INHERITANCE OF VENTRAL SPOTTING IN MICE

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The two best known types of white spotting in mice are "black-eyed white" and "piebald". The former, *Ww*, is dominant (lethal in a homozygous condition) while the latter, *ss*, is recessive to self. A possible third distinct form, "all white" (*whwh*) has been mentioned by KEELER (1931). In addition, a number of other types, at least some of which are the result of modifying genes on basic piebald, have been noted in the literature.

DUNN (1920, 1925) described two modifications of the piebald pattern. In one, which he designated as "white face spotting", the white areas were restricted to the face; and in the other, "belt", to a band around the body. By inbreeding, he succeeded in fixing the white face pattern but was less successful with belt.

LITTLE (1917, 1926) reported a form of spotting, "blaze", in which the animals showed a small, white forehead spot. Besides the main gene responsible for this condition, he concluded that there were several modifying genes influencing the amount of white.

The same author (1924) observed two localized forms of spotting, "white tail tip" and an unpigmented band around the tail, "white on tail". In the race in which these types were observed, he reported that occasionally the tail spotting was transferred to the belly, such animals behaving in inheritance like phenotypically tail-spotted mice.

Ventral spotting appears to be of rather frequent occurrence in mice. DUNN (1920) found its appearance dependent on a modifying gene in conjunction with piebald in the heterozygous condition (*Ss*). ALLEN (1914) considered a mid-ventral patch generally to be the first unpigmented area developing in mammals.

In one inbred strain in our laboratory more than 50 percent of all individuals show a white ventral patch. The mice of this strain (C-57 Brown) are intense brown non-agouti (*DDbbaa*) in color and directly descended, by brother-to-sister matings with some backcrosses, from two control animals of one of Dr. C. C. LITTLE's previous experiments. The mice reported on in this paper comprise undepleted litters of the thirteenth to the twenty-eighth filial generations, inclusive.

The patches vary in size from 0 to approximately 10 percent of the ventral surface. In the few mice of the highest grades the unpigmented area sometimes extends up onto the side of the animal. All determinations

of grade were made by the senior author, thus reducing the personal error incident to more than one observer, while the junior author is responsible for the computations and analysis. Some animals exhibited "white on tail" or "white tail tip" with or without ventral spotting. It seems probable, however, that in the strain of browns the tail markings and ventral spotting are not conditioned by the same factors. The C-57 Blacks in which LITTLE described tail spotting still produce a majority with such markings while belly spotting is now almost non-existent. The C-57 Browns, with a common origin, show both tail and ventral spotting. Moreover, satisfactory records as to the degree of tail spotting manifested by individual mice were not available so it was deemed advisable to consider only ventral white.

The distribution of the 2166 mice of undepleted litters by grade of ventral spotting is shown in table 1.

TABLE 1
Distribution of offspring in brown stock grade of ventral spotting.

	0	1	2	3	4	5	6	7	8	9	10	TOTAL
Sexes combined	984	658	260	92	80	46	13	9	15	4	5	2166
Percent	45.4	30.4	12.0	4.2	3.7	2.1	0.6	0.4	0.7	0.2	0.2	
Males	420	340	154	60	55	25	8	3	10	3	3	1081
Percent	38.6	31.5	14.2	5.6	5.1	2.3	0.7	0.3	0.9	0.3	0.3	
Females	563	319	106	32	25	21	5	6	5	1	2	1085
Percent	51.9	29.4	9.8	2.9	2.3	1.9	0.5	0.6	0.5	0.1	0.2	

From this table it is evident that not only are more males than females spotted but also that the grade of the former tends to be higher.

Table 2 gives distributions and mean grades of offspring from matings differing in degree of ventral spotting.

TABLE 2
Distribution of offspring in different types of matings.

MATING		GRADE OF VENTRAL SPOTTING											MEAN
		0	1	2	3	4	5	6	7	8	9	10	
♀ Self×♂ self	♂	130	82	36	7	5	2	1	1	1			.85
	♀	173	82	17	5	4	4		1	1			.63
♀ Grade 1× ♂ Grade 1	♂	38	37	15	11	10	5	2		1		1	1.63
	♀	65	30	14	2	2	4	1	3			1	1.06
♀ Grade 2-7× ♂ Grade 2-10	♂	22	23	9	7	6	6		2	5		1	2.22
	♀	27	26	6	6	5	6	1				1	1.56

It seems clear that a distinct correlation is present between grades of spotting in parents and offspring. This correlation, however, is imperfect since self parents produce offspring with a high grade of ventral spotting while spotted parents give birth to self animals.

The great majority of mice in the strain of browns are of three lines, A, C and CD. If the degree of ventral spotting is influenced by genetic factors, it might be expected that the lines would exhibit differences in the presence and extent of unpigmented areas. The distribution of ventral spotting in the three lines is listed in table 3.

TABLE 3
Distribution of ventral spotting in the three chief lines.

		GRADE OF VENTRAL SPOTTING											MEAN
		0	1	2	3	4	5	6	7	8	9	10	
Line A	♂	32	22	15	2	6	2			1			1.25
	♀	40	27	10	7	2	2		1				1.04
Line C	♂	122	102	37	8	9	6	3	1				1.01
	♀	178	96	26	2	9	5		3	2			.79
Line CD	♂	251	181	92	47	30	15	4	2	8	3	3	1.35
	♀	318	181	65	26	13	13	5	2	2	1	2	.95

The anticipated differentiation in the lines has apparently taken place since the mean grade is significantly lower, at least for the males, in Line C than in Line CD. Line A appears to be similar to CD although the numbers are few.

Since tables 2 and 3 make it seem probable that the presence and degree of ventral spotting are in part at least determined by genetic factors, parent-offspring correlation tables were constructed in order to show more exactly the extent to which variation in parental grade influenced variation in the grade of the offspring. The correlation between mid-parental grade and grade of offspring was $+0.258 \pm .014$. The square of this figure would indicate that slightly over six percent of the variation among the offspring was determined by variation among the parents.

The question which next suggests itself is the relative degree to which sire and dam influence spotting in the offspring. These correlations are given below:

Grade of spotting of sire—Grade of offspring $r = +0.269 \pm .013$

Grade of spotting of dam—Grade of offspring $r = +0.145 \pm .014$

These figures show that the correlation is positive and significant in both cases, but markedly higher with the sire than with the dam. A truer picture of the relative effects of the two parents may be given by the use of partial

correlations. This discloses that the correlation between sire and offspring with dam held constant is $+0.243$; that between dam and offspring with sire held constant is $+0.086$. The difference in the apparent influence of the two parents is thus further augmented.

The coefficients of correlation above have not taken into consideration the sex of the offspring. This factor is dealt with in the figures following:

	r	r (partial correlation)
Grade of spotting of sire		
—Grade of male offspring	$+0.300 \pm .019$	$+0.268$ (Dam held constant)
Grade of spotting of dam		
—Grade of male offspring	$+0.168 \pm .020$	$+0.093$ (Sire held constant)
Grade of spotting of sire		
—Grade of female offspring	$+0.226 \pm .019$	$+0.208$ (Dam held constant)
Grade of spotting of dam		
—Grade of female offspring	$+0.118 \pm .020$	$+0.077$ (Sire held constant)

Both sire and dam show slightly higher correlations with male than with female offspring although the differences probably lack significance.

It appears from the available evidence that heredity accounts for only a small portion of the variation in degree of ventral spotting in our strain of mice. The possibility that ventral spotting is due to either a single dominant or recessive gene is at once precluded. If dominant, self animals could not throw spotted offspring while if it were recessive, self young could not be produced by spotted parents. Of course if normal overlaps were postulated, these objections might be vitiated. That our ventrally spotted mice, like DUNN's, are heterozygous piebalds is likewise precluded, since matings involving such parents do not produce the requisite piebald young. A number of genes may be involved although it might be expected that practical homozygosity would have been attained after 13 generations of inbreeding. The reason for the greater influence of the male in determining the grade of spotting of the offspring is not at all clear.

Since heredity—as measured by the square of the parent-offspring coefficient of correlation—accounts for but little more than six percent of the variance, non-genetic factors must play the major part in determining the degree of ventral spotting. The data permit an analysis of several such possibilities.

WRIGHT (1926) found that the age of the dam was of more importance than heredity in determining the grade of spotting in an inbred race of guinea pigs. In our material, there was present a correlation of $+0.105 \pm .014$ between age of dam (in almost all cases the sire was of the same age) and grade of ventral spotting. Although significant, this is very low and would indicate that age accounts for about one percent of the variation in amount

of white in the offspring. Birth rank (position of litter in the series) likewise proves of slight importance as a factor with r equalling $+0.068$. In this case only males, both parents of which were self, were included. Since birth rank is largely a function of age it was to be expected that similar results would be encountered.

Still another possibility is that season of the year is a factor in influencing ventral spotting. Table 4, comprising offspring of self $\times$ self matings, affords scant evidence of this.

TABLE 4
Time of year and ventral spotting.

SEASON OF BIRTH		GRADE OF VENTRAL SPOTTING								TOTAL	MEAN	
		0	1	2	3	4	5	6	7			8
Dec. Jan. Feb.	♂	47	19	6	1	1	2				76	.63
	♀	45	20	5	1		2				73	.59
Mar. Apr. May	♂	29	27	8	2	1				1	68	.90
	♀	40	27	3		2	1			1	74	.73
June July Aug.	♂	17	8	4	2						31	.71
	♀	24	15	3	1	1	1				45	.73
Sept. Oct. Nov.	♂	37	28	18	2	3		1	1		90	1.06
	♀	64	20	6	3	1			1		95	.55

Although marked fluctuations occur, they are inconsistent and the differences are not certainly significant. Males born in the three autumn months, for example, show the highest average grade, while females born during the same three months display the lowest. Hence, it is probable that season of birth has little if any effect on grades of spotting.

SUMMARY

In an inbred strain of mice a white ventral patch ranging in size up to 10 percent of the ventral surface is present in a majority of the animals. These patches are not only more frequent in males than in females but average larger as well.

The presence of white ventral spotting seems to be due neither to a single dominant nor recessive gene. The occurrence and extent of these markings, however, do appear to have an hereditary basis. In this strain of mice, the three chief lines show a tendency towards differentiation in the amount of spotting present. The coefficient of correlation between mid-parental grade and grade of offspring is $+0.258$. When the method of partial correlation is employed, the value of r for grade of sire and grade of offspring (with dam held constant) is $+0.243$; that for grade of dam and grade of offspring (with sire held constant), $+0.086$. From these figures, it ap-

pears that the sire has more influence on the grade of offspring than does the dam. The total effect of heredity is relatively slight, most of the variation being non-genetic in origin.

The age of dam or sire apparently has a very slight influence in determining spotting since the coefficient of correlation is but $+0.105$. Birth rank and season of year likewise have little influence; so most of the non-genetic variation, whether it be due to accidents of development or to other causes, is still unaccounted for.

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