MUTATIONAL MOSAIC COAT PATTERNS
OF THE GUINEA PIG

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INTRODUCTION

Most of the guinea pigs which one sees have a mosaic coat pattern of some sort. The piebalds have a pattern of colored spots on a white ground, the tortoiseshells have a pattern of dark spots on a yellow ground and the tricolors have both yellow and dark colored spots of some sort on a white ground. It has been suggested (EYSTER 1924) that these patterns may be due to somatic mutations of an unstable gene, such as has been demonstrated in variegated corn. There certainly appears to be something akin to mutation as far as cell lineages are concerned. On the other hand, the more or less orderly relationship to the parts of the body indicates that the pattern is determined primarily by developmental processes of the type responsible for ordinary regional differentiation. The genes for piebald (s) and tortoiseshell (e^p) are simple recessives, seemingly as stable as any other genes in the germ-plasm. THE BUREAU OF ANIMAL INDUSTRY has maintained a number of inbred strains of guinea pigs since 1906. One of these families (No. 34) was tortoiseshell (SSe^pe^p) throughout its history. All of the others have bred consistently tricolor (sse^pe^p) except that in one of them (No. 13) true breeding red-white piebalds $(ssee)$ segregated out in

one line near the beginning. Some 35,000 guinea pigs have been recorded in these lines and from crosses between them, but there is not the slightest evidence that the piebald factor has ever mutated to its dominant allelomorph (S) or that the tortoiseshell factor has mutated either to dominant true-breeding black (E) or to the recessive true breeding red (e). Black-white and red-white bicolors appear not infrequently but breeding tests have indicated that these differ genetically in no respect from their tricolor relatives, their behavior contrasting sharply with that of blacks (EE) and reds (ee) obtained from other sources. With this type of mosaic pattern we shall have little further concern in this paper.

There are five sets of allelomorphs in guinea pigs which normally produce a uniform change in color throughout the coat except that the degree of effect may show an entirely regular regional differentiation. Mosaics in the effects of these factors are extremely uncommon, but when they do occur they presumably indicate some sort of a mutational or chromosomal change in the region affected. The purpose of the present paper is to give an account of the seven possible cases of this sort which the writers have noticed among over 40,000 guinea pigs which they have recorded.

The record of every guinea pig born in the experiments includes a sketch of the pattern made in a rubber stamp outline, similar to the patterns shown in the figures. These drawings have been made for the most part by the junior author, who has been on the lookout for any irregularities of the kinds to be described. The senior author has gone over all of the animals born each week for the purpose of recording the intensities of the various colors. Other opportunities for observation occur at the time of weaning and at times when weights are taken. Doubtless a few inconspicuous cases have been overlooked, especially in animals born dead. We feel safe in saying, however, that such mosaics are extremely uncommon in guinea pigs.

THE COLOR FACTORS OF GUINEA PIGS

The color factors which are known to have been present in this stock are given below. The black-eyed golden agouti variety with all 7 dominant factors is taken as the type, as having the factorial composition of the wild Cavia cutleri in these respects. In this variety each hair is black with a "red" (*ochraceous tawny*) subterminal band. This band is wider and lighter in color on the belly, which thus has a yellow appearance.

S, s s = piebald (white areas). Incomplete dominance.
$E, e^p, e.$ e^p = tortoiseshell (red areas).
        e = self red

A, a^r, a a^r = narrow red ticking, ticked belly

            a = self black

$C, c^k, c^d, c^r, c^a,$ c^k = slight dilution of black, marked dilution of red

            c^d = marked dilution of both black and red

            c^r = slight dilution of black, red replaced by white, eyes red

            c^a = black reduced to sooty white, red replaced by white, eyes pink (albino)

In all cases, intensification of black, but slight fading of yellow on exposure to cold and with age. Incomplete dominance in compounds of lower members of this series.

$F, f.$ f = dilution of red only (except in presence of p), effect increasing markedly with age.

$B, b.$ b = brown in place of black; dark red eyes. No effect on red.

$P, p.$ p = pale sepia in place of black; pink eyes. No effect on red.

♂   8400
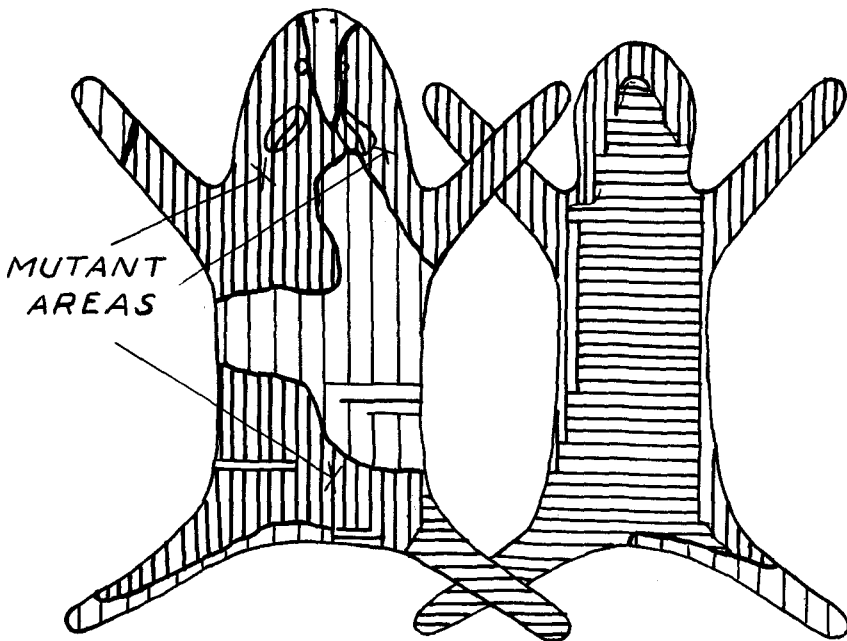
FIGURE 1.

The coat pattern of ♂8400. Vertical lines represent the agouti and horizontal lines the red or yellow of his tortoiseshell pattern. The heavily shaded portion represents the mutational intense portion (golden agouti and red) while the light shading represents the normal yellow agouti and yellow.

As already noted mutational mosaics could not easily be detected in piebalds (ss) or tortoiseshells ($e^p e^p$) because of their naturally mosaic patterns. The mosaics to be described apparently involved A in one case, the C series in one case certainly and possibly in two others, F in two cases

and P in one case. In only one case is there evidence that the germ-plasm was affected. We will describe this case first.

A SOMATIC AND GERMINAL MOSAIC $(Cc^d + c^d c^d)$

Male 8400 attracted attention at birth (December 23, 1918) through having a mosaic pattern of red agouti and yellow agouti. There were two separate red agouti regions as shown by the heavy bars in figure 1. One of these included the head about the eyes and ears, the shoulders and right fore leg. The other included both flanks and the right hind leg. Thus, the nose, left fore foot, a belt around the middle (extending forward on the right shoulder) and finally the left hind leg and left side of the rump were yellow agouti. The pattern was sufficiently striking at birth but became less easy to recognize later, largely, apparently, because of a relatively greater amount of fading of the red agouti parts. On brushing back the hair it may be seen that the black as well as the red is more intense in the red agouti areas. The differences are such as would be expected between an intense agouti (C-) and a dilute agouti $(c^d c^d)$[1]. Approximately 60 percent of the coat is red agouti dorsally. The entire belly appears yellow, but as there is little difference in intensity between "intense" and homozygous dilutes in this region, it is probable that the mutant patches extend over part of it.

This animal attracted special attention from the first because of the fact that both parents were dilutes and thus should not transmit the dominant intense coloration which he clearly showed. The sire (♂4849) was a self yellow of grade 8, believed to be $c^d c^d$ with $c^k c^d$ as a possibility. He was mated twice. His first mating was with a black-cream tortoiseshell necessarily $c^k c^r$ from her parentage. The progeny consisted of 3 with yellow in the fur $(c^k c^d)$ and one with cream $(c^d c^r)$. His second mating was with a dilute brown (♀6466) which later was proved by breeding tests to be $c^d c^r$. This mating produced 9 with yellow in the fur $(c^d c^d)$ and 4 with cream $(c^d c^r)$ in addition to the mosaic male (♂8400) showing both red and yellow which was thus assumed to be genetically $c^d c^d$. The color of the sire, together with his breeding record of 17 dilute young, from dilute females, omitting the intense dilute mosaic, agree in indicting that he was a homozygous dilute. His own sire, however, was an intense (agouti-red-white) necessarily Cc^d as coming from a cross between a yellow male $(c^d c^d)$ presented by Professor W. E. CASTLE and a golden agouti tricolor female of an inbred family (No. 39) which had always been CC. His dam was a cream that might have been either $c^d c^r$ or $c^k c^a$ as coming from a mat-

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[1] The colors of the different albino series compounds are described in detail elsewhere (Wright, 1925). The intensity of yellow is the best criterion. Using compound symbols, C– is typically red of grade 10 or 11, $c^{kd} c^{kd}$ yellow of grade 6 to 8, $c^{kd} c^{ra}$ cream of grade 4 or 5 and $c^{ra} c^{ra}$ pure white.

ing between a cream, $c^d c^a$, presented by Professor CASTLE and a black-cream $c^k c^r$. from a mating between a red-eyed brown ($c^r c^r$) presented by Professor CASTLE and a black-yellow from an inbred family (No. 18) homozygous $c^k c^k$ in the branch concerned. The brothers and sisters of ♂4849 were 3 with red (C-), 1 with yellow ($c^{kd} c^d$) and 3 with cream ($c^d c^{ra}$) in harmony with the formula assigned his parents.

The possibility that ♂4849 may have transmitted C from his father must of course be borne in mind, but the assignment of formula Cc^d to him raises difficulties in accounting for his own color and his failure to sire any unequivocal intense among 18 young, without assisting much in accounting for his mosaic son.

Going back to the dam of the mosaic, ♀6466 was a brown, a color in which the effects of the C series are not easily distinguished. She was mated three times, however, with results that make it certain that she was $c^d c^r$. Her first mating was with ♂4849, in which, as above noted, she produced 9 young with yellow ($c^d c^d$), 4 with cream ($c^d c^r$) in addition to the mosaic. Her second mating was with an albino male ($c^a c^a$) made especially as a test. She produced two sepia-cream young clearly $c^d c^a$ from their color, 2 sepias proved to be $c^d c^a$ by breeding tests, and 2 red-eyed sepias, clearly $c^r c^a$ from coat and eye color. Her third mating was with a red-eyed dark sepia ($c^r c^r$). She produced 9 black-eyed dilutes ($c^d c^r$) and 9 of the appearance of homozygous red-eyed dilutes ($c^r c^r$). She thus had 38 graded young to 23 of which including the mosaic she supplied c^d and to 15 of which she supplied c^r. It is perhaps worthy of record that she produced her 16th litter at the advanced age of five years and one month. She died a month later. Like ♂4849, she had an intense parent but in view of her extensive breeding record in which it was proved conclusively that she transmitted both c^d and c^r, the possibility that she transmitted C seems negligible. The formulae of the ancestors of the mosaic are shown below:

$$
\text{♂8400 (Red-yellow) agouti} \ (Cc^d + c^d c^d)
\begin{cases}
\text{♂4849 Yellow} \\ c^{kd} c^d
\begin{cases}
Cc^d
\begin{cases}
c^d c^d \\
CC
\end{cases} \\
c^d c^r \text{ or } c^k c^a
\begin{cases}
c^d c^a \\
c^k c^r
\begin{cases}
c^r c^r \\
c^k c^k
\end{cases}
\end{cases}
\end{cases} \\[2em]
\text{♀6466 Dilute Brown} \\ c^d c^r
\begin{cases}
c^d c^r
\begin{cases}
c^d c^d \\
c^r c^r
\end{cases} \\
Cc^d
\begin{cases}
CC \\
c^d c^a
\end{cases}
\end{cases}
\end{cases}
$$

Before leaving the ancestry, it may be well to state that a careful investigation was made at once to determine the possibility that the parentage of the mosaic had been incorrectly assigned. He was born in his parents' second litter, with two litter mates, a sepia-yellow ($c^d c^d$) and a sepia-cream ($c^d c^r$). There was no evidence that any intense guinea pigs had been in the pen in which he was found except his reputed parents for seven months. Female 6466 undoubtedly had a litter at this time. Breeding tests showed that the mosaic transmitted e and b, factors necessarily transmitted by ♂4849 (ee) and ♀6466 (bb) but which could have come from only a small number of other animals in the stock, descended from a few animals presented by Professor CASTLE. It happened that all but one of these other matings produced a litter within two months before or two months after. The one exception had been sterile for a year and could have produced the mosaic only through a double mutation. There is thus exceptionally complete evidence in this case that there was no mistake in parentage.

The genetic constitution of the mosaic was tested by matings with albinos ($c^a c^a$) red-eyed dilutes ($c^r c^a$) and one dark-eyed sepia ($c^d c^a$). The matings with albinos and red eyes were desirable since the distinction between the red of Cc^{ra} and the cream of $c^d c^{ra}$ is more striking than that between the red of Cc^d and the yellow of $c^d c^d$. In order to obtain as many young as possible he was moved in a ten-week cycle through three pens, in each of which there were usually two or three females.

The litters are shown in table 1 in chronological order. The first litter contained a golden agouti (intense) in addition to a cream agouti, thus proving that he transmitted intensity. The next litter confirmed this conclusion. Altogether, he produced 79 intense young and 149 dilutes. The expectation on the basis of his parentage and the appearance of the lighter areas in his coat was 100 percent dilutes. If, however, he were a heterozygous intense (Cc^d) the expectation would be 114 intense to 114 dilutes. The actual result is, of course, wholly out of harmony with the first hypothesis and deviates from the second by 35 ± 5.0, or seven times the probable error. The chance of obtaining such a deviation in this direction is about 1 in a million. Extensive experiments with the albino series have given no other significant departures from the expected ratios. Thus it seems safe to conclude that ♂ 8400 did not breed like a normal Cc^d. The obvious suggestion is that he was a mosaic germinally as well as somatically. If his germinal epithelium were 70 percent Cc^d and 30 percent $c^d c^d$, the observed ratio would be obtained. The dilute progeny and

TABLE 1

The breeding record of ♂8400. All of the females with which he was mated were as indicated albinos ($c^a c^a$) or red eyed dilutes ($c^r c^a$) with one exception, No. 8084, a dark eyed dilute ($c^d c^a$).

DATE OF BIRTH	No.	DAM formula	INTENSE	DILUTE	DATE OF BIRTH	No.	DAM formula	INTENSE	DILUTE
1919 Sept. 2	215	$c^a c^a$	1	1	1921 Sept. 20	7928	$c^a c^a$	1	2
Nov. 5	215	$c^a c^a$	1	1	Oct. 14	7533	$c^a c^a$	3	1
Nov. 30	8084	$c^d c^a$	2	2	Oct. 19	752	$c^r c^a$	1	2
Dec. 17	752	$c^r c^a$	1	1	Nov. 1	1317	$c^r c^a$	1	2
Dec. 29	9154	$c^r c^a$		1	Nov. 25	8203	$c^a c^a$	1	4
1920 Jan. 23	1317	$c^r c^a$		2	1922 Feb. 8	7928	$c^a c^a$	1	2
Jan. 28	8203	$c^a c^a$	1	3	Feb. 26	752	$c^r c^a$		2
Feb. 23	752	$c^r c^a$		1	Mar. 5	7533	$c^a c^a$		3
Mar. 9	215	$c^a c^a$	1	1	Mar. 31	1305	$c^a c^a$	2	2
Mar. 31	1317	$c^r c^a$	1	1	May 20	752	$c^r c^a$		2
Apr. 9	8084	$c^d c^a$	1	3	Sept. 5	7928	$c^a c^a$	1	1
Apr. 29	752	$c^r c^a$		3	Sept. 26	8203	$c^a c^a$		1
May 29	215	$c^a c^a$	1	2	Sept. 27	752	$c^r c^a$	2	2
June 9	8203	$c^a c^a$	1	3	Oct. 10	14963	$c^a c^a$		1
July 3	9154	$c^r c^a$		1	Nov. 15	7045	$c^a c^a$	1	1
July 6	752	$c^r c^a$		3	Nov. 22	14789	$c^a c^a$		2
Aug. 4	1317	$c^r c^a$	1	2	Dec. 14	7928	$c^a c^a$		3
Aug. 7	215	$c^a c^a$		1	1923 Jan. 7	752	$c^r c^a$	1	2
Sept. 4	4496	$c^r c^a$		1	Jan. 8	14963	$c^a c^a$		1
Sept. 9	4497	$c^r c^a$		1	Feb. 14	14962	$c^a c^a$	1	1
Sept. 10	752	$c^r c^a$		2	Feb. 20	7928	$c^a c^a$	1	1
Sept. 10	9154	$c^r c^a$		2	Mar. 14	752	$c^r c^a$ ⎫	1	3
Oct. 18	2	$c^r c^a$	2	2	Mar. 14	14963	$c^a c^a$ ⎭		
Oct. 30	8203	$c^a c^a$	1	3	Mar. 20	16355	$c^a c^a$		2
Nov. 14	4497	$c^r c^a$	3	1	Apr. 7	7045	$c^a c^a$	2	1
Nov. 18	752	$c^r c^a$		1	May 19	14963	$c^a c^a$	1	2
Dec. 6	215	$c^a c^a$	1		May 26	16355	$c^a c^a$	1	1
Dec. 15	1317	$c^r c^a$	1	1	July 4	14962	$c^a c^a$		2
Dec. 24	2	$c^r c^a$	1	4	July 9	7928	$c^a c^a$		2
Dec. 26	4496	$c^r c^a$	2	1	Aug. 1	16355	$c^a c^a$	2	1
1921 Jan. 23	752	$c^r c^a$	1	1	Aug. 13	17608	$c^a c^a$	1	2
Mar. 27	7523	$c^a c^a$	1	1	Aug. 25	7045	$c^a c^a$	1	4
Mar. 28	4497	$c^r c^a$	1	2	Sept. 11	7928	$c^a c^a$	3	2
Apr. 1	752	$c^r c^a$	1	2	Sept. 20	14963	$c^a c^a$		3
Apr. 20	1317	$c^r c^a$	2	1	Oct. 1	752	$c^r c^a$	1*	
Apr. 23	215	$c^a c^a$	1	1	Oct. 5	16355	$c^a c^a$	1	2
May 7	7970	$c^a c^a$		2	Nov. 26	14962	$c^a c^a$		3
May 8	7928	$c^a c^a$		3	Dec. 9	752	$c^r c^a$ ⎫	5	1
May 13	8203	$c^a c^a$		1	Dec. 9	14963	$c^a c^a$ ⎭		
June 7	752	$c^r c^a$		2	Dec. 12	16355	$c^a c^a$	1	3
July 5	1317	$c^r c^a$		1	1924 Jan. 18	17608	$c^a c^a$	1	2
July 13	7928	$c^a c^a$	5	1					
Aug. 5	7533	$c^a c^a$	1	3	Total			79	149
Aug. 13	752	$c^r c^a$	2	2					
Sept. 17	8203	$c^a c^a$	3	1					

*A "black-white" born dead is not included, as it might have been either Cc^{ra} or $c^d c^r$.

their descendants showed grades of sepia which indicated that the dilution factor which he transmitted was always c^d rather than c^k.

There is some indication that he did not produce the same ratio of intense to dilute at all times. Up to the end of 1919, his record was 5 intense to 6 dilute, giving no indication that he was breeding differently from Cc^d. During the next nine months, however, he produced only 7 intense to 32 dilute. The total results, summarized to this point, deviated from equality by 5.4 times the probable error and were presented by the senior author at the meeting of the American Society of Naturalists in 1920 as fairly conclusive evidence of an aberrant ratio. There followed, however, a period of thirteen months in which his record 34 intense to 42 dilute showed a much less impressive departure from equality. Indeed, in one four-month period, July to October, 1921, an excess of intense (16:13) was produced. During the next seventeen months there was again a marked deficiency of intense: 13 intense to 38 dilute. The final ten months with 20 intense to 31 dilute, seemed to show another shift toward equality. These variations in ratio can only be taken as suggestive, however, since on comparing with the expected figures on the basis of a constant proportion (34.7 percent) of intense, we obtain a value of P of .125 for the χ^2 test. Thus irregularities as great as those observed would be expected to occur one time in eight purely by chance. Another test can be obtained by comparing the record of 34 intense to 42 dilute produced in 13 months with the entire remaining record. The result is a contrast of 44.7 ± 3.8, with 29.6 ± 2.5 percent, a difference of 15.1 ± 4.6, about 3.3 times the probable error which might be expected to occur about 1 time in 35 by chance. Neither of these tests is quite fair in that they involve a selection of the periods for comparison. Nevertheless, there is a distinct suggestion that the proportion of germ cells carrying intense and dilute varied from time to time. This could be explained on the hypothesis that the germinal epithelium was mosaic and that the relative activity of different portions varied. A belated attempt of an experimental test of this point was made by removing the left testis (October 18, 1923). Only one litter was sired following the operation. This litter included 1 intense to 2 dilute, proving that both C and c^d were transmitted by the germinal epithelium of the right testis. Male 8400 died, (December 30 1925) at the rather advanced age of seven years, but produced no young since the litter referred to above, although mated with eight females for much of the time.

A number of his progeny have been tested by mating with albinos or red eyes, or with each other. There is nothing unusual in their records. Six intense young mated with albinos or red eyes have produced 46 intense

to 59 albinos or red eyes, a ratio which does not depart significantly from equality. Two matings between intense young have produced a total of 24 intense to 8 albinos, exact expectation. One homozygous dilute son, from the one mating in which ♂8400 was paired with a dilute, has produced 9 typical dilute young in a mating with an albino. Two heterozygous dilute sons mated with albinos have produced 8 dilute to 5 albinos where equality is the expectation. A mating between two dilutes produced two dilutes. The intense grandchildren of ♂8400 appear to be exactly like ordinary intense animals.
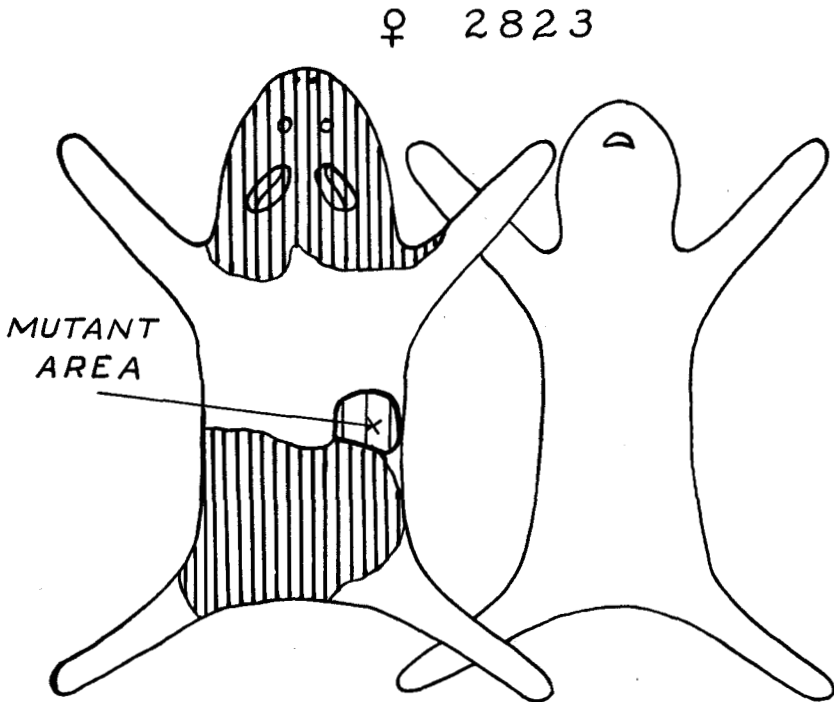
FIGURE 2.

The dorsal coat pattern of ♀ 2823. The heavy vertical lines represent black and the light vertical lines sepia. There was a red spot and another sepia spot on the belly, not shown in the early record. The mutational significance of the sepia spots is very doubtful.

The simplest explanation of this case is that ♂8400 was initially $c^d c^d$ but that a mutation to the dominant allelomorph C occurred in a cell which was ancestral both to part of the soma and part of the germinal epithelium.

It must be confessed, however, that it is difficult to entirely dismiss the thought that one of the intense grandparents somehow transmitted his

intensity through the apparently dilute sire or dam. The writers, however, have been unable to devise any explanation along this line which does not raise more difficulties than it solves.

TWO INTENSE-DILUTE MOSAICS

Two intense dilute mosaics may be noted very briefly. One of these (♀2823) was born in one of the inbred families (No. 38) homozygous in
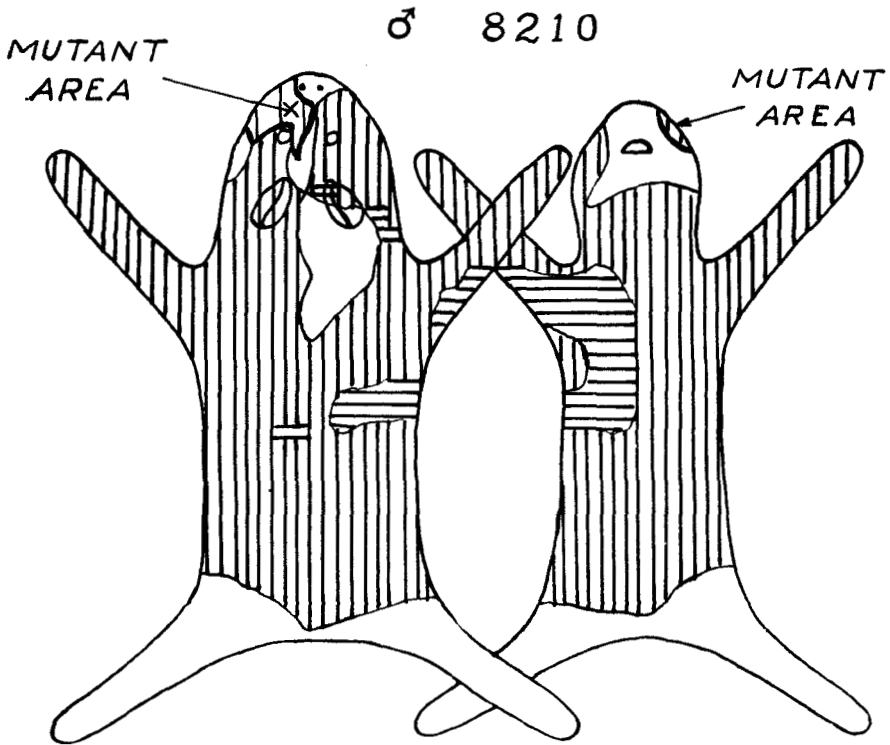
FIGURE 3.

The coat pattern of ♂ 8210 showing black (heavy vertical lines), sepia (light vertical lines) and red (horizontal lines). The mutational significance of the sepia spot is very doubtful.

all color factors. This guinea pig had four sharply distinct colors in the coat, black, sepia, red and white (figure 2). Incidentally, she had the peculiarity of lacking both eyeballs, a trait which appeared sporadically in family 38. Her 11 progeny were all blacks without any of the abnormal sepia color. A grandson, however, ♂8210, born December 3, 1918, was somewhat like her in his quadri-colored coat. He had a sepia patch on his nose contrasting sharply with the surrounding black as well as with his

red spots (figure 3). He came from a mating which brought together four different inbred families (13, 39, 34 and 38) from all of which he could have received only the intensity factor C in the albino series, except for a possibility of receiving albinism, c^a, from family 13. There was no evidence from the numerous progeny of his grandparents and parents or from his own progeny, which included 3 normal blacks from a mating with his dam, and 4 normal blacks from a mating with his sister, that he received or transmitted anything but C in the albino series, or that other factors pro-
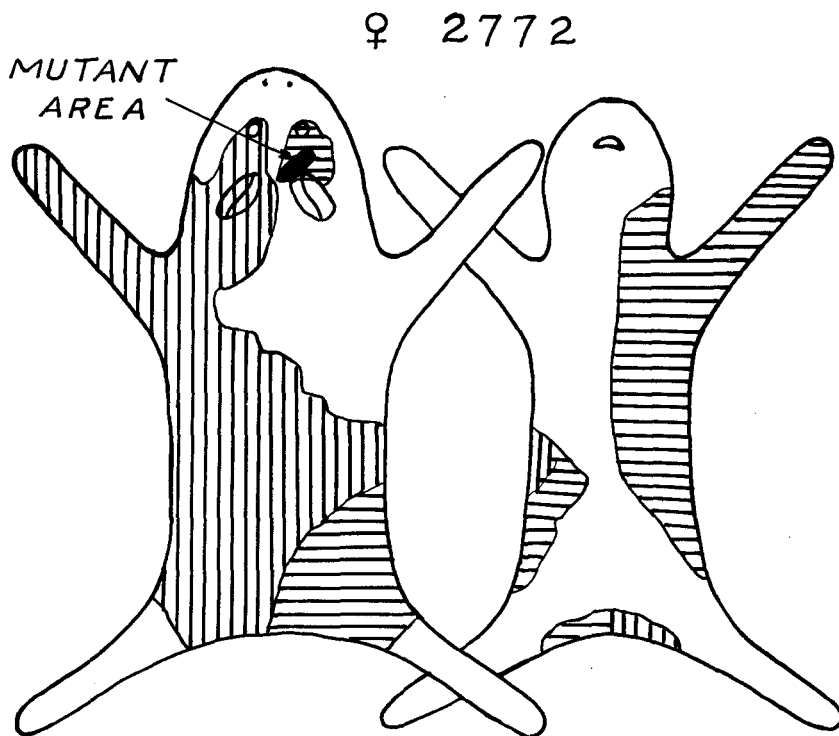
FIGURE 4.

The coat pattern of ♀ 2772 showing golden agouti (vertical lines), black (solid) and red (horizontal lines).

ducing dilution of black were present. A possible explanation is that the sepia spots represented modified brindled spots. Tortoiseshells usually show not only clear-cut black and red areas but brindled areas in which black and red hairs are intermingled. In these areas the black is usually much reduced in intensity. A spot composed exclusively of such hairs, that is, dilute black unassociated with red hairs, would have much the appearance of the observed spots on ♀ 2823 and ♂ 8210. If this is the

explanation, the mosaic pattern has no mutational significance, being simply a spot due to factor e^p, in which both animals were homozygous. It could be assumed that a peculiar combination of modifying factors gave these spots their unusual appearance.

AN AGOUTI-BLACK MOSAIC $(AA+aa)$

We will next consider the case of an agouti-black-red-white quadricolor, ♀2772, born November 24, 1919, in stock B, the control stock for
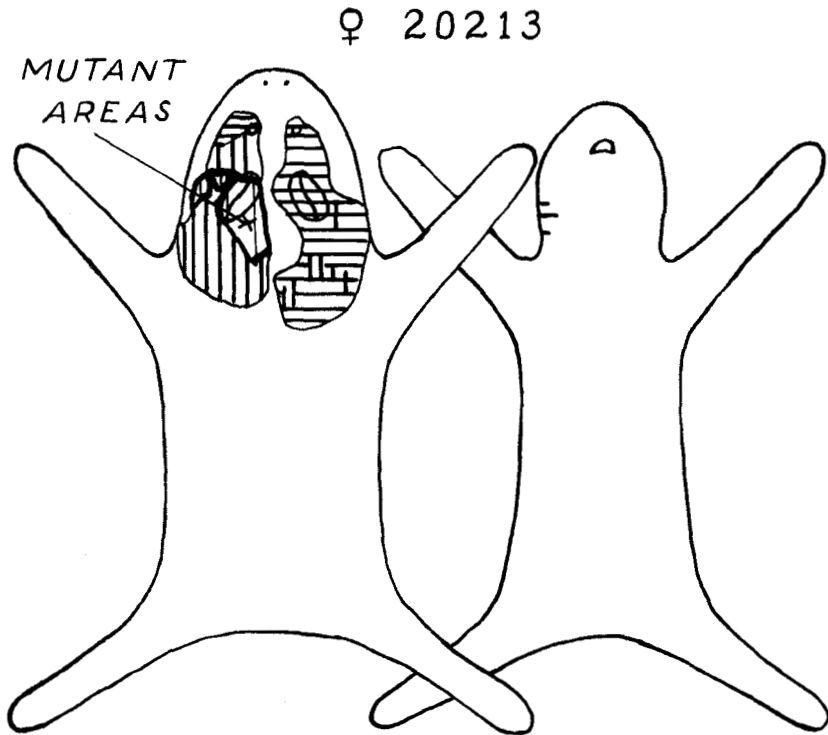

FIGURE 5.

The coat pattern of ♀ 20213 showing golden agouti (heavy vertical lines), cream agouti (light vertical lines) and red (horizontal lines).

the inbred families. This female had a clear-cut black spot in the fur in front of her right ear, surrounded by red (figure 4). She is the only agouti guinea pig on which the writers have ever noticed as much as a solid black hair. Her parents, grandparents and great-grandparents were all agoutis, except for one red-white bicolored great-grandparent, probably an agouti genetically. Three out of the 16 great-great-grandparents, however, were black. ♀2772 was one of fourteen agoutis produced by her parents. She

herself produced only 14 agoutis in a mating with a black male. Two of her daughters were mated with black males and produced 23 agoutis to 25 blacks, in addition to red-whites and albinos in which the agouti factor can produce no visible effect.

The ancestry and breeding record of ♀2772 make it reasonably certain that she was a homozygous agouti (AA) genetically. If the black spot was due to the ordinary recessive black factor (a) both genes must have mutated or been lost. The possibility remains, of course, that a mutation to an unknown dominant black occurred in some other locus.

TWO INTENSE-DILUTE MOSAICS $(Ff+ff)$

The next case is that of a golden agouti tricolor, ♀20213, born in the control stock B, September 4, 1923. In this case a much broken yellow agouti spot was noted on the left side of the head (figure 5). This spot changed later to a very pale cream agouti, markedly in contrast with the surrounding golden agouti. The black base of these cream agouti hairs was of full intensity however. These effects all indicated the kind of dilution due to factor f rather than the dilution of the albino series.

The sire was an albino, whose sire came from mating B211 which (with its parent matings) is the only known source of factor f. The paternal great-granddam of ♀20313, curiously enough, was ♀2772, the agouti-black mosaic discussed above. The dam of ♀20213 was a red-white from golden-agouti tricolor parents and grandparents. The parents produced 23 golden-agouti tricolors, 7 black-red-white, 2 red-white in addition to the mosaic. This result indicates that the dam was CCFF, the sire being probably $c^a c^a Ff$.

Female 20213 was herself tested by mating with a black-yellow-white male, known to be $Cc^a ff$ from his parentage. She produced 2 golden agoutis. 2 yellow agoutis, 2 black-yellows and 2 albinos. The yellow-agoutis and black-yellows were clearly of the kind due to factor f and not to c^k or c^d. It was thus clear that ♀20213 was of constitution $Cc^a Ff$. The mutant spot can be explained as due either to a mutation from F to f in the ancestral cell, or to loss of the whole chromosome carrying F.

The case of ♂23538 is very similar to that just described. This animal, born April 20, 1924, in the control stock B, was originally called a golden-agouti tricolor. When three months old a conspicuous cream-agouti spot was observed on the left side (figure 6). As in the previous case, the appearance suggested factor f. Guinea pigs of formula ff typically show yellow of grades 6 to 8 at birth, but in a few cases there has been very little

dilution (grade 9) at this time. This probably accounts for the failure to note the spot earlier. Whatever the color at birth, there always seems to be a fading to pale cream, if not to white, later in life.

ᵢ The parents were both golden-agouti tricolors. They produced 19 golden agoutis (including ♂23538) and 5 yellow agoutis, proving that both carried a dilution factor. The dam was a granddaughter of an ff dilute from mating B211, previously spoken of as the source of this factor. The
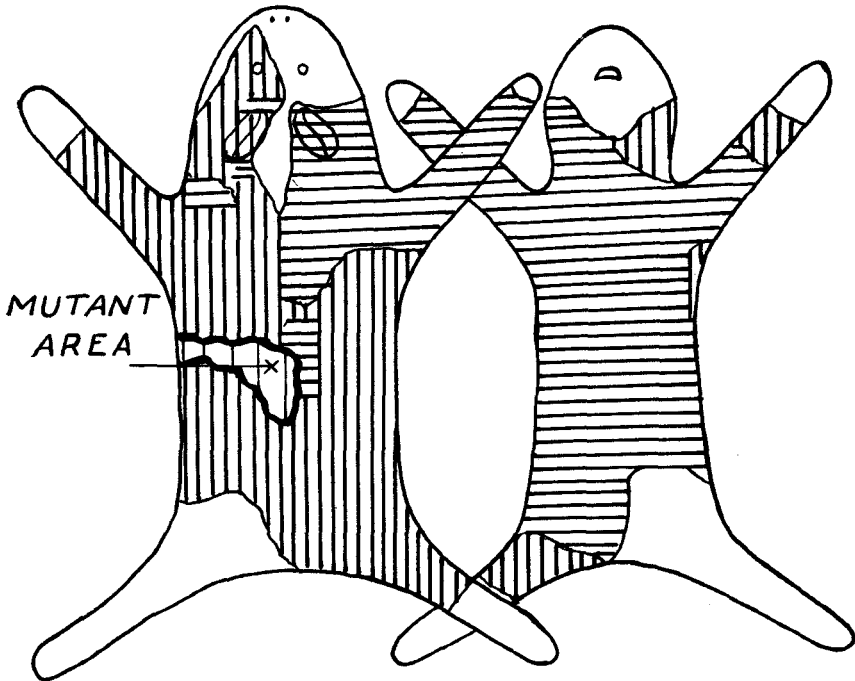
FIGURE 6.
The coat pattern of ♂ 23538, showing golden agouti (heavy vertical lines), cream agouti (light vertical lines) and red (horizontal lines).

sire traced through three generations to the mating which produced the female in B211 and which must thus have transmitted factor f. Dilution of the albino series (c^k) was also present on the sire's side, but seems to have been absent from the dam's pedigree. The sire was probably Cc^kFf, the dam $CCFf$. Male 23538 so far has produced 4 intense young from a mating with a black-yellow (ff) 4 intense from a meeting with an albino (c^ac^aFF) aside from four intense from a mating with an intense female. In all probability, he is Ff although the breeding test has not yet proved it.

The appearance of the cream-agouti spot suggests, as in the preceding case, that either F mutated to f or that the whole chromosome which carries it, was lost in the ancestral cell.

AN INTENSE BROWN-PALE BROWN MOSAIC $(Pp+pp)$

The last case is that of ♀ 25593, born September 5, 1924. She shows four colors, a typical intense brown and a sharply contrasting pale brown ex-
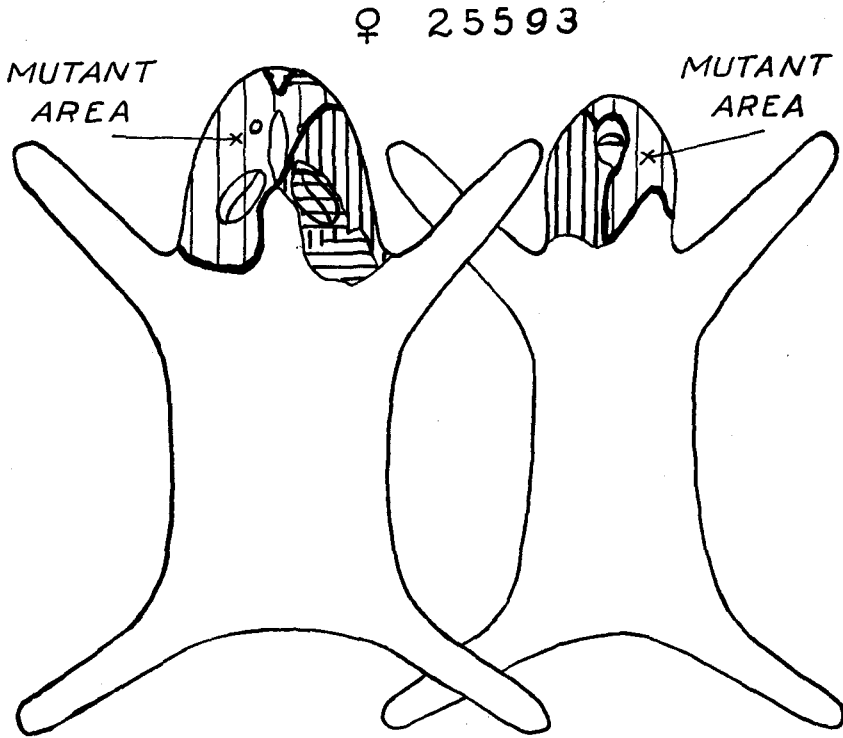

FIGURE 7.

The coat pattern of ♀ 25593 showing intense brown (heavy vertical lines), very pale brown (light vertical lines) and red (horizontal lines).

actly like that due to the pink eye factor p, in addition to the red and white of a tricolor (figure 7). The pale brown covers most of the head and left shoulder. An intense brown spot begins back of the right eye. Although the left eye is entirely surrounded by a pale brown fur and the right eye is more than half surrounded by it, the eyes are both of an intense brown, giving the head a very peculiar appearance to one familiar with guinea pig colors. The retina of the eye has, of course, such a different lineage,

ontogenetically, from the skin of the head that the lack of agreement requires no explanation except that required for the mosaic pattern as a whole.

This mosaic came from a back-cross involving six color factors, $SsEe^{\textit{p}}AaCc^kBbPp \times sse^{\textit{p}}e_{\textit{p}}aac^kc^rbbpp$. The appearance of ♀25593 indicates the constitution $sse^{\textit{p}}e^{\textit{p}}aa\ Cc^{kr}bb\ (Pp+pp)$. The pale brown spots can be explained as due either to a mutation from P to p or to loss of the chromosome carrying P. In a mating with a pink-eyed dilute brown tricolor $(sse^{\textit{p}}e^{\textit{p}}aac^kc^kbbpp)$ she has produced 6 brown-eyed young and 2 pink-eyed young, demonstrating that she transmits factor P.

<div align="center">DISCUSSION</div>

Bud mutations and many cases of variegation have been reported in plants in which the abnormal parts have been shown to transmit a corresponding mutant character. These results indicate that mutation may take place at any time in the life history. In animals, we naturally look to Drosophila for the most extensive data. Here also many somatic mutations have been found (BRIDGES 1919; MULLER 1920). BRIDGES finds, however, that most mutations occur as single individuals which he interprets as meaning that mutation is most likely to occur at or very near maturation. He reports a few cases in which a fly has produced a number of mutant offspring, indicating that mutation relatively early in the germ tract had caused the individual to be germinal mosaic. He also reports mutants which appear as somatic mosaics due, presumably, to mutation subsequent to cleavage in a cell ancestral to the germ tract and part of the soma. MULLER (1920) reports similar cases as well as a case of a purely somatic mosaic. MOHR (1923) and MORGAN, BRIDGES and STURTEVANT (1925) report cases in which both soma and germ-plasm were mosaic, as in the mutant guinea pig No. 8400 reported here. MULLER points out that even if mutation is equally likely to occur at all stages of development, most mutations will actually be observed as single individuals, thus taking issue with BRIDGES' interpretation. Gynandromorphs in Drosophila are somatic mosaics which seem ordinarily to be due to dropping out of one of the X chromosomes in cells subsequent to cleavage (MORGAN and BRIDGES 1919). BREITENBECHER has reported numerous dominant purely somatic mutations in the cowpea weevil, Bruchus.

In vertebrates, relatively few such cases have been reported where there was any knowledge of the genetic situation. Three cases described by CASTLE and by CASTLE and PHILLIPS may be mentioned. One of these (CASTLE 1912) concerned a guinea pig which was close to an albino in

appearance but had small areas of sepia on the right side of the head, the hips and dark streaks in the iris of each eye. The parents were both colored but one at least was known to transmit albinism. CASTLE (1922) interprets the case as probably a heterozygote, $c^d c^a$, in which factor c^d was lost from a cell at a very early stage by non-disjunction. He explains similarly a tricolor rat, gray, yellow and white, known to be heterozygous for pink-eyed yellow (Pp). This rat had many separate yellow spots. Breeding tests carried to F_2 gave no indication that he transmitted any new factors. The third case occurred in CASTLE and PHILLIPS' experiments on changing the hooded pattern of rats by selection. In the tenth generation of plus selection an ordinary "plus" rat sired two mutants from different females and presumably many normal plus young. These mutants, intermediate between the plus hooded stock and self color, proved to be heterozygous for a new third allelomorph of the hooding factor, dominant over the latter but recessive to self color. This dominant mutation occurred apparently in at least two germ cells of the sire who was thus a germinal mosaic.

Returning to the guinea pigs described in the present paper no one explanation seems to fit the 7 mosaics discussed above. In the last three cases the mutant animals were certainly or very probably heterozygous in the factor affected (Ff two cases, Pp one case). The loss of the chromosome carrying the dominant factor in one of the somatic divisions seems to be the most plausible explanation, with mutation to the recessive as a possible alternative. The case of the black spot on a homozygous agouti (AA) requires the loss of two chromosomes (not necessarily simultaneously) or a double mutation or a mutation to an unknown dominant black. The two black-sepia mosaics were similarly homozygous in all known factors affecting intensity of color, but the possibility that the sepia was merely an aberrant effect of the tortoiseshell factor e^p, in which they were homozygous, makes them of little value.

The case of ♂8400 is the most remarkable one observed. His record may be summarized as follows:

(1) He was a dilute-intense mosaic somatically.

(2) He was produced by extensively tested dilute (recessive) parents each of which, however, had one intense parent.

(3) He transmitted the dominant mutant factor for intensity.

(4) He was a mosaic germinally. His germ cells were about one-third C, two-thirds c^d as indicated by a ratio of 79:149 in backcrosses.

(5) The proportion of C gametes seems to have varied from time to time.

(6) Both intense and dilute progeny bred normally.

These results can all be explained by the hypothesis that he was $c^d c^d$ initially but that one c^d mutated to C in a cell ancestral to part of the soma and also to part of the germinal epithelium and that the activity of different parts of the latter varied from time to time. The possibility of a rather complicated explanation involving aberrant chromosome behavior is not perhaps entirely ruled out.

The appearance of these mosaics throws some light on a number of questions. Factors which affect coat color may be conceived either as producing their effects by local action or by means of substances carried in the blood. The differently colored spots of a tricolor are quite obviously determined locally. Even here, however, it is not necessary to suppose that the piebald and tortoiseshell factors act locally. Sex is a factor which modifies the extent of colored spots in piebalds and of black spots in tortoiseshells but which need not be thought of as acting locally. The relatively uniform color differences due to factors a, c^d, f, b, and p, it would seem, might well be constitutional rather than local. Nevertheless, the cases of persistent somatic mosaics, in all probability due to mutation or loss of certain of these factors in particular somatic cells, indicate that the effects are produced locally or, in other words, that the pigment produced by a particular cell depends, in the main, on the genes in its own nucleus. The evidence is reasonably satisfactory for factors c^a, f and p, less so for a. No case apparently involving b has yet been found.

Another point of interest is the shape of the mutant spots. If each is due to a single mutation or chromosome loss, it appears that a single cell may give rise to rather widely scattered descendants. This seems to have been the case with CASTLE's tricolor rat mosaic. The mutant areas of ♂8400 are widely scattered, as may be seen from the figure. The wide separation of the head and shoulder spots of red-agouti on ♂8400 from the rump spot is especially important in view of the completeness of this record, including evidence that his germinal epithelium was also mosaic.

The cream-agouti spots in ♀20213 and ♂23538 are very irregular in shape. In ♀20213 the cream-agouti is all on the left side of the head, but is broken into at least three portions, separated by red-agouti. In ♂ 23538, the spot runs irregularly from the mid-dorsal line to the belly down the middle of the side. In both of these cases, the shape is more irregular than is characteristic of either the colored or white spots of a piebald. Similar spots could perhaps be found on a tortoiseshell. The pale brown area of ♀25593 is compact enough except that it is cut by the white nose streak. The genetic condition of the mutant area doubtless is present

in this streak. Similarly, ♀2823 had two separate sepia spots but as these were separated merely by white, there is not necessarily any genetic discontinuity. Male 8210 and ♀2772 each had merely one compact mutant area.

Another curious fact is the relationship between certain of the mutants. Female 2823 (black-sepia) was the granddam of ♂8210, also black-sepia. Female 2772 agouti-black ($AA + aa$?) was the great-granddam of ♀20213 (red-cream-agouti) ($Ff + ff$) agouti and ♂23538 ($Ff + ff$) was related fairly closely to both of these. The case of the two black-sepias may, as noted in the text, involve merely inheritance of certain peculiar modifiers and not belong in the class of mosaics discussed here. The other cases may indicate an hereditary tendency toward germinal instability. LITTLE (1916) notes as possibly due to such a cause the occurrence of mutation from wild gray to brown-agouti (B to b) and from ordinary wild gray to white-bellied gray (A to A^1) in the descendants of a certain wild-gray mouse. The relationships here noted are rather closer than would be expected by chance in the large stock of guinea pigs of many distinct strains maintained by the BUREAU of ANIMAL INDUSTRY.

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