

## NOTES AND LITERATURE

### RECENT EXPERIMENTS ON THE INHERITANCE OF COAT COLORS IN MICE

The domesticated varieties of rodents, rabbits, guinea-pigs, rats and mice, have furnished exceptionally favorable material for analyzing the facts of Mendelian inheritance. The simple formulæ that at first sufficed to explain the results have become more complex as the work has progressed until, at present, the situation has become not a little intricate owing to the different interpretations that the facts have received. This complication is, however, paralleled by progress in the study of plants, fowls, pigeons, sheep, swine, beetles, moths, snails, etc. Despite the elaboration that Mendel's originally simple law has undergone, it is significant how little there is in later discoveries that is believed to be incompatible *in principle* with this law, which may seem to vindicate itself in every direction where new facts come to light. This is nowhere better illustrated than in the latest facts and newest theories relating to inheritance of color in mice.

The earlier work of Allen, Darbishire, Davenport and Cuénot has given the relative order of dominance of the colors. These stand yellow (Y), gray (G), black (B), chocolate (Ch) and white (W). Each color is dominant to all that follow it in the order given and recessive to all that precede. Cuénot's results with white mice—albinos—showed that albinos stand in a class by themselves. White mice may carry *latent*<sup>1</sup> the factor for producing any color, although so long as white mice are mated, they produce only white. Cuénot's suggestion has been widely adopted, namely, that two factors are essential to produce any color; one of these is common to all colors and is called the color producer (C), the other is specific for each special color (Y, G, B or Ch). When C is absent, no color can arise, although the other factor, the determinant, may be present; hence white mice are characterized by the absence of the color producer (C)

<sup>1</sup>The term "latent" has come to have another significance in recent work. In general it now means the presence of one factor only when two are necessary for the development of a character.

although they carry one or more of the color determiners. In fact no white mice are known in which all determiners are absent, and from the nature of the case none could arise. An example may make this clearer. It is assumed that white mice first arose by the loss of the factor C. Suppose this occurred in a gray mouse, CG. It would then contain only the factor G and no C. For convenience the absence of C is represented by the letter A. It might appear that nothing—no symbol—would better represent this condition, but in practise it is convenient to indicate the absence of C; or in other words, to represent the paired character (negative here) of C. A, therefore, is the allelomorph of C, *i. e.*, C and A form a pair of contrasted characters. An example will again make this evident. A gray mouse CG crossed with an albino mouse AG, produces a colored mouse with the formula, CGAG. In the germ cells of this mouse the contrasted characters are  $\frac{C}{A}$  and  $\frac{G}{G}$ , which give, as possible combinations, CG and AG. If we suppose two such mice, male and female, are paired, the possible unions of their germ cells may be represented thus:

$$\begin{array}{rcc}
 A\ G & & C\ G \\
 A\ G & & C\ G \\
 \hline
 AGAG & A\ G\ C\ G & \\
 & A\ G\ C\ G & CG \\
 \hline
 1AGAG; & 2AGCG; & 1CGCG
 \end{array}$$

The first term is a pure albino (extracted recessive); the second, a gray mouse carrying white recessive (a dominant recessive or heterozygote); the third term, a pure gray (extracted dominant). If the A's were omitted in the formulæ the outcome would be the same, but its presence is useful in arranging the contrasted characters in the germ cells; for, C always has A or C as its allelomorph, never G (or any other determiner). Hence the advantage of the symbol A. Failure to arrange the pairs of allelomorphs properly will give results incompatible with the theory.

In another graphic way the utility of representing an absent factor by some symbol can readily be shown. Suppose the characters are carried by certain material bodies in the egg—a purely preformation conception that dominates (or is latent in) all recent Mendelian speculation. If the color determiner is

carried by one body and the color producer by a different one, the pairs of allelomorphs will be  $\frac{C}{C}$ ,  $\frac{G}{G}$ ; every gray mouse carries these two pairs which separate at some time in the germ cells so that each germ cell (egg or sperm) carries one of each, C, G. Now an albino must arise by failure of a germ cell to contain C, the germ cell is simply 0 (zero) G, but since the same body that carried C may still be present (only one of its characters, namely C, being absent) the presence of that body is represented by A.

Let us now work out the case a step further. If this germ cell, AG, combines in fertilization with another germ cell, CG, of another individual, the resulting individual will be CGAG.

The allelomorph pairs will be  $\frac{C}{A}$ ,  $\frac{G}{G}$ . If such a mouse again pairs with a gray one, only gray mice will result. In time, however, enough mice of the formulæ CGAG will arise so that two such may meet; then and only then will an albino mouse *appear* amongst the gray offspring. Thus the conditions that produce the albino must arise two or more generations before the actual albino mouse is discovered.

This example shows, *on the theory*, how sports of this kind (recessive) that appear in nature are due to conditions that arise in the germ cells of an individual several generations earlier. The only possibility, on the theory, that such recessive sports could appear at once would be when several individuals changed in the same direction at the same time. Then the possibility of two germ cells of the same kind meeting would be realized. Recognizing the rarity of the appearance of sports, one may hesitate to assume that two such forms appear at the same time and pair with each other.

This view is based on the assumption that sports arise by the dropping out of one character in a germ cell. If the absent characters arise in some other way, after the germ cells have met for example, the situation is different, but the assumptions here made are in conformity with present-day development of Mendelian inheritance.

Our case was selected, however, not to illustrate how recessive sports arise and later appear, but to show how absent factors may be represented by bodies that in hybridizing become the partners of bodies containing that factor. Hence the supposed advantage of representing such absent factors by a definite

symbol standing for imaginary bodies; for such bodies, on this assumption, may carry other characters that remain, even though one be lost, and these other characters would still be subject to Mendelian rules and be associated with the absence of a character.

In the earlier work on mice and other forms the different colors, Y, G, B, Ch, W, are represented as allelomorphic pairs. Thus Y pairs with G, or G with B, or Y with Ch, etc. It follows, that if these color determiners are carried by definite bodies, these must always be the same kind of body or homologous bodies; otherwise they would not stand in this relation to each other. Thus a gray mouse paired with a chocolate would give a gray mouse, GCh whose germ cells would give the pair  $\frac{G}{Ch}$ . Two such mice paired would give:

$$\begin{array}{rcc}
 & G & Ch \\
 & G & Ch \\
 \hline
 G & G & G & Ch \\
 & & G & Ch & Ch & Ch \\
 \hline
 1 & G & G, & 2 & G & Ch, & 1 & Ch & Ch
 \end{array}$$

Similarly for every other combination. As a matter of fact gray by chocolate gives not only gray and chocolate but some black mice in the second generation. The formulæ fail to explain this result. Bateson, who was one of the first to point this out, was led therefore to a new formulation of the facts, and Cuénot to still another. Their views will be given later.

Another difficulty in connection with the inheritance of yellow was soon discovered by Cuénot. Yellow mice bred to yellow give not only yellow, but other colors as well. This would occur, of course, if the yellows were heterozygous. Thus YG by YCh would give yellows (YY, YG, YCh) and grays (CG). Some of the yellows should be YY, and two such paired should give only yellows. Cuénot was unable to produce such pure yellows. He therefore adopted a special explanation (selective fertilization) for this case. His view will come up again later.

A third complication arose in the case of dilute colors. In certain experiments, that need not be given here in detail, Cuénot found that the only assumption that would account for the facts was that two other factors—a strengthening or enforcing character (foncé) F, and a weakening or diluting factor

(dilué) D. The presence of F changes chocolate to black, the presence of D (in the absence of F) changes black to chocolate, and chocolate to dilute chocolate (or silver fawn).

In certain races of colored mice, the eyes are pink (absence of pigment) as in albinos. The presence of the factor that produces this condition has an effect on the coat color, according to Cuénot, hence he introduces a further set of factors that affect the color. By means of these several factors the inheritance in complex cases was explained.

It has been pointed out that in all gray rodents the color gray is due to a banded or barred condition of each hair. Each hair, in fact, contains bands of yellow, black and chocolate, arranged in definite sequence and in definite regions of limited extent. Hence gray is not a color in the sense that yellow or black or chocolate are colors, but is made up of all three. It is their arrangement that is the chief agent in producing gray animals. For this reason Castle has introduced a further factor, a barring or ticking factor instead of a gray factor. Hence gray is no longer allelomorphous to the other colors, but these colors are characterized by the absence of the barring factor and by the presence of one (or more) of the other colors.

Finally the hairs of black mice are known to contain chocolate pigment, so that black is not strictly allelomorphous to chocolate, although crossed with chocolate the Mendelian ratio for black and chocolate appears.

These and other discoveries show that the first representation of the pairs of characters will no longer suffice to account for the conditions that exist, although they give the Mendelian expectation for the cases first studied. We may next proceed to examine in more detail the hypotheses advanced to meet the more complex situation.

Bateson and his co-workers have discovered certain cases of inheritance which have led them to assume that *in crosses* the allelomorph of a given character is the absence of that character. For mice the following symbols are used:

CGB	.....	Gray or agouti
CgB	.....	Black
CGg	.....	Cinnamon agouti
Cgb	.....	Chocolate

So long as gray is bred to gray each character has its like for its allelomorph;  $\frac{C}{C}$ ,  $\frac{G}{G}$ ,  $\frac{B}{B}$ . But each germ cell will contain only one C, one G, one B. Similarly for any other color bred to its like.

If gray (CGB) is bred to chocolate (Cgb) the resulting mouse has the composition CGBCgb. The allelomorphs are  $\frac{C}{C}$ ,  $\frac{G}{g}$ ,  $\frac{B}{b}$ . These hybrids bred together give the results shown in the next table. The possible germ cells of each will be CGB, Cgb, CgB, Cgb, which by combination give the results here shown: 12 grays, 3 blacks, 1 chocolate.

CGB	CGB	CGB	CGB
CGB	Cgb	CgB	Cgb
gray	gray	gray	gray
Cgb	CGB	CGB	CGB
CGB	Cgb	CgB	Cgb
gray	gray	gray	gray
CgB	CgB	CgB	CgB
CGB	Cgb	CgB	Cgb
gray	gray	black	black
Cgb	Cgb	Cgb	Cgb
CGB	CGB	CGB	Cgb
gray	gray	black	chocolate

Thus the black mice that appear in this cross in the second generation are due to the absence of G and to the presence of the factor B. The single chocolate amongst the 16 mice is due to the absence of both G and B in the presence of C. Hence, Miss Durham recognizes chocolate (Ch) and color factor (C) as the same. Cuénot accounts for the results as follows. The gray mouse has the strengthening factor F along with C and G. The chocolate mouse has the diluting factor D along with C and Ch. The combination gives FCGDCh. The pairs are  $\frac{F}{D}$ ,  $\frac{C}{C}$ ,  $\frac{G}{Ch}$ . Omitting C, present in all combinations, we find the possible combinations are FG, FCh, DG, DCh. Two such mice crossed give the kinds of offspring shown in table on page 500.

The results are 9 gray, 3 dilute gray, 3 black, 1 chocolate, and these are the actual numbers realized. The dilute grays are grays without black and are known as cinnamon agoutis. Whenever F occurs with Ch the combination gives black, whenever D occurs alone with Ch (once) the result is chocolate.

FG	FG	FG	FG
FG	FCh	DG	DCh
gray	gray	gray	gray
FCh	FCh	FCh	FCh
FG	FCh	DG	DCh
gray	black	gray	black
DG	DG	DG	DG
FG	FCh	DG	DCh
gray	gray	gray	gray
DCh	DCh	DCh	DCh
FG	FCh	DG	DCh
gray	black	gray	chocolate

Both hypotheses account for the numerical outcome. Some other criterion must decide between them. The criterion is found in the recent work of Miss Florence M. Durham who has pointed out that chocolate can not be dilute black, since a dilute form of black is known, which is quite different from chocolate.<sup>2</sup> Let us examine her results.

Black and chocolate are found either in a dense condition when the mouse is called black or chocolate, or in a dilute state, *i. e.*, with the pigment granules scattered. Dilute black is blue and dilute chocolate is silver fawn in the "fancy." Black dominates blue and chocolate dominates silver fawn on the older terminology. But it is known that black mice often contain chocolate whose presence is obscured by the darker color, black. This relation Bateson calls epistatic. In the same sense black is epistatic to blue; and chocolate is epistatic to silver fawn.

Black crossed with blue gives black only. Such heterozygous blacks inbred give 3 blacks to 1 blue. Similarly chocolate crossed with silver fawn gives chocolate. These inbred give 3 chocolate to 1 silver fawn.

The most interesting result reported by Durham, is seen when black, *i. e.*, blue, is crossed with chocolate. The result is black, because the chocolate supplies the strengthening factor and makes the dilute black dense black which is epistatic to chocolate.<sup>3</sup> In

<sup>2</sup> There may be two quite distinct meanings however attached to "dilute." Cuénot means the black pigment is changed to chocolate pigment. Durham means that the black pigment granules are sparse in the dilute form. See next footnote.

<sup>3</sup> This experiment shows that Durham's interpretation of the dilute color is correct; Cuénot's is incompatible with the experiment, unless the factor for Durham's dilute colors is different from the diluting factor of Cuénot.

the second generation such black mice give approximately  
9 black, 3 blue, 3 chocolate, 1 silver fawn,  
which is the Mendelian expectation.

When blues are mated to silver fawns the offspring are all blue. These inbred give three blues to 1 silver fawn.

Miss Durham's hypothesis gives a consistent account of the relation of the dense and dilute colors to each other.

The dilute colors are modified to some extent, as Cuénot first showed, by the condition of the eye color. Most mice with colored coats have black eyes. The black eye is due to black pigment in most cases, but in chocolates and in some yellows the dark eye is due to chocolate pigment, as Castle and Durham have independently found. A silver fawn with pink eyes may be of a different color from a silver fawn with dark eyes. How this modification results is not yet known. In fact, this relation of dilute colors to eye color offers a promising field for further inquiry.

An examination of the hair of dilute mice shows great differences in the amount of pigment in each hair and the color of the animal is modified by the average number of hairs of a given kind. A considerable range of shades is evident. Whether this is only a fluctuating character, or whether pure races of different shades can be made that give Mendelian proportions, if crossed, remains to be worked out. It is not entirely certain, I think, that the pigment granules themselves are not only scattered to varying degrees but may be even lighter or darker. Whether this is due only to size or to another factor is not yet known.

These dilute colors should combine with ticking to produce different shades of gray in addition to cinnamon agouti. Some of the grays that I have met with appear to fall under this head.<sup>4</sup> Whether the diluting factor for black and chocolate will act as a diluter for yellow is not known. Here we meet with a question of great importance in further study of the colors in mice.

In addition to albinos with pink eyes, white animals with black eyes are known to occur in many groups of animals. Such a race of fancy mice exists. Miss Durham reports that these white mice crossed with colored mice with uniform coats produce

<sup>4</sup> Thus cinnamon agouti crossed to silver fawn may produce in the second generation a pinkish agouti with light chocolate in place of dense chocolate.



in the first generation some spotted mice. This result I have also repeatedly obtained. It remains to be discovered what relation exists between the white of such mice and the white of common spotted mice, for in these the spotting disappears in the first generation. It appears that the white mice with black eyes are derived from spotted mice in which the spotting has been carried so far that pigment remains in the eyes alone. If these mice are only extremes of the spotted conditions the results seem to indicate that a recessive character has been changed to a partially dominant one. Perhaps one might say that physiologically it has become stronger. On the other hand, these black-eyed white mice may have arisen not from extremes of ordinary spotted mice but from a different relation between black and white. It is interesting, however, to note that in rats the recessive spotted coat also partially dominates in the first generation.

Cuénot has shown that ordinary spotted mice behave towards mice with uniform coats as a simple recessive, appearing in the second generation as 1 to 3. But I have found in practise that it is almost impossible to give an exact classification of the mice in the  $F_2$  generation. In some individuals there may be only a small white tip to the tail, or only a few hairs may be white. Whether to classify such mice as dominant or recessive is largely arbitrary. White hairs not infrequently appear in mice that seem to be uniform in color. I find them quite abundant in wild black rats (*Mus rattus*). In man they appear in old age, and in horses when the skin is injured, etc. These considerations raise the question whether the problem may not after all be physiological, the result being due to the activity of the cells rather than to the absence of factors in the sense in which that term is ordinarily used in Mendelian hypotheses. If so, the entire result may be one of physiological activity rather than one of presence and absence of factors in a morphological sense.

The inheritance of the yellow color in mice has been a standing puzzle. Cuénot attempted to explain the facts on the assumption that a yellow bearing sperm can not fertilize an egg bearing this color, but can fertilize any other sort of egg. In other words selective fertilization takes place. Hence every yellow individual contains latent another color; it is yellow because yellow "dominates" (?) the other colors. But if selective fertilization can take place in regard to the individual characters

carried by the germ we introduce a conception entirely foreign to the whole Mendelian scheme. There is no evidence of selective fertilization *in this sense* known elsewhere and it seems a very questionable advantage to introduce the factor into the Mendelian process. The evidence that Cuénot brought forward in a second paper to show that selective fertilization takes place is open to criticism. He points out that since half the eggs can not be fertilized by half the sperm, there should be fewer young born when yellow is crossed with yellow than when yellow is crossed with any other color. His data show in fact a lower birth rate for yellow by yellow than when yellow is fertilized by other colors. Two objections to this argument may be advanced. First we must suppose that there are sufficient sperm present to fertilize the few eggs set free at each menstruation. Even if a yellow egg is not fertilized by a yellow sperm it should be fertilized by one of the other sperms. Second the fertility of the yellow mice is in my experience lower than that of other colors.

In order to avoid the hypothesis of selective fertilization and accepting Cuénot's statement that pure (homozygous) yellow mice do not exist, I suggested tentatively that the yellow-producing factor is not allelomorphie to the other colors, but that the germ cells of yellow mice are represented by the symbols Y(B), B(Y), to take a single example; in other words that yellow and the other color, black in this case, alternately dominate and recede. In this way the numerical results follow. I went so far as to suggest, as a theoretical possibility, that a similar mechanism might explain the alternate nature of the germ cells in all Mendelian cases and pointed out how this view could be tested. I have made one such test with entirely negative results, so that I think this interpretation must be abandoned.

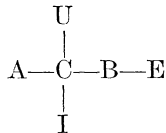
An experiment that I made with yellow mice showed, however, that the yellow bearing germ cells of yellow mice do carry other color factors than yellow, and this result, which is not in harmony with Cuénot's assumption for the behavior of yellow color in the gametes, offers the possibility of a different explanation. I crossed a yellow mouse with a spotted black mouse of known ancestry—it carried black only. Some of the offspring were yellow. Two of these inbred gave yellows, blacks, chocolates and albinos. Obviously the yellow bearing germ cells

of the grandparent carried the chocolate determiner since this was known to be absent in the black grandparent. Hence the yellow germ cells transmit the determiners for other colors.

Cuénot has objected to this conclusion on the ground that the chocolate grandchild was due to a diluting factor carried by the yellow grandparent. This objection would be valid if chocolate is the dilute form of black, but Miss Durham has shown that the dilute form of black is not chocolate and that chocolate itself has also a dilute form. This relation I have also seen in my experiments. Furthermore had there been a diluting factor in my original yellow, of which there is no evidence, I should have obtained blues and silver fawns in some of the descendants that were inbred for some time but this is not the case.

It is probable therefore that the yellow color is not the allelomorph of the other colors but may be transmitted along with them. Its allelomorph would be in Bateson's sense the absence of yellow. Even this assumption fails however to show why pure yellows do not appear, and we must look still further for an explanation of the behavior of yellow in inheritance.

Castle has made some important suggestions that bear on this question. The gray coat of rabbits is due, according to his analysis to at least five distinct unit characters represented in the formula



C is the color producer; A is the factor for ticking; B stands for black; U for uniform (*i. e.*, not spotted) distribution of color; I is the intensifier or strengthener; and E a factor that governs the extension of black over the body. For a black rabbit the same formula holds with A left out. For a yellow rabbit E is replaced by R, a factor that stands for the absence of black. A sooty yellow rabbit is like the last with A absent.

It will be noticed that there is no factor in these formulæ for yellow, because yellow is assumed to be present in all these rabbits, but since it has never been *lost* its claim to be looked upon as a unit character is not established. Castle believes that yellow is always present if C is present. Yellow rabbits therefore differ from gray, as stated above in the absence of E (not

of B, black) by which is meant that black is prevented from developing except in the eyes and the skin of the extremities. How far further analysis will justify these conclusions is uncertain, but the interest of the hypothesis lies in the character of the attempted analysis, for the composition of races of different colors is no longer explained as the result of a single color determiner but as the outcome of a considerable number of such determiners. The more recent speculations in Mendelian inheritance show a strong tendency to follow this direction. It might be said that color depends on the absence of certain determiners rather than on the presence of a special one.

It does not appear that Castle's scheme for rabbits will apply to mice unless amended, for the relation of yellow to the other colors appears to be different, and there is no evidence to show that it is present in black or in chocolate.<sup>5</sup>

The most recent attempt to account for the heredity of yellow in mice is that of Hagerdoorn. He points out that there are several kinds of yellow mice, a conclusion familiar to every one that has bred the animals for certain individuals give only certain other colors than yellow in the offspring. I have examples of this in my own experiments. Moreover, one can determine what those other colors may be by crossing yellows with other colors and breeding together the yellow offspring. Hagerdoorn also assumes that, in some yellows at least, an inhibiting factor must be present. This point may seem not improbable<sup>6</sup> from the fact that two yellows may produce in addition to yellows, grays and blacks or chocolates. Since the parents carried the factors for these colors and since they did not appear their absence may be attributed to suppression. So far little exception can be taken to the view since it is in harmony with certain facts. But it is further assumed that the barring factor that determines the distribution of the pigments on the individual hairs is "composed of two factors, one of which is the modifying factor present in the 'dominant' strain of yellow rodents. Its action, we see, is a partial inhibiting of the two darker pigments whenever these are present with it in one zygote."<sup>7</sup> I therefore propose the name of 'inhibiting factor' for it." The other

<sup>5</sup> The grounds for this statement are given later in the case of mice.

<sup>6</sup> Unless yellow is formed by combination.

<sup>7</sup> As shown by the absence of black or chocolate in the yellow band of the hair.—T. H. M.

component of the barring factor is called the "marking factor." If the marking factor is present and not the barring, the mouse would be black. A black mouse therefore contains a yellow band but this can not be seen because the black and chocolate pigments obscure it. If this is correct one would expect to extract from a black mouse the yellow pigment by a solvent for yellow. I shall give below the evidence that negatives this conclusion.

Hagerdoorn also thinks that yellow may be due in some cases to the absence of all pigments but yellow. In such a case either the marking or the inhibiting factor may also be present without its presence being noticeable. The following six classes of yellow mice are recognized:

- (a) Present black, chocolate and yellow plus inhibiting factor.
- (b) Present chocolate and yellow plus inhibiting factor.
- (c) Present yellow plus inhibiting factor plus marking.
- (d) Present yellow plus inhibiting factor.
- (e) Present yellow plus marking factor.
- (f) Present yellow.

Hagerdoorn states that he has "proof" of the existence of five of these six groups. Group (e) alone has not yet been recognized. Moreover he obtained homozygous individuals of each of these groups. Homozygous individuals of the same group bred to each other produce pure yellow strains, that is, strains that never produce any other color than yellow. The reason that Cuénot and others never obtained pure yellow is due to the fact that they crossed yellows of different strains and under such circumstances mice of other colors will appear. In passing, however, it should be noted that in Hagerdoorn's classification of yellows if individuals of strains (a), (b), (d) and (f) were crossed only yellows should appear in the first and in all subsequent generations. Thus the chance of getting pure yellows is as four to two, and it does not seem probable with so much in favor of hitting upon these combinations that such strains would not have been obtained by Cuénot or Durham, who have studied the problem extensively.

Hagerdoorn's evidence in favor of his classification of yellow is obtained by crossing yellows, not with each other, but with mice of other colors or with albinos of known (?) composition. The pairings are too complicated to discuss here in detail and in the absence of numerical data, to show how often the results

cited occurred it would not be profitable to attempt to go further into the matter. One example alone of extreme importance may be cited. One yellow male mated to chocolate gave only chocolate young; the same male mated to black gave only black young. If the number of young is large enough to establish the case conclusively it is a distinct advance in our study of yellow mice. Hagerdoorn assumes that this yellow male contains yellow alone and that neither the barring nor the inhibiting factor is present. Hence the cross with black gives only black because the black obscures the yellow in the hair. Similarly for chocolate. If this is the correct interpretation as much yellow could be extracted from these hybrids as from a yellow mouse but this test was not made. The only other possible conclusion would be that not enough young were obtained to show that yellows were not produced by this pairing. We must await the publication of the numerical data. It should be added that the yellow male was tested by crossing with an albino strain possessing the barring factor and only yellow young appeared. This shows the absence of black or chocolate in the yellow, for were they present some gray mice should have appeared according to the hypothesis. Whatever discoveries the future has in store for us these experiments are of great interest, especially in so far as they point out a better method for studying yellows than any so far reported. The assumption that yellow pigment is present in black and chocolate can be readily tested. I have made such a test and find that black hairs put into caustic potash give no evidence of yellow to the extent that yellow exists in yellow hair as shown by the same solvent.<sup>8</sup> The fact that caustic potash also extracts chocolate to some extent complicates the result.

The hypothesis seems also to call for the presence of yellow pigment throughout the gray hair and not only in the yellow band. It is more difficult to test this view and observation would be of no avail since the yellow might be obscured by the presence of black or chocolate. It is a point of no small importance to remember that if an inhibiting factor combined with a marking factor gives the barred or ticked hair of gray mice these factors act at only a particular period in the formation of the hair by suppressing the development of black and chocolate, for the tip and the base of such a hair are dark. If mark-

<sup>8</sup> Whether some blacks exist without yellow is a further question not touched by this test.

ing here and elsewhere in animals is due to factors of the sort postulated they are controlled (?) by a periodic function of the hair bud. We meet here with the same problem the embryologist encounters in proportionate development or interrelation of the parts. Whether this is a dynamic *function* (epigenetic) or can be referred to a system of *factors* in the germ is a difficult problem and for the future to decide.

Before leaving this question of yellow mice a few well known facts may be stated. Yellows exist from a deep orange to a pale lemon yellow. All intermediate gradations may be found. Whether these are in reality a graduated series or a series of overlapping conditions we do not yet know. The presence of other pigments combined with yellow is also familiar to every student of these mice. If yellow is due to an inhibiting factor that factor must at times very imperfectly do its work of inhibiting. I have a race of sports of the house mouse with white bellies, gray backs and yellow sides. The hairs on the sides may be pure yellow, which should be due to the action of the inhibiting factor in this particular region only, since on the rest of the upper surface the hairs are ticked. Even in gray mice single hairs may be yellow.

In some yellow mice the belly is pure white. This must be due to a further factor that in this region inhibits the yellow, the yellow itself being the result of another inhibiting factor. In other words an inhibitor of yellow must also be postulated. It might be assumed of course that the white belly is due to the absence of yellow in the region, but since the mouse can produce yellow its absence in the belly must also be accounted for by some special assumption. Again we meet with the localization factor—a problem that Mendelian studies have scarcely yet approached except by the purest symbolic representations.

The fact that many rodents change the color of their hair according to age indicates that the physiological condition of the animal is an important factor in determining its color. If the mechanism of Mendelian inheritance involves only the shuffling of morphological determinants, as implied in many current conceptions of the mechanism of inheritance, the changes that take place in the same individual are difficult to understand unless it be admitted that temporal and local conditions affect the development of the determiners. Such an admission is practically equivalent to referring the development of a color,

for example, to the *extent* to which physiological (chemical) processes are carried out in an individual or part of an individual. Inheritance from this point of view would be a physiological process depending on an inherited degree of activity of the protoplasm (subject to local modifications) rather than the result of sorting out of morphological unities.

Since the preceding review and criticism was written an important paper by Oscar Riddle has appeared in which he takes the same position that I have done elsewhere<sup>9</sup> in regard to the process of Mendelian inheritance. He bases his criticisms on some facts concerning the changes that certain melanin colors undergo as the result of the stage of oxidation to which they are carried. If what happens outside the body furnishes any hint in regard to what takes place in the formation of color in animals and plants these facts rehearsed by Riddle are of great importance in relation to the inheritance of color-production. He writes:

Here is then a *possible* picture of the basis of Mendelian segregation and proportion, but without recourse to hypothetical "particles" or to immutable and immortal factors. An apparently very specific end-result of an oxidation would be traceable in the germ only in the strength or pitch of a general vital process, and not at all in mnemons or representative particles packed with unthinkable precision, order and potentiality into (presumably) the chromosomes. . . The nature of present Mendelian interpretation and description inextricably commits to the "doctrine of particles" in the germ and elsewhere. It demands a "morphological basis" in the germ for the minutest phase (factor) of a definitive character. It is essentially a morphological conception with but a trace of functional feature. Although heredity is quite surely a functional process of major complexity, it may be recalled that the primary and fundamental Mendelian conception of this process utilizes not a single finding of the science of biochemistry, . . . With an eye seeing only *particles*, and a speech only symbolizing them, there is no such thing as the study of *process* possible. . . It has been possible, I think, to show by means of what we know of the genesis of these color characters that the Mendelian description—of color inheritance at least—has strayed very wide of the facts; it has put factors in the germ cells that it is now quite certainly our privilege

<sup>9</sup> See Chapter XXVII in my "Experimental Zoology," 1907, where the same problem is discussed in relation to Sex Inheritance; and in my paper "What are 'Factors' in Mendelian Explanations," read January 1909, before the American Breeders Association, Vol. V, 1909.



to remove; it has declared discontinuity where there is now proved continuity; it has postulated preformation where there is now evident epigenesis.

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#### SOME EXPERIMENTS IN BREEDING SLUGS

Certain large naked mollusca or slugs, common in Europe, are noted for their numerous and striking color-variations, some of which seem to be correlated with climatic conditions. Little has been known concerning the inheritance of these color-forms, but Mr. Walter E. Collinge has recently made some experiments in breeding two of the species, *Arion ater* (or *empiricorum*) and *A. subfuscus*. The results of this work are given in the *Journal of Conchology*, the short paper containing them being Mr. Collinge's address as president of the Conchological Society, delivered October 17, 1908. As the publication is available to few in this country, and the facts cited are very interesting, it seems worth while to abstract part of them.

*Arion ater* is a very large and handsome slug, of which the following color-varieties were used or appeared in the experiments:

- (1) *ater*, pure black. I was not quite clear about the meaning