

ON THE GENETICS OF SEVERAL TYPES OF SILVERING IN THE GUINEA PIG¹

SEWALL WRIGHT

Department of Zoology, The University of Chicago, Chicago, Illinois

Received October 19, 1946

INTRODUCTION

A SPRINKLING of white or light colored hairs among ones of a darker color in the coat of a mammal is variously known as silvering, roan or gray. At least four distinct patterns of this general sort are known in guinea pigs. The most familiar is one in which silvering, on the ground color determined by the rest of the genotype, is present at birth and does not change. A second type of stationary silvering is restricted to the blacks and browns and their modifications since it is due to the reduction of the yellow of the tortoiseshell pattern of intermingled yellow and dark pigmented hairs to white by certain genotypes. Third is a progressive type of silvering or grizzling, in which the color at birth is wholly that due to the rest of the genotype but scattered white hairs appear later and increase in number as the animal ages. Finally there is a retrogressive type which affects only intense browns. Scattered dark tipped pale brown hairs give a dingy appearance at birth which tends to be reduced or even to disappear in later pelages, especially in females. The second type has long been understood. The others have been in need of further investigation because of paucity of published data or conflicting interpretations.

STATIONARY SILVERING

Description

The common silvering of the guinea pig varies enormously in degree and character. In its weakest development there are merely a few light or white hairs, usually on the mammary region of the belly. In higher grades, the belly may be more or less uniformly silvered or there may be irregularly distributed blotches of white within silvered areas. Extensive silvering of the belly is correlated with the occurrence of patches of silvering on the sides and middle of the back. More rarely slight silvering of the back occurs without silvering of the belly. In the highest grades, the belly becomes almost white, usually sprinkled here and there with dark hairs or blotches, and the back becomes strongly silvered. The head and feet show little or no silvering even in the highest grade, as in roan horses. Red hairs are more conspicuously diluted in silvered areas than are black ones. It is sometimes difficult to decide whether a tortoiseshell with apparently dilute yellow hairs, intermingled with intense black, but no white, is to be considered a low grade silver or not. Silvered self reds and yellows are also difficult to classify unless the silvering is strong.

¹ This investigation was aided by a grant from the Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago.

Previous Accounts

CASTLE (1912) produced a strongly silvered strain from low grade silvers by selection but arrived at no factorial interpretation. WRIGHT (1917) stated (on the basis of a few crosses between a strongly silvered inbred strain, No. 34, and nonsilvers) that F_1 usually showed slight silvering on the belly but that there was no clear cut segregation in F_2 . IBSEN (1932) tentatively attributed what seems to be the same pattern to an incompletely dominant gene, *Ro* (roan). He gave no data, however. PICTET and FERRERO (1940) have published extensive data on silvering which seems from the description and photographs to be identical with that considered here. They ascribe whitening of the belly (blanchiment du ventre, partiel ou total) to a dominant gene, *V*. Silvering of the back first appeared in their colony on a whitebellied animal. They found it to be separable, however, and describe it as behaving as a simple recessive (*d*) in crosses with nonsilvers, and capable of increase by selection. The effect of *d* is referred to in most places as restricted to the back but in one place (p. 83) it is stated that it may reach the ventral surface. The evidence for their two factor interpretation will be discussed later.

Experiments

The silvering of the following experiments traced, except where otherwise stated, to an inbred strain, No. 13, in which the average extent of colored areas was so small (about 2 percent of the coat, WRIGHT and CHASE 1936) and so nearly restricted to the head that silvering was rarely evident. Silvering of all grades appeared, however, in the descendants of crosses with a tortoiseshell strain. No analysis of the early segregating generations is practicable; partly because the young were not graded with sufficient care in this respect and partly because the large amount of white in many of them made classification highly uncertain. It is, however, important to give an idea of the range of variability among those descended wholly from animals with more than slight silvering and from crosses between these and inbred strain 13. In table 1, a distinction is made between matings (A) in which both parents had more than slight silvering and (B) ones in which one or both parents had only slight, if any, silvering, though descended wholly from the former group. Class C consists of the crosses between either of these (strain I-13) and strain 13. Among the offspring a distinction is made between those with 50 percent or more of color in the coat, including color on the posterior belly, and the rest in which classification is of little value. The former are classified on the basis of descriptive terms used in the records, such as "no silver," "very slight," "medium," "strong," and "very strong." In most cases, however, "medium" and "strong" here mean merely that silvering was ascribed to the belly alone or to both belly and back, respectively. It is probable from later results that more careful examination would have raised most, if not all, of those called "nonsilver" to the category "very slight silver."

The most important conclusion from this table is that animals tracing exclusively to conspicuously silvered ancestors may range from ones with at

least no easily recognized silvering to ones with very strong silvering.

A series of experiments to explore the mode of inheritance was begun by mating medium, strong, or very strong silvers from strain I-13 with nonsilvers

TABLE I

Distribution of grades of silver in strain I-13, from parents (A) both of which were at least of medium grade, or (B) of which one or both were no more than slightly silvered but were derived from the preceding or (C) one parent was derived from (A) or (B), the other from strain (I3), the original source of silvering in I-13.

PARENTS	NO MAT-INGS	MORE THAN 50% COLOR IN COAT						LESS THAN 50% COLOR			
		% OF YOUNG OF EACH GRADE						NO. YOUNG	% NO SILVER	% SILVER	NO. YOUNG
		NO SILVER	V.SL.	SL.	MED.	STR.	V.STR.				
A I-13×I-13	30	3.1	1.8	6.6	36.1	41.0	11.4	227	63.0	37.0	46
B I-13×I-13	19	16.1	1.6	14.5	32.3	29.0	6.5	62	78.0	22.0	41
C I-13×I3	15	10.7	4.8	11.9	40.5	30.9	1.2	84	70.4	29.6	54
Total	69	7.0	2.4	9.1	36.5	36.7	8.3	373	70.2	29.8	141

from various sources. Grades of silver have been assigned at birth to back and belly separately to test the hypothesis of PICTET and FERRERO that silver in these areas is determined by independent genes.

Grade 0	no silver
Grade 1	trace of silvering (irregular dilution or few scattered white hairs)
Grade 2	slight but unmistakable silvering in a small area
Grade 3	silvering over less than half the area
Grade 4	strong silvering and blotching with white over more than half the area
Grade 5	white predominates

Doubtful grades were checked at weaning if possible. In some cases a trace of silvering was apparent at weaning which had not been observed at birth and in other cases an apparent trace at birth could not be detected later. Changes were rarely made in the higher grades.

The principal results are given in table 2. The grades of back and belly are here averaged: averages 0.5 and 1.0 are called 1, 1.5 and 2.0 are called 2, etc.

The results in F_1 indicate that silver is more nearly recessive than dominant. In five matings, no trace of silver was detected in 69 percent of the 39 young and only one individual was assigned grade two. Another F_1 mating gave high grade silvers as well as nonsilvers and low grades. The nonsilver parent in this case, however, may well have been heterozygous since silvering has been rather widely distributed in the colony.

Crossbreds showing no silver or only a trace have been backcrossed generation after generation to animals of I-13 that were strongly silvered at least on

the belly. If only one major factor is involved, 50 percent of the F_1 type should appear in each generation in spite of the continued attempt at dilution. With two major factors only a little more than 25 percent should continue to be of grades 0 and 1, while if multiple minor factors are involved backcrossing should soon produce a strain like I-13 in spite of selection of one parent for low grade. The first of these possibilities is the one that was realized. There were

TABLE 2

Distribution of grades of silvering from matings derived from outcross of silvers of I-13 to miscellaneous nonsilvers.

	PARENT (LOWER)		PARENT (HIGHER)	NO. MAT- INGS	GRADES OF SILVERING						TOTAL	% 0-1	% 2-5	
					0	1	2	3	4	5				
F_1	<i>SiSi</i> (Misc)	0	<i>sisi</i> (I-13)	4.0	5	27	11	1				39	97.4	2.6
F_1	<i>Sisi</i> (Misc)	0	<i>sisi</i> (I-13)	3.5	1	2	1	2	2	1		8	37.5	62.5
1BC	<i>Sisi</i> (F_1)	0.1	<i>sisi</i> (I-13)	3.7	10	37	25	17	18	7	5	109	56.9	43.1
2BC	<i>Sisi</i> (1BC)	0.5	<i>sisi</i> (I-13)	3.9	10	14	14	13	12	7	1	61	45.9	54.1
3BC	<i>Sisi</i> (2BC)	0.5	<i>sisi</i> (I-13)	2.9	3	9	8	3	3	4	2	29	58.6	41.4
4BC	<i>Sisi</i> (3BC)	0.0	<i>sisi</i> (I-13)	3.5	1	2	6		3	3	1	15	53.3	46.7
5BC	<i>Sisi</i> (4BC)	0.5	<i>sisi</i> (I-13)	4.5	1		1	1		1	1	4	25.0	75.0
Total BC	<i>Sisi</i>	0.3	<i>sisi</i>	3.9	25	62	54	34	36	22	10	218	53.2	46.8
$(F_1)^2$	<i>Sisi</i> (F_1)	0.0	<i>Sisi</i> (F_1)	0.0	2	9	3	2				14	85.7	14.3
(1BC) ²	<i>Sisi</i> (1BC)	0.5	<i>Sisi</i> (1BC)	0.5	5	10	28	4	5	2		49	77.6	22.4
(2BC) ²	<i>Sisi</i> (2BC)	0.0	<i>Sisi</i> (2BC)	1.0	1	1	1	1		1		4	50.0	50.0
(3BC) ²	<i>Sisi</i> (3BC)	0.4	<i>Sisi</i> (3BC)	0.9	2	9	7	2				18	88.9	11.1
Total (BC) ²	<i>Sisi</i>	0.4	<i>Sisi</i>	0.5	10	29	39	9	5	3		85	80.0	20.0
(BC) ²	<i>sisi</i> (BC)	2.1	<i>sisi</i> (BC)	3.1	3		1	2	7	2	6	18	5.6	94.4
2 BC	<i>sisi</i> (BC)	3.0	<i>sisi</i> (I-13)	4.3	5		3	5	6	4	2	20	15.0	85.0
Total	<i>sisi</i>	2.6	<i>sisi</i>	3.7	8		4	7	13	6	8	38	10.5	89.5
	<i>Si-</i> (BC) ²	0.6	<i>Sisi</i> (BC)	0.6	2	10	7					17	100.0	0.0
	<i>Sisi</i> (BC) ²	0.1	<i>Sisi</i> (BC)	0.1	2	8	13	4	4	3		32	65.6	34.4
(BC) ²	<i>Sisi</i> (BC)	0.6	<i>sisi</i> (BC)	2.1	4	7	3	2	4	5		21	47.6	52.4

56.9 percent of grades 0 and 1 among 109 young from the first backcross and 49.5 percent of these grades among the same number of young from later backcross generations.

The hypothesis that silvering depends on an incomplete recessive (to be called *si*) has been confirmed by other tests. Backcross silvers of the higher grades (2-5) mated with I-13 or with each other have given no nonsilvers and no more of grade 1 than can be accounted for from the distribution in I-13 itself, and are thus indicated to be *sisi*. Matings between nonsilvered parents or ones with only a trace, whether from F_1 or the first to third backcross gave largely (80 percent) nonsilver or grade 1, but 20 percent of grades 2 to 4, indicating that these matings were of type *Sisi* × *Sisi*.

A few matings which do not fall into the preceding categories gave results easily interpreted as in harmony with the conclusion that there is only one major pair of alleles.

TABLE 3

Distribution of backcross progeny by sex and type of mating with respect to sex.

♀ (♀ ♂)	MATINGS	OFFSPRING				TOTAL
		FEMALES		MALES		
		0-1	2-5	0-1	2-5	
R(RD)	6	16	15	15	18	64
R(DR)	4	9	7	12	11	39
(RD)R	2	5	2	3	3	13
(DR)R	13	24	16	32	30	102
Total	25	54	40	62	62	218

The progeny of the backcross matings are classified in table 3 by sex of parents and of offspring. R(RD) means a mating of recessive (silver) female by a male from recessive mother and dominant father. The other possibilities, R(DR), (RD)R and (DR)R are to be interpreted similarly. Matings of type R(RD) and R(DR) test the possibility of partial sex-linkage on the preferred hypothesis that males are heterogametic while (RD)R and (DR)R are tests on the less probable hypothesis that females are heterogametic. The absence of significant differences in the distribution of grade classes (0-1) and (2-5) among male and female progenies indicate that there is no sex-linkage of any sort.

It is evident that the range of silvering in heterozygotes overlaps both homozygotes. To get a more accurate idea of the amount of overlap than can be obtained merely by inspection of table 2, the 459 individuals in this table have been apportioned to genotypes and grades in as nearly exact Mendelian ratios as possible from each type of mating, and with a minimum of overlap. Table 4 shows the results.

TABLE 4

Apportionment of individuals of table 2 to genotypes on the assumption of as nearly exact Mendelian ratios as possible and a minimum of overlap.

PARENTS	NO. MATINGS	PROGENY									TOTAL
		<i>SiSi</i>	<i>Sisi</i>				<i>sisi</i>				
		0	0	1	2	1	2	3	4	5	
<i>SiSi</i> × <i>sisi</i>	5		27	11	1						39
<i>Sisi</i> × <i>sisi</i>	30		71	52		6	38	42	28	10	247
<i>Sisi</i> × <i>Sisi</i>	12	29	8	51		1	13	9	6		117
<i>sisi</i> × <i>sisi</i>	8					4	7	13	6	8	38
<i>SiSi</i> × <i>Sisi</i>	2	9	2	7							18
Total	57	38	108	121	1	11	58	64	40	18	459
% within genotypes		100.0	47.0	52.6	0.4	5.8	30.4	33.5	20.9	9.4	
Mean		0.0		0.5				3.0			

There is no clear evidence that *SiSi* ever showed any silvering although in one mating, parents both called grade 1, *SiSi* or *Sisi*, produced ten young all of grades 0 or 1.

The heterozygotes must be supposed to be distributed in varying proportions between grades 0 and 1 and only very rarely grade 2. In the total, 47 percent of *Sisi* had no detectable silvering and 53 percent had a trace. Genotype *sisi* is indicated to cover the range from a trace to very strong silvering with a mean at 3.0, medium silvering.

Table 5 shows the relation between the grades of silvering of back and belly among the 218 young from the backcrosses.

TABLE 5

Joint distribution of grades of silvering of back and belly in the backcross population.

	GRADE OF BELLY						TOTAL		IN TOTAL	IN UPPER 50%
	0	1	2	3	4	5				
	0	62	28	22	12	1	125	Back	$1.03 \pm .09$	$2.02 \pm .13$
	1	2	2	3	13	2	22	Belly	$1.96 \pm .11$	$3.38 \pm .08$
Grade	2			5	16	9	30	Correlation	$.80 \pm .024$	$0.68 \pm .054$
of	3			1	8	14	3			
Back	4					5	6			
	5						4			
Total		64	30	31	49	31	13	218		

The strong correlation, $.80 \pm .024$, between back and belly, demonstrates again that there can not be random assortment of two major genes, acting separately in these two regions. The rather large number (63) with silvering of the belly but not of the back as compared with the small number (2) in which the opposite was true, seems merely to reflect an average difference in threshold. This difference might to some extent account for the dominance of ventral silvering and recessiveness of dorsal silvering, noted by PICTER and FERRERO, but only as different effects of the same gene, not of independent genes.

The correlation between back and belly in silvers, homozygous in *si* but segregating in minor factors, may be estimated roughly by considering only the upper 50 percent of the backcross population (those in which the sum of dorsal and ventral grades is 3 or more, plus seven from the class graded 2 on the belly, 0 on the back). The correlation in this group is $.68 \pm .054$, which indicates that 68 percent of the variability in silvers of genotype *sisi*, but otherwise heterogeneous, is due to factors (nongenetic or minor genetic), that act alike on back and belly, leaving only 32 percent to factors that act more locally. That there is considerable nongenetic variability is indicated by the frequency of marked asymmetry and other irregularities on both back and belly and is, of course, to be expected of a character, the very nature of which implies different thresholds among hair follicles that all presumably have the

same genetic constitution. The efficacy of selection indicates, however, that minor genetic factors play some role.

Varying degrees of silvering have appeared in a stock of reds and yellows. The character is manifested in these by a usually rather slight but apparently rather uniform dilution of the color of the back, associated with a sprinkling of white hairs which is less conspicuous than on a black ground, and with a marked reduction of color on the belly which appears light yellow, blotched yellow and white, or solid white, depending on the grade. This silvering was independent of strain 13 in origin. The grading within this stock has not been sufficiently accurate for presentation but strong silvering has seemed to behave on the whole as recessive. Crosses of strongly silvered reds with silvers of strains I-13 or 13 have given silvered black-red tortoise shells of the following grades:

	MATINGS	0	1	2	3	4	5	TOTAL
White bellied light red × silver (I-13, 13)	5	0	2	3	2	2	9	18

From this result, there seems little doubt that the same recessive gene *si* is involved.

Not all unexpectedly dilute reds and yellows are *sisi*, however. Two unexpectedly pale creams (*ee c^kc^r FF* and *ee c^kc^a FF*), from an experiment in which the amounts of yellow pigment in diverse genotypes were being determined, were mated with silver from I-13. These pale creams did not have bellies appreciably lighter than their backs. The results (included in F₁ in table 2) indicate that these animals were *SiSi*.

	MATINGS	0	1	2	3	4	5	TOTAL
Pale cream × silver (I-13)	2	7	2	1				10

Discussion of previous interpretations

The results obtained in these experiments agree with the earlier statements by the author (1917), IBSEN (1932) and PICTET and FERRERO (1940) that silver may have at least some degree of dominance, manifested by silvering of the belly in the crossbreds. The gene, called *si* here, may be the same as that listed by IBSEN with the symbol *Ro*. It is obvious, however, that the gene is quite unusable as a dominant in the experiments described here, not only because about half of the heterozygotes show no silvering whatever, but those that are called silver have such a slight trace that their classification is often doubtful. The gene can be used as a recessive on the other hand with about the same degree of reliability as in the case of the spotting factor, *s*, by drawing an arbitrary line according to the expected ratio (cf. WRIGHT 1941).

The relation of *si* to PICTET and FERRERO's *V* and *d*, if any, is a puzzling matter. It seems unlikely that two apparently identical series of variations should have nothing in common genetically yet it is certain that the present results can not be explained by separate genes for silvering of back and belly and on the other hand PICTET and FERRERO's published results appear to

substantiate their interpretation and certainly do not lend themselves readily to interpretation in terms of *Si,si*. There are, however, certain difficulties in the interpretation. The original dorsal silver (which also had ventral white and was considered to be *VV dd*) was mated with a ventral white which had produced normals and was therefore assigned the formula *VvDD*. The progeny, 16 in number, were all ventral whites, presumably *VvDd* and *VVDd*. Two matings among these gave the following results. In the authors' terminology *Vbl* means ventral white alone, *Vbld* is ventral white associated with dorsal silvering and *arg* is dorsal silvering alone.

MATING	<i>Vbl</i>	<i>Vbld</i>	NORMAL	<i>arg</i>	TOTAL
<i>Vbl</i> (F ₁) × <i>Vbl</i> (F ₁)	17	10	0	6	33
<i>VvDd</i> × <i>VvDd</i>	(9/16) <i>V-D-</i>	(3/16) <i>V-dd</i>	(3/16) <i>vv D-</i>	(1/16) <i>vvdd</i>	

The most striking thing here is the absence of normals (*vvD-*) although the ratio as a whole is far from good. It should be said, however, that these matings gave much the poorest fit of any reported in the paper. They contribute about one-third of the total χ^2 referred to later. Six later matings are reported as between ventral whites without dorsal silvering, but with dorsally silvered young (necessarily *VvDd* × *VvDd*).

	<i>Vbl</i>	<i>Vbld</i>	NORMAL	<i>arg</i>	Total
<i>Vbl</i> (<i>VvDd</i>) × <i>Vbl</i> (<i>VvDd</i>)	105	36	0	12	153

Here again there are no normals, *vvD-*, although this class should constitute 3/16 of the young from this type of mating. The numbers in the other classes are however in excellent agreement with expectation. The authors advance the hypothesis that the normal genotype is lethal when produced by *VvDd* × *VvDd*. This is supported by the smaller size of litter in this case (2.25) as compared with 2.785 from 89 litters from *vvDd* × *vvDd* (which produces the same kinds of normals). The difference almost exactly accounts for the missing normal young.

According to this hypothesis, the union of a *vd* sperm with a *vD* egg, or of a *vD* sperm with either a *vd* or a *vD* egg gives lethal results but only if both parents are *VvDd*. Compare for example the results of the following matings (from which parents of the anomalous lethals were at least in part derived) which show that *VvDd* individuals of either sex produce the four expected types of germ cells in the expected 1:1:1:1 ratio and that two at least of the three alleged types of lethal unions give viable young when only one parent is *VvDd*.

MALE	FEMALE	<i>Vbl</i>	<i>Vbld</i>	NORMAL	<i>arg</i>	TOTAL
<i>Vbl</i> (<i>VvDd</i>) × <i>arg</i> (<i>vvdd</i>)		17	18	18	14	67
<i>arg</i> (<i>vvdd</i>) × <i>Vbl</i> (<i>VvDd</i>)		8	5	6	8	27
Total		25	23	24	22	94

The burden of proof on such an hypothesis seems so great that it would seem preferable to interpret the matings between *Vbl* parents cited above, as

ones in which both were homozygous in a gene for silvering (*sisi*) which might manifest its action in any of the three forms *Vbl*, *Vbld* or *arg* according to minor factors, genetic or otherwise.

Here, however, we must take cognizance of the closeness with which the observed results are matched by the calculated ones. The data are collected in tables 16 and 17 in PICTET and FERRERO's paper. A series of 48 matings, beginning with ones between extracted dorsal silvers (*vdd*) and normals (*vd-*) are reported in table 16 as giving only these two classes, in close agreement with expectation for every individual mating. Similarly close agreement is exhibited by the 47 matings (table 17) in which one or both parents had gene *V*. An analysis of the segregating progenies from these matings gives the following results:

	DEGREES OF FREEDOM	χ^2	PROBABILITY
Table 16	27	3.5	.999,996
Table 17	62	17.7	.999,999,8
Total	89	21.2	.999,999,999,99

According to the descriptions, both whitening of the belly and dorsal silvering varied from mere traces to strong; and dorsal silvering (in the category *arg*) might invade the belly. It would seem that there must have been intergrading of all four categories and many doubtful cases. One can only conclude from the extraordinary goodness of fit that doubtful cases were resolved in favor of the expected ratios.

It is possible to account for PICTET and FERRERO's results in terms of *Si* and *si* but this means little since normals may be either *SiSi* or *Sisi*, *Vbl* and *arg* either *Sisi* or *sisi* and even *Vbld* may occasionally be *Sisi* as well as *sisi*. A record of degree of silvering, rather than mere occurrence is necessary for an analysis. The possibility that the heterozygotes overlap both homozygotes can hardly be tested adequately without determining the resistance to dilution of the F_1 type by repeated backcrossing to pure recessives, supplemented by breeding tests of supposed recessive segregants. It may be concluded that the postulated independent genes for ventral (*V*) and dorsal (*d*) silvering cannot be accepted as demonstrated and that it is at least possible that the same incomplete recessive (*si*) may underlie all stationary silvering of the type which may be manifested on all ground colors.

SYNTHETIC STATIONARY SILVERING

In genotypes SSe^{pe^p} or SSe^{pe} there is a sprinkling of yellow hairs on a ground of one of the darker colors in the tortoiseshell pattern (IBSEN 1919), with more yellow on the average in SSe^{pe} than in SSe^{pe^p} (CHASE 1939). To some extent in Sse^{pe^p} or Sse^{pe} and to a greater extent in sse^{pe^p} and sse^{pe} , yellow tends to occur in large areas resembling in form and location the white areas which also appear in these tricolors (WRIGHT (1917), ILJIN (1928), CHASE (1939)). There is, however, considerable sprinkling of yellow in the black areas and of black in the yellow areas. It has long been known that

replacement of gene C by lower alleles tends to reduce the intensity of yellow disproportionately and in certain cases ($c^r c^r$, $c^r c^a$, $c^k c^r ff$, $c^k c^a ff$, $c^d c^r ff$, $c^d c^a ff$) the reduction is to white (WRIGHT 1915, 1927). There may be considerable resemblance to the preceding type of stationary silvering as manifested in silvered blacks and browns, but not of course in silvered reds and yellows.

PROGRESSIVE SILVERING (OR GRIZZLING)

Lambert's results

A type of silvering of the guinea pig that first appears after the first pelage and which progresses with age, like gray hair in man, and gray (as opposed to roan) in horses, seems to have been described only by LAMBERT (1935). It has been observed in my colony only in a few animals, kindly presented by DR. LAMBERT, and in descendants of these.

The character consists of the occurrence of totally white hairs, scattered principally over the posterior region of the back but in extreme cases over all the back and sides and to a lesser extent on the head and belly. At birth the animals may be of any color, depending on the residual genotype. According to LAMBERT, 40 days is the earliest at which white hairs appear (in the posterior dorsal region). LAMBERT's principal results (substituting grizzled for his term silver) were as follows:

MATING	GRADE OF GRIZZLING					TOTAL
	NONE	TRACE	LOW	MEDIUM	HIGH	
Grizzled×grizzled		1	6	10	22	39
Grizzled×nongrizzled (outcross)	12	2				14
Grizzled×heterozygote	35	28	24	21	13	121
Heterozygote×heterozygote	17	7		5	1	30

These results point clearly toward an incompletely recessive major factor (LAMBERT's interpretation) although reports of breeding tests of the supposed segregants are needed to clinch the demonstration. Thus in a cross between inbred normal and polydactyl strains of guinea pigs an apparent one factor difference, from evidence more extensive than that above, was completely disproved on testing the supposed segregants (WRIGHT 1934). Accepting provisionally the one factor interpretation, it may be noted that the amount of overlap of the heterozygotes with both homozygotes is remarkably similar to that inferred earlier in this paper for stationary silvering. In both cases the situation is also very similar to that found for spotting (s) (WRIGHT and CHASE 1936). LAMBERT gives no symbol. I shall use gr (grizzling) to avoid confusion with stationary silvering (si) and to suggest its progressive character.

Experiments

My own data are not very extensive but confirm LAMBERT's interpretation as far as they go. The pure stock derived from his stock produced 54

young which were saved beyond weaning. All of these became grizzled, some as early as two months. A few were ungrizzled at four months but became grizzled, usually of a high grade, later.

Reciprocal crosses to ungrizzled animals of my colony gave 21 young which were saved to six months or more. Only one of these developed a trace of grizzling (first noted at nine months). These include a mating to a silver of stock I-13. At birth one of the young showed slight silvering of the belly, three showed traces on the belly, five showed no silvering and 13 others were born before careful grading began, but no silvering was recorded and presumably no more than a trace was present if any. Four of the young, including one with a trace of ventral silvering, were kept to ten or more months. None developed any dorsal grizzling. Thus there appears to be no relation between stationary silvering and progressive grizzling.

A backcross to the pure grizzled stock gave 12 nongrizzled (at six months or more) to eight grizzled (two slight, six stronger). Two of the nongrizzled were backcrossed again to pure grizzled and gave five nongrizzled (at six months or more) to two slightly grizzled. These results tend to indicate a normal gene that behaves as a unit in withstanding successive attempts at dilution by backcrossing to the pure recessive strain. Analysis of these progenies by sex of parents and offspring gives no indications of sex-linkage. Using $R(DR)$ for recessive (grizzled) female by male from dominant female and recessive male and $(DR)R$ for the reciprocal backcross, the results were as follows.

TABLE 6
Backcross progeny classified by character, sex and nature of the mating.

MATING	FEMALE		MALE		TOTAL	
	NON-GRIZZLED	GRIZZLED	NON-GRIZZLED	GRIZZLED	NON-GRIZZLED	GRIZZLED
R(DR)	3	4	4	2	7	6
(DR)R	6	3	4	1	10	4
Total	9	7	8	3	17	10

Matings between heterozygotes gave eight nongrizzled (at six months or more) to three grizzled. Matings between heterozygotes and pure nongrizzled gave 24 young all nongrizzled. Extracted grizzled mated *inter se* have given 14 that were grizzled at six months or later and three not grizzled when last examined (six months in two cases, nine months in the other). As three of those ultimately recorded as grizzled showed no grizzling at six, nine and ten months respectively, the nongrizzled might have become grizzled if they had lived long enough. It is obvious that the grizzling extracted from the outcrosses was not as strong as that from LAMBERT'S selected stock.

The increase in grizzling with age is shown in table 7 for the pure stock, for the segregants which ultimately become grizzled and for the descendants of extracted grizzled. Grade 0 is nongrizzled, 1 means a trace, and 2 slight, 3

medium, 4 strong and 5 very strong grizzling. The nongrizzled are included in the averages.

In conclusion, there seems little doubt that there is one major pair of alleles (*Gr*, *gr*) although more extensive tests of segregants would be desirable. The degree of effect is undoubtedly subject to minor factors. With the usual modi-

TABLE 7

Increase in grizzling with age. The number of animals examined, the number nongrizzled and the average grade are shown by two month periods to 17 months, for ages 18 to 23 months and for 24 months and over.

		AGE IN MONTHS										
		0-	2-	4-	6-	8-	10-	12-	14-	16-	18-	24-
LAMBERT Stock	number		14	27	27	17	10	8	13	7	12	3
	nongrizzled		4	1	0	0	0	0	0	0	0	0
	av.	0	0.9	1.5	2.4	2.8	2.7	2.9	3.2	3.6	3.5	4.3
Segregants	number			7	7	3	7	3	2	3	4	1
	nongrizzled			3	2	1	0	0	0	0	0	0
	av.	0	0	0.7	1.3	1.3	2.6	2.3	2.0	3.0	2.3	2.0
Extracted Strain	number			20	10	10	5	3	3	0	2	0
	nongrizzled			12	3	2	1	0	0	0	0	
	av.	0	0	0.4	1.0	1.1	1.4	1.7	2.0		1.5	

fiers, grizzling is completely or almost completely recessive and even in homozygotes may not appear until the animal is nearly a year old. A residual heredity can be built up by selection that enables grizzling to appear at two months or even less and to become very strong in time and which enables a trace of the character to appear in heterozygotes.

RETROGRESSIVE SILVERING OR DINGINESS OF BROWN

IBSEN (1932) included in his list of variations of the guinea pig a white tipping for which he suggested an incompletely dominant factor (*W*). "*W* causes the distal half of all chocolate (*b*) hairs, on the back especially, to become white, provided the animal carries *C*, the factor for full color (red is present). It has no effect in *c*' (absence of red) animals. The effect on black hair (*B*) is very slight; homozygotes have a few white tipped hairs on the head, while heterozygotes do not show any white tipping. Red hair (*CCee*) is entirely unaffected by *W*. There is also a sex-limited effect in that nearly all females gradually lose their white tipping while males tend to retain it." No data were given.

A variation with some of the above characteristics has been present in browns (chocolates) of my colony and has been referred to briefly in a previous paper (WRIGHT 1942). EATON (1943) has described a similar condition as occurring in browns of the stock of the U. S. BUREAU OF ANIMAL INDUSTRY

(from which my stock split off in 1926) and as following an irregular mode of inheritance. There are a number of respects in which the condition in my stock differs from IBSEN'S account while agreeing more nearly with EATON'S description. Not all brown hairs are affected, even on the head, except in the more extreme cases. There is instead a sprinkling of light colored hairs among ones of full intensity. Moreover brown seems never to be reduced to white in any part of the hair in my stock, even in the highest grades, nor is the lightest portion of the hairs at the tip. Some two or three mm. at the tip of the hair is of full or nearly full intensity. Below this, some hairs merely show a band in which brown is reduced to a color comparable to that of a very pale brown ($E\ bbc^d c^d p p F F$) followed by less dilute brown to the base. Other hairs are uniformly pale brown except for the tip. In the most extreme grades all hairs are pale brown with dark tips. According to EATON dilution is more extreme in brown agoutis than in browns and this dilution occurs only below the yellow subterminal band of the agouti pattern. The term white tipping obviously does not apply to the condition in these stocks. The term dinginess gives the general impression given by these browns in contrast with intense browns and will be used here for this type of variation.

It was noted in the previous paper that this condition could not be transferred to browns with $c^k c^k$ (c^k is a higher allele of albinism than c^r referred to by IBSEN) or with $p p$, extreme diluter of brown and sepia but could be transferred to browns with $f f$ (i.e. $E-bbCCPPff$). Replacement of F by f has no appreciable effect on browns or sepias in the presence of P although it removes these colors in combination with $p p$. The paradoxical effect of dinginess in reducing brown only when it would otherwise be most intense made further study of its effects of interest.

Experiments

Strong dinginess of brown first appeared in some segregants from a cross made by DR. E. C. COLIN between the same black-red-white tricolor strain No. 13 that was the source of stationary silvering and a stock (C) which carried brown. DR. COLIN began experiments with these in 1930. He developed a strongly dingy strain and mated one of these with a pink eyed dilute brown tricolor ($s s e^p e^p a a b b c^k c^k F F p p$) from a strain (B) that was the most inbred strain of browns in the colony at the time. F_1 consisted of intense browns with no dinginess. Absence of dinginess persisted through three successive back crosses to the dingy stock in more than 50 percent of the young (total 61 non-dingy, 19 slightly dingy and 30 strongly dingy). Extracted dingies, mated *inter se* gave four nondingy, 18 slightly dingy and 94 strongly dingy. These results indicate that nondingy differs from dingy primarily in one major dominant gene. From later results, however, it appears probable now that this "dominant" gene was the well known recessive p , introduced in the original mating.

A stock (S) of browns from DR. COLIN'S experiments was carried on for a number of years before an attempt at semiquantitative analysis was made by

means of grades. Grade 0 is complete absence of dinginess. In grade 1, there is a trace of dinginess, restricted to scattered hairs on the cheeks and perhaps the nape. In grade 2, there is unmistakable dinginess of scattered hairs, restricted to head and nape. In grade 3, scattered dingy hairs are found on the back but substantial nondingy areas are also present. In grade 4, all parts of the back (as well as the head) are sprinkled with dingy hairs and there may be some dinginess on the belly. Grade 5 was adopted later for cases in which practically all hairs are affected.

Many animals of this stock, especially in the earlier generations, had only small areas of color on a white ground due to *ss*, derived as in the case of the silver stock, from strain 13. Grading of these presented less uncertainty than in the case of silver since dinginess can be graded from observation on the head, the commonest location of colored spots in extreme piebalds in contrast with silver, which cannot be graded satisfactorily in the absence of color on the posterior belly. There is no indication that the dinginess of colored spots is at all affected by genes *S*, *s*. Nearly all animals have been graded at birth. A second grade has usually been given when possible at about 30 days, when low grade dinginess is sometimes more conspicuous than at birth. Following are the averages of live born and still born intense browns at birth and of those that reached weaning, from matings that trace wholly to animals of grades 3 and 4 in the stock *S* referred to above and similar averages from the progeny of animals of grades 3 to 5 that segregated from outcrosses (*SP*, *SK*, *SA*) to other stocks referred to later. In both cases, matings that produced dilutes (*c^kc^k* etc.) are excluded. All were probably *bbC-PPFF*, but undoubtedly some individuals were heterozygous for albino alleles (*Cc^k*, *Cc^a* etc.). (Table 8.)

Descendants of high grade dingies

TABLE 8

Mean grades of dinginess at birth among live born and still born young, and at weaning, from the high grade stock S and from matings between high grades deriving from outcrosses.

TIME OF GRADING	STOCK S			EXPERIMENTS SP, SK, SA		
	NO.	MEAN	SE	NO.	MEAN	SE
Birth (live born)	326	2.93 ± .06		182	3.02 ± .09	
Birth (still born)	84	2.36 ± .12		64	2.61 ± .13	
30 days	233	3.00 ± .06		139	3.32 ± .09	

The grades of still born young are significantly lower than those of the live born young, possibly because of difficulties in grading in some cases (short hair, wetness, etc.). It has seemed best to exclude them from the data. The correlation between grade at birth and that at weaning was $.75 \pm .03$ in series *S* and $.85 \pm .02$ in the later group. The difference between the grades was not significant in the former but is in the latter.

The grades at weaning are undoubtedly more reliable than those at birth

but it has not seemed desirable for the purposes of this paper to exclude the grades of live born young when no later grade was given. The grade in all later tables is thus the last grade up to weaning of the live born young.

There was segregation of E and e^p in these experiments. The average grades of young without red spotting (largely E) and with red spotting ($e^p e^p$) are as follows in the two groups.

	STOCK S			EXPERIMENTS SP, SK, SA		
	NO.	MEAN	SE	NO.	MEAN	SE
Brown	111	2.06 ± .10		100	3.36 ± .12	
Brown-red	215	3.02 ± .07		87	3.09 ± .11	

It is obvious that there are no consistent differences and no distinction will be made later.

The full distribution of grades in these two groups is given below by sex.

TABLE 9

Distribution of grades by sex in stock S and among offspring of high grades derived from outcrosses.

		PERCENTAGE					NO.	MEAN	SE
		0	1	2	3	4			
Stock S	♂	1.2	4.1	18.7	35.1	40.9	—	171	3.11 ± .07
	♀	2.6	7.1	24.5	31.0	34.8	—	155	2.88 ± .08
	Total	1.9	5.5	21.5	33.1	38.0	—	326	3.00 ± .06
SP, SK, SA (parents 3-5)	♂	1.1	6.5	14.1	25.0	44.6	8.7	92	3.32 ± .11
	♀	0	11.6	13.7	28.4	40.0	6.3	95	3.16 ± .11
	Total	0.5	9.1	13.9	26.7	42.3	7.5	187	3.24 ± .08

The males are slightly higher in grade in both stocks but the difference is of somewhat doubtful significance. If both stocks are combined the difference ($.191 \pm .092$) is 2.1 times its standard error.

The wide variability of stock S suggests great genetic heterogeneity. The parents in the 58 matings in which both were graded (308 young) ranged from grade 1 to 4. The correlation between father and offspring was $+.280$, between mother and offspring $+.086$, giving an average of $+.183$. There was a low correlation between the parents, $+.212$, due to a considerable number of brother-sister matings rather than to intentional assortative mating. On the simplest hypothesis (no dominance, no interaction effects, a constant tendency to inbreeding) the correlation between parent and offspring is $(1/2)h^2(1+m) = .183$ where h^2 is degree of determination by heredity and m is the correlation between the genotypes of parents. This indicates less than 37 percent determination by heredity. The correlation between parents (often littermates) may include a nongenetic component. The nongenetic variance includes that

due to inconsistencies of grading, but the scale is such a coarse one that this can hardly be the major component.

Mated animals have been graded at the time of birth of each litter. Table 10 shows the averages for males and females of each initial grade. The males are distinctly less dingy at four or five months than at first but rise slightly in

TABLE 10
Grades of dinginess at successive ages of males and females of each initial grade.

		AGE IN MONTHS											
		0-	2-	4-	6-	8-	10-	12-	14-	16-	18-	24-	6-40
	no.		1	49	37	24	24	19	20	14	22	24	184
	av.	4.0	4.0	2.7	3.2	3.1	3.2	2.8	2.9	2.4	2.5	2.2	2.84
	no.		1	35	23	21	17	14	10	7	21	27	140
	av.	3.0	1.0	2.1	2.5	2.2	2.1	2.2	2.4	2.0	2.3	1.6	2.14
♂	no.		1	28	19	16	15	7	8	2	6	9	82
	av.	2.0	2.0	0.9	1.4	1.8	1.5	1.9	1.5	1.5	1.8	0.4	1.47
	no.		2	26	20	15	11	11	10	11	15	9	102
	av.	1.0	2.0	0.5	0.7	0.6	0.9	0.8	0.6	0.6	0.7	0.9	0.71
	no.		3	10	12	12	1	11	6	3	10	4	59
	av.	0.0	0.0	0.0	0.1	0.1	0.0	0.2	0.5	0.0	0.3	0.3	0.20
	no.		18	47	37	23	21	20	16	13	16	5	151
	av.	4.0	2.7	2.4	1.8	1.4	1.4	1.7	1.4	1.0	1.3	1.4	1.49
	no.		14	39	25	18	21	16	7	10	14	12	123
	av.	3.0	2.1	1.6	1.0	0.7	0.8	0.7	1.1	1.4	0.9	0.9	0.90
♀	no.		14	37	30	30	24	24	13	11	11	6	149
	av.	2.0	1.4	0.8	0.5	0.5	0.5	0.6	0.5	0.4	0.2	0.0	0.47
	no.		11	31	23	24	21	15	9	6	8	3	109
	av.	1.0	0.3	0.2	0.3	0.3	0.3	0.2	0.1	0.2	0.0	0.3	0.24
	no.		7	15	14	9	3	2	4	5	5	5	47
	av.	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.05

the next pelage and thereafter remain about the same or, in the case of high grades, decline slightly. The females lose most of their dinginess in the first six or eight months but thereafter change little on the average. The grand averages of all grades after six months bring out the difference between the sexes in loss of dinginess.

A number of characters of the guinea pig, most notably the occurrence of polydactyly and the amount of color in the spotting pattern have been shown to be greatly affected by the age of the mother (less polydactyly and more

white among the progeny of mature than of immature females) (WRIGHT 1926). It is of some interest to see whether dinginess belongs in this group, especially as in this case the females lose their dinginess as they become mature which, on a Lamarckian view might be supposed to have a corresponding effect on the offspring. The average grades according to age of mother in the high grade derivatives of stock S and of experiments SP, SK and SA are shown in table 11.

TABLE 11

Relation of age of mother to average grade of dinginess of offspring in Stock S and from matings between high grades in experiments SP, SK and SA.

AGE OF MOTHER (MONTHS)	STOCK S		EXPERIMENTS SP, SK, SA	
	NO.	MEAN SE	NO.	MEAN SE
3-	100	2.91 ± .11	51	3.30 ± .13
6-	82	2.90 ± .11	51	3.16 ± .15
9-	90	3.03 ± .10	58	3.14 ± .16
15-36	54	3.26 ± .11	28	3.46 ± .22

There are no consistent differences among the averages. In stock S, the distributions yield $\chi^2=9.4$, $n=9$, Probability, 0.30-0.50. In the other group $\chi^2=20.3$, $n=12$, Probability, 0.05-0.10.

Interactions with known color factors

Dinginess is not expressed in the white areas of the piebald pattern, due to the incomplete recessive *s*, but, as noted earlier, seems to be as strongly expressed in the brown spots of piebalds as in the corresponding areas of self browns.

Similarly dinginess is not expressed in self yellows (*ee*) or in the yellow hairs of tortoiseshells (*e^pe^p*, *e^pe*) but seems to be equally expressible in brown hairs of tortoiseshells and of self browns (*E*-).

Dinginess occurs in the brown of brown agoutis (*A*-) and according to EATON is more strongly developed than in nonagouti browns (*aa*). In my experiments, there have not been a sufficient number of litters with segregation of brown agoutis and browns for an adequate comparison.

The brown factor *b* is necessary, at least for more than a trace of dinginess. According to IBSEN, traces of white tipping may be present in blacks (*B*). I have not observed anything in black littermates of dingy browns that could be said with confidence to be the same condition but such litters have not been produced in adequate numbers. There is also, as noted, some doubt as to whether IBSEN'S white tipping is the same as the dinginess of brown in my colony.

The remaining three major series of alleles are concerned with the intensity of black, brown and yellow. Their interaction with each other in nondingy browns are shown in table 12 in which the amount of brown pigment ex-

tractible in genotype (*S E aabb*) *C-P*- is taken as 100 (WRIGHT 1942). The albino series (*C*, *c^k*, *c^d*, *c^r*, *c^a*) is represented by the three alleles that have been studied most intensively in connection with dinginess. Replacement of *c^k* by *c^d* or *c^r* gives somewhat smaller amounts of brown. *C* and *P* appear to be completely dominant and replacement of *F* by *f* in the presence of *P* appears to have no effect in nondingy browns. *F* is not completely dominant over *f* in pale browns, genotype *bbC-Ffpp* having only about 24 percent as much brown as *bbC-P*- instead of 30 percent as in *bbC-FFpp*. The very pale yellow or cream of *bbC-ffpp* seems to contain no brown.

TABLE 12

The appearance and amount of brown pigment relative to that with C-P- in combinations of C, c^k, c^a; F, f and P, p.

	(<i>F, ff</i>) <i>P</i> -	<i>FF pp</i>	<i>ff pp</i>
<i>C</i> -	Brown (100)	Pale Brown (30)	Pale Cream (0)
<i>c^kc^k</i>	Brown (96)	Pale Brown (25)	White (0)
<i>c^kc^a</i>	Brown (83)	Pale Brown (15)	White (0)
<i>c^ac^a</i>	White (0)	White (0)	White (0)

The effects of these genes on black (*B*) are somewhat parallel to those on brown. Replacement of either *C* or *F* by lower alleles reduces the intensity of yellow. Thus *c^kc^k* can easily be distinguished from *C*, and *ff* from *F* in tortoiseshells though not in self browns. Replacement of *B* by *b* or of *P* by *p* has no effect on intensity of yellow.

The observation that the occasional brown-yellow tortoiseshells (*e^pe^pbbc^kc^kP-FF*) and pink eyed pale browns (*bbC-ppFF*), that segregated out in early generations of stock S, never showed the dinginess which was usually present in their brown-red littermates (*e^pe^pC-P-FF*), led to experiments (SK, SP) intended to test these apparent interaction effects more thoroughly. Another experiment (SF) was made to test whether dinginess could be introduced into brown-yellow tortoiseshells that owed their dilution of yellow to *ff* instead of to *c^kc^k*. As the interpretation of the results in the last case turned out to involve fewer complications these data will be considered first.

Effect of F, f

High grade dingies of stock S were mated reciprocally with brown-yellow tortoiseshells of a strain (F) in which at this time all animals were homozygous *CCffPP*. Most of the young (table 13) showed low grades of dinginess (average 1.5 ± 0.1). There were no significant differences by direction of cross or sex of young (averages for 16(*DR*) ♀'s 1.6, for 25(*DR*) ♂'s 1.5, for 12(*RD*) ♀'s 1.2 and for 3(*RD*) ♂'s 1.3).

Backcrosses to stock F gave 41 young of which 24 had red spots (*Ff*), 16 had dilute yellow spots (*ff*) and one had no yellow spots and therefore might either be *Ff* or *ff*. Only seven of the 24 known to be *Ff* had any dinginess (average for *Ff* 0.4 ± 0.1) and none of the 16 known to be *ff* were dingy.

The significant reduction of the average for Ff ($1.5 \pm .10$ to $0.4 \pm .13$) on backcrossing to stock F shows that the latter must have introduced an independent factor or factors that inhibit dinginess. Results in later generations show that there is, in fact, no difficulty in obtaining Ff of grade 4. Brown-reds from $Ff \times ff$ in which both parents were half to three-quarter blood of stock S average $2.57 \pm .13$. This is significantly lower than FF of stock S but is higher than the average for Brown-reds from $Ff \times Ff$ and about the same

TABLE 13

The distribution of grades of dinginess in the offspring of matings involving only segregation of F, f among known factors. The ancestry (stock S, or F, F_1 , $\frac{3}{4}$ blood stock S, etc.) is indicated in parentheses and is followed by the average grade.

DINGIER PARENT	LESS DINGY PARENT	MAT-INGS	GENO-TYPE	0	1	2	3	4	NO.	AV.	SE	
FF (S)	3.7 ff (F)	0.0	8	Ff	5	24	24	3	56	1.45	$\pm .10$	
Ff (F_1)	2.2 ff (F)	0.0	5	FF	17	5	2		24	0.38	$\pm .13$	
				?		1			1	1.00		
				ff	16				16	0.00		
FF (S)	4.0 Ff (F_1)	0.5	2	$F-$	1		5	2	3	11	2.55	$\pm .37$
Ff (F_1 , ($\frac{3}{4}$) S)	2.3 $F-$ (ca ($\frac{3}{4}$) S)	2.3	3	$F-$		1	7	1	3	12	2.50	$\pm .29$
FF (ca $\frac{1}{2}$ S)	3.4 ff (ca ($\frac{3}{4}$) S)	0.8	7	Ff	5	9	13	7	2	36	1.78	$\pm .18$
FF (S)	3.6 ff (ca ($\frac{1}{2}$) S)	1.2	8	Ff	2	7	20	8	3	40	2.08	$\pm .15$
Ff ($(\frac{1}{2})-(\frac{3}{4})$ S)	2.8 ff ($(\frac{1}{2})-(\frac{3}{4})$ S)	1.3	28	Ff	6	6	17	31	15	75	2.57	$\pm .13$
				?		3	4	1		8	1.75	
				ff	12	20	23	17	2	74	1.69	$\pm .13$
				$F-$	3	15	27	24	17	86	2.43	$\pm .12$
Ff ($(\frac{1}{2})-(\frac{3}{4})$ S)	2.6 Ff ($(\frac{1}{2})-(\frac{3}{4})$ S)	1.6	24	?		1	5	3		9	2.22	
				ff	10	8	9	5	1	33	1.36	$\pm .20$
ff ($(\frac{1}{2})-(\frac{3}{4})$ S)	1.6 ff ($(\frac{1}{2})-(\frac{3}{4})$ S)	0.7	18	ff	11	42	35	9		97	1.43	$\pm .08$

amount of ancestry of stock S although about one-third of these should be FF . The data give no reliable evidence for any difference between FF and Ff where the rest of the genotype is the same.

The results in the later generations show that it is also possible to introduce dinginess into ff . But while a few have been given grade 4, it is clear that the average is systematically lower than for Ff . In the case of matings of type $Ff \times ff$ the young known (by their dilute yellow spotting) to be ff are lower than those known (by their red spotting) to be Ff by $0.88 \pm .18$. In the case of matings $Ff \times Ff$, the brown-yellows (ff) are lower than the brown-reds (Ff or FF) by $1.07 \pm .23$. Those without yellow spotting and thus unclassifiable are intermediate in both cases. The average for young from $ff \times ff$ (extracted) is very low ($1.43 \pm .08$) in view of the amount of S ancestry and thus confirms the effect of ff indicated by the preceding results.

The data from the backcrosses of F_1 to stocks F and S are not adequate for a decision on whether stock F differs from S by one incompletely recessive gene (other than f) or by multiple factors although the fact that the upper

50 percent of Ff in the backcross to stock F is below F_1 in average, while the lower 50 percent in the backcross to stock S is above F_1 , suggests more than one factor. The small numbers are, however, compatible with the one factor interpretation.

It is noteworthy that the antagonistic effect of ff on dinginess is the first clear effect of f on dark pigmentation in the presence of P . It is also noteworthy that this effect, which is in the direction of intensification of brown, is in the opposite direction to the elimination of brown by ff in the combination $ffpp$.

Effect of P, p

Dingy browns of stock S were mated with pale browns ($C-p\bar{p}FF$ and $c^k c^k p\bar{p}FF$) from various sources as the first step in an attempt to introduce dinginess into this color. The young in F_1 (intense brown) consisted of 40 nondingy and only three with a trace of dinginess. In outcrosses of stock S to browns (nondingy or nearly so) from similar sources but known to be Pp , half the young showed some dinginess and two were of grade 4. F_2 from the first cross also included high grade dingies as well as ones of low grade and nondingies. The pink-eyed pale brown-red segregants ($C-p\bar{p}$) lacked all trace of dinginess as did a few brown-yellow ($c^k c^k P-$) and pale brown-yellow ($c^k c^k p\bar{p}$) segregants. Table 14 gives these results and those in later generations, except that the few animals shown to be $c^k c^k P$ or $c^k c^k p\bar{p}$ by their yellow spotting are omitted. None of these showed any dinginess.

The results in F_1 and F_2 show that the pale brown parent must have introduced a gene or genes that tend to suppress dinginess, that there is segregation of high grade dinginess in F_2 and that dinginess is at least difficult to introduce into pale brown.

The complete absence of dinginess in the $p\bar{p}$ segregants of F_2 continued into later generations even when the amount of ancestry of stock S was increased to three-fourths or more. The attempt to obtain pale browns from high grade dingy parents, was, however, a failure. The brown young from matings that produced pale browns at all were moreover predominantly nondingy or of low grade. With one exception, matings in which either parent was of high grade (3, 4) produced no pale brown young. Matings in which either parent was $p\bar{p}$ produce only low grade dingies (and pale browns) except for one individual called grade 3. Nearly all matings in these experiments between animals of grades 0 or 1, or between such animals and pale brown produced some pale browns. All of the results point to the conclusion that p strongly reduces dinginess even in heterozygotes. Only three animals of grade 3 and none of grade 4 have yet been found which were Pp . One of these is shown in the table as coming from a class of matings of type $PP \times p\bar{p}$. The second came from the same class but was born dead and so does not appear in the table. The third came from a mating of type $Pp \times Pp$ and was proved by a breeding test to be Pp . All of these were about three-fourths blood of stock S.

Linkage of p with a suppressor of dinginess is an alternative interpretation. The fact that p from all sources seems to have this effect and that nothing

suggesting crossingover has occurred in the course of the experiments, indicates that the effect is inherent in p rather than linked.

This conclusion was unexpected for two reasons. First there has been no indication from other experiments that P ever falls short of complete dominance over p even when other factors tend to reduce black or brown pigmentation to such a point that slight differences between PP and Pp should be easily

TABLE 14

Distribution of grades of dinginess among the offspring of matings involving p but not f . F_1 was largely from $CCPP \times c^k c^k pp$. Some later matings produced yellow spotted young ($c^k c^k P-$, $c^k c^k pp$). These young are omitted. Ancestry and average grade of parents are indicated. $PP?$ and $Pp?$ refer to animals which may have been either PP or Pp by ancestry and descendants but are questionably assigned a genotype by grade. These were all ($\frac{1}{2}$) blood or more of stock S .

PARENT (HIGHER GRADE)	PARENT (LOWER GRADE)	NO. MAT- INGS	pp	GRADE OF OFFSPRING						NO. P-	
				0	1	2	3	4	5		
PP (S)	3.5 pp (Misc.)	0.0	10	0	40	3				43	
PP (S)	3.1 Pp (Misc.)	0.1	8	0	17	9	8		2	36	
Pp (F_1)	0.2 Pp (F_1)	0.2	10	16	27	11	6	5	3	52	
PP ($(\frac{1}{2})S$)	2.9 pp ($(\frac{1}{2})S$)	0.0	3	0	26	11	2			39	
Pp ($(\frac{1}{2})S$)	1.0 pp ($(\frac{1}{2})S$)	0.0	4	4	3	1				4	
Pp ($(\frac{1}{2})S$)	1.4 Pp ($(\frac{1}{2})S$)	0.8	6	11	16	4	7	6	3	36	
PP (S , ($\frac{3}{4}$) S)	3.1 pp ($(\frac{1}{2})S$, ($\frac{3}{4}$) S)	0.0	9	0	18	35	20	1		74	
Pp (ca ($\frac{3}{4}$) S)	2.3 pp ($(\frac{1}{2})S$, ($\frac{3}{4}$) S)	0.0	5	20	8	9	2			29	
Pp (ca ($\frac{3}{4}$) S)	1.3 Pp (ca ($\frac{3}{4}$) S)	1.1	13	38	24	17	15	22	10	1	89
PP (S , ($\frac{3}{4}$) S)	3.2 Pp ($(\frac{1}{2})S$, ($\frac{3}{4}$) S)	0.8	5	0	18	8	7	8	4	45	
$PP?$	3.5 $PP?$	3.3	8	0		1	12	18	25	8	64
$PP?$	3.6 $PP?$	2.0	4	0	1	3	9	10	20	43	
$PP?$	2.0 $PP?$	2.0	2	0		1	4	5	7	17	
$PP?$	3.8 $Pp?$	2.0	4	0	6	1	4	2	3	16	
$PP?$	3.6 $Pp?$	0.3	6	0	15	4	6	5	8	38	
$PP?$	2.0 $Pp?$	0.3	3	0	12	6	7	4	3	32	
$P-$	0.5 Pp	0.0	2	0	7	1	4			12	
$P-$	1.0 $Pp?$	0.0	1	0	2		1		1	4	

detected if present. Secondly, Pp gives a more intense brown than either pp or PP . In extreme dinginess of grade 5, PP may be even paler, though more irregular, than pp .

Effect of C series

The few brown-yellow tortoiseshells ($c^k c^k$) that segregated out in experiment S completely lacked dinginess and often appeared to be more intense in the brown parts of their coats than their dingy brown-red littermates. This called to mind IBSEN'S observation that white tipping could not be introduced into browns of genotype $c^r c^r$. As c^k is the closest of the albino alleles to C in its effects on color, an experiment (SK) was started with the purpose of introducing dinginess into $c^k c^k$ browns if possible. Table 15 gives the data from this experiment excluding all matings in which either parent was definitely

known from its ancestry or descendants to be Pp . Unfortunately this excludes all of F_1 and most of the early matings as the effect of Pp on dinginess was not anticipated. Some of the matings included may involve Pp and this may account for some of the young of low grade.

The results resemble those with P, p in that no clear case of dinginess has been observed in the recessive segregants, here brown-yellow tortoiseshells ($c^k c^k$). In two or three cases there was some suggestion of dinginess on the cheeks but not enough to be sure that this was not a manifestation of the tor-

TABLE 15

Distribution of grades of dinginess among offspring of matings involving C, c^k but not F, f . Matings (including all of F_1) in which either parent was known to be either Pp or pp are excluded. Matings of type $Cc^k \times Cc^k$ are divided into a group in which both parents were of high grade (3, 4) and one in which one parent was of grade 2 and the other 2 or 3. In all cases both parents are 50% or more of stock S. The average grades of higher and lower parents in the matings in each group are shown.

PARENT (HIGHER GRADE)	PARENT (LOWER GRADE)	NO. MAT- INGS	GENO- TYPE	GRADE OF OFFSPRING					NO.	AV.		
				0	1	2	3	4				
CC	3.9	$c^k c^k$	0	5	Cc^k	9	7	2	13	6	42	2.00
					Cc^k	1	7	11	8	9	36	2.47
Cc^k	2.6	$c^k c^k$	0	14	?	4	1	2			7	1.57
					$c^k c^k$	35					35	0.00
					$C-$	4	1	8	7	6	26	2.38
Cc^k	2.2	Cc^k	2.0	7	?		1	2	1		4	3.00
					$c^k c^k$	17					17	0.00
					$C-$		1	9	4	20	34	3.26
Cc^k	3.8	Cc^k	3.6	7	?			1	2	1	4	3.00
					$c^k c^k$	14					14	0.00

toiseshell pattern. The results differ from those with P, p in that high grade parents often turned out to be heterozygous (Cc^k) as shown by the production of brown-yellow young. In such cases, moreover, the brown-red young were predominantly of high grade. Again matings between a $c^k c^k$ parent and either CC or Cc^k produced many high grade dingies.

These results suggest that Cc^k does not differ from CC in relation to dinginess. The average grades for the brown-red young are, however, rather low for the amount of ancestry of strain S (one-half to three-fourths). Moreover the average grade of brown-reds from matings of type $Cc^k \times Cc^k$ which should include 33 percent homozygotes is higher (2.90) than the average from matings which can not produce homozygotes (2.20). This comparison does not, however, have the validity of a comparison between classes of young from the same matings. It has not been possible to obtain a decisive answer to this question by more detailed analysis of these data.

In another experiment (SA) an attempt was made to produce albinos ($c^a c^a$) capable of transmitting dinginess. Table 16 gives a condensed account of the results. Again no matings are included in which either parent was definitely

known to be other than PP from ancestry or descendants. Unfortunately the available brown eared albinos ($EEaabbcc^aP\text{-}FF$) all had p in their recent ancestry and some of them may well have been Pp and again this could be responsible for some of the low grade young.

The average for F_1 (stock S by the foundation albinos) was low (1.36) and included none of grade 4. In later generations, however, with more ancestry of stock S, young were obtained from matings of type $CC \times c^a c^a$ and $Cc^a \times c^a c^a$.

TABLE 16

Distribution of grades of dinginess among offspring of matings involving C, c^a but not F, f. Parents known to be Pp or pp are excluded. In all except the first row both parents are 50% or more of stock S. The average grade of higher and lower parent in the matings of each group are shown.

PARENT (HIGHER GRADE)	PARENT (LOWER GRADE)	NO. MAT- INGS	$c^a c^a$	GRADE OF C OFFSPRING					NO. C-	AV. C-		
				0	1	2	3	4				
CC (S)	3.4	$c^a c^a$ (EBA)	5	0	15	14	19	8		56	1.36	
CC	3.4	$c^a c^a$	7	0	8	17	21	13	2	61	1.74	
Cc^a	2.6	$c^a c^a$	8	44	1	3	17	16	6	43	2.53	
Cc^a	2.1	Cc^a	1.5	17	46	29	20	41	22	10	122	1.70
CC (S)	4.0	Cc^a	1.1	3	0		2	8	4	4	18	2.56

that were of grade 4. Thus Cc^a , like Cc^k , can not have as great a suppressive effect on dinginess as does Pp . The rather low averages throughout in comparison with stock S suggest, however, that Cc^a may have some effect but the average is no higher in the progenies that include CC than in those that do not.

No systematic attempt has been made to introduce dinginess into browns with other combinations of albino alleles. The following have, however, segregated out of matings in progenies that contained red spotted dingies (C-): 12 $c^k c^r$, 24 $c^k c^a$, 14 $c^d c^a$, 6 $c^r c^r$, 3 $c^r c^a$. The young in the first three of these classes were identifiable by cream spotting (and by ancestry), the last two by white spotting or silvering of the synthetic type (and by ancestry). No trace of dinginess was observed in the brown of any of these. It seems safe to conclude that gene C is necessary for the expression of dinginess.

Joint effects of P, p and the C series

Genes c^k and c^a and to a less extent c^d and c^r were present in experiment SP and it is possible that some of the suppression of dinginess attributed to Pp may have been due to joint effects of Pp and heterozygosis in the C-series. An enumeration (table 17) of known double heterozygotes yields the following in which c^x here refers to cases in which it was merely known that a lower albino allele was present.

It is noteworthy that 82 percent of the known double heterozygotes were completely lacking in dinginess and none of the rest showed more than a trace. Thirty-six of these were from the first cross between stock S and unrelated ani-

mals and might owe their low grade to such a factor or factors as was indicated to be present in stock F. The remaining 21, however, had *S* ancestry, usually 50 percent or more, on both sides.

TABLE 17

Distribution of grades among individuals known to be Pp and also heterozygotes of C with a lower allele.

	F ₁ (S×MISC.) GRADE		BOTH PARENTS WITH S ANCESTRY GRADE	
	0	1	0	1
<i>Cc^kPp</i>	17	2	6	2
<i>Cc^rPp</i>	—	—	5	0
<i>Cc^aPp</i>	—	—	5	3
<i>Cc^xPp</i>	14	3	—	—
<i>Total</i>	31	5	16	5

Effect of age on different genotypes

The average for all grades after six months of age was found for each mated animal. Table 18 shows the relation between initial grade and the average for each genotype and sex after six months. Genotype *C-P-FF* includes all animals known to be carrying *C* and *P* and not known from ancestry or descendants to carry *p* or any lower allele of *C* (though heterozygosis may be suspected because of grade in some cases).

The initial grades of these mated animals agree fairly well with those based on the progeny in the preceding discussion.

The grades after six months show the reduction previously referred to, but otherwise tend to parallel the grades at weaning. It is, however, noteworthy that *Cc^kP-FF* and *Cc^aP-FF* in both males and females show a much greater loss of dinginess than does *CCPPFf* although the initial grades differ but little. These adult grades give more reliable evidence for effects of *Cc^k* and *Cc^a* than obtained from the initial grades. The very low grades of *CCPPff*, *C-PpFFF* confirm the previous conclusions and the exceptionally low grade of *Cc^xPpFFF* in males supports the view that *Cc^x* and *Pp* act cumulatively.

The effects of unrecognized *Pp* (in *P-*) and of residual factors can be largely eliminated by confining attention to animals that were of grades 3, 4 or 5 initially. This is done in table 19. The group *C-PPFF* is subdivided into those from stock *S*, experiment *SP*, and experiments *SK* or *SA*.

The initial grades mean nothing here because of the selection, which is more drastic in *CCPPFf* and *Cc^xPPFF* than for *C-PPFF*. The grades after six months bring out clearly the tendency of *Cc^xPPFF* to lose dinginess more than does *C-PPFF* from the same experiments. It appears indeed that *C-PPFF* from *SK* and *SA* has been selected to an even higher level of dinginess than in

TABLE 18

Average grade after 6 months of age of animals of indicated genotypes and each initial grade. The class ♂ C-P-FF initial grade 4 includes 2 of initial grade 5 which averaged 3.70 after 6 months.

GENOTYPE	INITIAL GRADE										TOTAL		
	0		1		2		3		4		INI- TIAL	AFTER 6 MONTHS	
	NO.	AV.	NO.	AV.	NO.	AV.	NO.	AV.	NO.	AV.			
♂ C-P-FF	1	0.00	4	0.73	4	2.60	21	2.97	43	3.28	73	3.41	2.97 ± .13
♂ CCPPff	1	0.00	3	0.50	11	2.02	6	2.90	7	3.29	28	2.54	2.30 ± .22
♂ C-PPff	9	0.28	6	0.67	6	1.25	—	—	1	3.70	22	1.00	0.80 ± .25
♂ Cc ^h P-FF	1	0.00	2	2.15	5	0.78	6	1.08	10	1.91	24	2.92	1.41 ± .18
♂ Cc ^a P-FF	2	0.00	6	0.73	5	1.30	8	1.25	1	4.00	22	2.00	1.13 ± .23
♂ C-PpFF	3	0.37	6	0.25	4	1.30	1	1.50	—	—	14	1.21	0.66 ± .19
♂ Cc ^h PpFF	3	0.17	2	0.20	—	—	—	—	—	—	9	0.44	0.18 ± .09
♂ Cc ^a PpFF	2	0.35	2	0.00	—	—	—	—	—	—			
♀ C-P-FF	6	0.00	7	0.50	15	0.83	21	1.26	46	1.73	95	2.99	1.29 ± .11
♀ CCPPff	2	0.00	5	0.20	8	0.59	7	1.69	4	2.20	26	2.23	1.01 ± .20
♀ C-PPff	4	0.00	6	0.17	11	0.68	4	1.00	—	—	25	1.60	0.50 ± .15
♀ Cc ^h P-FF	1	0.00	3	0.17	7	0.23	5	0.36	6	0.82	22	2.55	0.40 ± .09
♀ Cc ^a P-FF	2	0.50	9	0.24	12	0.37	7	0.60	3	1.70	33	2.00	0.51 ± .11
♀ C-PpFF	3	0.03	5	0.04	19	0.10	—	—	—	—	19	1.11	0.10 ± .04
♀ Cc ^h PpFF	2	0.00	2	0.50	—	—	—	—	—	—	8	0.38	0.13 ± .08
♀ Cc ^a PpFF	3	0.00	1	0.10	—	—	—	—	—	—			

stock S. The difference between C- and Cc^h in males in experiments SK, SA alone is 2.29 ± .30. Using all males of genotype C-PPFF the difference is 1.60 ± .23 and in females .83 ± .18, highly significant in spite of the great reduction in grade in all females. Genotype Ff of initial grade 3 or 4 does not, on the other hand, differ significantly from FF after six months, either in males or females.

TABLE 19

Average grade after 6 months of age of animals of the indicated genotypes and of grade 3 or more initially. The group C-PPFF is divided into 3 classes according to source.

GENOTYPE	NO.	INITIAL GRADE	AFTER 6 MONTHS
♂ C-PPFF(S)	39	3.72	3.05 ± .14
♂ C-PPFF(SP)	12	3.58	2.85 ± .30
♂ C-PPFF(SK, SA)	13	3.77	3.87 ± .23
♂ CCPPff(SF)	13	3.54	3.11 ± .19
♂ Cc ^h PPFF(SK, SA)	25	3.44	1.58 ± .20
♀ C-PPFF(S)	46	3.70	1.57 ± .15
♀ C-PPFF(SP)	13	3.54	1.51 ± .30
♀ C-PPFF(SK, SA)	8	3.88	1.84 ± .51
♀ CCPPff(SF)	11	3.36	1.87 ± .31
♀ Cc ^h PPFF(SK, SA)	21	3.43	0.76 ± .13

The only evidence for an effect of *Ff* is in the unselected initial grades and here the undoubted presence of unfavorable residual heredity in many *Ff* and the likelihood that *Pp* is present in some of those called *C-P-FF* make comparisons unreliable.

Developmental Factors

To some extent at least dinginess tends to develop most in the regions of the body (head and back as opposed to belly) and of individual hairs (subterminal region) in which brown would otherwise be most intense. Apparently there is a certain optimum in the complex of factors of all sorts that control the intensity of brown. Either excess or defect in this complex results in less than maximum intensity. The actual amount of brown pigment in dingy hair has not yet, however, been investigated.

SUMMARY

Four types of silvering of the coat of the guinea pig are discussed.

There is a stationary type in which white or light colored hairs are mingled with those of the color determined by the rest of the genotype. It is usually restricted to the belly in lower grades but in higher grades appears also on the back. The head and legs are least affected. Silvering depends in the main on a single incompletely recessive autosomal gene (*si*) but varies continuously over a wide range because of minor factors, genetic and non-genetic.

There is a synthetic-type in which the tortoiseshell pattern of mingled dark and yellow hairs is reduced to a pattern, sometimes simulating the preceding, by action of genotypes which reduce yellow disproportionately. The genetics of this type is well known.

There is a progressive type of silvering or grizzling which appears only after the first pelage. White hairs appear first on the posterior back but become sprinkled later over the entire back, head, and belly, among hairs of the color determined by the rest of the genotype. This depends on an incompletely recessive autosomal gene (*gr*), in confirmation of LAMBERT.

There is a retrogressive type of silvering or dinginess which is manifested only in otherwise intense browns (*bb C P*). In the lowest grade there are scattered hairs on cheeks and nape in which there is subterminal banding with pale brown. In higher grades, such hairs are sprinkled over the whole head and back, and in the highest practically all hairs are affected. Dinginess is reduced with age, especially in females. At least four series of alleles are involved. One or more autosomal factors, again incompletely recessive, are necessary for any dinginess. If these are favorable, all known series of alleles, that affect intensity of brown in any combination, tend to modify dinginess, but in the opposite direction from that which would be expected from their ordinary effects. *CCPPF*- is necessary for the highest grade of dinginess. $Cc^x (= Cc^k, Cc^d, Cc^r \text{ or } Cc^a)$ reduces dinginess, at least in mature animals. No dinginess appears in combinations lacking $C(c^k c^k, \text{ etc.})$. *Pp* reduces dinginess more than does Cc^x and acts cumulatively with the latter. There is no dinginess in pale browns (*pp*). It is uncertain whether *Ff* affects dinginess, but *ff* reduces it considera-

bly. To some extent at least dinginess tends to appear most in the region of the body and of the hairs in which brown would otherwise be most intense.

The factors that affect dinginess give good illustrations of the principle that gene replacements that increase development of a character in certain combinations may reduce development in others.

LITERATURE CITED

- CASTLE, W. E., 1912 The inconstancy of unit characters. *Amer. Nat.* **46**: 352-362.
- CHASE, H. B., 1939 Studies on the tricolor pattern of the guinea pig. *Genetics* **24**: 610-643.
- EATON, O. N., 1943 Silvering in a strain of guinea pigs. *J. Hered.* **34**: 105-108.
- IBSEN, H. L., 1919 Tricolor inheritance. IV. The triple allelomorphous series in guinea pigs. *Genetics* **4**: 597-606.
- 1932 Modifying factors in guinea pigs. *Proc. 6th Int. Congress. Genetics* **2**: 97-101.
- ILJIN, N. A., 1928 The distribution and inheritance of white spots in guinea pigs (Russian). *Trans. Lab. Exp. Biol. Zoopark, Moscow* **4**: 255-349.
- LAMBERT, W. V., 1935 Silver guinea pigs. *J. Hered.* **26**: 279-283.
- PICTET, A. and A. FERRERO, 1940 Recherches sur l'hérédité de la dilution et du blanchiment du pelage dans le genre *Cavia*. *Genetica* **22**: 1-122.
- WRIGHT, S., 1915 The albino series of allelomorphs in guinea pigs. *Amer. Nat.* **49**: 140-148.
- 1917 Color inheritance in mammals. V. The guinea pig. *J. Hered.* **8**: 476-480.
- 1926 Effects of age of parents on characteristics of the guinea pig. *Amer. Nat.* **60**: 552-559.
- 1927 The effects in combination of the major color-factors of the guinea pig. *Genetics* **12**: 530-569.
- 1934 The results of crosses between inbred strains of guinea pigs, differing in number of digits. *Genetics* **19**: 537-551.
- 1941 Tests for linkage in the guinea pig. *Genetics* **26**: 650-669.
- 1942 The physiological genetics of coat color of the guinea pig. *Biol. Symp.* **6**: 337-355.
- WRIGHT, S., and H. B. CHASE, 1936 On the genetics of the spotted pattern of the guinea pig. *Genetics* **21**: 758-787.