06 in female
	2	C	Full color	13.89 in male
		c^{ch}	Chinchilla	
		c^{d}	Extreme dilution	
		c	Albinism	
				2.5
	3	S^{h}	Non-shaker	
		s^{h}	Shaker	
2	4	A^{y}	Yellow	
		A^{w}	White-bellied agouti	
		A	Agouti	
		a^{t}	Black-and-tan	
		a	Non-agouti	
3	5	B	Black	
		b	Brown	
4	6	D	Density	
		d	Dilution	
				0.06
	7	S^{e}	Normal-ear	
		s^{e}	Short-ear	
5	8	S	Self	
		s	Piebald	
				9.8 in female
	9	H^{r}	Haired	2.6 in male
		h^{r}	Hairless	
6	10	W	Black-eyed white	
		w	Self	
7	11	V	Normal walking	
		v	Waltzing	
8	12	R	Rodded retinae	
		r	Rodless	
				12 ?
	13	S^{l}	Non-silver	
		s^{l}	Silver	
9	14	N	Naked	
		n	Normal coat	
?	15	H	Normal head	
		h	Haemoragic head	
?	16	T	Tailless	
		t	Normal tail	
?	17	D^{w}	Non-dwarf	
		d^{w}	Dwarf	

any given case is a difficult matter. If, however, in mouse crosses the maximum possible number of young is raised from each mating involving heterozygotes, lethal factors if present would ordinarily be revealed. According to GATES (1926a) and KIRKHAM (1920), the production of as many as 75 or 80 young from a pair is not impossible.

While it is both customary and useful to speak of genes as either dominant or recessive, it would seem that in mice many if not most of the genes are, strictly speaking, neither. It is possible to list as incompletely dominant, or incompletely recessive characters, albinism and its allelomorphs, yellow, brown, black-eyed white, shaker, piebald, hairless, naked, tailless, and perhaps dilution. Some of these, for example hairless and albinism, reveal their presence in single dose only under special conditions; and it is not unlikely that by proper experimental methods a number of the other factors would be found also to be detectable in the heterozygous condition.

THE LINKAGE OF SHORT-EAR AND DILUTION

As first discovered and reported by GATES (1927), there exists a remarkably close linkage in the house mouse between the characters short-ear and density and their allelomorphs normal-ear and dilution. To date only one crossover between these two pairs of characters has been reported. GATES (1927, 1928a) has reported the test of 426 individuals of F_2 and later generations from a cross of short-ear and dense with normal-eared and dilute without finding evidence of a single crossover. The present author (1928) has reported the test of 579 individuals from a similar cross. Of this number only one was the carrier of a crossover chromosome. From this single crossover individual was derived a stock of short-eared dilute mice, and a backcross undertaken with a view to obtaining further data on the linkage. From this backcross I have obtained a total of 1034 individuals but no crossovers.

One crossover, however, apparently has been obtained by Miss COPELAND in a backcross generation of 106 individuals. In one litter of seven young, she found a normal-eared dense male along with 4 normal-eared dilute individuals and 2 short-eared dense ones. I have tested this male and find him to be the correct constitution for a crossover, namely, S^eD/s^ed. This is the second crossover to occur between the two loci.

Totalling all data, the number of gametes so far tested is 3150, the number of crossovers 2, and the crossover percent 0.06. These results are summarized in tables 2, 3, and 4.

TABLE 2

Summary of F_2 data from crosses of short-ear×dilute.

	MATING	S^eD	S^ed	s^eD	s^ed	AUTHOR
Observed	$\varphi\frac{S^ed}{s^eD}\times\sigma\frac{S^ed}{s^eD}$	827	404	393	0	GATES 1928a
Expected		*812*	*406*	*406*	*0*	
Dev./P.E.		1.1	0.2	1.1		
Observed	Same	1407	722	603	0	SNELL 1928
Expected		*1366*	*683*	*683*	*0*	
Dev./P.E.		2.3	3.5	5.2		

TABLE 3

New data from backcross.

	MATING	S^eD	S^ed	s^eD	s^ed	AUTHOR
	$\varphi\frac{S^ed}{s^eD}\times\sigma\frac{s^ed}{s^ed}$	0	481	432	0	SNELL
	Same	1	55	50	0	COPELAND
	$\varphi\frac{s^ed}{s^ed}\times\sigma\frac{S^ed}{s^eD}$	0	64	57	0	SNELL
Observed		1	600	539	0	Total
Expected with complete linkage		*0*	*570*	*570*	*0*	
Dev./P.E.			2.6	2.6		

TABLE 4

Summary of data showing linkage of short-ear and dilution.

MATING	NUMBER OF OFFSPRING TESTED	NUMBER OF CHROMOSOMES TESTED	NUMBER OF CROSSOVERS	CROSSOVER PERCENT	AUTHOR
F_2	426	852	0	0	GATES 1928a
F_2	579	1158	1	0.09	SNELL 1928
Backcross	1034	1034	0	0	SNELL
Backcross	106	106	1	0.94	COPELAND
Total	2145	3150	2	0.06	Total

As was suggested to me by Doctor EAST, the two individuals interpreted above as crossovers may also be interpreted as mutants, for a mutation on chromosomes of the constitutions S^ed or s^eD would give chromosomes S^eD or s^ed that would be indistinguishable from those produced

by crossing over. Hence the hypothesis of mutation would satisfactorily account for the observed results. I am inclined, however, to regard the occurrence of a crossover as the more probable explanation. Mutations at the loci for short-ear and dilution have never been known to occur in laboratory stocks, except as already noted, and must be of very rare occurrence. Moreover, to explain the normal-eared dense individual obtained by Miss COPELAND otherwise than as a crossover it would be necessary to postulate a reverse mutation, that is, one from the mutant type back to the normal or wild type, and such mutations have been shown by observations on Drosophila to take place only with great rarity. This fact of the difference of mutation rate in the two directions, while not enabling us to choose finally between the two explanations with the data at present available, would enable us to make a choice were a larger amount of reliable data to be obtained. If an extensive backcross $(S^e d)/(s^e D) \times (s^e d)/(s^e d)$ yielded approximately the same number of double dominant $(S^e D)/(s^e d)$ offspring as of double recessive ones, it would be safe to infer that crossing over rather than mutation was responsible for their production.

In the F_2 generation which I obtained from matings of mice heterozygous for short-ear and dilution there is a significant deficit of short-eared dense individuals as indicated by the Dev./P.E. of 5.2 (table 2). Likewise, in the backcross generation there are less than the expected number of short-eared dense offspring, though here the Dev./P.E. is only 2.5 and hence not surely significant (table 3). These departures from the expected are attributable to lesser viability of short-eared mice as compared with normal-eared ones. All young had to be raised to at least fourteen days before they could be identified and during this period there were numerous deaths in the majority of litters, most of them due to paratyphoid. There is reason to believe that an undue proportion of these deaths were among short-eared dense individuals. Had the conditions for raising the young been more favorable, all ratios would probably have been normal.

REVERSAL OF DOMINANCE OF DILUTION

In the course of the backcross experiment two young were born which were first classified as short-eared dilutes and hence as crossovers, but which it now seems were almost surely short-eared and intense. The first of these, by female 155, lived only about a month, but during this time was examined on three occasions and carefully compared as to coat color with other dilute individuals. On each occasion its coat was unmistakably

dilute, and were it not for the second individual discussed below it would have been classified as a crossover. It was noticeably smaller than the single sib which survived the first week of life, and its hair was slightly thinner than normal.

The second case was a female, one of four young produced by a mating of female 71 to a short-eared dilute male. This female was examined at 17, 23, and 24 days of age, and on each occasion was unmistakably a short-eared dilute cinnamon. Its sibs, two short-eared intense and one long-eared dilute, were killed at the time of the first examination in order that this one might receive the full care of the mother. The next examination was made at 44 days of age and revealed the unexpected fact that the supposed crossover had moulted to a clear cut intense cinnamon. As in the case described just above, the apparently short-eared dilute individual was smaller than its sibs.

In the course of tests for possible linkage of naked with dilute a third case appeared, similar to the above, though not quite so well checked. A naked female, R177, mated to a dilute chocolate male, gave birth to a litter of seven young. These were examined at 10 and 15 days of age and one of the young, female R352, a cinnamon naked, was classified on both occasions as dilute. When the next examination was made, however, this female, then 36 days old, had regenerated a second coat which was clearly intense.

These three cases, of which one was very carefully checked, indicate that under certain conditions mice heterozygous for dilution may appear for about the first month of life as if homozygous dilute, the dominance of the gene for density being temporarily reversed. More cases would be necessary to prove that only individuals carrying dilution and never those homozygous for density can exhibit this phenomenon, but it seems probable that this is the case. It may be added that of the 603 short-eared intense ($s^e s^e DD$) F_2's none were of this pseudo-dilute type; if they had been they would have been classed as crossovers. It is of interest to note that all the pseudo-dilutes described above were cinnamons, but the significance of this is doubtful.

TESTS FOR LINKAGE OF NAKED

In June, 1928, there were received at the BUSSEY INSTITUTION from Doctor N. G. LEBEDINSKY of Riga, Latvia, six albino mice, two males and four females, heterozygous for the dominant Mendelian character, naked. They were sent at the request of Doctor CASTLE, and brought to

this country through the kindness of Doctor HANS NACHTSHEIM of Berlin and Doctor SCHRATA. From these six parents were derived the stock used in the linkage experiments here described. The original albino naked animals proved to be vigorous and good breeders, and the F_1 generation from crosses with other mice was exceptional in these respects. F_1 naked females not uncommonly produced and raised litters of six to eight young, and one such female gave birth to thirteen young of which twelve were raised to two weeks of age.

To date linkage tests of naked with rodless, hairless, piebald, black-eyed white, agouti, brown, pink-eye, albinism, waltzing, dilution, and short-ear have been completed, in every instance with negative results. It can therefore be concluded that the gene for naked does not lie on any one of the eight chromosomes occupied by these characters. All data were derived from backcrosses, the fact that naked is dominant making it unnecessary to raise an F_2 generation. With a few exceptions, pregnant females were removed to isolation pens, thus avoiding any mistake as to the identity of the mother and providing more favorable conditions for the young. All litters were classified at two weeks of age or within a few days thereafter, as by three weeks loss of hair was usually so complete as to make identification of coat color difficult or impossible. In many cases a preliminary record of coat color was made prior to two weeks of age. The linkage data are summarized in table 5.

In the case of every character but one, short-ear, free reassortment with naked is unquestionable, most of the characters showing more than 50 percent of crossovers. Short-ear shows only 43.3 percent and a Dev./P.E. of 3.5; but in view of the fact that dilution shows 49.5 percent crossing over and a Dev./P.E. of only 0.1, it seems highly probable that the gene for naked lies in a different chromosome from that occupied by the genes for these two characters.

The figures showing absence of linkage with hairless also prove the two characters to be not allelomorphic. Mice which are both hairless and naked ($h^rh^rN_n$) can be identified by the short, rough coat prior to shedding, by the loss of hair on the feet at the fourteenth day, and especially by the wrinkled skin at from two to three weeks of age, though as they get older they become almost indistinguishable in general appearance from ordinary hairless mice.

THE LINKAGE OF HAIRLESS AND PIEBALD

The hairless mice used in the experiments here described were descended from one homozygous hairless male and two heterozygous hairless fe-

TABLE 5

Backcross data showing absence of linkage of naked with other characters.

CHARACTER	NON-CROSSOVERS		CROSSOVERS		*Expected Crossovers*	CROSSOVER PERCENT	DEV. / P.E.
Rodless	*Rn*	*rN*	*RN*	*rn*			
	7	8	12	12	*19.5*	61.5	2.1
Waltzing	*VN*	*vn*	*Vn*	*vN*			
	5	7	6	12	*15.0*	60.0	1.6
Hairless	H^rN	h^rn	H^rn	h^rN			
	13	14	19	22	*34.0*	60.3	2.5
Piebald	*SN*	*sn*	*Sn*	*sN*			
	28	32	42	33	*67.5*	57.0	2.4
Agouti	*AN*	*an*	*An*	*aN*			
	66	91	88	99	*172.0*	54.3	2.4
Brown	*BN*	*bn*	*Bn*	*bN*			
	67	79	88	80	*157.0*	53.5	1.8
Pink-eye	*PN*	*pn*	*Pn*	*pN*			
	45	45	50	54	*97.0*	53.6	1.5
Albinism	*Cn*	*cN*	*CN*	*cn*			
	15	15	14	10	*27.0*	44.4	1.2
Black-eyed white	*Wn*	*wN*	*WN*	*wn*			
	13	14	10	14	*25.5*	47.0	0.6
Dilution	*DN*	*dn*	*Dn*	*dN*			
	32	27	31	27	*58.5*	49.5	0.1
Short-ear	S^eN	s^en	S^en	s^eN			
	65	57	52	45	*109.5*	44.3	3.5

TABLE 6

Backcross data showing 1:1 ratio of naked to normal coat.

OBSERVED		*Expected*		DEV.	P.E.	DEV. / P.E.
Naked	Normal	Naked	Normal			
361	373	*367*	*367*	6	9.14	0.7

males derived from BROOKE'S original stock (BROOKE 1926). This stock has been maintained in CREW'S laboratory in Edinburgh. They were brought to this country by Doctor DUNN and very kindly given by him to the author.

Before any large amount of data had been gathered in crosses involving hairless and the various other coat characters in mice it became evident that hairless and piebald were linked. Thereupon all other linkage tests were dropped and every effort concentrated on this one experiment. By a fortunate coincidence the original hairless individuals were piebalds so that it was unnecessary to raise an F_2 generation to obtain double recessive individuals for a backcross. Moreover, the piebald which they carried was of a rather high grade and therefore excellent to work with as the homozygous and heterozygous piebald segregates were usually distinguishable from one another without the slightest difficulty.

Owing to the sterility of the hairless females it was impossible to use the usual backcross mating to test the crossover rate in doubly heterozygous males. Hence the following matings were used:

$$♀ \frac{Sh^r}{sh^r} \times ♂ \frac{sh^r}{sh^r}$$

$$♀ \frac{sH^r}{sh^r} \times ♂ \frac{SH^r}{sh^r}$$

The first of these is the ordinary backcross. The second was adopted in preference to an F_2 coupling cross because, while no more efficient in showing the presence of a linkage, it reveals crossovers in the male only. The crossover percent for this mating was calculated by a modification of the method of maximum likelihood described by R. A. FISHER (1928, pp. 243-244).

In order to insure the accuracy of the data gathered, the following precautions were adopted. All pregnant females (with a few exceptions due to failure to detect pregnancies) were isolated in separate pens. In some cases where the litter was large and the mother unable to furnish sufficient milk, all young in excess of three or four and occasionally the entire litter, were given, when between one and four days of age, to foster mothers. All litters were classified at two weeks of age or a few days thereafter, and in most cases preliminary records were made as to the self or piebald character of the coat at between ten and fourteen days of age.

Despite these precautions, the data are still subject to one possible

source of error. Though the piebald used was in general of a high grade it showed considerable variation, and it is thus possible that some individuals genetically homozygous piebald were phenotypically self, while others genetically heterozygous self were phenotypically piebald. Such

TABLE 7

Backcross data showing 1:1 ratio of haired to hairless.

OBSERVED		*Expected*		DEV.	P.E.	$\frac{\text{DEV.}}{\text{P.E.}}$
Haired	Hairless	Haired	Hairless			
92	101	*96.5*	*96.5*	4.5	4.69	1.0

TABLE 8

F_2 data showing 3:1 ratio of haired to hairless.

OBSERVED		*Expected*		DEV.	P.E.	$\frac{\text{DEV.}}{\text{P.E.}}$
Haired	Hairless	Haired	Hairless			
115	40	*116.25*	*38.75*	1.25	3.64	0.3

TABLE 9

Data showing the linkage of hairless and piebald.

MATING	SH^r	Sh^r	sH^r	sh^r	CROSSOVER PERCENT
$\frac{SH^r}{sh^r} \times \frac{sh^r}{sh^r}$ ♀ × ♂	50	6	3	56	7.8 in ♀
$\frac{Sh^r}{sH^r} \times \frac{sh^r}{sh^r}$ ♀ × ♂	0	2	7	1	10.0 in ♀
$\frac{NSH^r}{nsh^r} \times \frac{nsh^r}{nsh^r}$ ♀ × ♂	27	4	5	32	13.3 in ♀
					Total 9.8 in ♀
$\frac{sH^r}{sh^r} \times \frac{SH^r}{sh^r}$ ♀ × ♂	77	1	38	39	2.6 in ♂

individuals would have been classified as crossovers. In view of this difficulty, it would be desirable, were further linkage studies made, to test all supposed crossovers genetically. In the experiments here reported, only one individual, a female given me by Miss THIGPEN and thus not a product of my own crosses, was established genetically as a crossover.

She was of the constitution *Sh*^{r}/*sh*^{r}. Of the other crossovers about half are open to very little doubt owing to the clean-cut phenotype, but in view of the doubt as to the remaining half it is possible that the calculated crossover percent is somewhat too high.

The results are recorded in table 9. Those from crosses in which naked was involved are given under a separate heading, as they are slightly less reliable than the remainder owing to the difficulties of classification when naked is present. When totaled they show a crossover percent of 9.8 in the females and 2.6 in the males. It is of interest to note that in this linkage, as in that of pink-eye with albinism, the data show a higher crossover rate in the female than in the male.

PROBABLE MUTATIONS TO BLACK-AND-TAN

During the progress of the crosses here reported there occurred four probable mutations to black-and-tan. The mutants are listed in table 10, together with the date of their birth, and the known facts as to their own and their parents' genetic constitution. Unfortunately, at the time the mutations occurred, there were other black-and-tan individuals in the laboratory, so the evidence for the occurrence of mutation is not as convincing as in the earlier instance reported from the same laboratory by PINCUS (1929). In the case of female H382, however, a good check was possible. Her father, male H26, was the son of an albino and hence carried albinism. Her mother, female H66, on the other hand, was homozygous for color, as shown by the production of 16 young, all colored, when mated to male H26. All black-and-tan mice in the author's stocks, and so far as can be determined in the whole laboratory, were from lines probably not carrying albinism. Hence when female H382 was shown by mating to an albino male to carry albinism, she was fairly definitely established as the offspring of female H66 and male H26, both dark-bellied individuals, and therefore as a mutation.

Of the other possible mutants, H433 and H588 died before any breeding tests were possible, and S263 lacked characters which would have served as a possible check. H433 and S263 were born in pens from which females were not being isolated, so in each case the mother may have been either one of two females in the pen, both of which had litters at about the same time. H433 was noted at about 2 weeks of age as appearing perhaps slightly older than its sibs, a fact possibly indicating that it had been accidentally transferred from another cage. At the time, however, there were no black-and-tan individuals in neighboring pens. We

therefore regard these three cases as being, rather more probably than not, mutations to black-and-tan.

In only one of the above four cases, that of male S263, were both parents homozygous for non-agouti so only in this case can we be sure that the mutation occurred in a non-agouti rather than an agouti locus. In all the other cases, however, both the parents at least carried non-agouti (table 10).

These four probable mutations to black-and-tan, together with the one reported by PINCUS (1929), and four to white-bellied agouti reported by LITTLE (1916), indicate that the light-bellied form appears much more

TABLE 10

Probable mutations to black-and-tan.

MUTANT	DATE OF BIRTH	MOTHER	FATHER
♂ S263 $a^t addPPD^wD^w$	March 28, 1929	♀ S100 $aaBBDdPpD^wD^w$ or ♀ S101 $aaBbDdPpD^wd^w$	♂ S103 $aaDdPpD^wd^w$
♀ H382 $a^taBbCcH^rh^rRR?Ss$	April 20, 1929	♀ H66 $aaBbCCH^rh^rssS^es^e$	♂ H26 $AaBbCcH^rh^rRrSs$
H433 a^tadd	April 27, 1929	♀ H57 $AabbDdH^rh^rss$ or ♀ H17 $aaBbH^rh^rss$	♂ H119 $AaBbCcDdH^rh^rRrSs$
H588 a^ta	June 11, 1929	♀ H271 $AaBbH^rh^rss$	♂ H429 $AabbH^rh^rSsS^es^e$

frequently as a mutation than the other known dominant characters of the house mouse. Comparison as to mutation rate with the known recessive characters is at present impossible owing to the much greater difficulty of detecting recessive mutations.

SUPPLEMENTARY EFFECTS OF THE GENE CAUSING SHORT-EAR

The gene for short-ear manifests itself principally by a reduction in the length of the ears, but other effects are also produced. Thus, GATES (1926a) has remarked that it produces morphological variations of the head and skull, and there is evidence that it causes reduction in general size and viability. Kinky-tail is also an effect of this gene as my data show, and not the effect of a linked gene.

In table 11 are recorded the mean measurements of the skulls of thirteen short-eared ($s^e\ s^e$) and twelve normal-eared ($S^e\ s^e$) mice, each measurement being expressed as a percentage of the basilar length, and accompanied by its probable error. In the next to the last column is found the difference of the means and the probable error of the difference. In the last column is given a measure of the significance of the difference, P, the values of P being calculated from formulae and tables given by R. A. FISHER (1928, p. 107 and p. 139). Values of P of 0.05 or less may be taken to indicate a surely significant difference. This test of significance is more accurate for small samples than the test furnished by Dev. / P. E.

TABLE 11

Mean measurements of the skulls of 13 short-eared (s^es^e) and 12 normal-eared (S^es^e) mice. Each measurement is expressed as a percentage of the basilar length (A).

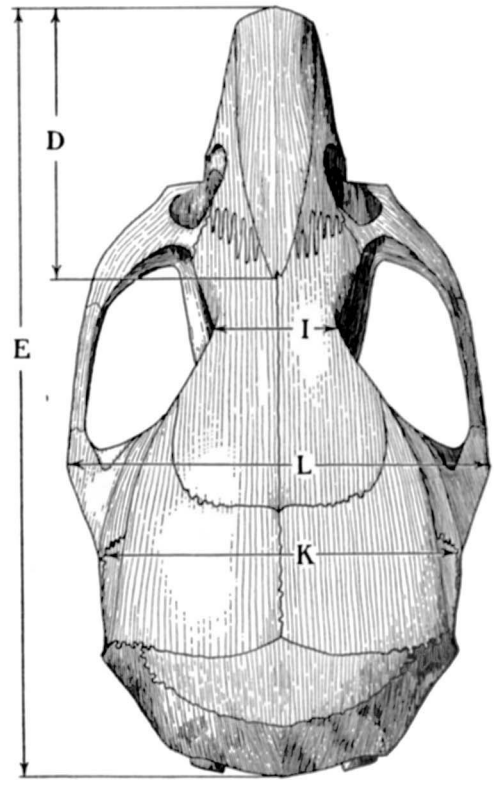
	MEASUREMENT	NORMAL-EARED	SHORT-EARED	DIFFERENCE	P
B	Condylo-basal length	120.27±.16	120.05±.17	.22±.24	.47
C	Length of tooth row	20.27±.11	20.13±.10	.14±.15	.46
D	Length of nasal bone	44.37±.28	43.95±.31	.42±.42	.45
E	Distema	31.07±.20	30.68±.10	.39±.22	.15
F	Greatest length	125.78±.32	124.58±.30	1.20±.30	.05
G	Palatilar length	55.68±.12	54.92±.13	.76±.17	P<.01
H	Width across auditory bullae	42.71±.27	42.38±.34	.33±.44	.57
I	Interorbital width	21.09±.17	21.35±.16	.26±.23	.40
J	Width foramen magnum	24.22±.11	24.62±.21	.40±.23	.21
K	Width brain case	56.14±.27	57.38±.29	1.24±.40	.03
L	Zygomatic width	64.47±.26	65.60±.25	1.13±.37	.03
M	Width outside molars	26.33±.11	26.85±.12	.52±.16	.02
N	Maximum height	37.36±.18	37.75±.32	.39±.36	.43
O	Height from basion to inion	34.17±.16	34.74±.17	.57±.24	.08
P	Height of rostrum	19.83±.10	17.42±.15	2.41±.18	P<.01

All twenty-five skulls used were obtained from eight litters from matings of the type ♀ $S^e\ d/s^e\ D \times$ ♂ $s^e\ d/s^e\ d$ so that the short-eared individuals were sibs of the normal-eared controls. Hence it may be safely concluded that all differences noted are due to the action of the gene for short-ear and not to any multiple factor differences present in the short-eared and normal-eared strains.

All measurements were made with vernier callipers.

Of the measurements used (figures 5, 6, 7, and table 11), A, B, C, E, G, J, K, L and N were employed by GATES (1926a); D, F, I, and M were suggested by Doctor ALLEN; O was adopted from JAYNE (1898, p. 509); and H and F were developed to show special peculiarities of the short-eared skull. They reveal that the skull of short-eared mice is proportion-

ately shorter and wider than that of normal-eared, the palatiler length being especially reduced. Even more marked is the reduction in the height of the rostrum. These changes account for the slightly stubby-nosed appearance of the short-eared mice. Of the measurements of width, only one, that across the auditory bullae, was less for the short-eared than the normal-eared, this slight reduction of the bones in the region of the ear being a natural accompaniment of the reduction of the external ear itself.



FIGURES 5, 6, and 7.—Three views of mouse skull, showing the measurements used. In figure 7, the right auditory bulla is removed.

In addition to the cranial measurements, some preliminary measurements similar to those used by GATES (1926a) were made on various features of the external anatomy, but as these failed to reveal any new differences between the two genetic types they were discontinued. Weighings of the two types indicated that the short-eared mice probably average smaller than their normal sibs, but a larger number of weighings than

has so far been made will be necessary to establish the difference statistically. The difference in viability has already been mentioned.

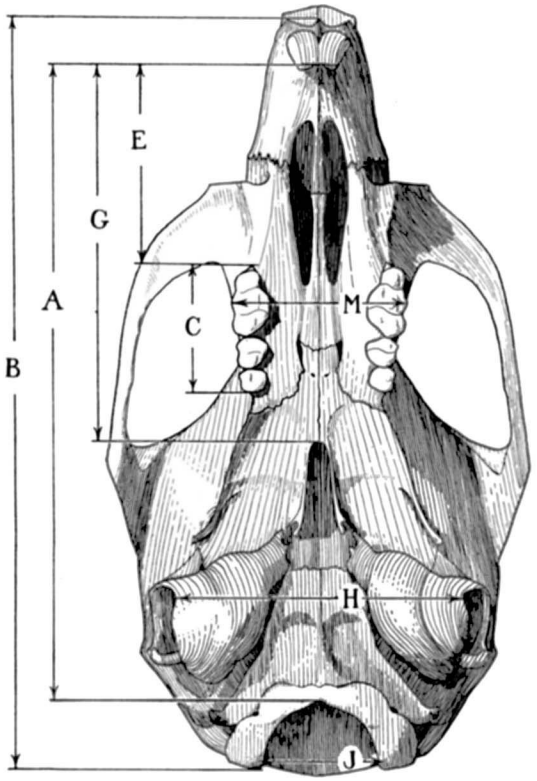


FIGURE 6.

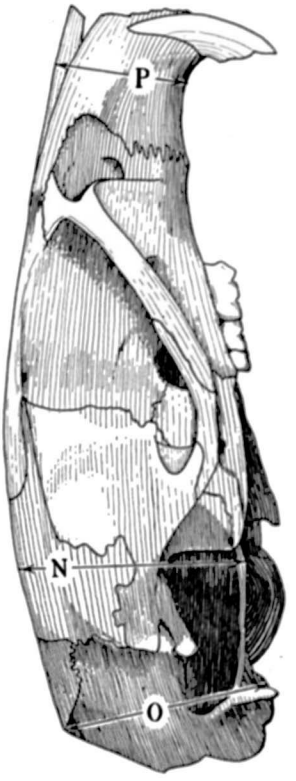


FIGURE 7.

SUMMARY

A description is given of most of the unit characters that have been reported in the house mouse.

The recessive and dominant forms of hairlessness are proved to be due to different genes located on different chromosomes. Recessive hairless is established as a clear-cut Mendelian character.

Data are presented showing the absence of linkage of dominant hairless or naked with rodless, hairless, piebald, black-eyed white, agouti, brown, pink-eyed, albinism, dilution, short-ear, and waltzing.

A close linkage of hairless with piebald is established. Three hundred forty-eight young from matings made to measure the intensity of the linkage show a crossover percent of 9.8 in the female and 2.6 in the male.

New data on the linkage of short-ear and dilution are reported. In a backcross generation of 1140 young, of which 106 were raised by Miss COPELAND at SMITH COLLEGE, 1 crossover was obtained by Miss COPELAND, none by the author.

Measurements are given of the skulls of 13 short-eared and 12 normal-eared mice which show the gene for short-ear to produce pronounced changes in the shape of the skull, especially a proportionate increase in width of the brain case and a reduction in height of the rostrum. Kinky-tail is also shown to be due to this gene and not to a closely linked gene as has been twice reported.

Three cases of reversal of dominance in young mice of the gene for dilution are described. These mice, all heterozygous for dilution, appeared dilute when young but changed to intense when they grew older.

Mention is made of 4 probable mutations to black-and-tan.

ACKNOWLEDGMENTS

The writer wishes to thank Doctor DUNN, Doctor PINCUS and Miss THIGPEN for mice given him for use in these experments; Doctor LEBEDINSKY, Doctor NACHTSHEIM, and Doctor SCHRATZ for making it possible to obtain a stock of naked mice in this country; Doctor KEELER for sectioning the eyes of litters in crosses involving rodless; and especially Doctor CASTLE, under whose direction the experiments were carried out, for invaluable advice and assistance, and actual care of the crosses during the summer of 1928 when the writer, owing to illness, was unable to attend to them.

LITERATURE CITED

ALLEN, G. M., 1904 The heredity of coat color in mice. Proc. Amer. Acad. Arts Sci. **40**: 59–163.

BAGG, H. J., 1925 Hereditary abnormalities of the viscera. Amer. J. Anat. **36**: 275–311.

1929 Hereditary abnormalities of the limbs, their origin and transmission. Amer. J. Anat. **43**: 167–220.

BAGG, H. J., and HALTER, C. R., 1927 Further studies on the inheritance of structural defects in the descendants of mice exposed to Roentgen-ray irradiation. Anat. Rec. **37**: 183.

BATESON, W., 1894 Materials for the stuty of variation. London: Macmillan and Co.

BLANK, E., 1916 Die Knickschwänze der Mäuse. Arch. EntwMech. Org. **42**: 333–406

BROOKE, H. C., 1926 Hairless mice. J. Hered. **17**: 173–174.

CAMMIDGE, P. J., and HOWARD, H. A., 1926 Hyperglycaemia as a Mendelian recessive character in mice. J. Genet. **16**: 387–392.

CAMPBELL, A., 1907 *Mus musculus* var. *M. nudo-pilcatus*. Zoologist, 4th series **11**: 1–3.

CASTLE, W. E., and ALLEN, G. M., 1903 The heredity of albinism. Proc. Amer. Acad. Arts Sci. **38**: 603–622.

COCKS, W. P., 1852 Trans. Cornwall Polytech. Soc.

CUÉNOT, L., 1902 La loi de Mendel et l'hérédité de la pigmentation chez les souris. Arch. Zool. exp. gén. **10**: 27–32.

1904 L'hérédité de la pigmentation chez les souris. Les formules héréditaires. Arch. Zool. exp. gén. **2**: 45–56.

1928 Génétique des souris. Bibl. genet. **4**.

DOBROVOLSKAIA-ZAVADSKAIA, N., 1927 Sur la mortification spontanée de la queue chez la souris nouveau née et sur l'existence d'un charactère (facteur) héréditaire "non-viable." C. R. Soc. Biol. Paris **97**: 114–116.

DUBOSCQ, O., 1922 Une lignée de souris anoures et extromèles. Ass. franç. p. avanc. Sci., Montpellier pp. 399–402.

DUNN, L. C., 1920 Types of white spotting in mice. Amer. Nat. **54**: 465–495.

1928 A fifth allelomorph in the agouti series of the house mouse. Proc. Nat. Acad. Sci. Wash. **14**: 816–818.

DUNN, L. C., and DURHAM, G. B., 1925 The isolation of a pattern variety in piebald house mice. Amer. Nat. **59**: 36–49.

DURHAM, F. M., 1911 Further experiments on the inheritance of coat colour in mice. J. Genet. **1**: 159–178.

FISHER, R. A., 1928 Statistical methods for research workers. 2nd Edit. London: Oliver and Boyd.

GASKOIN, J. S., 1856 On a peculiar variety of *Mus musculus*. Proc. Zool. Soc. London **24**: 38–40.

GATES, W. H., 1926a The Japanese waltzing mouse; its origin, heredity and relation to the gametic characters of other varieties of mice. Pub. Carnegie Instn. Washington **337**: 83–138.

1926b A case of non-disjunction in the mouse. Genetics **12**: 295–306.

1927 Linkage of short-ear and density in the house mouse. Proc. Nat. Acad. Sci. Wash. **13**: 575–578.

1928a Linkage of the factors for short-ear and density in the house mouse. Genetics **13**: 170.

1928b Linkage of the characters albinism and shaker in the house mouse. Anat. Rec. **41**: 104.

GORDON, G., 1850 Variety of the common or house mouse (*Mus musculus*). Zoologist **8**: 2763–2764.

HANCE, R. T., 1927 Altering a matured genetic character. J. Hered. **18**: 377–380.

1928 Detection of heterozygotes with X-rays. J. Hered. **19**: 481–485.

HUNT, H. R., and PUMAR, D., 1928 Flexed tail, a mutation in the house mouse. Anat. Rec. **41**: 117.

JAYNE, H., 1898 Mammalian anatomy. Philadelphia: J. B. Lippincott.

KEELER, C. E., 1927 Rodless retina, an ophthalmic mutation in the house mouse. J. Exp. Zool. **46**: 355–407.

1929 The occurrence of a heritable twisted nose in the house mouse, *Mus musculus*. Proc. Nat. Acad. Sci. Wash. **15**: 838–839.

1930 Hereditary blindness in the house mouse with special reference to its linkage relationships. Howe Laboratory, Harvard Medical School Bull. 3.

KIRKHAM, W. B., 1920 The life of the white mouse. Proc. Soc. Exp. Biol. N. Y. **17**: 196–198.

LANG, A., 1912 Vererbungswissenschaftliche Miszellen. Z. indukt. Abstamm.-u. VererbLehre **8**: 233–283.

LEBEDINSKY, N. G., and DAUVART, A., 1927 Atrichosis und ihre Vererbung bei der albinotischen Hausmaus. Biol. Zbl. **47**: 748–752.

LITTLE, C. C., 1916 The occurrence of three recognized color mutations in mice. Amer. Nat. **50**: 335–349.

1920 Note on the occurrence of a probable sex-linked lethal factor in mammals. Amer. Nat. **54**: 457–460.

LITTLE, C. C., and BAGG, H. J., 1924 The occurrence of four inheritable morphological variations in mice and their possible relation to treatment with X-rays. J. Exp. Zool. **41**: 45–91.

LORD, E. M., and GATES, W. H., 1929 Shaker, a new mutation of the house mouse (*Mus musculus*). Amer. Nat. **63**: 435–442.

MARSHALL, C. C., 1887 Hairless mice in Humboldt county. W. Amer. Sci. **3**: 72–73.

MORGAN, T. H., 1914 Multiple allelomorphs in mice. Amer. Nat. **48**: 449–458.

MORGAN, T. H., BRIDGES, C. B., and STURTEVANT, A. H., 1925 The Genetics of Drosophila. 262 pp. S-Gravenhage: Martinus Nijhoff.

MULLER, H. J., 1928 The measurement of gene mutation rate in Drosophila, its high variability, and its dependence upon temperature. Genetics **13**: 279–357.

PAINTER, T. S., 1927 The chromosome constitution of GATES' non-disjunction (*v—o*) mice. Genetics **12**: 379–392.

PEARSON, E. S., 1924 Congenital eye anomalies in albino mice. Nature **114**: 433.

PINCUS, G., 1929 A spontaneous mutation in the house mouse. Proc. Nat. Acad. Sci. Wash. **15**: 85–88.

PLATE, L., 1910 Die Erbformeln der Farbenrassen von *Mus musculus*. Zool. Anz. **35**: 634–640.

POCOCK, R. I., 1904 Proc. Zool. Soc., London **2**: 133.

RABAUD, E., 1914 Sur une anomalie héréditaire des membres postérieurs chez la Souris. C. R. Soc. Biol. Paris **77**: 411–412.

1919 Recherches sur l'hérédité et la variation. Bull. biol. Suppl. **1**: 1–316.

SNELL, G. D., 1928 A crossover between the genes for short-ear and density in the house mouse. Proc. Nat. Acad. Sci. Wash. **14**: 926–928.

1929 Dwarf, a new Mendelian recessive character of the house mouse. Proc. Nat. Acad. Sci. Wash. **15**: 733–734.

SO, M., and IMAI, Y., 1920 The types of spotting in mice and their genetic behavior. J. Genet. **9**: 319–333.

WRIGHT, S., 1917 Color inheritance in mammals. II. The mouse. J. Hered. **8**: 373–378.