CHAPTER XVIII

STABILITY OF THE GENE

IN what has been said, so far, it has been implied that the gene is a stable element in heredity, but whether it is stable in the sense that a chemical molecule is stable, or whether it is stable only because it fluctuates quantitatively about a persistent standard, is a question of theoretical and perhaps of fundamental importance.

Since the gene cannot be studied directly by physical or chemical methods, our conclusions concerning its stability must rest on deductions from its effects.

Mendel's theory of heredity postulates that the gene is stable. It assumes that the gene that each parent contributes to the hybrid remains intact in its new environment in the hybrid. A few examples will serve to recall the nature of the evidence for this conclusion.

The Andalusian race of poultry has white, black, and blue individuals. If a white bird is mated to a black one, the offspring are slate-colored or blue. If two of these blue-colored birds are mated, the offspring fall into three classes, black, blue, and white, in the proportion of 1:2:1. The gene for white and the gene for black separate in the blue hybrid. Half the mature germ-cells come to carry the black-producing element and half the white-producing element. Chance fertilization of any egg by any sperm will give the observed proportions 1:2:1 in the second filial generation.

The test of the correctness of the assumption that the germ-cells of the hybrids are of two kinds is as follows. If a blue hybrid is back-crossed to a pure white bird, half

the offspring will be blue and half white. If a blue hybrid is back-crossed to a pure black bird, half the chicks will be black and half blue. Both results are consistent with the postulate that the genes of the blue hybrid are pure, half for black and half for white. Their occurrence in the same cell has not resulted in contamination or mutual infection.

In the example just given the hybrid is unlike either parent and, in a sense, is intermediate between them. In the next example the hybrid is indistinguishable from one parent. If a black guinea pig is bred to a white one, the offspring are black. If these are inbred, the offspring are three blacks to one white. The extracted whites breed as true as the original race of whites. The white gene has not been contaminated by the black gene in their sojourn together in the hybrid.

In the next example a case is chosen in which the two original forms are much alike, and the hybrids, while intermediate to some degree, are so variable that, at the ends of the series, they overlap the parental types. The types differ in a pair of genes.

If an ebony Drosophila is bred to a sooty one, the offspring are, as stated, intermediate, but variable. If these are inbred, they produce an array of shades that give a practically continuous series. There are ways, however, of testing the grades. When this is done it is found that the array is made up of individuals that are pure for ebony, others that are hybrids, and others that are pure for sooty, in the ratio of 1:2:1. Here again we have evidence that the genes have not been mixed. The continuous series of shades is merely due to overlapping variability of the characters.

All this is simple and clear because we are dealing in each case with a single pair of genes that act as differentials. These cases serve to establish the principle at stake.

In practice, however, the actual conditions are not always so simple. Many types differ from each other in several genes, each of which has an effect on the same character. Consequently, when they are crossed simple ratios are not found. For example, if a race of corn with a short cob is crossed to a race with a long cob, the next generation has cobs of intermediate length. If these are inbred the following generation has cobs of all sizes. Some are as short as the cobs of one of the original races, others as long as the original long. These stand at the ends. Between them is a series of intermediate sizes. A test of the individuals of this generation shows that there are several pairs of genes that affect the size of the cob.

Height in man is another such case. A man may be tall because he has long legs, or because he has a long body, or both. Some of the genes may affect all parts, but other genes may affect one region more than another. The result is that the genetic situation is complex and, as yet, not unraveled. Added to this is the probability that the environment may also to some extent affect the end-product.

These are the multiple factor cases, and students of heredity are trying to determine in each cross how many factors are present. The results are complex only because several or many genes are involved.

It is this sort of variability that in the earlier days, before Mendel's discovery had been made known, supplied natural selection with the evidence on which that theory was based. This question will be considered later, but first must be described the great advance in our understanding of the limitations of the selection theory that was made in 1909 by Johannsen's brilliant work.

Johannsen carried out his experiments with a garden plant, the princess bean. This bean reproduces exclusively by self-fertilization. As a result of long-continued in-

breeding each individual has become homozygous. This means that the two members of each pair of genes are identical. Hence such material is suitable to carry out

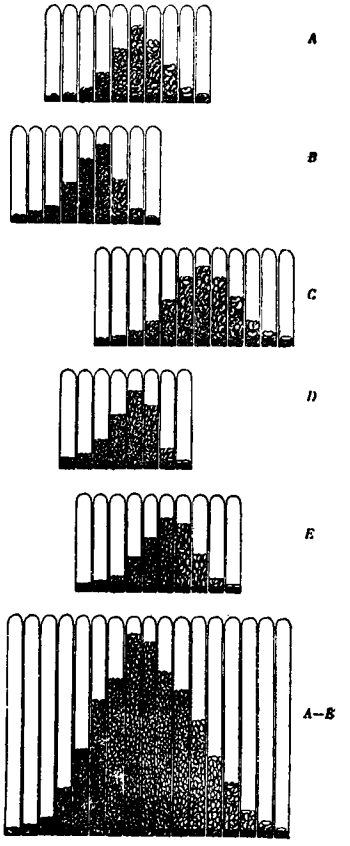

FIG. 150.

A-E groups of beans representing five pure lines. Below A-E the group formed of the combination of the other five. (After Johann sen.)

critical experiments to determine whether *individual* differences shown by the beans are affected by selection. If selection changes the character of the individual, it

must, under these conditions, do so by changing the gene itself.

The beans produced by each plant are somewhat variable in size, and when arranged according to sizes they give the normal curve of probability. All the beans from any one plant and all of the descendents of this plant have the same distribution (Fig. 150), no matter whether large beans are continually selected, or small beans are picked out in each generation. The offspring always give the same groups of beans.

Johannsen detected nine races of beans in those he examined. He interpreted his results to mean that the differences in size of the beans from a given plant are due to its environment in the widest sense. It was possible to demonstrate this with material in which the members of each pair of genes were identical when selection began. Selection is shown to have no effect in changing the genes themselves.

When sexually reproducing animals or plants are selected that are not homozygous at the start, the immediate outcome is different. There are numerous experiments showing what happens, such as Cuénot's results with spotted mice, or MacDowell's results with ear-length in rabbits, or East and Hayes' experiments with corn. Any of these might serve as an example of what takes place under selection. One example will suffice.

Castle studied the effects of selection of the color-pattern of a race of hooded rats (Fig. 151). Starting with the offspring of commercial animals, he selected in one direction those rats that had the broadest stripes, and in the other direction the rats that had the narrowest stripes, keeping these two lines apart. In the course of a few generations the two populations became measurably different—in one the dorsal stripe was broader, on the average, than in the original group of rats; in the other,

the stripe was narrower. Selection had in some way changed the width of the stripe. So far there is nothing in the results to show that this change may not have been due to the sorting out by selection of two sets of factors that determine the width of the dorsal stripe. Castle argued, however, that he was dealing with the effect of a

FIG. 151.
Four types of hooded rats. (After Castle.)

single gene, because when the striped rats are crossed to a rat with uniform coat (all black or all gray) and the hybrid (F_1) rats are inbred, their offspring give three uniform to one spotted coat. This Mendelian ratio does show, in fact, that a spotted coat is due to a recessive gene, but it does *not* show that the effects of this gene may not also be influenced by other genetic factors that determine the width of the stripe, and this is really the question at issue.

A later experiment, devised by Wright and carried out by Castle, showed, in fact, that the results had been due to the isolation of modifying genes for width of stripe. The test was as follows: Each of the highly selected races was back-crossed to wild rats, that is, rats with uniform coat color, and a second (extracted) generation of spotted rats obtained. The process was repeated with the (F_2) spotted rats obtained from the first back-cross. It was found after back-crossing for two or three generations that the selected stock began to change back, so to speak, to its original state. The selected race with a narrower stripe changed toward a broader stripe and the selected race with a broader stripe changed toward a narrower stripe. In other words, the two selected races became more and more like each other, and more like the original race from which they had started.

This result is completely in accord with the view that modifying factors are present in the wild rats that affect the width of the stripe in animals that are already striped. In other words, the original selection had changed the character of the stripe by sorting out those genes that made it broader or narrower.

At one time Castle went so far as to claim that the results of the experiments with hooded rats reëstablished a view that he ascribed to Darwin, namely, that selection itself brings about a change in the hereditary materials in the direction in which the selection takes place. If this were really Darwin's meaning, such an interpretation of variability might seem greatly to strengthen the theory of natural selection as the method by which evolution has taken place. Castle said in 1915: "All the evidence we have thus far obtained indicates that outside modifiers will not account for the changes observed in the hooded pattern, itself a clear Mendelian unit. We are forced to conclude that this unit itself changes under repeated

selection *in the direction of the selection;* sometimes abruptly, as in the case of our 'mutant' race, a highly stable plus variation; but much oftener gradually, as has occurred continuously in both the plus and the minus selection series."

In the following year he said: "Many students of genetics at present regard unit-characters as unchangeable. . . . For several years I have been investigating this question, and the general conclusion at which I have arrived is this, that unit-characters are modifiable as well as recombinable. Many Mendelians think otherwise, but this is, I believe, because they have not studied the question closely enough. The fact is unmistakable that unit-characters are subject to quantitative variation. . . . Selection, as an agency in evolution, must then be restored to the important place which it held in Darwin's estimation, an agency capable of producing continuous and progressive racial changes."

A careful reading of Darwin's books will fail to furnish a single clear statement to the effect that he believed that the selection process determines or influences the direction of future variation, unless we bring into the field another theory held by Darwin, namely, the theory of inheritance of acquired characters.

Darwin held strongly to the belief in Lamarck's theory. He did not hesitate to make use of it whenever his theory of natural selection was in difficulty. It would be logical, therefore, for anyone who cared to do so (although Darwin himself does not appear to have put the two views together, nor does Castle) to point out that whenever a more advantageous type is selected its germ-cells are exposed, so to speak, to the pangenes produced by its own body, and might be expected to be changed in the direction of the character selected. Hence each new advance would start from a new base, and if scattering variations

occurred about this as a new mode that overstepped the previous boundary, further advances would be expected to appear in the direction in which the last advance took place. In other words, selection would bring about further advances in the direction in which each selection had taken place.

But, as I have said, Darwin never made use of this argument in favor of his selection theory, although it might be claimed he did so in principle whenever he found natural selection inadequate to explain a situation and appealed to Lamarck's principle to carry through the new advance.

Today we regard the selection process, whether natural or artificial, as capable, at most, of causing changes only to the extent to which recombination of the genes already present may affect a change; or, in other words, selection cannot cause a group (species) to transcend the extreme variations that it naturally shows. Rigorous selection can bring a population to a point where all of the individuals are nearer to the extreme type shown by the original population, but beyond this it cannot go. Only by the occurrence of a new mutation in a gene, or by a mass-change in a group of old genes, is it possible, as it now appears to us, for a permanent advance—a step forward, or backward—to be made.

This conclusion is not only a logical deduction from the theory of the stability of the gene, but rests on numerous observations showing that whenever a population is subjected to selection, a rather rapid change begins, but quickly slows down and soon comes to a standstill at or near the extreme type shown by a few individuals of the original population.

So far the problem of the stability of the gene has been examined with respect to gene-contamination in the hybrid, and from the point of view of selection. The possible

influence of the body itself on the constitution of the gene has been only touched upon. The clean separation of the genes in the hybrid, that is the basal postulate of Mendel's first law, would not be possible if genes were subject to influences from the bodily characters of the hybrid.

This conclusion brings us face to face with the Lamarckian theory of the inheritance of acquired characters. It would take us too far afield to attempt to consider the varied claims of this theory, but I may be allowed to call attention to certain relations that would be expected, if, as this theory postulates, the germ-cells are affected by the body in the sense that a change in a character may bring about corresponding alterations in specific genes. A few examples will illustrate the essential facts.

When a black rabbit is bred to a white rabbit the hybrid young are black, yet the germ-cells produced in this hybrid are black- or white-producing, in equal numbers. The black hair of the hybrid has no influence on the white germ-cells. No matter how long the genes for white are carried by black hybrids, the white genes remain white.

Now if the white gene is interpreted as an entity of some sort, it should show, *if* the Lamarckian theory holds, some effect of the body character of the individual in which the gene is carried.

Suppose, however, the white gene is interpreted as the absence of the black gene. Then, of course, there is no reason for supposing that the black color of the hybrid could produce any influence on nothing. To anyone holding the presence and absence theory this argument against Lamarck's theory is not cogent.

There is, however, another line of approach that may be more to the point. A white four-o'clock, bred to a red one, produces an intermediate hybrid with pink-colored flowers (Fig. 5). If we interpret the white color as an absence, the red must be due to a presence. The color of

the flower of the hybrid—pink—is weaker than the red, and if the character affects the gene, the red-producing gene in this hybrid should be diluted by the color of the flower. No such effects here, or elsewhere, have been recorded. The red and the white genes separate in the pink hybrid without showing any somatic effects.

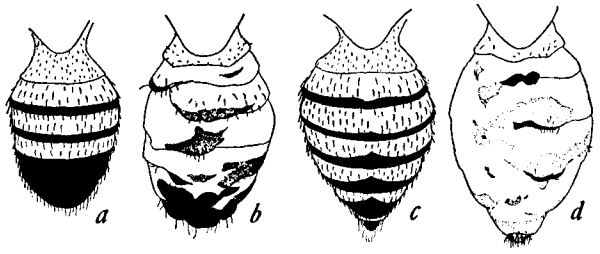

FIG. 152.

a, Abdomen of normal male; *b*, of "abnormal" male; *c*, of normal female; *d*, of "abnormal" female of Drosophila melanogaster.

The evidence from another source is perhaps even a stronger argument against the theory of the inheritance of acquired characters. There is a race of Drosophila—called abnormal abdomen—in which the regular banding of the abdomen is more or less obliterated (Fig. 152). This condition, in its most extreme form, appears in the first flies that emerge from a culture when the food is abundant and the culture is moist and acid. As the culture gets older and dryer, the flies that emerge become more and more normal in appearance, until at last they cannot be distinguished from wild flies. Here we have a genetic character that is extremely sensitive to the environment. Such characters as these furnish a favorable opportunity to study the possible effects of the body on the germ-cells.

If we breed the first hatched flies with very *abnormal*

abdomens, and at the same time and under like conditions we breed the late hatching flies with *normal* abdomens, we obtain exactly the same kinds of flies in the next generation. The first to emerge are abnormal, the later ones more normal. It has made no difference whether the abdomen of the parent was normal or abnormal, so far as the germ-cells are concerned.

If it be said that the effects might be too small to be seen at first, then I may add that late-hatching flies have been bred from for ten successive generations without any observed difference in the results.

Another example is equally convincing. There is a mutant stock of Drosophila called eyeless (Fig. 30). The eyes are smaller than the normal eye and very variable. By selection, a uniform stock has been produced in which most of the flies are without eyes, but, as each culture gets older, more and more flies have eyes, and larger ones. If, now, we breed from the late-hatched flies, the offspring are the same as when eyeless flies are used.

Here the presence of eyes in the older culture is a positive character and might be considered to furnish better evidence than the abnormal abdomen, where the symmetry and pigmentation of the late hatching larvae is less obviously a present character. The outcome is, however, the same in both cases.

It is quite unnecessary to attempt to consider here the numerous claimants that have appeared in the last few years, who have furnished "proof," as they say, of the inheritance of acquired characters. I choose only one case, that is the most complete of its kind, since it gives the numerical and quantitative data on which the conclusions are based. I refer to the recent work of Dürken. The experiment seems to have been carefully made and appears to Dürken to furnish proof of the inheritance of acquired characters.

Dürken worked with the chrysalids (or pupae) of the common cabbage butterfly (Pieris brassicae). Since 1890 it has been known that when the caterpillars of some butterflies pupate (that is, when they transform into the resting chrysalis) the color of the pupa is to some extent influenced by the background, or by the color of the light that falls on it.

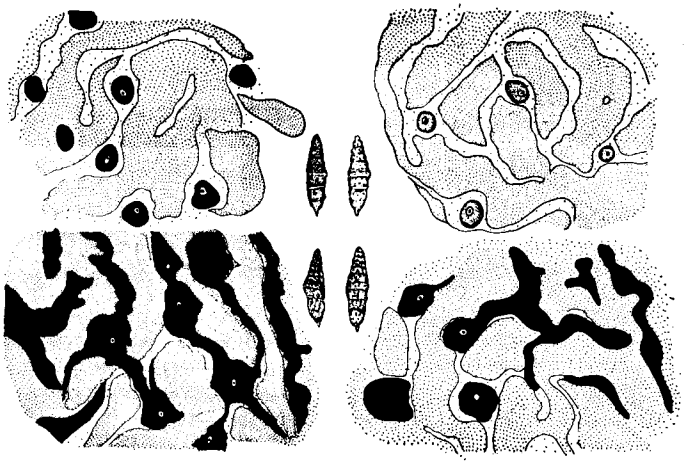

FIG. 153.

In the center four differently colored pupae of the cabbage butterfly. Around them is shown the characteristic arrangement of the pigment cells in the epidermis in different color types. (After Leonore Brecher.)

For example, the pupae of the cabbage butterfly are quite dark, if the caterpillars live and transform in daylight, or even in a faint light; but if the caterpillar lives in yellow or red surroundings or behind a yellow or red screen the pupae are green. The green color is due to the absence of superficial black pigment. In its absence the greenish yellow color of the interior shows through the skin (Fig. 153).

Dürken's experiments consisted in rearing caterpillars in orange (or red) light, where the pupae assumed a light or green color. The butterflies that emerged were reared in open cages and their eggs collected. Some of the young from these eggs were reared again in colored light, others in bright light or in darkness. The latter are the controls. The results are summarized in the chart (Fig. 154). The number of dark chrysalids is indicated by the length of the black band, and the green or light ones by the light band in the chart. As a matter of fact, the pupae were classified in five color groups. Three of these were then lumped together as dark and the other two as light.

As shown in Fig. 154 at 1 (which gives the normal coloration), nearly all pupae, collected at random or in normal surroundings, are dark; only a few are light or green. The caterpillars that came from these were reared in an orange environment. When they transformed into pupae there was a very high percentage of light-colored types, 2. If the light-colored types only are now picked out and reared, some in orange, some in the light, and others in the dark, the results are shown in 3a and 3b. In the former, there are more light pupae than before; since two generations have been in orange, the effect is augmented. It is the other set, 3b, however, that is more significant. As the bands show there were more light pupae than in the wild pupae, 1, that were reared in the light or dark. This increase Dürken attributes in part to the inherited effect of the orange light on the preceding generation, and in part to the new environment, whose effect is in the opposite direction.

Now this interpretation, from the point of view of genetics, is not satisfactory. The experiment shows, in the first place, that not all caterpillars respond to the orange light. If those that do respond are genetically different, then of course when they—the light pupae in the experi-

ment—are selected for the second orange trial and for the control in light and dark, we are dealing already with a more responsive type, a selected group, and these are expected to again respond in the next generation, as they do in fact.

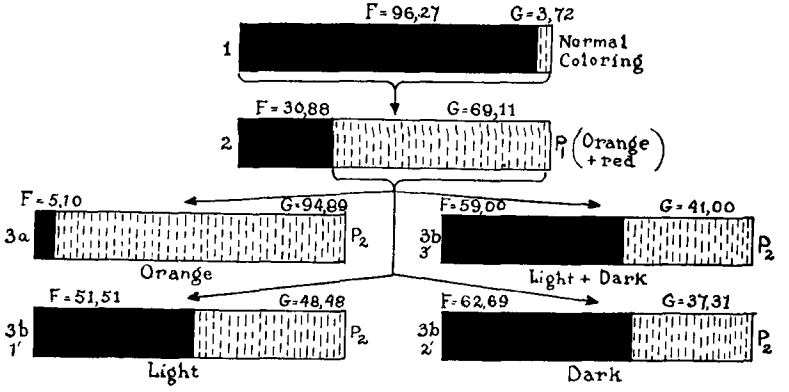

FIG. 154.

Diagram illustrating the results of selection of dark and light pupae of the cabbage butterfly. (After Dürken.)

Therefore, unless the material is genetically homogeneous at the start or unless other controls are used, the evidence fails signally to establish the inherited effect of the environment.

The same error runs through nearly all the work of this sort that has been done. Modern genetics, if it had accomplished nothing more, would have justified itself in showing the worthlessness of such evidence.

We may pass now to a group of cases in some of which it seems probable that the germ-cells themselves have been directly injured by special treatment, and that the injured germ-material is transmitted to later generations. Owing to this injury, malformations may appear in successive generations. This means that the treatment

has not affected the germ-material by first causing defects in the embryo, but has affected both the embryo and its germ-cells at the same time.

Stockard carried out a prolonged series of experiments on the effects of alcohol on guinea pigs. The guinea pigs were treated by placing them in closed tanks over strong

FIG. 155.
Two abnormal young guinea pigs whose ancestors were alcoholics. (After Stockard.)

alcohol. They breathed the air saturated with alcohol, and after a few hours became completely stupefied. The treatment was carried over a long time. Some of the guinea pigs were bred while undergoing treatment, others only at the end of the treatment. The results were essentially the same. Many young were aborted or absorbed, others were born dead, others showed abnormalities, especially in the nervous system and eyes (Fig. 155). Only those that themselves showed no defects could be bred. From these, abnormal young continued to appear

along with other individuals normal in appearance. In later generations abnormals continued to appear, but only from certain individuals.

If we examine the pedigrees of the alcoholic series there is no evidence that the results conform to any of the known Mendelian ratios. Moreover, the varied localization of the effects shown by the abnormals is not of a kind that resembles what we meet with when single gene-changes are involved. On the other hand, the defects have many points of resemblance to the kind of changes that we are familiar with in experimental embryology when abnormal development is brought about by treating eggs with toxic agents. Stockard has called attention to these relations, and interprets his result to mean that an injury of some sort to the germ-cells has been produced by the alcohol—an injury to some part of the machinery that is involved in heredity. The effects are localized only in so far as they pertain to those parts of the body that are most sensitive to any departure from the normal course of development. These parts are most frequently the nervous system and the sense organs.

More recently Little and Bagg have carried out a series of experiments on the effects of radium on pregnant mice and rats. When the treatment is properly administered, the young mice in utero may develop abnormally. When examined before birth many of them show hemorrhagic areas (Fig. 156) in the brain and cord, or elsewhere (especially in the leg rudiments). Some of these embryos die before parturition, and are absorbed, others are aborted. Still others are born alive and some of these survive and may procreate. The offspring often show serious defects in the brain or in the appendages. One or both eyes may be defective. Both eyes may be absent, or one only may be present, much reduced in size. Bagg has bred some of these mice and finds that they produce many

abnormal offspring that show defects similar, in a general way, to those induced directly in the original embryos.

How shall we interpret these experiments? Has the radium first produced its effects on the brain of the de-

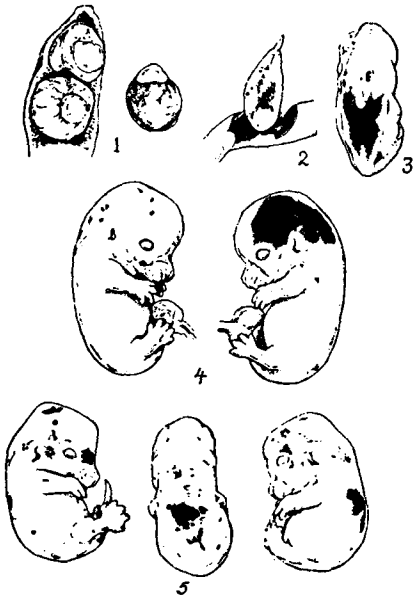

FIG. 156.

Young rat embryos with hemorrhagic areas whose mother had been treated with radium when the young were in utero. (After Bagg.)

veloping embryo, causing defects, and is it owing to the presence of these defects that the germ-cells of the same embryo become affected? There is an apparent objection to this interpretation. We should expect when the brain alone is affected, the next generation should show brain defects; when the eye is the principal organ affected, the next generation should show only eye defects. So far as

reported the results are not like this, for a mouse with abnormal brain and full-sized eyes may produce offspring that have defective eyes. In other words, there is not here a specific effect, but a general one.

The other interpretation is that the germ-cells of the young mouse in utero are affected by the radium. When, in turn, these germ-cells produce a new generation, the individuals are defective because the same organs whose normal development was most disturbed are the organs that are most easily affected by any alteration in the course of development. They are, in a word, the weakest or most delicately balanced phases of development, and therefore the first ones to show the effect of any departure from the normal course of events. This is, I think, at present the most plausible explanation of these and similar experiments.