

THE FACTORS OF THE ALBINO SERIES OF GUINEA-PIGS AND THEIR EFFECTS ON BLACK AND YELLOW PIGMENTATION

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INTRODUCTION

Genetic studies on various animals have shown that albinism is the extreme in a series of grades of dilution of color and that it is independent, genetically, of white spotting, the "partial" albinism of many authors. Albinism and its allelomorphs affect the intensity of all kinds of melanin pigmentation,—black, yellow, brown, etc., and affect all parts of the body in which such pigment occurs, but most conspicuously the skin, fur and eyes. They have no effect on the localization of the different kinds of pigment. The highest allelomorph in guinea-pigs, for example, is found alike in golden agoutis, blacks, reds and black-red tortoise-shells, which are all "intense" varieties, while a lower allelomorph is found, alike, in yellow agoutis, sepias, yellows, and sepia-yellow tortoise-shells, which are all "dilute" varieties.

The general nature of the effects suggests that the albino series has to do simply with the rate of some process which is essential to all melanin pigmentation. On this hypothesis, one might expect to be able to arrange the compounds in a certain order of intensity of color. This, however,

turns out not to be possible. In a description of four allelomorphs in this series in guinea-pigs (WRIGHT 1916) it was shown that a compound with a more intense yellow than another might have a less intense black. The intensities of black, of yellow and of eye color in the various compounds were described as in table 1.

TABLE 1

COMPOUND	YELLOW FUR	BLACK FUR	EYE COLOR
$C-$	Red	Black	Black
$c^d c^d$	Yellow	Dark sepia	Black
$c^d c^r$	Cream	Dark sepia	Black
$c^d c^a$	Cream	Light sepia	Black
$c^r c^r$	White	Dark sepia	Red
$c^r c^a$	White	Light sepia	Red
$c^a c^a$	White	White	Pink

The homozygous red-eyed dilutes, $c^r c^r$, were found to lack the power to produce yellow, the parts of the fur which would otherwise be yellow being white, yet they were much blacker in the black parts of the fur than the black-eyed dilutes carrying albinism ($c^d c^a$) which nevertheless had the power to produce a pale yellow or "cream."

It was recognized that this result could be interpreted as meaning that the factors of the albino series act independently on eye color, black in the fur, and yellow in the fur, or indeed, that the so-called allelomorphs are merely combinations of very closely linked factors with no necessary similarity in physiological effect. The writer preferred the view, however, that the factors of the albino series have a single effect on pigmentation and that the irregularities in the order of effect in different cases are due to secondary processes in the physiology of pigment production. It was suggested first that the threshold for yellow is higher than that for black; second, that above the threshold for yellow its process of production interferes with the production of black even in black parts of the coat; and finally, that conditions relative to the threshold of yellow are different in eye and skin.

Since this paper was written, a fifth allelomorph of the albino series has been found in guinea-pigs (WRIGHT 1923). A fourth (chinchilla) has been added in rabbits to the long-known series, intense, Himalayan and albino (CASTLE 1921), and multiple allelomorphs of albinism have been found in rats (WHITING and KING 1918) and in mice (DETLEFSEN 1921, FELDMAN 1922).

The purpose of the present paper is to present more fully than before the evidence on the allelomorphism of the five factors in the guinea-pig together with a study of the average intensity of black and yellow in each of the fifteen compounds now known.

MATERIAL

Three albino-series allelomorphs have been found in the stock of guinea-pigs maintained by the Bureau of Animal Industry. These are the "intensity" factor, C , the new "dark-dilution" factor, c^k , and albinism, c^a . A few animals with "light dilution," c^d , and "red-eyed dilution," c^r , were kindly presented by Professor CASTLE and are the sole sources of these factors in the present experiments. The light dilutes traced to Professor CASTLE'S "dilute selection" stock which was the principal source of the animals used by the writer in the experiments described in the paper of 1916. It should be added that one of the animals sent by Professor CASTLE, an animal descended from his importations from Arequipa, Peru (CASTLE 1916), transmitted a dark dilution apparently identical with c^k from the stock of the Bureau of Animal Industry. The dark dilutes described in the present paper, however, all owe their dilution factor to the Bureau stock rather than to this source. The present discussion will be based primarily on the data from 192 matings in certain experiments (J and K) the chief purpose of which was the study of the effects of the albino series on black and yellow. All young born in these experiments, from their beginning in 1919 to the end of 1923, are included in the data as far as their records are complete, with two classes of exceptions.

One of these includes all descendants of a certain male whose appearance and breeding record constitute the only clear exception to the ordinary mode of inheritance of the five allelomorphs, which the writer has observed. This male was produced by dilute parents ($c^d c^d \times c^d c^r$) in another experiment. He attracted attention when first recorded, as an intense-dilute mosaic, somatically, an extremely rare condition. In matings with lower recessives (albinos, $c^a c^a$, and red-eyed dilutes, $c^r c^a$) he produced both intense and dark-eyed-dilute young. The occurrence of the intense young (C—) proves him to have been a mutant, while the ratio, 79 intense to 149 dilute, departs so widely from equality as to indicate that he was a germinal as well as a somatic mosaic. There has been great variation in the ratio at different times in the five years during which he has been producing young. Altogether, his case is a very peculiar one and will be described in more detail elsewhere. Both his intense and dilute young and

their descendants have behaved normally. They happened to be recorded in experiment K, but it has seemed best to exclude them from the data to be presented here.

The second class of exceptions includes all animals which descend along any line from a certain mating (B211) which has been the sole source of an independent dilution factor (f) (WRIGHT 1923). Nearly all possible combinations between this factor and the albino series have now been made, yielding a number of new color varieties, among which black-eyed silver agoutis ($c^k c^a f f A -$), slightly creamy black-eyed whites ($c^d c^d f f e e$), pink-eyed cream-yellow mosaics ($C - f f p p$) and a new kind of apparent albino ($c^d c^a f f p p$) may be mentioned. While all of the data are in harmony with those presented here, it has seemed best to avoid discussion of the complications arising from the bringing together of two dilution series whose effects simulate each other more or less.

There is a great deal of data on the albino series from experiments carried on for other purposes. As far as this has been critically analyzed, it is all in harmony with the data from experiments J and K except for the mutant male referred to above. It will be convenient to use certain of these data to supplement the rather scanty data from experiments J and K as regards the intensity of sepia in certain compounds, especially $c^k c^r$ and $c^k c^k$. The purpose of experiment L has been to make all combinations between the albino series and the "pink-eye" factor (p). In experiment N, all combinations between the albino series and the brown factor (b) have been made. Experiment UR includes matings leading up to the production of a stock recessive in eight sets of factors. The matings of these experiments have been analyzed critically for the source of the albino-series factors involved and with respect to the appearance and breeding record of all descendants. Use is made here only of animals of known constitution, which showed sepia in the fur (factors p and b absent).

Experiments J and K were largely a self-contained group of matings. The matings made in 1923 had on the average between 4 and 5 generations of ancestry of J or K matings. As homozygous stocks were not available for starting the experiments, most of the early matings produced more than one class of progeny. It was thus necessary to mate many animals whose genetic constitution was not uniquely determined from their parentage. A genetic constitution has been assigned each mated animal only after an exhaustive investigation. That assigned is in every case consistent with the constitutions assigned the parents and all of their ancestors as far back as known, with its own color within the range of

variation of the various compounds, with the classes of progeny produced and with all later descendants. As to color, there is, as will be seen, considerable overlapping of the various compounds, especially with respect to sepia. The following statements may be made here: Intense red in any part of the coat occurs only in the presence of the intensity factor C ; yellow or cream (in the present experiments) only with c^k or c^d as the highest member of the series present; a white brindle (tortoise-shell pattern) associated with more or less dark-red eyes only with c^r as the highest member.

Pink-eyed white in the present data has always meant a true albino ($c^a c^a$), although in other experiments such combinations as $c^r c^r p p e e$ (IBSEN 1919) and $c^d c^d f f p p$ have been responsible for apparent albinos.

The factors most difficult to distinguish by appearance have been the two dilution factors c^k and c^d . In the great majority of cases, however, the matings have been made in such a way that a black-eyed dilute could be definitely assigned to one or the other by its ancestry alone.

The evidence for the allelomorphism of the five factors will be considered chiefly from the standpoint of particular critical crosses. It may be noted here, however, that the consistency of the results within a large net-work of matings such as represented by experiments J and K affords perhaps the most convincing evidence, but evidence of a kind which it is difficult to present in a compact form. The great variety of crosses which have been made and the consistency of the results with the hypothesis of allelomorphism may be seen, however, from tables 13 to 20 which give all of the data in experiments J and K through 1923 with the exceptions previously noted.

METHOD OF GRADING

Series of sepia and yellow skins have been used for grading the intensity of the colors. The sepia series runs from 3 for a light sepia to 14 for intense black. The yellow series runs from grade 3 for a light cream to 13 for the most intense red. Each series gives the appearance of a nearly continuous gradation.

A guinea-pig which has a reasonably large amount of sepia or yellow in a compact spot can easily be graded, with only an occasional question of one grade. Sepia can not, however, be graded satisfactorily in agoutis because of the replacement of the blackest part of each hair by yellow. Consequently, no attempt has been made to assign them sepia grades. Non-agouti tortoise-shells ($aa e'e'$) have been given preference in the matings in order to obtain animals which could be graded with respect to

both sepia and yellow as far as possible. Many agoutis, self-yellows and self-sepias came in the early generations, however, because of the association of c^d and c^r with the factors determining these patterns in the foundation animals.

There has been considerable difficulty in keeping a constant set of sepia grades. It has been found that the sepia skins gradually fade and become browner, making necessary restandardization from time to time. Errors in grading from this cause probably make each class appear slightly more variable than it really is. Comparison of class averages for different years shows, however, that there has been no serious error in averages due to this cause. There has been no such tendency to fade among the yellow standards. Grades 7, 10 and 13 were taken from three inbred families, No. 35 ($c^k c^k$), No. 2 (CC) and No. 32 (also CC). The guinea-pigs of these families are uniform in intensity of color at any given time and can safely be assumed to be so from year to year. Frequent comparison of the standards with living young from these families make it certain that there has been no change in the meaning of the yellow grades.

The grades based on comparison with standard skins have all been made by the writer. There are additional data, useful in connection with the young which died before the accurate grade was given, in the color terms in the daily record of births kept by Mr. O. N. EATON. These color terms are given simply by inspection. While there is naturally some overlapping, it is found that in general they compare with the numerical grades as follows:

<i>Color</i>	<i>Grade</i>	<i>Color</i>	<i>Grade</i>
Light sepia	3-6	Cream	3-5
Medium sepia	7-10	Yellow	6-8
Dark sepia	11-12	Red	9-13
Black	13-14		

CHANGE IN COLOR WITH AGE AND EFFECT OF COLD

Unless otherwise stated, all grades refer to the color within a week or two after birth. There is seldom any change in the grade of yellow later in life but the sepias regularly become darker. This effect is greatest in the red-eyed varieties. Even the heterozygotes ($c^r c^a$) usually become a glossy iridescent black, at least on the back, at maturity, while the black-eyed sepias merely become a darker brown. Thus, while a red-eyed sepia $c^r c^a$ usually differs but little from a black-eyed sepia of type $c^d c^a$ at birth, and is distinctly lighter than $c^k c^a$, at maturity it will in general be found to be the darkest of the three. This darkening of the sepia is probably an effect of cold. In harmony with the experiments of LENZ (1923) and of

SCHULTZ (1918, 1922) on Himalayan rabbits, it has been found that after plucking a patch of hair from a sepia part of the fur, in any of the compounds (including intense blacks, C) the new hair, especially in winter, is of a distinctly darker color. It is possible to bring out pale sepia patches in this way even in albinos. In agreement with the natural age effect the darkening is greatest in red-eyed dilutes.

If yellow hair is plucked, either there is no visible difference between the new hair and that around it, or the former comes out slightly lighter in color.

The grades in the series of skins used here were defined without relation to the grades used in the previous study (WRIGHT 1916). They compare approximately as follows (the comparison with RIDGWAY'S color charts as given in the above paper is repeated):

<i>Grades of sepia</i>		
1916	1925	RIDGWAY
Black 0	14	Black
Sepia 3	10	16'''n, warmer and darker than clove brown 17'''m.
Sepia 6	6	16'''l, warmer and lighter than clove brown 17'''m.
Sepia 9	3	17'''i, hair brown, somewhat purer, however.

<i>Grades of yellow</i>		
1916	1925	RIDGWAY
Red 0	11	15'i, ochraceous tawny.
Yellow 3	7	16''b, redder than cinnamon buff 17''b.
Cream 6	4	19''b, cartridge buff.

COMPOUNDS $c^k c^a$ AND $c^d c^a$

The distinction between the two dilution factors, c^k of the Bureau stock and c^d of Professor CASTLE'S stock, was demonstrated by crossing dilutes from each source with albinos whose sire or dam was a dilute of the other kind (WRIGHT 1923). The process was repeated generation after generation. If the difference in intensity were due to independent modifying factors, the latter should be transmissible through the albinos as well as through the dilutes themselves and the two sets of matings should give identical results. If, on the other hand, the two types of dilution are due to different allelomorphs of albinism, albinos should not be able to transmit their difference, and the results of the two sets of matings should maintain their distinctness. The latter turned out to be the case (Table 2).

All but one of the 77 graded sepias from matings of type 1 were below grade 10 in intensity. Among those which were not graded, 7 were called light or medium sepias at birth by Mr. EATON and only one, found dead at birth and probably wet, was called a black-cream. Two had no sepia in the fur. The sepias from matings of type 2, on the other hand, were graded

between 10 and 13. Of those not graded, 12 were called dark sepia or black by Mr. EATON, 6 had no sepia in the fur and only one was called medium sepia. Thus, with a few doubtful exceptions, light and medium sepias have produced only light and medium sepias (and albinos), and dark sepias have produced only dark sepias (and albinos) in matings with albinos, regardless of the ancestry of the albino parent. These results demonstrate that c^d and c^k are different allelomorphs of albinism.¹

TABLE 2

The grades of sepia among the young from matings between dilutes, heterozygous for albinism, and albinos. In matings of type 1, the dilutes (light sepia and cream) trace their dilution to Prof. CASTLE'S dilute selection stock while in the matings of type 2 the dilutes (dark sepia and cream) trace their dilution to Bureau stock. Each type of dilute is mated with albinos produced by the other type of mating. The young not graded either had no sepia in the coat or died too soon.

TYPE NUMBER	MATING	GRADE OF SEPIA												NOT GRADED	DILUTES		TOTAL DILUTES	ALBINO
		3	4	5	6	7	8	9	10	11	12	13	14		3-9	10-13		
1	$c^d c^a$ (from 1) $\times c^a c^a$ (from 2)	1	3	6	8	22	34	2	1	10	76	1	87	105
2	$c^k c^a$ (from 2) $\times c^a c^a$ (from 1)	7	15	34	10	..	19	..	66	85	77

TABLE 3

The same matings as in table 2, but with the young classified with respect to grade of yellow instead of black.

TYPE NUMBER	MATING	GRADES OF YELLOW											NOT GRADED	TOTAL DILUTES	ALBINO	
		3	4	5	6	7	8	9	10	11	12	13				
1	$c^d c^a$ (from 1) $\times c^a c^a$ (from 2)	2	53	6	26	87	105
2	$c^k c^a$ (from 2) $\times c^a c^a$ (from 1)	..	24	23	5	33	85	77

The grades of the creams from these matings are shown in table 3. There appears to be a slight difference in average grade, but there is so much overlapping that the grade of cream is practically worthless as a means of distinguishing $c^d c^a$ and $c^k c^a$.

Types $c^d c^a$ and $c^k c^a$ have been obtained from other matings. The grades of those which came from matings which could produce no other dark-eyed

¹ The reciprocal matings, female albino by male dilute and female dilute by male albino, are combined. This is justified by the absence of sex-linked inheritance in this case and the absence of appreciable sex differences in intensity of color. Matings of type $c^d c^a \times c^a c^a$ produced 24 dilute sons, 25 dilute daughters, 28 albino sons and 26 albino daughters. The reciprocal matings produced 13 dilute sons, 25 dilute daughters, 22 albino sons and 29 albino daughters. The average grades of the sons were sepia 7.31, cream 4.00, those of the daughters were sepia 6.95, cream 4.11. No distinction of sex has seemed necessary in the later tables.

type of dilute are given in groups A (experiments J and K) and C (experiments L, N and UR) in tables 9 and 10 (see appendix). The numbers are considerably larger than the special crosses given in tables 2 and 3, but the results are essentially the same. There is still only one example of overlapping in grade of sepia, a $c^d c^a$ of grade 10. The assignments to types $c^d c^a$ and $c^k c^a$ from matings which produced more than one type of black-eyed dilute, as given in groups B and D in tables 9 and 10, are consistent with the figures for those of more certain constitution. The grand totals are given in tables 11 and 12.

TABLE 4

The grades of yellow among the progeny of matings between black-eyed dilutes heterozygous for albinism ($c^k c^a$ or $c^d c^a$).

MATING	GRADE OF YELLOW													NOT GRADED			$c^k c^d$	$c^k c^a$	$c^d c^a$
	3	4	5	6	7	8	9	10	11	12	13	Cream	Yellow	No yellow					
$c^d c^a \times c^d c^a$	2	42	11	4	17	2	15	7	15	37	78	24	
$c^k c^a \times c^k c^a$..	13	12	3	11	2	1	3	5	17	33	19	
$c^k c^a \times c^d c^a$..	19	9	5	11	1	1	4	1	18	33*	10	

* Composed of 20 $c^k c^a$ and 13 $c^d c^a$ as indicated by grade of sepia.

COMPOUNDS $c^k c^k$, $c^k c^d$ AND $c^d c^d$

On crossing dilutes from matings of type 1 with each other ($c^d c^a \times c^d c^a$) it is found that a considerable number of the young are well outside the limits of variation of $c^d c^a$, being more intense in both the sepia and yellow parts of the fur than their parents. Closely similar results have been obtained from matings of types $c^k c^a \times c^k c^a$ and $c^k c^a \times c^d c^a$. The distribution of the grades of cream and yellow are shown in table 4. Comparison with table 3 suggests that all or nearly all of grades 7 and 8 and probably some of grade 6 (at least in the case of light dilutes) are homozygotes, $c^d c^d$ or $c^k c^k$, or are heterozygotes between the two types of dilution, $c^k c^d$. The ratios agree reasonably well with this interpretation. In each of these matings, we have an analogue of the Blue Andalusian fowl case,—cream being the unfixable heterozygote between yellow and white. There was no difficulty in obtaining a reasonably true-breeding strain of medium sepia-yellow color ($c^d c^d$) by selecting the yellow segregates from the matings between heterozygotes. The distribution of all of definitely known constitution (A, C) or of probable constitution (B, D) are given in tables 9 and 10 (appendix) with grand totals in tables 11 and 12 as before. These show considerable overlapping with $c^d c^a$ with respect to sepia, but only a small amount with respect to yellow. Similar results are shown for $c^k c^k$ and $c^k c^d$ in these tables. A homozygous race of dark dilutes ($c^k c^k$) has been

developed from segregates in these experiments since the period covered by the data. They are uniformly dull black (usually grade 13) with yellow markings (usually of grade 7 or 8). They agree in these colors with the inbred family (No. 18, now extinct) to which in the main they traced their dilution factor.

Eight of those which, on account of their color, were thought to be $c^k c^d$, were tested by mating with albinos. As shown in table 13 (appendix), they produced 32 dark dilutes ($c^k c^a$) and 40 light dilutes ($c^d c^a$) whose colors, included in group B in tables 9 and 10, were typical of these varieties. The segregation was clear-cut in the litters which contained both kinds.

It may be interesting at this point to summarize in table 5 the intensity relations of the three allelomorphs, c^k , c^d and c^a , indicated by the data so far considered.

TABLE 5

	GRADES OF INTENSITY					
	$c^k c^k$	$c^k c^d$	$c^d c^d$	$c^k c^a$	$c^d c^a$	$c^a c^a$
Sepia	13.1	12.4	9.9	11.5	7.0	0.0
Yellow	7.1	7.2	7.0	4.6	4.2	0.0

It may be seen that c^k and c^d are almost indistinguishable in effect on yellow. Lumping them together under the symbol c^{kd} , the homozygotes have a yellow of about grade 7.1 and the heterozygotes a cream of about grade 4.4. On the other hand, c^k and c^d differ markedly in effect on black, whether homozygotes or heterozygotes are compared. In relation to each other, c^k seems almost fully dominant over c^d . It must be remembered, however, that the grades are not measurements of the actual amounts of pigment, but are based on a scale in which successive grades can just be distinguished. It is certain that the addition of a given amount of pigment to white or to the lower grades would produce a more easily recognized difference than the addition of the same quantity of pigment higher in the scale. The approach to dominance of c^k may therefore be merely apparent.

There is one other point to which attention may be called. The type $c^k c^a$ is more intense in the sepia parts of the fur than $c^d c^a$, but less intense in the yellow parts, furnishing another case in which it is impossible to arrange the compounds in a single order of intensity.

COMPOUNDS $c^k c^r$ AND $c^r c^a$

A series of color varieties with red eyes, in which the yellow parts of the fur are replaced by white, although the black parts remain more or less

intense, seem to trace back exclusively, as far as known in this country, to a few animals which Professor CASTLE obtained in Peru in 1912 (CASTLE 1914). The eyes show more or less black pigment in the iris, but give a red glow from the pupil because of deficient retinal pigmentation. They are thus intermediate between the ordinary dark eyes and the pigmentless eyes of albinos. Evidence that these varieties contain a factor (c^r) allelomorphous with albinism (c^a), dilution (c^d) and full intensity (C) has been presented in previous papers (WRIGHT 1915, 1916, CASTLE 1916). Inspection of tables 8 to 15 will show that the present data are in full agreement with this result. Red-eyed dilutes mated with each other never produce the dark-eyed varieties showing red, yellow or cream in the fur. They segregate as expected in crosses involving the compounds Cc^r , $c^k c^r$ and $c^d c^r$. It will not be necessary to go into more detail on this point.

Examination of tables 8 to 15 shows a large number of matings which should produce heterozygotes, $c^r c^a$, but not homozygotes $c^r c^r$. In other cases, only $c^r c^r$ should appear, while in still other cases both are expected. The red-eyed young which actually appeared where only $c^r c^a$ was expected, were relatively light sepia in color (at birth) with light-red eyes, while those which appeared where only $c^r c^r$ was expected were almost black at birth with dark-red eyes, sometimes difficult to distinguish from the eyes of intense or black-eyed dilute varieties. The actual grades are shown in table 9 (A and C). The table brings out clearly the intermediate character of the heterozygote in grade of sepia, although a small amount of overlapping is indicated.

Matings such as $c^r c^a \times c^r c^a$ produced both types. There is seldom if ever any difficulty in distinguishing the homozygotes from heterozygotes within a given litter. After making as careful a classification as possible on the basis both of grades of sepia and of notes on eye color, mating $c^r c^a \times c^r c^a$ is credited with producing 26 $c^r c^r$: 50 $c^r c^a$: 20 $c^a c^a$ in reasonable agreement with expectation. The grand average for intensity of black (table 11) comes out 13.1 for $c^r c^r$ and 8.5 for $c^r c^a$. There is no trace of yellow in either case in the white regions which correspond to the yellow of other varieties.

COMPOUNDS $c^k c^r$ AND $c^d c^r$

A considerable number of crosses in experiments J and K were such as to produce only $c^d c^r$ among the dark-eyed dilute varieties. These are brought together in tables 9 and 10 ($c^d c^r$, row A). Most of them are sepia grade 12 and cream grade 4, the averages being 12.2 and 4.1, respectively. The same result is found among those brought together from experiments UR, L and N (row C in the above tables), the averages again being sepia 12.2

and cream 4.1, respectively. Those assigned to $c^d c^r$ on less certain grounds, in experiments J and K (row B) and UR, L and N (row D), are consistent with the above figures. It will be noticed that $c^d c^r$ has a cream indistinguishable from $c^d c^a$, but that it has a much darker sepia. In fact, it averages distinctly darker than $c^d c^d$ with respect to sepia, although much lighter with respect to yellow. Curiously enough it is practically indistinguishable from $c^k c^a$ in both sepia and cream, although having no factor in common. A breeding test with albinos, of course, immediately separates them (compare table 13).

No mating in experiments J and K produced $c^k c^r$ as the only expected dark-eyed dilute class. A number were produced by experiments UR, L and N, however, (tables 9 and 10, $c^k c^r$, row C). They proved to be almost intense black (sepia 13.3) with cream spots (cream 4.5). The results from matings which should produce both $c^k c^r$ and some other dark-eyed class (rows B and D in tables 9 and 10), agree with this result after apportioning the young to the classes as fairly as possible from the expected ratio and the known range of variation of the other dilute class (largely $c^k c^a$ or $c^d c^r$). A considerable number of those assigned to $c^k c^r$ in experiments J and K on the basis of their appearance, have been mated and have produced young of the expected classes. Thus, 5 thought to be $c^k c^r$, mated with albinos, produced 23 dark dilutes in the range of variation of $c^k c^a$ and 21 red-eyed light or medium sepias of class $c^r c^a$.

THE INTENSE COMPOUNDS

It has been pointed out that there is imperfect dominance among the compounds of the four lower allelomorphs in the series, as far as there are recognizable differences in effect. The highest factor, C , on the contrary, appears to be completely dominant. Black is represented by intense black, grade 14, in the homozygotes and all of the heterozygotes. There is considerable variation in the grade of red, but no average differences which can be relied upon. Table 10, it is true, shows a slightly higher average for Cc^k than Cc^d or Cc^a , but it happens that the former had a relatively higher percentage of blood from a particular inbred family, No. 32, characterized by a very intense red (grade 13). It has been shown that the difference between this family and certain others (No. 2 and No. 13) characterized by a dull red (grade 10) is inherited independently of albinism. One of these inbred families, No. 13, still occasionally transmits albinism. Inspection gives no indication of a difference between the ordinary homozygotes, CC , of this family and those known to transmit albinism, and thus, Cc^a ; both are grade 10.

DIFFERENCES WITHIN LITTERS

As previously noted, the comparison of different compounds has been complicated by the presence of modifying factors and by the difficulty in maintaining standard sets of skins, especially in the case of sepia. It seemed of interest, therefore, to make comparisons between the compounds as they segregated out within litters. There is no difficulty in determining which of two young guinea-pigs, compared directly with each other, is the darker, and to measure the difference on the basis of the standard skins. There is, of course, danger of arguing in a circle where the relative intensity of color is both the character which is being studied and the criterion determining genetic constitution. Fortunately, the relative intensity of yellow, regarding which there is seldom any doubt, can be used as the genetic criterion in comparing grades of sepia in many cases. Using compound symbols, there is seldom difficulty in distinguishing the four groups of compounds, C — (red), $c^k d c^k d$ (yellow) $c^k d c^r a$ (cream) and $c^r a c^r a$ (white). In dealing with a mating such as $c^d c^r \times c^d c^r$, it is usually safe to assume that the more intense yellows in a litter are $c^d c^d$, the less intense, creams, $c^d c^r$, and those with white in a pattern resembling tortoise-shells and with red eyes, $c^r c^r$. Comparisons of grades of sepia in the three compounds can be made accordingly.

In cases of segregation in which the grade of yellow is of no assistance, the separation can be made with more or less certainty, depending on the amount of overlapping as found in those of certain constitution. As already noted, there is seldom if ever any uncertainty in separating $c^r c^r$ from $c^r c^a$, or $c^d c^a$ from any of the compounds $c^k c^a$, $c^d c^r$ or $c^k c^r$. It is impossible to separate $c^d c^r$ and $c^k c^a$ with any reliability except by a breeding test and no attempt has been made to do so. In the case of $c^k c^r$ and $c^k c^a$ separation has been attempted, but doubtless with a considerable number of errors, due to overlapping.

Table 21 shows the differences which were found within litters. It is shown, for example, that $c^k c^a$ varied from 3 to 7 grades darker than $c^d c^a$. In most cases the average difference is very close to the difference between the average grades as given in table 11.

On comparing $c^r c^a$ and $c^d c^a$ as they segregate from the litter, it is found that $c^r c^a$ is not so much darker as the data in table 11 indicate, the difference being only 0.5 instead of 1.5. Indeed, in two cases out of 19, the red-eyed sepia was judged lighter than its dark-eyed litter mate, in nine cases there was no difference and in eight cases the red-eyed sepia was judged darker. On comparing $c^d c^d$ and $c^d c^a$, on the other hand, a somewhat greater difference was found between litter mates (3.9 grades) than

indicated by the grand average (2.9 grades). These are the most important discrepancies. On the whole, this comparison confirms the grand averages very satisfactorily.

DISCUSSION

The data indicate that there are at least five allelomorphs in the albino series of guinea-pigs. The results could also, of course, be explained by complete linkage among a number of factors, as far as the purely genetic evidence is concerned, but the relations among the characters makes this explanation as artificial here as in the many other cases which have convinced geneticists that multiple allelomorphism is a phenomenon entirely distinct from very close linkage. It is merely necessary to point out that the four recessives resemble each other in general effect, in contrast with the usual lack of correlation between linkage relation and nature of effect, and that none of the recessives are complementary to each other, a surprising coincidence on the linkage hypothesis.

The situation is thus the simplest possible, as far as the mode of inheritance is concerned, but the irregularities in the order of effect of the compounds indicate that it is not so simple with regard to the effects of the factors in development.

The average grades of black and yellow in the fur, and of black in the eyes, are summarized in table 6.

TABLE 6

	BLACK	YELLOW	EYE COLOR
$C-$	14.0	10.6	Black
$c^k c^k$	13.1	7.1	Black
$c^k c^d$	12.4	7.2	Black
$c^k c^r$	13.5	4.6	Black
$c^k c^a$	11.5	4.6	Black
$c^d c^d$	9.9	7.0	Black
$c^d c^r$	12.1	4.1	Black
$c^d c^a$	7.0	4.2	Black
$c^r c^r$	13.1	0	Dark red
$c^r c^a$	8.5	0	Light red
$c^a c^a$	0	0	Pink (no pigment)

Figure 1 presents the relation between intensity of black and yellow, graphically. The impossibility of arranging the compounds in a linear order of intensity is obvious. It may be of interest to point out the

differences in interpretation which would probably have been reached if different pairs of factors had been studied separately. Stocks containing only c^r and c^a or only c^k and c^d would appear to vary only in a modifier of black. Stocks containing only c^k and c^r would seem to involve only a modifier of yellow. With only C and c^d present, the latter would be considered to be a diluter of both black and yellow, while with only c^d and c^r present, c^r would be considered a diluter (or rather annihilator) of yellow, but an intensifier of black.

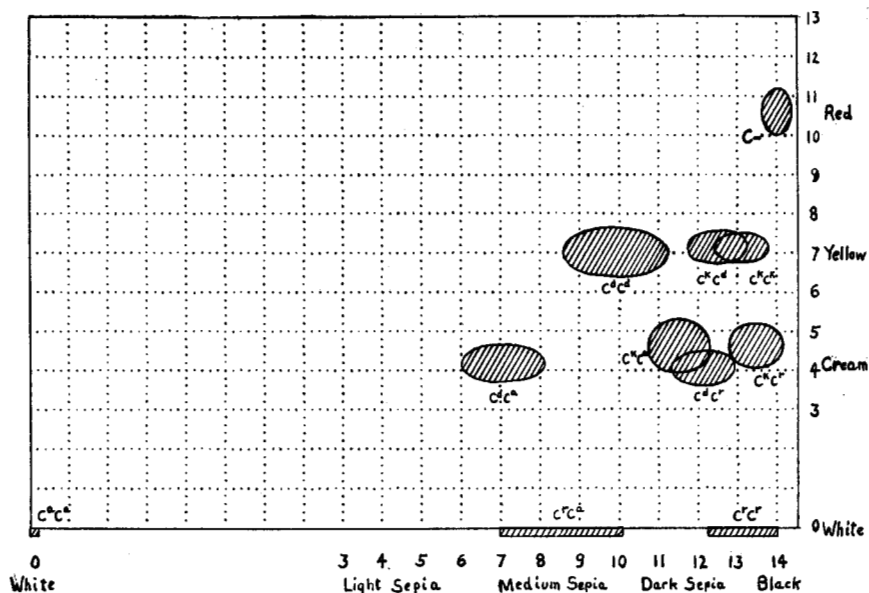


FIGURE 1.—The grades of intensity with respect to both sepia and yellow, of the albino-series compounds of guinea-pigs. The shaded areas extend horizontally to a distance above and below the mean equal to the standard deviation with respect to grade of sepia, and extend vertically the corresponding amount with respect to grade of yellow. This range includes about 68 percent of the individuals. The area should thus include about 47 percent of them.

An explanation of these irregularities may be sought either in the nature of the gene or in its effects on development. The simplest conception of an allelomorph series is, perhaps, that the different genes differ merely quantitatively. ANDERSON and DEMEREC, in a paper read before the 1921 meeting of the Genetics Sections, and EYSTER (1924) have suggested such an explanation for the constantly mutating allelomorphs involved in the variegation of pericarp color in maize, and STURTEVANT and MORGAN (1923) have shown in the case of bar and ultra-bar in *Drosophila*, that the latter probably consists merely of two ordinary

bar genes. It would be far from safe, however, to generalize from these peculiarly-behaving cases to multiple allelomorphs in general.

If genes are complex chemical entities, it would seem likely that they would be subject to variation in many different directions. Thus, *a priori*, both quantitative and polymorphic variations seem probable.

Data such as the present can throw no light on these alternatives, since in either case the visible effects may or may not fall into an apparently quantitative series. Thus, however diverse the variations of a gene, if it acts on only one process in ontogeny, the allelomorphs can produce only quantitative differences in that process, and thus are likely to produce a regular gradation in visible effects. If factor *C*, for example, is interpreted as acting on only one fundamental process in the production of melanin pigment, it is quite possible that there may be many diverse modifications of it, each merely weakening this process as far as visible effect is concerned. There may be dozens of distinct albino factors, alike only in that some change in the factor *C* in each case prevents its normal activity. Such allelomorphs could not be separated by breeding tests.

On the other hand, it is quite possible that a purely quantitative series of changes of a gene may be accompanied by polymorphic visible effects, in case the gene affects a number of different but interacting processes in ontogeny with thresholds at different levels of the gene. Thus the nature of the effects in an allelomorphic series gives no evidence on the nature of the gene, but only on the nature of its effects in ontogeny. The question as to the ultimate nature of the differences between factors *C*, c^k , c^d , c^r and c^a may thus be dismissed at this point as one to which the data are not pertinent.

The black and yellow pigments of guinea-pigs are both melanins, and the processes by which they are produced doubtless have much in common. The albino series is not, indeed, the only series which affects them more or less similarly, since the white piebald pattern and white silvering may appear on either a black or yellow ground.

The existence of two series of factors in guinea-pigs (the agouti series *A*, a' , *a*, and the tortoise-shell series *E*, e' , *e*), which determine the localization of black and yellow in the fur relative to each other, also indicate a common element. On the other hand, there is considerable independence. Two sets of factors are known in guinea-pigs (the "pink-eye" and "brown" factors), which modify black wherever it occurs (skin, fur and eyes) without any apparent effect on yellow, while one factor (*f*) is known

which seems to have the opposite effect, to dilute yellow with little if any effect on black.²

It would thus be possible to interpret albinism either as affecting a single process fundamental to any melanin pigment production or as affecting the production of black and yellow for different reasons. If the latter be assumed, with the further assumption of polymorphic variation of the gene, the problem raised by the lack of agreement in the order of intensity in black and yellow parts of the fur ceases to exist. Under such conditions there need not be any correlation at all. This dismissal of the whole situation seems rather arbitrary, however, especially in connection with the imperfect correlation between the effects on black pigmentation in the eye and in the fur, and in view of the parallelism between the albino series in different mammals. Without further discussion at this point, it will be assumed, provisionally, that the albino series has only one primary type of effect on pigmentation and that the irregularities in the effects on different kinds of pigment or different parts of the body are due to developmental processes subsequent to the effect of the albino factors.

The first conclusion which is suggested by the data is, that the threshold for yellow is higher than that for black. The red-eyed dilutes ($c^r c^r$ and $c^r c^a$) may have a great deal of black in the fur, but no yellow. The typically yellow parts of the tortoise-shell or the agouti patterns are represented by pure white. Even albinos develop black in the ears, nose and feet, and sometimes sootiness of the back, but never a trace of yellow. Since this difference in threshold was suggested (WRIGHT 1915) to account for the situation in guinea-pigs and in the Himalayan rabbit, it has been confirmed by the discovery of several albino allelomorphs in other animals in which more or less black is developed, but no yellow. WHITING and KING (1918) found a "ruby-eyed" dilute variety (c^r) of this sort in the wild rat. The homozygotes had light sepia in place of black, but no yellow. The heterozygotes, obtained from matings with albinos, were still paler in color and with brighter-red eyes, in agreement with the imperfect dominance of c^r in guinea-pigs. DETLEFSEN (1921) reported on an allelomorph of albinism (c^d) found in wild mice, apparently intermediate in character

² This factor was described in a previous paper (WRIGHT 1923) as diluting yellow and probably intensifying black. The latter conclusion seems now to have been based on an error. A black-cream variety appeared in the progeny of the cross $Cc^a Ff \times Cc^d Ff$. These were at first thought to be the desired combination $c^d c^a ff$. Breeding tests proved them to be $C-ff$, considerably more extreme in the dilution of yellow than previously observed in this constitution. The combination $c^d c^a ff$ has since been produced in considerable numbers and thoroughly tested. It is light sepia-white with dark eyes, the light sepia being apparently identical in grade with that in ordinary light sepias ($c^d c^a F-$). An apparent effect on black has been noted only in combinations with the pink-eye factor.

between the red-eyed and albino guinea-pigs. The homozygotes were dirty white at birth, although with dark-red eyes, only slightly less intense than those of normal wild mice. They acquired a more general pale sepia color later in life with especially large amounts of dark pigment in the exposed parts of the skin. They also seem to be entirely lacking in yellow. Finally, CASTLE (1921) has found that the chinchilla variety of rabbit has a fourth allelomorph of albinism, that reduces black to a dark sepia, yellow to white, and, while not affecting the pigment of the iris appreciably, causes sufficient reduction in the retinal pigment to make it relatively easy to obtain a red reflection through the pupil.

In addition to these three albino allelomorphs above the threshold for black, but below that for yellow, and with red eyes, apparently more or less homologous to the red-eyed guinea-pigs, FELDMAN (1922) has described a fourth allelomorph of the mouse (c^r), which seems to be more comparable to factor c^d in guinea-pigs. This variety is described as having dark eyes, a very dark, dull slate color in place of black, and a yellow (in the agouti pattern) intermediate between white and the yellow of wild gray mice. The heterozygotes were paler in color (brownish) and with yellow practically reduced to white.

The albino series of these four rodents may be classified as follows with respect to the thresholds for yellow and black. No exact identification of the genes in the different cases is intended. As DETLEFSEN (1921) has emphasized, such an identification is out of the question. It may perhaps be well to call attention to the fact that c^d and c^r are used in more or less reversed senses in guinea-pigs and mice. Factor c^r in mice, however, seems to give distinctly lighter eyes than C .

TABLE 7

THRESHOLD	FUR COLORS	EYES	GUINEA-PIG	RABBIT	RAT	MOUSE
Yellow	Black-red	Black	C c^k	C	C	C
	Sepia-yellow	Black	c^d			c^r
Black	Sepia-white	Red	c^r	c^c	c^r	c^d
	Sooty white-white	Pink	c^a	c^h		
	Pure white	Pink		c	c	c

There are cases in other mammals which suggest a threshold difference. PEARSON, NETTLESHIP and USHER (1913) found that the F_2 from a cross between albino Pekingese dogs and black Pomeranians (F_1 being black)

included reds and "lilacs," the latter with albinotic eyes, in addition to the grandparental colors. The case appears to be exactly comparable to the cross between red-eyed white guinea-pigs ($c^r c^r ee$) and blacks ($CCEE$), which produces reds ($C-ee$) and red-eyed sepias ($c^r c^r E-$) in F_2 in addition to the blacks and red-eyed whites. It would appear that the "albino" Pekingese is really well above the threshold for black, as far as its albino factor is concerned, although below it with respect to red, and that it is a white in appearance because an independent factor tends to replace black with red.

The similarity of the Siamese variety of cat to the Himalayan rabbit was first pointed out by BATESON (1913). These cats are white or nearly so at birth, but later develop considerable brownish pigment, especially on the ears and extremities. No yellow seems to be produced, however. The red pupils (in a favorable light) indicate deficient retinal pigmentation. CASTLE (1922) has obtained data from a breeder, which indicate that the variety is a simple recessive. Dominance of the ordinary intense varieties is not quite complete, however.

The agreement in these six mammals, including those whose genetics has been most exhaustively studied, goes far to prove that a difference in threshold of black and yellow is characteristic of the physiological process affected in albinism, and that the situation described in the guinea-pig is not a mere accident, resting on a few mutations of a polymorphically varying gene.

In attempting to develop further the idea that the albino series affects primarily only one process in pigmentation, the question arises as to whether it is the 15 compounds or the 5 genes which are to be arranged in a linear order of effectiveness with respect to this process.

The first hypothesis implies that the primary products of the activity of the two genes come together before there is any modification of their quantitative relations, while the second implies that such modifications take place before the union of the primary products, and that the results are the same as if the two genes acted on black and yellow pigmentation in entire independence of each other. A third view, that there is reaction with other substances both in a period of separate gene activity and a period of activity of cell products as a whole, would seem more likely than either extreme view. Before considering this compromise hypothesis, however, it will be well to see how far the facts fall into order under the two extreme views.

The possibilities and difficulties of the first hypothesis can be somewhat crudely illustrated by the following scheme. The five genes c^a , c^r , c^d , c^k ,

and *C* are assigned effects in the proportion 0, 1, 3, 4 and 10. If their primary products come together without modification, the effects of the compounds should be in proportion to the sums of the two genic effects. This brings the compounds into the order shown in table 8.

TABLE 8

	HYPOTHETICAL PRIMARY EFFECTS	OBSERVED GRADES		EYE COLOR
		Yellow	Black	
<i>C</i> —	10–20	10.6	14.0	Black
$c^k c^k$	8	7.1	13.1	Black
$c^k c^d$	7	7.2	12.4	Black
$c^d c^d$	6	7.0	9.9	Black
$c^k c^r$	5	4.6	13.5	Black
$c^d c^r$	4	4.1	12.0	Black
$c^k c^a$	4	4.6	11.5	Black
$c^d c^a$	3	4.2	7.0	Black
$c^r c^r$	2	0	13.1	Dark red
$c^r c^a$	1	0	8.5	Light red
$c^a c^a$	0	0	0	Pink

The grades of yellow fall into four distinct levels, white (0), cream (4.1 to 4.6), yellow (7.0 to 7.2) and red (10.6); the grades of black rise within each level (of yellow) but fall in the passage from one level to the next (except the last).

The similarity in appearance of the compounds $c^d c^r$ and $c^k c^a$ is explained as due to the identity of the sum of the effects of their combined genes. The scheme thus brings out a certain order among the facts. The levels in intensity of yellow and the drop in intensity of black in the transition from one level to the next require explanation in terms of later reactions. The previously advanced hypothesis that production of yellow interferes with the production of black may be used to explain the second of these phenomena, while the unbroken rise in intensity of black in the eye may be explained as due to the lack of competition with yellow in that region through a higher yellow threshold.

There are, however, rather serious objections to this view, aside from its complexity. It is difficult to formulate any quantitative scheme which can account for the very marked drops in intensity of black in the transitions from $c^r c^r$ to $c^d c^a$ and from $c^k c^r$ to $c^d c^d$. Such a scheme, moreover, leaves it a mere coincidence that each heterozygote is intermediate (or nearly so)

between the corresponding homozygotes and, more generally, that each gene difference has practically the same effect in all cases.

This leads to consideration of the second hypothesis under which each gene has its characteristic effect, primary and secondary as well, on black and yellow, the effects of the compound being merely the sum of the effects of the genes acting independently of each other.

The lines in figure 2 show the intensity of yellow in compounds in which one gene is constant and in which the differences are therefore to be explained as due wholly to the other gene. It will be seen that c^r and c^a are

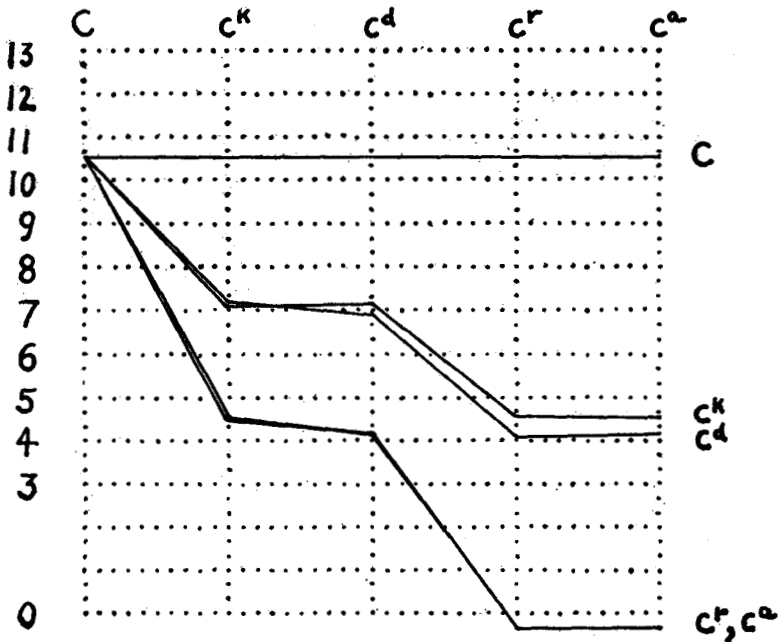


FIGURE 2.—The average grades of intensity of yellow in the albino-series compounds. Each line represents the grade for the compounds in which the factor to the right is combined in succession with each of the factors at the top.

practically identical in effect (or lack of effect) in whatever way they may be combined. Not only is yellow reduced to white in the compounds $c^r c^r$, $c^r c^a$ and $c^a c^a$, but $c^d c^r = c^d c^a$ (4.1, 4.2), $c^k c^r = c^k c^a$ (both 4.6). Similarly, c^k and c^d are very close together in effect, with c^k usually giving a little more intensity. Compare $c^k c^a$ with $c^d c^a$ (4.6, 4.2), $c^k c^r$ with $c^d c^r$ (4.6, 4.1), $c^k c^k$ with $c^d c^k$ (7.1, 7.2).

Figure 3 deals similarly with intensity of black. The tendency toward parallelism between the different lines, each representing a series of com-

pounds in which one gene is constant, is obvious. The order, however, is different from that with respect to intensity of yellow.

Disregarding the compounds with the completely dominant intensity factor, there is only one minor exception to the order of effectiveness, c^k , c^r , c^d , c^a . The differences are brought out most strongly in the compounds with c^a ($c^k c^a = 11.5$, $c^r c^a = 8.5$, $c^d c^a = 7.0$, $c^a c^a = 0$). The combinations with c^d give the series $c^k c^d = 12.4$, $c^r c^d = 12.1$, $c^d c^d = 9.9$, $c^a c^d = 7.0$. The combinations with c^r give the series $c^k c^r = 13.5$, $c^r c^r = 13.1$, $c^d c^r = 12.1$ and $c^a c^r = 8.5$. Finally, the combinations with c^k give $c^k c^k = 13.1$, $c^r c^k = 13.5$, $c^d c^k = 12.4$, and $c^a c^k = 11.5$.

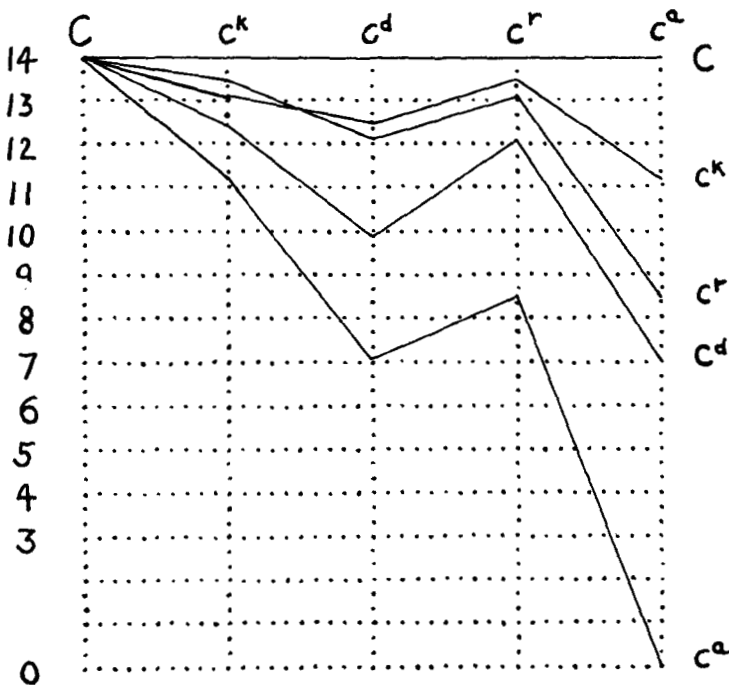


FIGURE 3.—The average grades of intensity of sepia in the albino-series compounds. Each line represents the grade for the compounds in which the factor to the right is combined in succession with each of the factors at the top.

The doubled effects of the genes on both yellow and black are shown in the series of homozygotes in figure 4. The order of the genic effects is the same as in figures 2 and 3.

As pointed out previously, the agreements in these series are mere coincidences on the first hypothesis. This seems too much to assign to coincidence. It can thus hardly be doubted that the genes act in independence

of each other to at least a considerable extent. On the other hand, there are irregularities which indicate that there is not complete independence.

As c^a is below the threshold for yellow and nearly so for black, the lowest lines in figures 2 and 3 (repeated in figure 5) should represent the effects of the five single genes, the lines in figure 4 representing the doubled effects of the same genes. Under completely independent activity of the two genes in a compound, the homozygotes (figure 4) should produce exactly

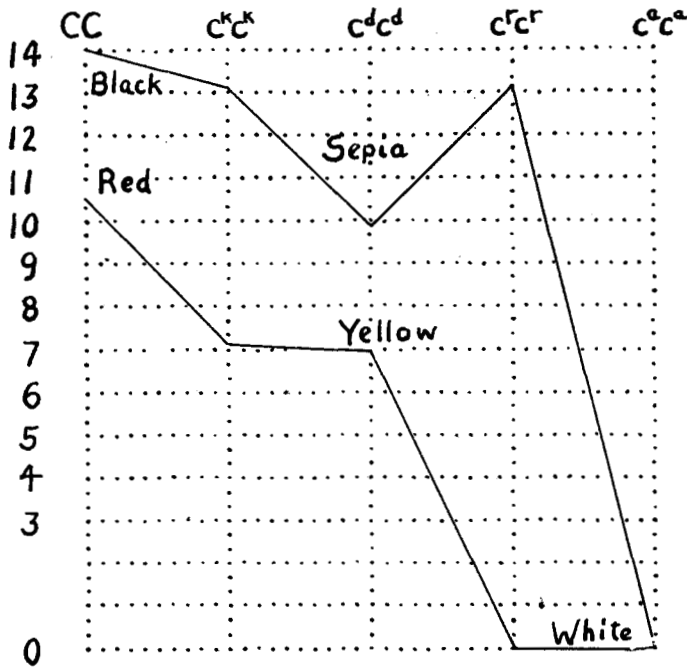


FIGURE 4.—The average grades of sepia and of yellow in the five homozygotes of the albino series.

twice the amount of pigment as the heterozygotes with albinism. The different factors should contribute fixed amounts in every compound in which they enter. Unfortunately, the scale used for measuring intensity can not be considered sufficiently close to a quantitative one to enable final conclusions to be drawn as to how far the data meet these conditions. As already pointed out, it is certain that smaller differences in the absolute amount of pigment are recognizable in the light sepias than in the dark sepias, with the consequence that the scale needs stretching in the upper part relative to the lower. In spite of the unsatisfactory character of the scale in this connection, there are certain points which indicate that the action of the genes is not wholly independent. In the first place, the com-

plete dominance of factor C can hardly be a mere question of imperfection of the scale, at least as regards red. Most intense reds, whether homozygous CC or heterozygous with albinism Cc^a , are of grades 10 and 11. This is well below the limit of intensity (grade 13) found regularly in a particular inbred family. Thus, it can hardly be maintained that there is twice as much pigment in CC as in Cc^a . There probably are limiting factors in intensity of pigmentation independent of the albino series which are responsible for the complete dominance of factor C .

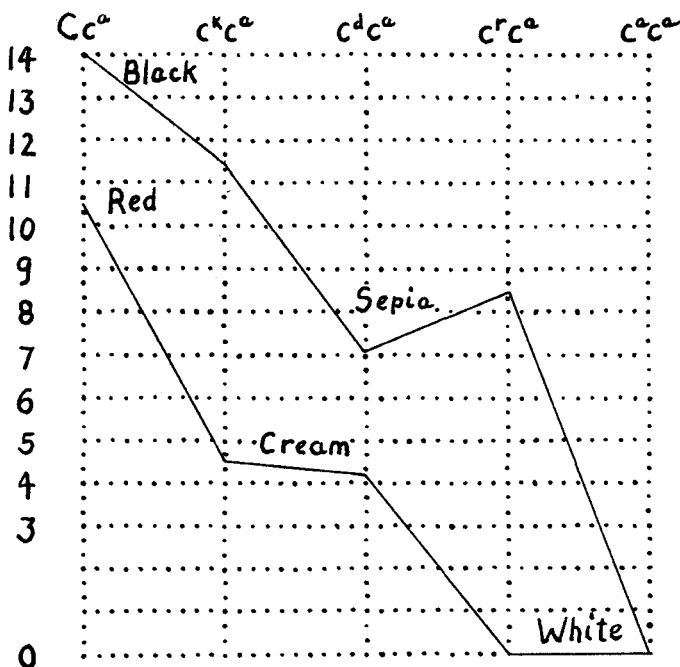


FIGURE 5.—The average grades of sepia and of yellow in the five compounds with albinism of the albino series.

Aside from the dominance of C , the most serious departure from expectation on the basis of independent activity of the genes comes in the effect of factor c^r , which, in combination with c^a , seems decidedly more like c^d than c^k in effect on black, although in other combinations it approaches very closely to c^k in effect, or even rises above it. However, the entire process of pigment production is hardly likely to be localized in the immediate vicinity of the two chromosomes carrying the albino factor. The surprising thing is that the effects of the compounds agree as well as they do with the hypothesis that the genes act independently on pigment production, or at least that the most important modifications of their effects takes place before the separate identity of their products is lost.

The problem thus reduces in the main to the explanation of the different effects of the five genes on black and yellow in fur and skin and on eye color.

Figures 4 and 5 suggest a rising trend in effect on pigmentation in the series c^a , c^r , c^d , c^b and C , but a tendency toward negative correlation between black and yellow in their deviations from this trend. The evidence for different thresholds for yellow and black, as responsible for the peculiar effects of c^r ,—rather intense black, no yellow,—has already been discussed. This threshold difference is one which must be traced back to the separate activities of the genes. The rates of production of the primary products of factors c^r and c^a (on the view adopted) appear to be below the threshold for yellow, with the consequence that these genes contribute nothing to intensity of yellow in any compound in which they enter.

The drop in intensity of black with c^d as compared with c^r in all compounds accompanying the first appearance of the power to produce yellow, suggests some sort of physical antagonism between the processes of black and yellow pigmentation, perhaps competition for some other substance. The absence of any such drop in the intensity of black in the eye (c^d , black eye; c^r , red eye) requires the further hypothesis that this interference with black production by yellow is absent in the eye, perhaps because the threshold for yellow is never passed in this location.

The hypotheses suggested to account for the irregularities in the effects of the albino series, namely, the threshold difference between black and yellow, the antagonistic action of yellow on black above the threshold of the former, and the difference in threshold for yellow in the eye and skin, are the same as those previously advanced. It is suggested here, however, that they apply to the primary products of the genes instead of to the compounds.

ALBINISM AND DILUTION IN OTHER ANIMALS

Albinism is one of the commonest types of color variation among all sorts of animals which have melanin pigmentation. How far is it safe to identify the albinism of different species physiologically, and how far genetically? In the first place, all the piebalds, roans and dominant whites must be eliminated from consideration. They are doubtless as distinct from true albinism, physiologically, as experiments with the laboratory rodents have shown them to be, genetically. There remain, however, numerous pink-eyed, red-eyed, perhaps even black-eyed, whites, reported in all classes of vertebrates, which may be truly homologous (HAECKER 1918, DUNN 1921). The genetical studies indicate that true

incomplete albinism is to be looked for in varieties in which both black and yellow are reduced in intensity, the latter more drastically. Dilution of black alone or of yellow alone, when both colors are present, may be rejected. Moreover, not all simultaneous dilution of black and yellow is related to albinism. The type of dilution in which black is reduced to a maltese color, and yellow to cream, as found in blue mice and rabbits and in maltese cats, has been shown in all three of these cases to be transmitted independently of albinism. In albino-series dilution, black seems always to be reduced to a brown color resembling human brown hair.

It is a remarkable fact that only one series of factors answering the above description has been found in each of the four laboratory rodents. This is not because of the rarity of mutations, as multiple allelomorphs of albinism have been found in each case. At least two were first found in animals caught wild. There is a strong indication here that just one physiological process, interference with which can lead at a single step to albinism, is involved in each case, and that in each case this is controlled primarily by just one gene.

There is direct genetic evidence tending to connect albino factors in three species. Albinism in the rat is linked very closely with "red-eyed yellow" and less closely with "pink-eyed yellow," two varieties in which black is greatly reduced in intensity, but yellow is unaffected (CASTLE 1916, 1919, DUNN 1920). Albinism in the mouse is also linked, but not very closely, with a pink-eyed variation closely resembling that of the rat (HALDANE, SPRUNT and HALDANE 1915, CASTLE 1919, DUNN 1920). Complete albinism in the wood mouse, *Peromyscus maniculatus*, is closely linked with "pallid," a variation closely resembling red-eyed yellow of rats (SUMNER 1922). In the guinea-pig, it is true, albinism seems to be wholly independent of a variation (*p*) resembling pink-eyed yellow of rats and mice. It is asking a good deal of the chromosomes, however, to expect them to maintain their identity in the enormous period since the separation of the hystricomorph and murimorph rodents.

No other mammals have been investigated with sufficient thoroughness to give evidence as to whether more than one apparent albino series occurs within the same species. Albinism of apparently the same kind as in those cited above is, however, very widespread. In the human species, albinism is, of course, well known. Unfortunately, there seems to be much confusion in the literature with types of dilution of color of entirely different kinds. The researches of PEARSON, NETTLESHIP and USHER (1913) indicate that human albinos often have considerable brown pigment. They also, however, describe albinos with yellow or even red in the hair, but no brown.

These seem to be more comparable to the genetically unrelated red-eyed and pink-eyed yellows mentioned above, in which a factor which specifically reduces black pigment is involved. It seems clear that such dilute variations as the yellowish-haired, hazel-eyed "White Indians" of Darien discovered recently by the Marsh expedition and which the writer has had the opportunity of observing, have nothing to do with albinism as the term is understood in the laboratory rodents. If an albino allelomorph is responsible for the paleness of the yellow (as contrasted with red) in these White Indians, the same factor must also be present in the normally-colored brown Indians from whom they segregate, if the analogy with rodent albinism is carried out.

Among horses, WRIEDT (1918) finds that albinism (white with glass eye) is incompletely recessive to the intense colors, such as black, bay and chestnut. In the heterozygotes red or yellow pigmentation is reduced to a pale-cream, but black is not appreciably modified. There is thus indication of a more drastic dilution of red than of black. There are more or less similar dilute variations and also albinos in cattle, but the mode of inheritance has not been satisfactorily worked out.

Albinos with or without pink eyes are relatively common among birds. Perhaps the most interesting possible parallel to the series in rodents is that in the ring-doves. The white ring-dove, with only traces of brownish pigment in a half ring on the neck and with deficient pigmentation of the eyes, is a sex-linked recessive to the blond variety (*Streptopelia risoria*). The latter has a black half ring on the neck and sufficient brown pigment elsewhere in the plumage to give a pale fawn color and dark eyes (STRONG 1912, WHITMAN and RIDDLE 1919). WHITMAN made additional crosses involving a number of much more intensely colored wild species. There is clear evidence in certain of these crosses (as with *Streptopelia humilis* and *Turtur orientalis*) that white is a sex-linked recessive to the dark color. This might be the same sex-linked difference as that by which white differs from blond. Appropriate crosses indicated, however, that blond also is a sex-linked recessive to dark color. While the authors do not express their results in the Mendelian terminology, the simplest interpretation which is in harmony with the data (with one apparent exception) is that intense, blond and white form a series of triple allelomorphs. There is also a sex-linked pair of factors in pigeons,—dominant intensity of blacks, blues and reds as opposed to dilution of duns, silvers and yellows (COLE 1912), which has some similarity with the albino series of mammals. Whether there is any real homology between the dove and pigeon series or between either and albinism, it is too early to say.

Among lower vertebrates, HAECKER (1918) has shown that an incomplete albino of the salamander, *Ambystoma tigrinum*, is imperfectly recessive to the normal variety. These albinos had grayish areas in the skin, containing both black and yellow melanophores, and also had pigment in the iris, but red pupils, owing to deficient retinal pigmentation. WHITING (1919) has described two interesting tadpoles of the green frog (*Rana clamitans*). In one, yellow seemed entirely lacking, black was reduced to a very light sepia, but both iris and pupil were dark. The other was yellow with very little if any black, and with golden iris and pink pupil. The former might well be comparable to rodent albinism, the latter certainly was not. AIDA (1921) has investigated the genetics of a number of varieties of the fish, *Aplocheilichthys latipes*. One recessive factor reduces black to blue black. The same factor reduces red to white. There is thus some resemblance to the working of factor c^r in guinea-pigs.

The following general conclusions as regards homologies in different species seem warranted: Disturbances in melanin pigmentation which may be homologous to guinea-pig albinism, are relatively common throughout the vertebrate phylum. Certain of the peculiarities of the guinea-pig series of allelomorphs, a particular type of dilution of black associated with a more drastic dilution of yellow and occurring in eyes as well as skin, are found widely distributed as the effects of a more or less completely recessive unit-factor variation. In the mammals most intensively studied there is a rather strong indication that there is only one process liable to such an effect, and that this is controlled essentially by only one gene.

SUMMARY

As the writer may have gone into speculation at some points to a greater extent than the reader may think warranted, it will be well to distinguish carefully in the summary what is fact and what is speculation.

The existence of at least five allelomorphs in the albino series of guinea-pigs, C , c^k , c^d , c^r and c^a , the writer wishes to present as the simplest description of the genetic facts. The average grades of intensity of the 15 compounds of these factors, with respect to black and yellow pigmentation of the fur and black in the eyes, are also presented as facts within the limits indicated by the probable errors. It is desired to call attention to the fact that the order of intensity of the compounds with respect to black in the fur is unmistakably different from the order with respect to yellow in the fur or black in the eyes.

Certain speculations are presented in the attempt to find order in the grades of black and yellow in the fur and black in the eye. It is found

that the compounds are, in the main, such as would result if each of the two genes in the zygote affect pigment production independently. The relative effects of the genes on yellow (in the order c^a , c^r , c^d , c^k and C) are best illustrated by the grades of intensity of the compounds of each with albinism, namely, 0.0, 0.0, 4.1, 4.6 and 10.6, respectively. The relative effects on black may be illustrated by the sepia grades of the same compounds, namely, 0.0, 8.5, 7.5, 11.5 and 14.0, respectively. The relative effects on eye color may be indicated by the qualitative terms, pink, light red and black, for the last three.

There is complete dominance of the intensity factor C over all of the others, suggesting that in these compounds some factor outside of the albino series plays the rôle of a limiting factor.

It is suggested that the factors of the albino series determine the rate of some one process fundamental to all pigmentation and that the irregularities in the order of effect on different kinds of pigment, or in different regions of the body, are due to subsequent physiological processes with which the albino series of genes has nothing to do. Among such processes one which determines a higher threshold for yellow than for black finds extensive corroboration in the albino series of other mammals. A tendency for the production of yellow to interfere with the production of black is suggested by the guinea-pig series. The differences between intensity of black in the fur and the eye suggest that competition from yellow is lacking in the eye, which thus shows more simply than the fur the effects of the different genes on intensity of black.

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APPENDIX—TABLES 9 to 21

TABLE 9

The intensity of sepia among black-eyed and red-eyed dilutes of different genetic constitutions.

GENETIC CONSTITUTION	CRITERION*	GRADE OF SEPIA												NUMBER	MEAN
		3	4	5	6	7	8	9	10	11	12	13	14		
$c^k c^k$	A	1	1	2	13.50 ± .35
	B	4	6	5	15	13.07 ± .13
	C	3	12	5	20	13.10 ± .11
	D	3	5	4	12	13.08 ± .14
$c^k c^d$	A	1	..	1	2	11.00 ± .36
	B	1	10	12	..	23	12.48 ± .11
	C	1	1	14.00 ± .51
	D	1	1	..	2	12.50 ± .36
$c^k c^r$	A
	B	6	10	33	49	13.55 ± .07
	C	1	2	5	8	16	13.25 ± .12
	D	5	2	7	13.29 ± .18
$c^k c^a$	A	13	31	46	11	..	101	11.54 ± .05
	B	12	32	53	10	..	107	11.57 ± .05
	C	1	14	6	1	..	22	11.32 ± .11
	D	1	7	5	1	..	14	11.43 ± .14
$c^d c^d$	A	4	20	4	14	42	9.67 ± .14
	B	2	..	5	9	13	7	9	1	..	46	10.02 ± .14
	C
	D	2	1	2	1	6	10.33 ± .38
$c^d c^r$	A	3	20	8	..	31	12.16 ± .10
	B	1	..	3	12	22	29	67	12.10 ± .07
	C	3	15	9	..	27	12.22 ± .11
	D	7	2	1	..	10	11.40 ± .18
$c^d c^a$	A	1	3	10	28	43	48	6	1	140	7.04 ± .06
	B	13	28	40	29	9	119	6.94 ± .06
	C	1	1	8	7	2	19	7.42 ± .16
	D	1	1	6.00 ± .71
$c^r c^r$	A	3	21	10	..	34	13.21 ± .10
	B	1	..	2	4	11	10	28	12.93 ± .11
	C	1	3	2	..	6	13.17 ± .24
$c^r c^a$	A	1	5	10	25	12	5	7	6	71	8.59 ± .12
	B	1	11	15	12	1	2	42	8.17 ± .16
	C	5	10	6	3	3	1	28	8.70 ± .19

* Groups A and B include all in experiments J and K through 1923 (with the exceptions noted in the text). Group A includes those from matings which could only produce the type of black-

eyed or red-eyed dilute designated. Group B includes all other graded sepias in these experiments (compare tables 13 to 20). The grade of yellow was the principal criterion in distinguishing classes $c^k c^k$, $c^k c^d$, and $c^d c^d$ with yellow of grades 7 and 8, from classes $c^k c^r$, $c^k c^a$, $c^d c^r$, and $c^d c^a$ with cream of grades 3, 4 and 5). The grade of sepia and the expected ratio were used when necessary, however. Group C includes all of definitely known constitution from experiments L, N and UR during the same period. Group D includes sepias from L, N and UR which produced two or more types of black-eyed dilutes and for which the grade of yellow was used as a criterion for separation.

TABLE 10

The intensity of yellow among intense and dilute young of different genetic constitutions.

GENETIC CONSTITUTION	CRITERION*	GRADE OF YELLOW											NUMBER	MEAN		
		3	4	5	6	7	8	9	10	11	12	13				
CC	A	†	†
Cc^k	A	5	8	2	..	15	10.80 ± .11
Cc^d	A	1	18	2	21	10.05 ± .09
Cc^r	A
Cc^a	A	2	23	14	39	10.31 ± .07
C—	B	1	66	83	13	1	164	10.68 ± .03
$c^k c^k$	A	5	5	7.00 ± .10	..
	B	14	3	17	7.18 ± .05	..
	C	1	16	2	19	7.05 ± .05	..
$c^k c^d$	A	1	1	2	7.50 ± .20	..
	B	23	3	26	7.12 ± .06	..
	C	1	1	8.00 ± .34	..
$c^k c^r$	A
	B	1	12	25	1	39	4.67 ± .07	..
	C	1	8	6	2	17	4.53 ± .10	..
$c^k c^a$	A	2	49	33	8	92	4.51 ± .05	..
	B	..	34	35	11	2	82	4.77 ± .05	..
	C	..	17	3	1	21	4.24 ± .11	..
$c^d c^d$	A	3	32	7	42	7.10 ± .06	..
	B	2	10	45	7	64	6.89 ± .05	..
	C
$c^d c^r$	A	..	33	2	35	4.06 ± .04	..
	B	5	48	10	63	4.08 ± .03	..
	C	..	24	3	27	4.11 ± .05	..
$c^d c^a$	A	3	91	25	119	4.18 ± .03	..
	B	7	94	20	2	123	4.14 ± .03	..
	C	..	14	2	16	4.13 ± .08	..

* The groups A, B and C have the same significance as in table 9. Groups A and C include young whose constitution is uniquely determined from their ancestry, from experiments J and K and from L, N and UR, respectively. Group B includes all other graded yellows from experiments J and K assigned on the basis of both grade of yellow and sepia and of expected ratio of classes.

† Inbred family 2 is regularly graded 10, while family 32 is graded 13. Both are CC.

TABLE 11

The intensity of sepia in all compounds of the albino series. The figures are the sums of the separate groups (A, B, C and D) as given in table 9.

GENETIC CONSTITUTION	WHITE	GRADE OF SEPIA												NUMBER	MEAN	σ
		Light				Medium				Dark						
	0	3	4	5	6	7	8	9	10	11	12	13	14			
C—	x	...	14.00	...
<i>c^kc^k</i>	10	24	15	49	13.10 ± .07	0.74
<i>c^kc^d</i>	1	1	12	13	1	28	12.43 ± .10	0.75
<i>c^kc^r</i>	1	8	20	43	72	13.46 ± .06	0.71
<i>c^kc^a</i>	27	84	110	23	..	244	11.53 ± .03	0.79
<i>c^dc^d</i>	2	..	9	31	18	23	10	1	..	94	9.88 ± .09	1.36
<i>c^dc^r</i>	1	..	3	25	59	47	..	135	12.09 ± .05	0.84
<i>c^dc^a</i>	..	1	3	24	58	91	84	17	1	279	7.02 ± .04	1.05
<i>c^rc^r</i>	1	..	2	8	35	22	68	13.09 ± .07	0.86
<i>c^rc^a</i>	..	1	6	26	50	30	9	12	7	141	8.49 ± .09	1.52
<i>c^ac^a</i>	x	0.00	...

TABLE 12

The intensity of yellow in all compounds of the albino series. The figures are the sums of the separate groups (A, B and C) as given in table 10.

	GRADE OF YELLOW													NUMBER	MEAN	σ
	White	Cream			Yellow				Red							
	0	3	4	5	6	7	8	9	10	11	12	13				
C—	4	112	107	15	1	239	10.57 ± .03	0.64	
<i>c^kc^k</i>	1	35	5	41	7.10 ± .03	0.32	
<i>c^kc^d</i>	24	5	29	7.17 ± .05	0.42	
<i>c^kc^r</i>	..	2	20	31	3	56	4.63 ± .05	0.61	
<i>c^kc^a</i>	..	2	100	71	20	2	195	4.59 ± .04	0.73	
<i>c^dc^d</i>	2	13	77	14	106	6.97 ± .04	0.59	
<i>c^dc^r</i>	..	5	105	15	125	4.08 ± .02	0.39	
<i>c^dc^a</i>	..	10	199	47	2	258	4.16 ± .02	0.47	
<i>c^rc^r</i>	x	0	0	
<i>c^rc^a</i>	x	0	0	
<i>c^ac^a</i>	x	0	0	

TABLES 13 to 20.—These tables give the results of all matings in experiments J and K through 1923 (with the exceptions noted in the test). All young are included with the few exceptions noted below each table. The young are assigned to the expected classes on the basis of sepia and yellow, and eye color. The grade of yellow is the primary criterion where more than one class of young is expected. Compounds $c^k c^k$, $c^k c^d$ and $c^d c^d$ with yellow of grades 7 to 8 being separated from $c^k c^r$, $c^k c^a$, $c^d c^r$, and $c^d c^a$ with cream of grades 3 to 5. Within these groups of compounds the grade of sepia is used as a criterion. Thus, $c^d c^a$ is separated from $c^k c^r$, $c^k c^a$ or $c^d c^r$ as of grade 9 or less, the latter classes being considered as of grade 10 or more. The separation of $c^k c^r$ (grade 13 or 14) from $c^k c^a$ or $c^d c^r$ (grades 10 to 12) where both should be produced, is less satisfactory. In the few cases in which both $c^k c^a$ and $c^d c^r$ should be produced, these are assigned merely by expected ratio. There were no matings which produced more than one of the varieties with yellow ($c^k c^k$, $c^k c^d$, $c^d c^d$). Where both kinds of red-eyed dilutes were expected ($c^r c^r$ and $c^r c^a$), the contrast in eye color and grade of sepia within the litter was used as far as possible. In a few cases it was necessary to draw an arbitrary line between grades 11 and 12 to separate them. Young were only assigned classes possible from their ancestry. The range of variation in each compound which this necessitated may be seen by a study of groups A and B in tables 9 and 10, since all graded young included in tables 13 to 20 are there included.

TABLE 13

The results of the matings in experiments J and K between albinos ($c^a c^a$) and each of the compounds of the albino series. It may be added that matings of type $CC \times c^a c^a$ have been made in other experiments and have produced only intense young (Cc^a). Matings of type $Cc^r \times c^a c^a$ have also been made in other experiments and have produced the two expected classes, intense (Cc^a) and light sepias with red eyes ($c^r c^a$). Matings of albino by albino have produced only albino young.

PARENTS	NUMBER OF MATINGS	GENETIC CONSTITUTION OF OFFSPRING											TOTAL
		C—	$c^k c^k$	$c^k c^d$	$c^k c^r$	$c^k c^a$	$c^d c^d$	$c^d c^r$	$c^d c^a$	$c^r c^r$	$c^r c^a$	$c^a c^a$	
$CC \times c^a c^a$..	x	x
$Cc^k \times c^a c^a$	3	15	19	34*
$Cc^d \times c^a c^a$	2	13	8	21
$Cc^r \times c^a c^a$..	x	x	..	x
$Cc^a \times c^a c^a$	5	30	43	73
$c^k c^k \times c^a c^a$	5	18	18
$c^k c^d \times c^a c^a$	8	32	40	72†
$c^k c^r \times c^a c^a$	5	23	21	..	44
$c^k c^a \times c^a c^a$	11	85	77	162
$c^d c^d \times c^a c^a$	6	67	67
$c^d c^r \times c^a c^a$	3	11	..	8	..	19
$c^d c^a \times c^a c^a$	21	87	105	192
$c^r c^r \times c^a c^a$	1	4	..	4
$c^r c^a \times c^a c^a$	1	2	1	3
$c^a c^a \times c^a c^a$	1	3	3

* Two black-eyed whites (either Cc^a or $c^k c^a$) omitted.

† 29 with cream but no sepia (equally likely to be $c^k c^a$ or $c^d c^a$) omitted.

TABLE 14

The results of the matings in experiments J and K between heterozygous red-eyed dilute ($c^r c^a$) and compounds in the albino series (except the matings included with an albino) included in table 13.

PARENTS	NUMBER OF MATINGS	GENETIC CONSTITUTION OF OFFSPRING											TOTAL	
		C-	$c^k c^k$	$c^k c^d$	$c^k c^r$	$c^k c^a$	$c^d c^d$	$c^d c^r$	$c^d c^a$	$c^r c^r$	$c^r c^a$	$c^a c^a$		
$CC \times c^r c^a$	x
$Cc^k \times c^r c^a$	2	12	12	17	41*
$Cc^d \times c^r c^a$	4	27	11	17	55†
$Cc^r \times c^r c^a$	x
$Cc^a \times c^r c^a$	2	18	6	10	34
$c^k c^k \times c^r c^a$	1	5	15	20‡
$c^k c^d \times c^r c^a$	x
$c^k c^r \times c^r c^a$	1	4	3	2	2	11+
$c^k c^a \times c^r c^a$	7	19	18	16	13	..	66§
$c^d c^d \times c^r c^a$	1	4	5	9¶
$c^d c^r \times c^r c^a$	2	3	2	3	1	9
$c^d c^a \times c^r c^a$	5	10	15	..	13	13	..	51**
$c^r c^r \times c^r c^a$	1	1	1	2
$c^r c^a \times c^r c^a$	3	26	50	20	..	96

* 7 with cream only (grades 4, 5) assigned 4 to $c^k c^r$ and 3 to $c^k c^a$.
 † 10 with cream only (grade 4, 5) assigned 5 to $c^d c^r$ and 5 to $c^d c^a$.
 ‡ 2 with cream only (grade 4) either $c^k c^r$ or $c^k c^a$ omitted.
 § 2 with cream only (grades 4, 5) assigned 1 to $c^k c^r$ and 1 to $c^k c^a$.
 + 10 with cream only (1 grade 6, 6 grade 4, 3 ungraded) assigned 5 to $c^k c^r$ and 5 to $c^k c^a$.
 ¶ 6 with cream only omitted.
 ** 1 with cream only assigned to $c^d c^r$ (might equally well be $c^d c^a$).

TABLE 15

The results of the matings in experiments J and K in which one of the parents was a homozygous red-eyed dilute ($c^r c^r$) and which are not included in previous tables.

PARENTS	NUMBER OF MATINGS	GENETIC CONSTITUTION OF OFFSPRING											TOTAL	
		C-	$c^k c^k$	$c^k c^d$	$c^k c^r$	$c^k c^a$	$c^d c^d$	$c^d c^r$	$c^d c^a$	$c^r c^r$	$c^r c^a$	$c^a c^a$		
$c^k c^d \times c^r c^r$	2	7	6	13*
$c^d c^d \times c^r c^r$	3	23	23
$c^d c^r \times c^r c^r$	3	20	..	14	34†
$c^d c^a \times c^r c^r$	2	8	12	20
$c^r c^r \times c^r c^r$	3	18	18

* 4 ungraded black-and-cream tortoise-shells (either $c^k c^r$ or $c^d c^r$) omitted.
 † 9 of uncertain eye color and without cream or white tortoise-shell markings in fur omitted (either $c^d c^r$ or $c^r c^r$).

TABLE 16

The results of the matings in experiments J and K in which one of the parents was a light dilute carrying albinism ($c^d c^a$) and which are not included in previous tables.

PARENTS	NUMBER OF MATINGS	GENETIC CONSTITUTION OF OFFSPRING											TOTAL
		C-	$c^k c^k$	$c^k c^d$	$c^k c^r$	$c^k c^a$	$c^d c^d$	$c^d c^r$	$c^d c^a$	$c^r c^r$	$c^r c^a$	$c^a c^a$	
$CC \times c^d c^a$	2	7	7
$Cc^d \times c^d c^a$	1	3	5	..	5	13
$Cc^r \times c^d c^a$	1	5	3	4	..	12
$c^k c^k \times c^d c^a$	1	7	..	9	16
$c^k c^r \times c^d c^a$	1	2	..	2	..	2	5	..	11*
$c^k c^a \times c^d c^a$	4	18	..	20	13	10	61
$c^d c^d \times c^d c^a$	1	1	..	2	3
$c^d c^r \times c^d c^a$	2	3	7	4	..	6	..	20†
$c^d c^a \times c^d c^a$	8	37	..	78	24	139

* 4 dark sepia-cream, divided equally between $c^k c^a$ and $c^d c^r$.

† 1 with cream only (either $c^d c^r$ or $c^d c^a$) assigned to $c^d c^a$.

TABLE 17

The results of the matings in experiments J and K in which one of the parents was a light dilute carrying red-eye ($c^d c^r$), and which are not included in previous tables.

PARENTS	NUMBER OF MATINGS	GENETIC CONSTITUTION OF OFFSPRING											TOTAL
		C-	$c^k c^k$	$c^k c^d$	$c^k c^r$	$c^k c^a$	$c^d c^d$	$c^d c^r$	$c^d c^a$	$c^r c^r$	$c^r c^a$	$c^a c^a$	
$CC \times c^d c^r$	1	6	6
$Cc^d \times c^d c^r$	1	1	1
$c^k c^a \times c^d c^r$	1	4	5	6	..	5	..	20*
$c^d c^d \times c^d c^r$	6	25	33	58†
$c^d c^r \times c^d c^r$	6	18	38	..	21	77

* 1 cream (either $c^k c^r$ or $c^d c^a$) assigned to $c^d c^a$.

† 10 sepias (grades 9 to 12) divided equally between $c^d c^d$ and $c^d c^r$.

TABLE 18

The results of the matings in experiments J and K in which one of the parents was a homozygous light dilute ($c^d c^d$) and which are not included in previous tables.

PARENTS	NUMBER OF MATINGS	GENETIC CONSTITUTION OF OFFSPRING											TOTAL
		C-	$c^k c^k$	$c^k c^d$	$c^k c^r$	$c^k c^a$	$c^d c^d$	$c^d c^r$	$c^d c^a$	$c^r c^r$	$c^r c^a$	$c^a c^a$	
$CC \times c^d c^d$	3	22	22
$Cc^a \times c^d c^d$	1	23	15	38
$c^k c^a \times c^d c^d$	1	6	6	12
$c^d c^d \times c^d c^d$	8	65	65

TABLE 19

The results of the matings in experiments J and K in which one of the parents was a dark dilute ($c^k c^a$, $c^k c^r$ or $c^k c^k$) and which are not included in previous tables.

PARENTS	NUMBER OF MATINGS	GENETIC CONSTITUTION OF OFFSPRING											TOTAL
		C-	$c^k c^k$	$c^k c^d$	$c^k c^r$	$c^k c^a$	$c^d c^d$	$c^d c^r$	$c^d c^a$	$c^r c^r$	$c^r c^a$	$c^a c^a$	
$CC \times c^k c^a$	3	40	40
$Cc^r \times c^k c^a$	1	4	4	0	..	8
$Cc^a \times c^k c^a$	3	11	4	9	24
$c^k c^k \times c^k c^a$	1	..	1	4	5
$c^k c^a \times c^k c^a$	6	..	20	30	19	69*
$c^k c^k \times c^k c^r$	1	..	5	..	2	7†
$c^k c^r \times c^k c^r$	2	..	1	..	3	2	6‡
$CC \times c^k c^k$	1	14	14
$Cc^d \times c^k c^k$	1	6	..	2	8
$Cc^a \times c^k c^k$	1	7	5	12

* A black-eyed white (either $c^k c^k$ or $c^k c^a$) assigned to $c^k c^a$.

† 9 blacks (4 grade 14, 4 grade 13, 1 ungraded) omitted.

‡ 8 blacks (3 grade 14, 4 grade 13, 1 grade 12, eye colors uncertain) omitted.

TABLE 20

The results of the matings in experiments J and K between intense animals ($C- \times C-$).

PARENTS	NUMBER OF MATINGS	GENETIC CONSTITUTION OF OFFSPRING											TOTAL
		C-	$c^k c^k$	$c^k c^d$	$c^k c^r$	$c^k c^a$	$c^d c^d$	$c^d c^r$	$c^d c^a$	$c^r c^r$	$c^r c^a$	$c^a c^a$	
$Cc^a \times Cc^a$	2	28	8	36
$Cc^r \times Cc^r$	2	22	5	27
$Cc^d \times Cc^a$	1	10	3	13
$Cc^k \times Cc^k$	1	13	5	18
$CC \times C-$	3	34	34

TABLE 21

The differences in the grades of sepia of young of different genetic constitution born in the same litters in experiments J and K.

LITTER MATES	DIFFERENCE IN GRADE WITHIN LITTER											NUMBER	AVERAGE DIFFERENCE	AVERAGE DIFFERENCE FROM TABLE 11	
	-3	-2	-1	0	1	2	3	4	5	6	7				8
$c^k c^r - c^d c^a$	1	..	1	..	2	6.0	6.5
$c^r c^r - c^d c^a$	1	..	1	..	2	6.0	6.1
$c^k c^d - c^d c^a$	1	2	6	3	4	1	17	5.6	5.5
$c^d c^r - c^d c^a$	1	..	3	5	6	1	1	2	19	4.7	5.0
$c^k c^a - c^d c^a$	9	6	10	6	2	..	33	4.6	4.5
$c^d c^d - c^d c^a$	5	..	5	5	2	17	3.9	2.9
$c^r c^a - c^d c^a$	1	..	1	9	4	3	1	19	0.5	1.5
$c^k c^r - c^r c^a$	1	2	13	2	..	18	5.6	5.0
$c^r c^r - c^r c^a$	7	6	7	10	30	4.7	4.6
$c^k c^d - c^r c^a$	1	..	1	..	1	..	3	5.0	4.0
$c^d c^r - c^r c^a$	3	6	2	1	1	13	3.3	3.5
$c^k c^a - c^r c^a$	2	2	1	4	10	19	3.0	3.0
$c^r c^r - c^d c^d$	1	..	3	4	3.5	3.2
$c^d c^r - c^d c^d$	3	10	10	8	31	1.7	2.1
$c^r c^r - c^d c^r$	4	3	7	14	1.2	1.1
$c^k c^k - c^k c^a$	1	1	11	13	1.8	1.6
$c^k c^r - c^k c^a$	1	11	3	15	2.1	1.9
$c^k c^d - c^k c^a$	9	3	12	1.2	0.9