

GENETIC ASPECTS OF PIGMENT PRODUCTION IN THE GUINEA PIG¹

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Received March 14, 1941

INTRODUCTION AND REVIEW OF LITERATURE

THE purpose of the present study was to correlate the processes of pigment formation as observed in fetal and adult guinea pigs with the theory of color inheritance as presented by BOGART and IBSEN (1937). The effects of some of the color-determining factors of the guinea pig and the time and manner of their action have been described.

The foundations of the present knowledge of color inheritance in the guinea pig were laid by CASTLE and WRIGHT (1916), WRIGHT (1917, 1925, 1927), and others. WRIGHT (1917) advanced an enzyme theory of pigment production. In 1927 he presented this theory again in modified form and reviewed the literature on pigment production.

MAXIMOW and BLOOM (1934) summarized from a histological point of view the status of knowledge of pigment and its production in the skin and hair of man. GORTNER (1911) studied the chemical nature of the melanins. EDWARDS and DUNTLEY (1939) found a diffuse pigment in close association with granular pigment in the living human skin. GREMMEL (1939) reported that the coat color of horses was due to different arrangements and concentrations of one kind of granular pigment. He observed no diffuse pigment in horse hairs.

ESSKUCHEN (1927, 1930) described the development of pigment in cattle fetuses. He found two types of pigment cells in the skin; observed that dark color appeared earlier than red and that the skin of the extremities showed pigmentation first.

The relation of pigmentation to color inheritance in pigeons was investigated by HAWKINS (1931).

HUNT and WRIGHT (1918) made a number of microscopic observations on the hair of guinea pigs. They described black and "yellowish" granules and a yellowish diffuse pigment in sectioned hairs.

BOGART and IBSEN (1937) examined the hair and in some cases the skin of various domestic animals, particularly cattle, in an attempt to determine the effects of some color genes upon the pigmentation of the hair and skin.

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² The writers are indebted to DR. H. L. IBSEN and RALPH BOGART, who contributed valuable advice and criticism from the geneticist's point of view; and to LEE FENT, who prepared the photographs. DR. IBSEN selected the animals which were used; the KANSAS ACADEMY OF SCIENCE granted a part of the funds for the maintenance of the colony.

In guinea pigs, they found both granular and diffuse types of pigment in the hair. They distinguished between black and chocolate granules and found that variations in the shade of the diffuse pigment, as well as in the amount and kind of granular pigment, were responsible for the different shades of red hairs. These results formed the immediate basis of the present study.

MATERIAL AND METHODS

Guinea pigs of known genetic composition with regard to the factors studied were bred under observation, and fetuses were obtained which ranged from 43 to 57 days, copulation age. A few newborn animals were also studied. Blocks of skin were taken from the nose, ears, back, and belly of each fetus and adult animal killed. These tissues were studied microscopically as fresh smears and as fixed and sectioned material. A variety of fixatives were used, including 8 percent neutral formalin and 95 percent alcohol, neither of which altered the color of the pigment. Most of these tissues were sectioned and mounted without staining. Bouin's fluid was used as a fixative for tissues which were stained with hematoxylin and eosin and studied histologically. Whole mounts were made of hair samples from animals of various ages.

By these methods the effects of the following color-determining genetic factors were studied: The extension series: E , e^p , and e ; Black and chocolate: B and b ; The "albino" series: C , c^d , c^r , and c^a . Material was not available for a study of the factor c^k in the "albino" series.

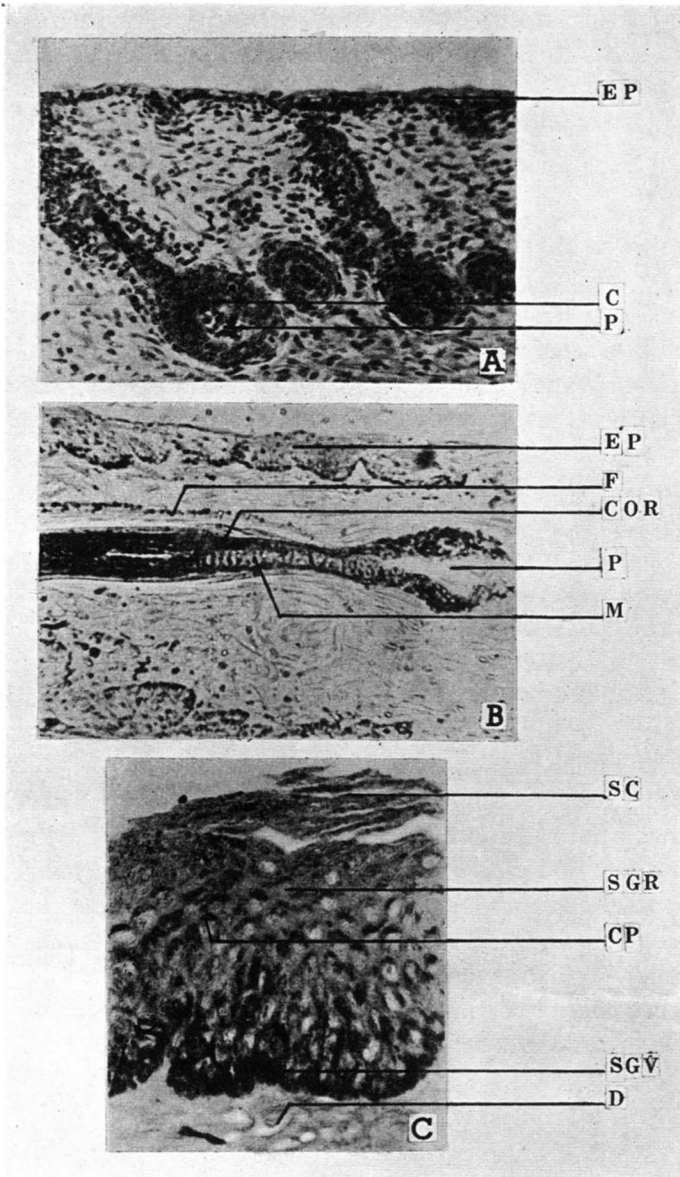
The appearance of the living animals at various ages was checked with the microscopic observations. Color in animals is influenced by non-genetic as well as by genetic factors; therefore, the food, light, and temperature in the colony were kept as constant and as favorable as possible, and the animals used for breeding were not subjected to any experimental treatment.

In the following discussion, the age of embryos is given in days calculated from the date of copulation; other specimens are described either as newborn (less than one week old) or as adult (more than four weeks old).

TYPES OF PIGMENT

Two types of pigment—granular and diffuse—were observed. Granular pigment was of three kinds—red, black, and chocolate, found in red, black, and chocolate hairs, respectively. Black and chocolate granules only were seen in the skin. Colorless granules were found in the white hairs of c^r and c^a animals. They occupied a position corresponding to that of the colored granules in pigmented hairs. In every instance, the color of the hair was the same as that of the granules which it contained.

Diffuse pigment ranged in shade from a pale yellow to a deep red-brown.



EXPLANATION OF PLATE I

FIGURE A.—Transverse section ($\times 148$) through the skin of the back of a self intense chocolate fetus, aged 45 days. Fixed in Bouin's fluid, stained with hematoxylin and eosin. The general histological relations of the developing skin and hair are shown. EP, epidermis; C, cone of pigment cells; P, papilla of the hair.

FIGURE B.—Transverse section ($\times 156$) through the tip of the ear of a self intense chocolate animal. Formalin-fixed, unstained. The distribution of pigment in the hair (seen in longitudinal

It was seen only in the cortex of the fully formed hair and was always found in association with red, black, or chocolate pigment granules.

DEVELOPMENT OF PIGMENT

The earliest stages of pigment formation were observed in fetuses of 43 days copulation age. Cells containing pigment granules were seen in the anlage of the hair, which was at this time a slight condensation of ectodermal cells projecting into the dermis. At the same time similar pigment cells were observed in the deep layer of the developing epidermis.

These pigment cells were larger than the ordinary cells of the dermis and epidermis and usually were irregularly star-shaped, with long pseudopodia-like processes which extended far out between the surrounding cells. Mitotic figures were often seen in them. Cells of this type were found both in the epidermis and in the hair, but none occurred in the dermis, nor in the dermal hair papilla.

At a later stage of development (45 and 46 days) the branched pigment cells in the base of the follicle were arranged in a dense conical cap over the hair papilla (fig. A). They were pushed upward by the division and growth of the cells next to the surface of the papilla, and they became differentiated into two types: the polygonal cells of the medulla and the spindle-shaped cells of the cortex of the hair. Branched pigment cells also occurred in the external root sheath of the follicle, especially in black and chocolate animals (fig. B).

The definitive hair was composed of a large medulla made up of star-shaped cells between which lay anastomosing air spaces; a rather thin cortex made up of flattened spindle-shaped cells; and a cuticle of thin overlapping scales (fig. B). The medulla was narrow and discontinuous toward the distal end of the hair and was absent at the tip.

The epidermis of the body was thin, and in pigmented animals branched pigment cells and scattered pigment granules were present in its deep layer. The epidermis of the nose and the ears became greatly thickened and contained, in addition to the branched type of pigment cells, several layers of small rounded cells in which granular pigment was found (fig. C).

Pigment granules were seen in the cytoplasm of both types of pigment cells. They were either scattered or gathered into caplike masses over the peripheral surface of the nucleus in the small rounded cells of the skin of

section) and in the skin are typical. EP, epidermis; F, pigment in the wall of the hair follicle; COR, cortex of the hair; M, medulla of hair; P, papilla.

FIGURE C.—Transverse section ($\times 443$) through the skin of the ear of a self intense black animal. Formalin-fixed, unstained. The stratum corneum is pulled away from the stratum granulosum. SC, stratum corneum; SGR, stratum granulosum; CP, "cap-like" mass of pigment granules at peripheral end of cell; SGV, stratum germinativum; D, dermis.

the nose and ear. The flat cells of the stratum corneum contained fewer granules than the cells in the deep layer. In the branched type of pigment cell the granules were scattered through the cytoplasm or clumped in one or more rounded masses which were often so compact that the individual granules could not be distinguished. Either masses of granules or scattered granules or both could be found in one cell. Pigment granules were also present between the cells of the hair bulb. Cytological observations indicated that the pigment did not originate directly from the nucleus but was formed in the cytoplasm of the cell.

The time and place of development were the same for black, chocolate, and red granules.

Study of the distribution of pigment granules in the hair was complicated by the presence of refractive surfaces in the medulla which appeared dark by transmitted light and often looked like pigment. The following methods were therefore employed in an effort to avoid confusion of pigment with "air spaces":

- (1) comparison of cleared, uncleared, and partially cleared hairs;
- (2) examination of these hairs with reflected as well as transmitted light;
- (3) examination of sectioned hairs.

The results show that while pigment is present in the medulla of many hairs, air spaces are always present and may look dark by transmitted light. It is possible that in some cases where pigment has been described in "albino" hairs, the air spaces might have been mistaken for pigment granules.

DESCRIPTION OF PHENOTYPES

Intense Black (C- E- B- P-)

The granular pigment of black animals was dark sepia in color. Rows and clumps of the granules were abundant in the cortex of black hairs, and "black" granules were densely packed in the shrunken cells of the medulla. A faint yellowish diffuse color was visible in the cortex of the hair. This diffuse pigment was somewhat darker at the tip of the hair and was almost absent at the base. "Black" granules were found in the pigment cells of the epidermis and of the wall of the follicle.

Intense Chocolate (C- E- bb P-)

Chocolate granules were more translucent and were of a lighter brown color than the "black" granules. The amount and distribution of granules in the hair and the skin of chocolate animals was the same as it was in black animals. The pigment cells were the same as to size, shape, and distribution in both types. Diffuse pigment in the cortex of a chocolate hair

was more intensely red and more conspicuous than it was in a black hair. Granular pigment in the skin was of the same color as that in the hair.

Black and chocolate granules appeared to be the same with regard to size, number, and distribution, and the time of their appearance. In the earlier stages of development, when only a few granules were present in the skin and hair, it was difficult to distinguish between black and chocolate granules. A difference in color was apparent only when a number of granules were observed together. Chocolate pigment appeared to be more susceptible than black to the effects of dilution factors such as c' and p .

Deep Cherry Red (C- ee B- P-), (C- ee bb P-)

All cherry red hairs which were studied contained translucent bright red-orange granules, abundant in the medulla and rather sparsely scattered in the cortex. A brilliant orange-red diffuse pigment was also present in the cortex. It was brighter near the tip of the hair than at the base. No black or chocolate granules were seen in any red hair, whether in a spot on an e^p animal or on a self red. Red granules were larger than black and chocolate granules, and they were more irregular in shape. Their color was entirely different from that of black or chocolate; no intergrades were found.

Red granules from different animals were sometimes different in shade; this variation seemed to be due in part to differences in the age of animals and in part to the influence of the factors B and b .

Sections of the skin of a spotted red-and-chocolate fetus were particularly valuable for comparing red and chocolate pigments. It was possible to observe, in one field of the microscope, follicles which were developing red hairs and follicles which were developing chocolate hairs. The differences could be observed easily and could not be ascribed to variations in the method of handling or preparation, since both were in the same tissue and were viewed under the same conditions of light and magnification. Red pigment in a spot on such a specimen appeared the same as that in a self red individual.

From observation of fresh whole mounts of the skin of black and red fetuses (litter mates) it was determined that the skin pigment is the same in both B - red and black animals. The branched pigment cells of the skin contained black granular pigment in both fetuses, although the hairs of the red fetus contained red granules and those of the black fetus contained black granules.

The skin of the nose and ear of B - red animals contained black granular pigment, although there was a little less present in red than in black animals. Chocolate granules were present in the same locations in bb red animals.

Newborn deep cherry red animals were a much deeper red and were more brownish than adults of the same genetic composition. This agrees with the observation that in the earlier stages of their development black, chocolate, and red granules look alike. However, microscopical observations showed that hairs from these young red animals were more like reds with very concentrated pigment than like chocolates or blacks.

Light Red ($c^d c^d ee bb smsm P-$)

Hairs from animals of this composition had a few pale red granules in the cortex and the medulla. There was a small amount of yellowish diffuse pigment present in the cortex. It could be seen only at the tip of the hair. No chocolate granules were seen in the hair.

c^r *Black and White* ($c^r c^r e^p B- P-$)
 c^r *Chocolate and White* ($c^r c^r e^p bb P-$)

Some of the c^r black animals were heterozygous for B ; hence they produced both c^r black and c^r chocolate fetuses, which could not be distinguished from each other at an early age. When the difference could be recognized, as was possible in older fetuses, it was the same as the difference between $C-$ black and $C-$ chocolate, which has already been described. For these reasons, c^r black and c^r chocolate animals are described together.

To gross observation, c^r black and c^r chocolate hairs appeared lighter in shade, especially near the base, than $C-$ black and $C-$ chocolate hairs. Microscopical examination showed that c^r hairs had fewer pigment granules both in the medulla and cortex than $C-$ hairs but that the granules themselves were typically chocolate or black.

Red diffuse pigment was found in the cortex of c^r chocolate and c^r black hairs. It was less conspicuous in black than in chocolate hairs.

White hairs from the c^r spotted animals contained neither red nor dark granules nor diffuse pigment; however, colorless granules were present in them. (The term "dark" is used here as it was by WRIGHT (1917) to include both black and chocolate granules, hairs, or animals, as distinguished from red or white.) The difference between white and dark hairs was especially evident in sections of the skin of these e^p (spotted) animals, which showed chocolate, white, and "mixed" hairs in the same field of the microscope. In the skin, scattered dark pigment granules were often present in regions where the hair was white as well as where it was pigmented.

c^r *White* ($c^r c^r ee bb P-$) ($c^r c^r ee B- P-$)
 "Albino" *White* ($c^a c^a ee bb P-$)

No difference was observed among the above three types of white hair. ($E- bb$ and $E-B-$ "albinos" were not available for study.) Neither red nor

dark pigment granules, nor diffuse pigment, were found in any of the white hairs which were studied. Colorless granules were seen in both c^r and c^a white hairs. They occupied a position in the cell and in the tissue comparable to that of the pigment granules in pigmented hairs.

DISCUSSION

Development of Pigment

In those tissues of the guinea pig examined in this study the pigment was confined to the epidermis and its derivatives. No pigment cells were seen in the dermis nor in the dermal papilla of the hair.

When the anlage of the hair first appeared, pigment cells could be identified in it. At the same time, similar pigment cells could be seen in the developing epidermis around the hair. The time of appearance of pigment was the same in all specimens studied, regardless of the genetic constitution. Hairs in several stages of development could be found on different body regions of a single fetus. It was possible to observe corresponding degrees of pigmentation in them.

These observations are in contrast with the findings of ESSKUCHEN (1927, 1930), who reported that the time at which pigmentation appeared in cattle fetuses varied with the color. Reddish-brown pigmentation appeared three and a half months later than black pigmentation. ESSKUCHEN (1927) also stated that in cattle the extremities were the first to show pigmented areas. The same was found by the present writers to be true in guinea pigs. In some types of guinea pigs, such as c^r whites and some albinos, the extremities are the only places where pigment ever appears.

ACTION OF GENETIC FACTORS

The following observations agree with those of BOGART and IBSEN (1937): (1) Pigment in the hair of guinea pigs occurs in two forms, granular and diffuse. (2) The granular pigment is black in black hairs and chocolate in chocolate hairs. (3) Diffuse pigment occurs as several different shades of red.

The observations given below disagree with the conclusions of BOGART and IBSEN (1937): (4) Red hairs contain red granular pigment, but no black or chocolate pigment. (5) White hairs from all animals studied may contain colorless granules, but no red, black, or chocolate granules. (6) Diffuse pigment is seen only in the cortex of the fully formed hair, and it is associated with some type of granular pigment. The intensity of the diffuse pigment is related to the type of granular pigment with which it is associated. (7) Diffuse pigment occurs in c^r dark hairs, as well as in C and c^d hairs. None is found in white hairs.

BOGART and IBSEN (1937) described the diffuse red pigment in guinea

pig hairs as if it alone accounted for the color of red hairs. They thought that in dark hairs the black or chocolate granules were "extended" so that they obscured the red diffuse pigment and that in red hairs, the black or chocolate granules were present but were not extended, thus permitting the red diffuse pigment to show through. They thought that a complete suppression of red diffuse pigment and the restriction of black or chocolate granular pigment to the medulla accounted for the colorless appearance of white hairs.

We found neither black nor chocolate pigment in ee (red and white) hairs. Red hairs contained red granules and white hairs contained colorless granules; however, the two may not be homologous. The red granules are probably comparable to the "yellowish" granules which HUNT and WRIGHT (1918) described in red and yellow guinea pig hairs. HAWKINS (1931) stated that the red coloring in the feathers of pigeons was due to red granular pigment.

Action of Factors in the Extension Series

On the basis of the above observations, it seems that the factors E ("extension") and e ("non-extension") should be described as determining the production of a definite type of granular pigment (dark or light), rather than the extension or non-extension of pigment granules over diffuse pigment. The light pigment produced in ee animals would then include the various shades of red granules, and possibly colorless granules. The dark pigment produced in E - animals would then include black and chocolate granules. The distribution of pigment in the hairs from the dark and light areas of e^p animals is the same as that in the hairs from E - and ee animals, respectively.

Action of Factors in the "Albino" Series

The factors in the "albino" series are discussed here in terms of their relation to the factors E and e .

In C - ("dark eyed") animals, the factor E determines the presence of dark granules in the hair. The factor e determines the presence of red granules in comparable positions. The action in the skin is probably quantitative rather than qualitative, for no red granules were seen in the skin of any type of guinea pig studied.

Too little work was done with c^d animals to give a basis for describing the effects of that factor.

In c^r ("red eyed," "non-red") animals, the factor E produces dark granules in the hair, but e does not produce red granules. Instead, it may produce the colorless granules which were observed. Dark granular pigment appears in the skin of c^r white animals, especially in the extremities.

The factor c^a ("albino") is epistatic to both E and e . Neither red nor

dark granules were seen in the hair of $c^a c^a$ animals of our stock; but colorless granules were seen there as they were in c^r animals. Here again, the action is not the same in the skin as it is in the hair. "Albino" guinea pigs usually have dark pigment in the skin of the extremities. Because of the presence of this pigment, $c^a c^a$ guinea pigs are not considered true albinos.

The Relation Between Diffuse and Granular Pigment

When the actions of the factors in the "extension" and the "albino" series are interpreted as above, it becomes evident that the diffuse red color need not be considered as one of the pigments which is primarily determined by the genetic composition of the animal. The granular pigments seem to be the direct expression of the action of the color-determining factors. The color of the hair in each case corresponds to the color of the granules in it. The red diffuse pigment appears to be formed in the cortex of the hair as a consequence of the presence there of some type of granular pigment. It behaves as if it were the product of a chemical or physical reaction between the granules and the cornified substance of the cortex of the hair. GORTNER (1911) in his description of two kinds of melanin says:

"Those melanins which are soluble in dilute acids are of a protein nature (melanoproteins). It appears probable that these melanoproteins are not present as granules, but that they are 'dissolved' in the keratin structure.

"The melanins which are insoluble in dilute acids are of an unknown constitution and are probably the 'pigment granules' which may be seen in the hair and tissues."

EDWARDS and DUNTLEY (1939), in studies of the living human skin, described a modified diffuse form of melanin which they called "melanoid." It resembled melanin closely in its spectrophotographic properties, and it occurred only in cells derived from melanin-bearing cells—that is, the cells of the stratum corneum. The amount of melanoid in any skin depended upon the amount of melanin found there. Because of these relations, the authors regarded "melanoid" as a degradation product of melanin. It was present as a dissolved pigment and reenforced the melanin, particularly in giving a purer yellow color than melanin alone.

The relations described by EDWARDS and DUNTLEY (1939) for the human skin are similar to those found in the hair of the guinea pig. These authors did not study the hair of their subjects.

In c^r guinea pigs, white hairs are found in place of the red hairs of C -animals. BOGART and IBSEN (1937) assumed that these hairs were white, because they lacked red diffuse pigment. They expected that c^r black and chocolate hairs would also lack diffuse red pigment. The presence of red diffuse pigment in c^r black and chocolate hairs at first seemed contradictory to the description of the c^r factor ("non-red"). Its presence may be

explained if one assumes that it is red granular pigment rather than red diffuse pigment, which is determined by the *C*- factor in the presence of *ee* and which will not appear in *c'ee* hairs. In the absence of these red granules no red diffuse pigment is formed; hence *c'ee* hairs are white. In *c'E*-hairs the diffuse pigment is formed as it is in *C-E*-hairs, in association with the black or chocolate granules which are present in the hair. The close association between granular and diffuse pigment is parallel to the description of the "albino" series as given by BOGART and IBSEN (1937), in which there is no separate factor for the red diffuse pigment.

The absence of all pigment from the hairs of "albino" (*c^ac^a*) animals may be explained similarly. In such animals neither red nor dark granules are present in the hair; hence no diffuse pigment is produced, and the hair is white.

Action of the Factors B (black) and b (chocolate)

The differences between black and chocolate pigment granules as seen in *E* animals have been described earlier in this paper. Part of the difference between the types of granules seems to lie in their relation to the diffuse type of pigment. Red granules are bright and translucent and are associated with a large amount of diffuse pigment. Chocolate granules are darker and denser, and less of the diffuse pigment is found with them. Black granules are darker than chocolate granules and are associated with an even smaller amount of diffuse pigment.

When deep cherry red (*ee*) guinea pigs are examined, it is seen that the *B*- red animals are of a deeper color than the *bb* reds and that this difference is due as much to the shade of the hair as it is to the color of the skin of the ears, nose, and other exposed parts. The differences in the color of the skin may be explained on the basis of the presence of black pigment in the skin of the *B*- red animals and chocolate pigment in the skin of *bb* red individuals. It was thought that the different shades of the red hairs might be due to the presence of black and chocolate granules in *B*- and *bb* hairs. Since in both types of hair, red granules only are present, some other explanation must be found for the difference in shade between the two types of red hair. It has already been mentioned that there is some variation in the shade of the red granules. They are somewhat lighter in *bb* red hairs than they are in *B*- red hairs. The difference was seen only in material from adult animals. This leads to the conclusion that the factors *B* and *b* may have the same kind of effect on red granules as they do on dark granules. They may produce "light" and "dark" red granules in *ee* hairs just as they produce chocolate and black granules in *E*- hairs.

CONCLUSIONS

The earliest stages of pigment formation in the hair and skin of the

guinea pig were seen in fetuses of 43 days. At this stage no difference was apparent among black, chocolate, and red pigment granules.

In older fetuses (44 to 57 days) and in adult animals, black, chocolate, and red granules were present in both the medulla and cortex of black, chocolate, and red hairs, respectively. Colorless granules, which may or may not have been homologous to the true pigment granules, were seen in white hairs. In every case, the color of the hair corresponded to the color of the granules which it contained.

Diffuse reddish pigment was seen only in the cortex of the fully formed hair in association with black, chocolate, or red granular pigment. Hence, it was present in *C*-red and dark hairs and in *c^r* dark hairs, but it was absent in *c^r* and *c^a* white hairs.

It is possible to explain the actions of the color determining factors in terms of their relation to granular pigment alone. The diffuse pigment may be considered as the product of the granular pigment. The following outline presents a possible explanation of the action on the hair of the color-determining factors which were studied: The factor *E* may determine the presence of dark granules. The factors *B* and *b* determine whether these granules are black or chocolate. The factor *e* in the homozygous condition may determine the presence of red granules. The factors *B* and *b* may produce "dark" and "light" red granules. In the presence of the factor *C*, both *E* and *e* may act as described above. In the presence of the factor *c^r*, in the homozygous condition, *E* may act as described, but *e* may produce only colorless granules, or none at all. Where the factor *c^a* is present in the homozygous condition, *E* does not produce dark granules and *e* does not produce red granules. Unless other factors are present, the hairs of *c^ree* and *c^a* animals are white. The action of the factors in the light and dark areas of *e^p* (spotted) animals corresponds to that in *e* and *E* animals, respectively. In the skin, the factors *E* and *e*, *C*, *c^r* and *c^a* may affect the amount rather than the kind of pigment present. Where there is a small amount, it is found chiefly in the extremities. The factors *B* and *b* may control the color of the pigment in the skin, and act in the presence of either *E* or *e*. Observations on the histological and cytological origin of pigment in the guinea pig indicated that the pigment cells were ectodermal in origin and that pigment granules were not formed directly from the nucleus of the cell.

LITERATURE CITED

- BOGART, R., and HEMAN L. IBSEN, 1937 The relation of hair and skin pigmentation to colour inheritance in cattle, with some notes on guinea pig hair pigmentation. *J. Genet.* 35(1): 31-59.
- CASTLE, W. E., and S. WRIGHT, 1916 Studies of inheritance in guinea pigs and rats. Part II. An intensive study of the inheritance of color and of other coat characteristics in guinea pigs, with especial reference to graded variations. By Sewall Wright. Carnegie Inst. Wash. Publ. No. 241. 192 p.

- EDWARDS, E. A., and S. Q. DUNTLEY, 1939 The pigments and color of living human skin. *Amer. J. Anat.* **65**(1): 1-33.
- ESSKUCHEN, E., 1927 Über die Entstehung der Färbung der Haussäugetiere. *Züchtungsk.* **2**(7): 337-351.
1930 The development of pigment in cattle embryos [in German]. *Z. Zücht., Reihe B, Tierzücht. u. Züchtungsbiol.* **19**(2): 268-295. (Original not seen. Abstract, *Expt. Sta. Rec. Wash.* **65**(6): 524. Oct. 1931.)
- GORTNER, R. A., 1911 On melanin. *Biochem. Bull.* **1**(2): 207-215.
- GREMMEL, F., 1939 Coat colors in horses. *J. Hered.* **30**(10): 437-445.
- HAWKINS, L. E., 1931 Studies on inheritance in pigeons. X. Relation of chocolate to black and dominant red. *Genetics* **16**: 547-573.
- HUNT, H. R., and S. WRIGHT, 1918 Pigmentation in guinea pig hair. *J. Hered.* **9**(4): 178-181.
- MAXIMOW, A. A., and W. BLOOM, 1934 A textbook of histology. 2nd ed. 662 pp. Philadelphia: Saunders.
- WRIGHT, S., 1917 Color inheritance in mammals. *J. Hered.* **8**(5): 224-235.
1925 The factors of the albino series of guinea pigs and their effects on black and yellow pigmentation. *Genetics* **10**: 223-260.
1927 The effects in combination of the major color factors of the guinea pig. *Genetics* **12**: 530-569.