THE RELATION OF ALBINISM TO BODY SIZE IN MICE

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IN PREVIOUS studies made in coöperation with former colleagues at the BUSSEY INSTITUTION of HARVARD UNIVERSITY, it was found that certain recessive mutant genes, when homozygous, increase the body size of mice, whereas other mutant genes decrease the body size.

In particular the brown (or chocolate) gene was found to increase adult body weight by 3 or 4 percent, and body length by about 1.5 percent. That the brown mutation increases body size was independently discovered and first reported by FELDMAN (1935), who made observations on the relative body weight of black and of brown individuals in three different races of mice in which the two alternative colors were occurring together in the same litter. He gives averages for a group of from 35 to 50 mice of each sex and color, weighed at monthly intervals between the ages of one month and six months. At each of the six weighings in both sexes, the brown mice were heavier than the blacks by from 1.6 to 5.6 percent. Combining the percent differences for both sexes, the series runs thus:

Age in months	1	2	3	4	5	6
Browns heavier, in percent	2.8	2.2	2.0	3.1	2.4	3.5

From this it would seem that the brown gene, in FELDMAN'S observations as in our own, when homozygous makes mice heavier by about 3 percent than when it is heterozygous, and further that this influence is of about the same strength at all ages. The growth period studied by FELDMAN covers that from an average weight of about 9 grams at one month of age to a weight of about 23 grams at six months of age in males of race H. In race J the corresponding weights are 10 and 32, and in the third race (IHJ) they are 9.8 and 26.6.

From the fact that the percentage difference is substantially the same at 1, 4, and 6 months of age in FELDMAN'S mice, it seems probable that it was already effective at birth or even earlier (as genetic size differences are in rabbits).

The dilution gene also was found by us to increase body weight and body length, though to a less extent than the brown gene, but tail length was in several crosses increased more strongly by dilution than by brown, indicating a special localized action of the dilution gene.

The combined action of the two genes, brown and dilution, was about equal to the sum of their effects when acting separately.

An opposite effect, decrease of body size was found to occur, when the gene for short ear or the gene for pink eye was present in homozygous state. The gene for short ear was thought to reduce body weight by about 5 percent, the gene for pink eye by less than one percent, though the evidence was not altogether clear.

In the case of the agouti gene, no evidence was found that it either increases or decreases body size.

In continuance of this line of research, an experiment has recently been made to ascertain what effect, if any, the albino mutation *c* has on body size. The conclusion reached is that it has no effect, since individuals homozygous for albinism do not differ in average size from their colored litter mates which are heterozygous for albinism. The evidence on which this conclusion is based will now be presented.

In the fall of 1936, in the Veterinary Science Laboratory of the UNIVERSITY OF CALIFORNIA, a cross was made between albino mice of the formula *AA bb cc* and dilute brown colored mice of the formula *aa bb CC*. The albino mice were kindly supplied by Dr. E. C. MACDOWELL, the dilute brown mice were obtained from the Supply Department of the ROSCOE B. JACKSON MEMORIAL LABORATORY. Both races had been long inbred and so would be theoretically of complete genetic uniformity. In making the cross albino females were mated with dilute brown males. The F_1 young, like their albino mothers, were animals of remarkable size, vigor, and fecundity. In color they were cinnamon and their genetic formula obviously would be *Aa bb Cc*. That is, they were heterozygous for agouti and for albinism, but like both parents were homozygous for the brown gene.

F_1 females were now backcrossed with males of a triple recessive albino race kindly supplied by Dr. L. C. STRONG, his long inbred race A, which is of the formula *aa bb cc*. The resulting backcross mice fall into four genetic classes expected to be numerically equal one to another, *Aa bb Cc* (cinnamon), *aa bb Cc* (brown), *Aa bb cc* (albinos potentially cinnamon), and *aa bb cc* (albinos potentially brown). The last two classes are indistinguishable in appearance and so there are really only three phenotypes, cinnamon, brown, and albino, and their expected proportions are 1:1:2. In a backcross population of 1252 mice raised to an age of six months, the actual numbers are 334 cinnamon, 308 brown, and 610 albino, a sufficiently close approximation to the expected 1:1:2 ratio.

A comparison of individuals of the three phenotypes should show whether genes *A*,*a* and *C*,*c*, in their alternative forms exercise any appreciable influence on body size. If the gene *A* exercises any influence on size different from that of its allele, *a*, then the cinnamon mice (*Aa*) should differ significantly in size from the browns (*aa*). And if gene *C* exercises

on size an influence different from that of its allele, *c*, then the average size of the colored mice (cinnamons and browns, which agree in being *Cc* in formula) should be different from that of the albinos, which are all *cc* in formula.

Animals of the backcross population were weaned at an age of three or four weeks. The sexes were caged separately, about 12 or 15 animals to a cage, and kept constantly supplied with Purina Dog Chow and water. They were weighed individually at monthly intervals from about four months of age, and the maximum weight recorded for each animal was regarded for statistical purposes as its adult weight. In the case of females, which were of course not allowed to breed, the final weight observation made was usually the maximum, or at any rate there was little decline up to six months of age from a maximum previously attained. In the case of males the maximum was often attained as early as four months of age, subsequent to which weight might be lost from fighting but this did not seem to affect either body length or tail length, if the tail remained uninjured. In case the tail was severely injured by fighting, its length was not included in the calculation of average tail length. This accounts in part for the smaller number of animals tabulated as to tail length. But there also occurred a certain number of animals in both sexes which had stubby tails obviously abbreviated at birth by an overzealous mother in the process of cleaning the new born young, or else congenitally shorter and stubbier than normal as to tail form. These also were omitted in tabulating the data on tail length.

The tail length in these backcross mice was measured from the point to which the body fur covers the tail (disregarding the longest contour hairs) to the tail tip (projecting hairs however being here disregarded). The tail measurement was made independently of the body measurement and the difficulty in determining the point on the *morphological* tail to which the body fur extended will account in part (but only in part) for the greater variability of the tail measurement, as compared with that of body length. Actually tail length varies more in relation to body length, than body weight does. This is indicated by the lesser magnitude of the correlation coefficient between tail and body when compared with the correlation coefficient between weight and body. Weighing was done with a Toledo scale, which proved both expeditious and accurate to within 0.2 gram.

When the animals were six months old they were chloroformed and measurements were taken of the body length and tail length of each animal after SUMNER's method, keeping the body slightly stretched under tension of 20 gram weights attached to teeth and tail respectively.

Table 1 contains a summary, for each sex separately, of the observa-

tions on body weight, body length, and tail length. Males are in all three respects larger than females and so are summarized separately, but no phenotype differs significantly from either of the other phenotypes of the same sex in weight, body length, or tail length.

Brown males average a trifle larger bodied by all three criteria than cinnamon males, but the difference is less than twice the probable error

TABLE 1

Comparative body size in a backcross population, of mice of the three phenotypes, cinnamon, brown and albino, as indicated by body weight, body length and tail length.

MALES	NO.	AVERAGE WEIGHT	NO.	AVERAGE BODY LENGTH	NO.	AVERAGE TAIL LENGTH
Cinnamon	173	39.45±.16	172	102.66±.10	165	93.75
Brown	153	39.91±.14	153	102.92±.10	146	93.82
Cin. and br. combined	326	39.67±.09	325	102.78±.07	311	93.77
Albino	310	39.54±.09	310	102.58±.07	304	93.82
Total	**636**	**39.61±.05**	**635**	**102.68±.03** $\sigma=1.90\pm.03$	**615**	**93.79±.07** $\sigma=2.91\pm.05$
FEMALES						
Cinnamon	161	30.78	161	98.38	161	90.89
Brown	155	31.34	155	98.10	154	90.68
Cin. and br. combined	316	31.09	316	98.22	315	90.78
Albino	300	31.47	300	98.75	295	91.02
Total	**616**	**31.27**	**616**	**98.33**	**610**	**90.90**

and so not significant. And in the case of females, this relation is reversed at least as regards body length and tail length, for cinnamon females exceed their brown sisters slightly in these measurements. We may conclude therefore that the *Aa* phenotype does not differ in body size from the *aa* phenotype, which conclusion agrees with that reached in experiments previously reported.

We come now to the prime objective of this experiment, to discover whether albinism has a tendency either to increase or to decrease body size. For this purpose we may compare the average body size of colored individuals with that of their albino litter mates. The combined cinnamon and brown classes constitute the colored individuals, the body size of which is to be compared with that of the albinos. The 326 colored males of table 1 have an average body weight of 39.67 grams; the 310 albino males average 39.54 grams. The difference between these averages is .13 gram, which scarcely exceeds the probable error, .12 gram, and so is not significant.

In body length, the colored males are just .10 mm longer bodied than the albinos, a difference which just equals the probable error. In tail length the difference between colored and albino males is also insignificant, being only .05 gram, actually less than the probable error. Albinism accordingly is without detectable influence on the body size of males.

A similar conclusion is reached in the case of females from a comparison of the body size of colored and of albino females. The average body weight of 316 colored females is 31.09 grams. For 300 albino females, it is .38 gram greater but this is less than the difference in weight between the two colored classes, cinnamon and brown, which on grounds already discussed was not considered significant. Also the relation between the colored and the albino females as regards body weight is the reverse of that observed among the males, since colored males were heavier than albino males, but colored females weigh less than albino females. Probable errors were not calculated for the female population, but if they are substantially the same as for the corresponding groups of males, the difference in weight between colored and albino groups would not have statistical significance.

The albino females, as regards body length and tail length, as well as body weight, are slightly larger bodied than their colored sisters, but this relation is doubtless a consequence of random sampling and not indicative of genetic differences, as is shown by the following considerations. As the data were accumulated, they were from time to time summarized. Three such partial summaries were made, about 200 individuals being included in each. In two of these summaries the average weight of the brown females was greater than that of the cinnamons, but in the third summary the cinnamons were heavier than the browns. Also in two of the partial summaries colored females are heavier than albinos, but in the third summary albinos are heavier than colored individuals.

That it is through general rather than local growth processes that genes commonly influence body size is indicated by the positive correlations which exist between body weight, body length, and tail length. An individual which is large by one of these criteria is also large by the other criteria, and an individual which is small by one criterion is also small by the others. This is true even within inbred races and populations derived by crossing such inbred races, as in the present experiment. Here genetic uniformity is nearly complete and such variability as exists must be referred almost wholly to accidents of development. Organic correlations are regularly less within inbred populations where genetic influences are uniform than in other populations in which genetic influences are variable. For example, in the backcross population described by CASTLE, GATES and REED (1936), where several genes affecting body size were segregating, the correlation between body weight and body length was found to be

$.65 \pm .01$ in the case of females, and $.66 \pm .01$ in the case of males. But in the present experiment in which variation is uninfluenced by genes affecting body size, the corresponding correlation for males is only $.55 \pm .01$.

Tail length shows a greater degree of independent variability than either weight or body length. The correlation between body length and tail length was found to be only $.26 \pm .02$ in the available male population of 613 individuals, in which were included only those with uninjured tails. In a previous publication the gene mutation dilution was found to exert a direct influence on tail length, in addition to the indirect influence which in common with the brown mutation it exerts through its action on general growth. In the present experiment homozygous dilution does not occur in the backcross population, so this complication is avoided.

SUMMARY

An experimental test was made of the influence of the albino mutation on the body size of mice. Albino females of an inbred race (*AAbbcc*) were crossed with dilute brown males (*aabbCC*). The F_1 mice, cinnamon in color, were *AabbCc*. F_1 females were backcrossed to triple recessive inbred males *aabbcc*. Mice of three phenotypes were produced, cinnamon (*AabbCc*), brown (*aabbCc*), and albinos (either *Aabbcc* or *aabbcc*). These three phenotypes in a backcross population of 1252 animals occurred in the expected ratio, 1:1:2. The animals were grown under uniform conditions to an age of six months, then killed and measured as to body length and tail length, having been previously weighed at monthly intervals. The body size of each individual was judged by three criteria, maximum weight at or prior to six months of age, body length and tail length.

No significant difference was found between body size, as estimated by any one of these criteria, among the three phenotypes. In particular the colored classes were neither larger nor smaller bodied than the albinos. The conclusion is reached that albinism (and incidentally also the non-agouti mutation) is without influence on body size. Among the 635 male individuals the correlation between weight and body length was found to be $.55 \pm .01$. Among 613 available males the correlation between body length and tail length was found to be $.26 \pm .02$.

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