CHAPTER IX

THE FACTORIAL HYPOTHESIS

In Mendelian heredity the word "factor" is used for something which segregates in the germ cells, and which is somehow connected with particular effects on the organism that contains it. For example, if a fly (♀) with red eyes is crossed to a fly (♂) with white eyes, there will be in F_2 three reds to one white, and this ratio can be explained by the assumption that in the F_1 hybrid something for red eyes has separated from something for white eyes.

We may express these factorial relations in another way by saying that a germ cell that produces white eyes differs from a germ cell that produces red eyes by one factor-difference. We think of this difference as having arisen through a factor in the red-eyed wild fly mutating to a factor for white.

Mendelian heredity has taught us that the germ cells must contain many factors that affect the same character. Red eye color in Drosophila, for example, must be due to a large number of factors, for as many as 25 mutations for eye color at different loci have already come to light. Each produced a specific effect on eye color; it is more than probable that in the wild fly all or many of the normal allelomorphs at these loci have something to do with red eye color.

One can therefore easily imagine that when one of these 25 factors changes, a different end result is produced, such as pink eyes, or vermilion eyes, or white eyes or eosin eyes. Each such color may be the product of 25 factors (probably of many more) and each set of 25 or more differs from the normal in a different factor. It is this one different factor that we regard as the "unit factor" for this particular effect, but obviously it is only one of the 25 unit factors that are producing the effect. However since it is only this one factor and not all 25 which causes the difference between this particular eye color and the normal, we get simple Mendelian segregation in respect to this difference. In this sense we may say that a particular factor (p) is the cause of pink, for we use cause here in the sense in which science always uses this expression, namely, to mean that a particular system differs from another system only in one special factor.

The converse relation is also true, namely, that a single factor may affect more than one character. For example, the factor for rudimentary wings in Drosophila affects not only the wings, but the legs, the number of eggs laid, the viability, etc. Indeed, in his definition of mutation, DeVries supposed that a change in a unit factor involves all parts of the body. The germ cells may be thought of as a mixture of many chemical substances, some of them more closely related to the production of a special character, color, for example, than are others. If any one of the substances undergoes a change, however slight, the end

product of the activity of the germ cell may be different. All sorts of characters might be affected by the change, but certain parts might be more conspicuously changed than are others. It is these more obvious effects that we seize upon and call unit characters. It is the custom of most writers to speak of the most affected part as a "unit character," and to disregard minor or less obvious changes in other parts. They frequently speak of a unit character as the result of a unit factor, forgetting that the unit character may be only one effect of the factor.

Failure to realize the importance of these two points, namely, that a single factor may have several effects, and that a single character may depend on many factors, has led to much confusion between factors and characters, and at times to the abuse of the term "unit character." It can not, therefore, be too strongly insisted upon that the real unit in heredity is the factor, while the character is the product of a number of genetic factors and of environmental conditions. The character behaves as a unit only when the contrasted individuals differ in regard to a single genetic factor, and only in this case may it be called a unit character. As soon as the individuals differ by two or more genetic factors that affect the same character the latter can be no longer considered a unit. So much misunderstanding has arisen among geneticists themselves through the careless use of the term "unit character" that the term deserves the disrepute into which it is falling.

In the following sections, several of the more important misconceptions arising from the confusion between factors and characters will be considered in turn:

1. There is a curious objection to the factorial hypothesis that is sometimes brought forward. It originated apparently as an objection to Weismann's idea that a single determinant stands for a single character. Weismann's idea of a sorting out of determinants undoubtedly implies something of this kind. The objection states that the organism is a whole—that the whole determines the nature of the parts. Such a statement, in so far as it has any meaning at all, rests on a confusion of ideas. That the different regions of the developing embryo do sometimes have an immediate influence on each other has been abundantly demonstrated, as well as the fact that in other cases parts have little or no influence on each other. That substances are produced in one place whose principal effects are seen in other places is not likely to be denied. It has even been insisted in the preceding pages that the evidence from heredity indicates with great probability that there are many factors whose combined effect is necessary for the production of each separate character, as in the production of eye color, for example. There is no reason why this interaction should always take place within the separate cells; in other words, why the products of factor A in one cell should not sometimes affect the products of factor B in another cell. The factorial hypothesis

does not assume that any one factor produces a particular character directly and by itself, but only that a character in one organism may differ from a character in another because the sets of factors in the two organisms have one difference. This point is not likely to be misunderstood by any one who grasps the meaning of the factorial hypothesis. The "organism-as-a-whole" argument, so long as it is not a vague and mystical sentiment incapable of clear expression, has no terrors for the factorial hypothesis, for this hypothesis disclaims any intention of making one unit character the sole product of one factor of the germ.

2. No one disputes that characters vary, but it has become necessary to explain what we mean by this statement. Many populations have been shown to be mixtures of different genetic types. This means that many of the individuals have different germ plasms. In man, for instance, there are blue-eyed, brown-eyed, black-eyed and pink-eyed individuals, and these variations of eye color have been shown by Hurst, the Davenports, Holmes and others to depend on different factorial constitutions. It has been shown in several cases, notably in corn, by Shull, and by East and Hayes, that populations may contain differences in many factors that have similar effects on the same character. In this case too the different factors that affect a part in the same way are shown to separate and recombine in successive generations. The result is variability, but variability of a sort that is compatible with the

invariability of the factors involved. When, however, these factors were sorted out so that strains became homozygous, some variability probably due to evironic differences still remained. That is, in addition to the variation due to recombination it has been found that even in pure races "unit characters" vary. Why, then, it may be asked, do not the factors that produce them vary also?

Johannsen's work on material of a kind suitable to give a definite answer to this question and by methods that have not been questioned, has brought out clearly certain facts only vaguely stated before. In a population of beans he found that each bean gave rise by self-fertilization to what he called a pure line. Each of the original beans proved to be homozygous for all of the factors involved. This was probably due to self-fertilization through many generations, a process that automatically produces homozygous lines. The weights of the descendants of any given bean gave a curve of frequency which was different from that of the whole population (Fig. 62). Within the group derived from one bean, however, it was found that any bean, whether heavier or lighter than the others, gave a curve exactly like the curve of the line from which it came. Evidently then the size differences within these pure lines are not inherited. They must be due to the environment of the plant, or to the position of the bean in the pod, etc.; in other words to conditions that are extrinsic to the germ plasm. Here is a demonstration that the factors do not vary, but give identical results in successive

generations. Of course this demonstration could not have been made with heterozygous individuals.

3. It has also been suggested that one factor may sometimes contaminate its allelomorph, when the two meet in the hybrid. There is no *a priori* reason why this might not occur so far as we can see. The question is whether there is any evidence to establish or even make probable such a view. The great body of Mendelian evidence points unmistakably to the conclusion that as a rule contamination does not occur. It will require equally clear evidence to show that contamination does sometimes take place. Until this evidence is forthcoming the facts which have been said to support the hypothesis of contamination find a more consistent explanation on the hypothesis of multiple factors.

4. Bateson has recently argued from the visible differences between characters that a process of fractionation of factors takes place. The argument is given in the following quotation:

"Some of my Mendelian colleagues have spoken of genetic factors as permanent and indestructible. Relative permanence in a sense they have, for they commonly come out unchanged after segregation. But I am satisfied that they may occasionally undergo a quantitative disintegration, with the consequence that varieties are produced intermediate between the integral varieties from which they were derived. These disintegrated conditions I have spoken of as subtraction—or reduction—stages. For example, the Picotee sweet pea, with its purple edges, can surely

be nothing but a condition produced by the factor which ordinarily makes the fully purple flower, quantitatively diminished. The pied animal, such as the Dutch rabbit, must similarly be regarded as the result of partial defect of the chromogen from which the pigment is formed, or conceivably of the factor which effects its oxidation. On such lines I think we may with great confidence interpret all those intergrading forms which breed true and are not produced by factorial interference.

"It is to be inferred that these fractional degradations are the consequences of irregularities in segregation. We constantly see irregularities in the ordinary meristic processes, and in the distribution of somatic differentiation. We are familiar with half segments, with imperfect twinning, with leaves partially petaloid, with petals partially sepaloid. All these are evidences of departures from the normal regularity in the rhythms of repetition, or in those waves of differentiation by which the qualities are sorted out among the parts of the body. Similarly, when in segregation the qualities are sorted out among the germ cells in certain critical cell divisions we can not expect these differentiating divisions to be exempt from the imperfections and irregularities which are found in all the grosser divisions that we can observe."

Bateson has assumed because the character appears to fractionate that we are to infer that some particular factor, that stands for it, fractionates too, but such a conclusion overlooks the fact that a character is produced by many factors in co-operation,

and that, in consequence, many factor differences may occur which will, in turn, cause the character differences in question. Secondly, Bateson argues that we should expect these irregularities to occur in the segregation of character-factors during germ-cell formation, because we find irregularities in the segregation of factors during development. Apparently Bateson holds the view that differentiation of characters is the result of sorting out of factors in the somatic divisions; in other words, he adopts Weismann's theory of embryonic development. Localization of factors is inferred from localization of characters. Hence his employment of the idea chiefly when patterns are involved. The conclusion to which most modern students of experimental embryology have arrived, a conclusion based on a considerable body of evidence, is that differentiation is not a consequence of sorting out of the hereditary (genetic) materials. This conclusion is not considered or else is ignored by Bateson in this argument.

5. The confusion of character with factor is nowhere more apparent than in the well-known presence and absence hypothesis, and since this hypothesis has been so widely employed in Mendelian literature it calls for somewhat more extended analysis. The hypothesis was first proposed to explain the inheritance of combs in poultry (Fig. 64). Rose comb by single comb gives in F_2 three rose to one single; pea comb to single gives in F_2 three pea to one single. When rose is bred to pea a new type of comb, called walnut, appears, and in F_2 there are nine walnut:

three rose: three pea: one single. Since single comb was not present in either of the grandparental strains,

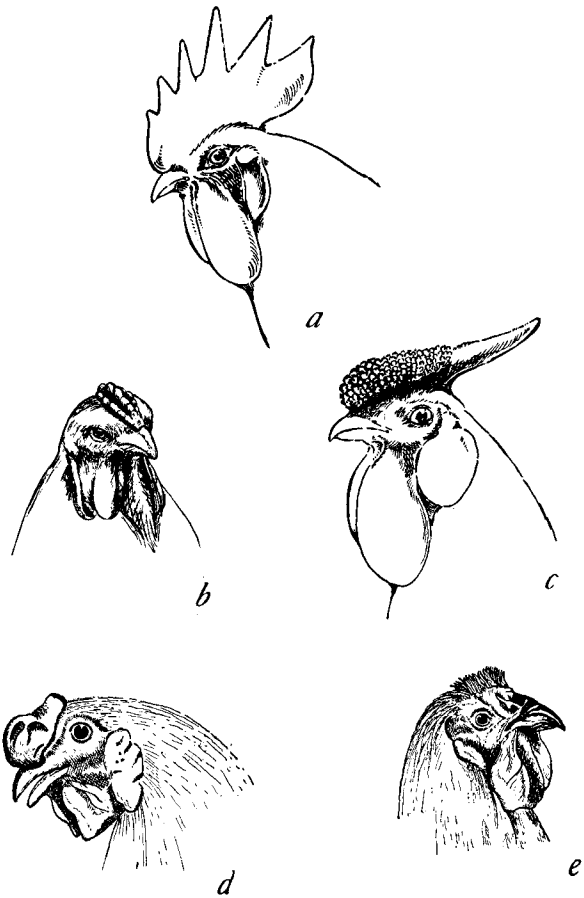

FIG. 64.—Combs of fowls. *a*, Single; *b*, pea; *c*, rose; *d*, walnut; *e*, Breda.

how then can its appearance in this cross be explained? The difficulty was met as follows: The ratio shows

clearly that two pairs of Mendelian factors are present. Pea comb was assumed to lack a factor for rose, and rose was assumed to lack a factor for pea. By recombination there should result in F_2 one individual in sixteen that was no-rose no-pea. This is the single comb. A single letter or symbol S was inserted in all of the formulæ so that when neither rose nor pea comb was present something would seem to be left to represent the single comb.

The verification of the latter point was supposed to be found in the relation of the single comb to a combless condition found in the Breda race of fowls, which, when crossed to single, gave in F_2 three singles to one combless. In other words the combless fowl was supposed to represent a race in which the lowest stage of the series had been reached and the last factor for comb had been lost. The series just described was represented on the presence and absence scheme as follows:

Rose	RpS
Pea	rPS
Walnut	RPS
Single	rpS

There is, obviously, no necessity to make these characters depend for their expression on *losses* of something; for the small letters that here stand for absences might just as well stand for actual factors different from those represented by the large letters. The formulæ would then of course work out as well as before. To those accustomed to the presence and

absence scheme it may, however, be difficult to think of the small letters as anything but absences. It may, therefore, be helpful to represent the same formulæ with other letters.

If the original comb was single, which in fact is the type of comb of the wild bird from which the domesticated races have come, a dominant mutation from A to A′ gave rise to a rose comb; another dominant mutation from the wild type that changed B to B′ gave rise to a pea comb; a third but recessive mutation that changed C to C′ gave rise to a "combless" comb. The normal allelomorphs would be represented by the same letters without the primes. The formulæ (in simplex) for the combs would then be as follows:

Wild type (single)	A B C
Rose	A′B C
Pea	A B′C
Combless	A B C′

The walnut comb that appears when pea is bred to rose is, of course, the double dominant form A′B′C.

If it seems desirable to use letters that give a clue to the name of the factor for which they stand, either of the next alternatives would cover the case under discussion. In the second of these the small letters are not absences, but only the recessive allelomorphs.

Wild type (single)	P R C or p′r′C
Rose	P R′C or p′R′C
Pea	P′R C or P′r′C
Combless	P R C′ or p′r′c

It is a matter of little theoretical importance what system of symbols is adopted, unless that system proves to be impracticable, or unless it implies relations that are unnecessary or unjustifiable. (See Appendix.)

We do not wish to appear to base our objection to the presence and absence hypothesis on the impracticability of its nomenclature in a new field, but rather on the grounds that the conception of presence and absence assumes that we do know something about the relation between character and factor that we can not possibly know. To assume the absence of a factor from the absence of a character is, in a sense, as naive as it was to assume that an animal moved toward light because it liked the light.

It need not be denied that losses of factors may occur, and it may even be probable that a loss in the germ plasm might lead to a loss in some part or parts of the body, but there still remains no justification for the assumption in any given case that we can infer from the lack of a character in an animal or plant a loss of factors. Such an assumption is entirely gratuitous; and gives a totally false impression concerning the factorial hypothesis of Mendelian heredity. Moreover, if taken literally it may lead to unwarranted conclusions in other fields.

It is similarly naive to assume the absence of a factor from the recessiveness of the character, yet the literature abounds with instances where the recessiveness of the character is taken as a criterion for

assuming the absence of the factor, the dominant character being considered as a "presence." Dominance, however, is often found to be incomplete if exact quantitative studies are made. In fact, characters are known to show all degrees of dominance and recessiveness over their alternative allelomorphs. Which character is to be considered dominant and which recessive when each allelomorph has an equal effect, as in the case of the red and the white Mirabilis, is entirely a matter of choice. Hence, no matter whether red or white is presence, the present factor is not truly dominant. It seems reasonable, then, to suppose that if presence and absence is true a hybrid (with one presence) might approach more nearly the type with two absences than to the type with two presences. In such a case the present factor would actually be the recessive. Such a case is in fact known. In the cross of horned by hornless sheep, the horned condition dominates in one sex and the hornless in the other. Here no matter which is considered as a presence it must be conceded that in one sex or the other it is recessive. The view that dominance of a factor proves its presence and recessiveness its absence should therefore be abandoned.

A further argument against the theory of presence and absence is found in the evidence, already given, which indicates the possibility of multiple allelomorphs. On the presence and absence system, only two kinds of allelomorphs, the presence and the absence, are possible, and no character differences

can be due to different kinds of factors, all of them "presences."

A word here may not be out of place concerning inhibitors. As pointed out, the adherents of presence and absence generally interpret the absence of a character to mean the absence of a factor; they also interpret recessiveness to mean the absence of a factor. When cases come up in which a character is absent, as horns in cattle, but the absence of the character is dominant, an attempt is made to reconcile fact and theory by assuming that the factor for the absent character is not really absent, but that an inhibitor is present whose activity prevents the appearance of the character.

Those who do not accept the presence and absence hypothesis need make no such assumption here of course. To them there is no reason why a factor for hornless should not dominate a factor for horns. Moreover, the facts do not even require one to assume that the hornless race differs from the horned because of the lack or inhibition of certain reactions, for it is possible in such cases that the reaction merely takes a different course, or may even proceed beyond the usual point.

These statements are not, however, intended to mean that factors may not at times act as inhibitors, but rather that we do not know, and in most cases can not know, in a single case enough about the nature of the reaction to demonstrate the existence of a factorial inhibitor.

Weismann's Præformation Hypothesis and the Factorial Theory

Weismann's theory of *development* postulates particles in the germ plasm that are sorted out in proper sequence to appropriate parts of the body as the embryonic cells divide. What determines the order of the sorting out of the factors was not explained. Weismann's speculation differed from other præformation theories mainly in that he made use of the chromosomal mechanism not only to carry the hereditary materials, but also to bring about the sorting out of the materials in order to reach their final destination in the body. His theory as applied to embryonic development failed, both because the facts concerning the behavior of the chromosomes during segmentation of the egg gave no support to his assumption of sorting out of the materials of the chromosomes, and also because the data from experimental embryology and regeneration indicated very clearly that no such sorting process takes place. On the other hand, Weismann's ideas of *heredity* concerning the segregation in the reduction divisions of the egg and sperm of inherited materials present in the chromosomes, furnish the basis of our present attempt to explain heredity in terms of the cell.

In common with Weismann's theory, the factorial theory of heredity rests on the assumption that the germ plasm contains a host of elements, that are independent of each other in the sense that one allelomorph may be substituted for another one without

alteration of either, and that these allelomorphs will now perpetuate themselves unchanged although in company with different factors. Today this assumption is no longer an *a priori* deduction, but a conclusion from experimental data.

The second real and important point of agreement between the factorial theory and Weismann's theory is that both maintain that at one period in the history of the germ cells, the factors derived from the mother separate from those derived from the father, each pair by itself. The precise way in which this is supposed to take place may differ slightly on the two views, but the essential point is the same. We owe to Weismann more than to any other biologist the conception of segregation at the reduction division of the egg and sperm—a conception of fundamental importance in the application of the chromosome theory to Mendelian heredity. The factorial hypothesis postulates only three things about the factors with which it works, viz.: (1) that they are constant, (2) that they are usually in duplicate in each cell of the body, and (3) that they usually segregate in the maturing germ cells. But the biologist is not likely to stop here, for, to him the problem involves cells about whose history and processes he has come to know certain facts. Weismann, following Roux, was the first to point out that these facts give a mechanism showing how separation of factors might take place. The specific application of the behavior of the chromosomes to heredity, then, is the third important contribution which modern genetics owes

to Weismann. Today, however, we have advanced beyond Weismann in this respect, and may more specifically interpret our numerical results of independent segregation, linkage, and even crossing over on the basis of a chromosome mechanism. Moreover, the new facts have given us ideas very different from those of Weismann regarding the arrangement of the factors in the chromosomes and the way in which the characters of an individual are determined by the chromosomal factors.

In the last edition of his Vortræge ueber Descendenztheorie (3d edition, 1913) Weismann modifies his earlier views in regard to the factorial nature of the chromosomes so that his conception of the germ plasm is brought into harmony with the Mendelian theory of heredity. Formerly he had supposed that the chromosomes are all alike, or nearly alike, in so far as each one carries a full assortment of "ids." Each id, in itself, represented the full complement of all the factors that go to make up the organism. But since the results of Mendelian heredity show that all sorts of characters, however trivial, may be segregated independently (which would not be the case, if, as Weismann formerly supposed, all the hereditary characters are carried by each chromosome), it follows that the chromosomes must be bearers of part ids (Theil Ids).

Weismann still adheres nevertheless to his mosaic theory of development, but as before stated the modern work on development does not support this interpretation of development. His view assumes

disintegration of the germ plasm when the body cells are produced in order to account for the localization of characters; the other view, following the experimental results and microscopical observations, assumes, so far as the chromosomal materials are concerned, that all of the hereditary factors are present in every cell in the body. This view is essentially that proposed by DeVries in his book on Intracellular Pangenesis. The cause of the differentiation of the cells of the embryo is not explained on the factorial hypothesis of heredity. On the factorial hypothesis the factors are conceived as chemical materials in the egg, which, like all chemical bodies, have definite composition. The characters of the organism are far removed, in all likelihood, from these materials. Between the two lies the whole world of embryonic development in which many and varied reactions take place before the end result, the character, emerges. Obviously, however, if every cell in the body of one individual has one complex, and every cell in the body of another individual has another complex that differs from the former by one difference, we can treat the two systems as two complexes quite irrespective of what development does so long as development is orderly.

It is sometimes said that our theories of heredity must remain superficial until we know something of the reactions that transform the egg into the adult. There can be no question of the paramount importance of finding out what takes place during development. The efforts of all students of experimental

embryology have been directed for several years *toward this goal. It may even be true that this* information, when gained, may help us to a better understanding of the factorial theory—we can not tell; for a knowledge of the chemistry of all of the pigments in an animal or plant might still be very far removed from an understanding of the chemical constitution of the hereditary factors by whose activity the pigments are ultimately produced. However this may be, the far-reaching significance of Mendel's principles remains, and gives us a numerical basis for the study of heredity. Although Mendel's law does not explain the phenomena of development, and does not pretend to explain them, it stands as a scientific explanation of heredity, because it fulfils all the requirements of any causal explanation.