CHAPTER XIX

GENERAL CONCLUSIONS

THE preceding chapters have dealt with two main topics: with the effects following a change in the number of the chromosomes; and with the effects following a change within a chromosome (a point mutation). The theory of the gene is broad enough to cover both these kinds of changes, although its main concern is with the gene itself. The term *mutation* also has come, through usage, to include the effects produced in both these ways.

These kinds of changes have important bearings on current genetic theories.

The Effects Produced by a Change in Chromosome Number and by a Change in a Gene.

When the number of the chromosomes is doubled, trebled, or multiplied any number of times, the individual has the same kinds of genes as before, and they stand in the same numerical ratio to one another. There is no *a priori* expectation that this kind of change would affect the character of the individual, were it not that the volume of the cytoplasm may not increase to correspond with the increase in the number of the genes. Just what a failure to attain a corresponding increase of cytoplasmic volume means is not clear at present. At any rate, the results show that triploid, tetraploids, octoploids, etc., do not differ markedly in any special characters (except size) from the original diploid type. In other words, the changes produced may be very numerous, but not strikingly different from the original ones.

On the other hand, the addition of a single chromosome or of two members of the same pair, or of two or more members of different pairs to the group, or the loss of a whole chromosome from the group, may be expected to produce more evident effects on the individual. There is some evidence that such additions or losses are less extreme when many chromosomes are present, or when the change takes place in a small chromosome. From the point of view of the theory of the gene, this result is what would be anticipated. For instance, the addition of one chromosome means that a large number of genes are now present in triplicate. The balance of the genes is changed in the sense that there are now present more genes of certain kinds than before, but since no new genes are added the effects would be expected to be distributed amongst many of the characters that might be somewhat enhanced or diminished in intensity. This accords with the facts as yet reported. It is interesting to note, however, that, as far as known, the general results are not beneficial but, if anything, deleterious. This, too, is expected if the adjustments, both to internal and to external relations, are as perfect as possible in the normal individual as its long evolutionary history might lead one to expect.

Because such a change affects many parts to a slight degree, it does not follow that such effects are more likely to lead to the establishment of a new viable type than when changes are brought about one step at a time by changes in single genes.

Furthermore, even the addition of two new chromosomes of the same kind, giving possibly a new stable type of inheritance, does not improve the situation, but, as far as we know,—the evidence is slight at present,—the maladjustments are even further increased. For these reasons it does not seem that a change from one chromo-

some group to another is easily brought about in this way, although the possibility of such a change cannot be entirely excluded. We need, at present, more evidence to decide this question.

The same arguments apply, though less strongly perhaps, to those cases when parts of chromosomes are added to, or subtracted from, the chromosome group. The effect produced is the same in kind, but less in degree, and it is correspondingly more difficult to determine whether the final effect on viability is injurious or beneficial.

The work of the last few years in genetics has made it clear that, despite the occurrence of the same number of chromosomes in related species and even in entire families and orders, it is hazardous to assume that the chromosomes, even in closely related species, are always identical as to their genes. The genetic evidence is beginning to make clear that readjustments may take place both within the chromosomes, where groups of genes may come to lie in reversed order, and between different chromosomes, where blocks of genes may be shifted, without giving a measurable difference in size. Even whole chromosomes might be recombined in different groupings without changing the actual number. Alterations of these kinds will affect profoundly the linkage relations, hence the modes of inheritance of the various characters, without, however, changing the total number or kinds of the genes involved. Unless, therefore, the cytological observations are checked by genetic studies it will always be unsafe to assume that identity in number of chromosomes means a correspondence in grouping of the genes.

Two methods by which changes in chromosome numbers take place are, first, the union of two chromosomes to form one, as in the attached X's of Drosophila, and the occasional breaking apart of chromosomes, as re-

ported by Hance in Oenothera and in several other cases. The temporary separation and reunion of certain chromosomes in moths, described by Seiler, also come under this heading, especially if, as he supposes, the separated elements may sometimes recombine reciprocally.

In contrast with the effect produced when large numbers of genes are involved, the effects produced by a change in a gene appear at first sight much more extreme. This first impression may, however, be very misleading. While it is true that many of the most striking mutant characters studied by geneticists are markedly different from the normal character with which they are contrasted, these mutant characters have often been chosen for study because they are sharply marked off from the typical character, and can, in consequence, be readily followed in succeeding generations. Their separation is accurate, and the results more certain than in cases where the differences are less marked, or where there is an overlap between the characters of the contrasted pair. Moreover, the more bizarre and extreme modifications, that sometimes amount to "abnormalities," are the ones that are most likely to attract attention and interest, hence are utilized for genetic study, while the less obvious modifications are overlooked or neglected. Geneticists are familiar with the fact that the more intensively any particular group is studied the more mutant characters are found which had been, at first, overlooked, and since these are those that more nearly approach the normal type, it becomes increasingly evident that the mutation process involves very small, as well as very great, modifications.

In the older literature the extreme, abnormal types were called sports, and for a long time it was supposed that these sports were sharply separated from the small or individual differences constantly present in all species

and commonly spoken of as variations. Today we know that there is no such sharp contrast, but that sports and variations may have the same kind of origin, and are inherited according to the same laws.

It is true that many of the small individual differences are due to the environmental conditions under which the development takes place, and superficial examination fails often to distinguish between this sort of variability and that due to minor changes brought about by genetic factors. One of the most important results of modern genetics is the recognition of this fact, and the invention of methods by which the smaller differences may be referred to one or to the other of these factors. If, as Darwin supposed, and if, as is generally accepted today, the process of evolution has taken place by the slow process of accumulation of small variations, it follows that it must be the genetic variations that are utilized, since these, and not those due to environmental effects, are inherited.

It must not be supposed, however, from what has just been said, that mutant changes produce only a single striking or even a single small change in one particular part of the body. On the contrary, the evidence from the Drosophila work, which is in accord with that from all other forms that have been critically studied, shows that even in those cases where one part is especially modified, other effects are commonly present in several or in all parts of the body. The subsidiary effects not only involve structural modifications, but physiological effects also, if one may judge by the activity, the fertility, and the length of life of the mutants. For example, the loss of positive phototropism, characteristic of Drosophila, accompanied a change involving a very slight alteration in the general color of the body.

The converse of this relation must also hold. Slight

changes due to a mutated gene that affect physiological processes and reactions may frequently be accompanied by alterations in external structural characters. If these physiological changes are of a kind to better adjust the organism to its environment, they may be expected to persist, and, at times, lead to the survival of new types. These types may then differ from the original type in superficial characters that are constant but trivial in themselves. Since many species differences appear to be of this kind, it is plausible to interpret their constancy as due not to their own survival value, but rather due to their relation to some other deeply seated character that is important for the welfare of the species.

In the light of what has just been said we can give a reasonable explanation of the differences that follow when a mutant change involves a whole chromosome (or part of one) and when only a single gene is involved. The former change adds nothing intrinsically new to the situation. More or less of what is already present is involved in the change, and the effects are small in degree but involve a large number of characters. The latter change—mutation in a single gene—may also produce widespread and slight effects, but, in addition, it often happens that one part of the body is changed to a striking degree along with other changes less striking. This latter kind of change, as I have said, supplies materials favorable for genetic study; these have been widely utilized. Now it is these mutational changes that have occupied the forefront of genetic publication, and have given rise to a popular illusion that each such mutant character is the effect of only one gene, and by implication to the fallacy, more insidious still, that each unit character has a single representative in the germ material. On the contrary, the study of embryology shows that every organ of the body is the end-result, the culmination of a long

series of processes. A change that affects any step in the process may be expected often to affect a change in the end-result. It is the final visible effect that we see, not the point at which the effect was brought about. If, as we may readily suppose, very many steps are involved in the development of a single organ, and if each of these steps is affected by the action of a host of genes, there can be no single representative in the germ-plasm for any organ of the body, however small or trivial that organ may be. Suppose, for instance, to take perhaps an extreme case, all the genes are instrumental in producing each organ of the body. This may only mean that they all produce chemical substances essential for the normal course of development. If now one gene is changed so that it produces some substance different from that which it produced before, the end-result may be affected, and if the change affects one organ predominatingly it may appear that one gene alone has produced this effect. In a strictly causal sense this is true, but the effect is produced only in conjunction with all the other genes. In other words, they are all still contributing, as before, to the end-result, which is different in so far as one of them is different.

In this sense, then, each gene may have a specific effect on a particular organ, but this gene is by no means the sole representative of that organ, and it has also equally specific effects on other organs, and, in extreme cases, perhaps on all the organs or characters of the body.

To return now to our comparison. The effect of a change in a gene (which if recessive means, of course, a pair of like genes) frequently produces a more localized effect than a doubling or trebling of the genes already present, because a change in one gene is more likely to upset the established relation between all the genes than is an increase in the number of genes already present. By extension, this argument seems to mean that each gene

has a specific effect on the course of development, and this is not inconsistent with the point of view urged above, that all the genes or many of them work together toward a definite and complicated end-product.

The best argument at present in favor of a specific action of each gene is found in the series of multiple allelomorphs. Here changes in the same locus affect primarily the same end-result not only in one organ, but in all the parts that are also visibly affected.

Is the Mutation Process Due to a Degradation of the Gene?

In his mutation theory de Vries spoke of types that we now call mutant recessive types as arising from the loss or inactivation of genes. Such changes he regarded as retrogressive. At about the same time, or a little later, the idea that recessive characters are due to losses of genes from the germ material became popular. At the present time several critics interested primarily in the philosophical discussion of evolution have attacked with violence the idea that the mutant types studied by geneticists have anything to do with the traditional theory of evolution. With this latter assertion we are not much concerned, and may safely leave the question at issue for the future to decide; but the suggestion that the mutation process, in so far as it involves an effect on single genes, is limited to the loss of genes or to their partial loss or degradation, as I venture to call such a change, is a matter of some theoretical interest; for, as Bateson elaborated in his 1914 address, it leads logically to the idea that the materials that we use in genetic work are due to loss of genes; that absences, in a literal sense, are the allelomorphs of wild type genes; and that, in so far as this evidence applies to evolution, it leads to the *reductio*

ad absurdum that that process has been a steady drain on the original storehouse of genes wherever they existed.

In chapter VI the genetic evidence at hand that bears on this question has been considered, and it is unnecessary to summarize again what was there said, but I may be allowed to repeat that it is not justifiable to conclude from the fact that many mutant characters are defective, or even partial or complete losses, that they must, therefore, be due to absences of a corresponding gene in the germ material. So far as there is any direct evidence that bears on this question, quite aside from the arbitrariness of the absence hypothesis, it does not, as I have attempted to show, support such a point of view.

There remains, however, a problem of some interest, namely, whether some or many of the changes in the genes that lead to the occurrence of mutant characters (whether recessive, intermediate, or dominant makes little difference) may not be due to a breaking up of a gene, or to its reconstitution into another element producing somewhat different effects. There is, however, no reason for assuming that such change, if it occurs, is a downhill one rather than the development of a more complex gene, unless it appears more probable, *a priori,* that a highly complex stable compound is more likely to break down than to build up. Until we know more concerning the chemical constitution of the genes, and how they grow and divide, it is quite futile to argue the merits of the two sides of the argument. For the genetic theory it is only necessary to assume that any kind of a change may suffice as a basis for what is observed to take place.

It is equally futile to discuss, at present, whether new genes arise independently of the old ones, and worse than futile to discuss how the genes arose in the first instance. The evidence that we have furnishes no grounds whatsoever for the view that new genes independently arise,

but it would be extremely difficult, if not impossible, to show that they do not arise. To the ancients it seemed not incredible that worms and eels arose from the river's slime, and that vermin in general arose in dark dusty corners. The origin of bacterial life from putrefying substances was believed in only one generation ago, and it was extremely difficult to prove that this does not happen. It may be equally difficult to prove convincingly, to one who insists on believing the contrary, that genes arise independently of other genes; but the genetic theory need not be anxious concerning this question until it meets with a situation where such a postulate becomes necessary. At present we find no need of interpolating new genes in the linkage series, or at the ends of the series. If the same number of genes is present in a white blood corpuscle as in all the other cells of the body that constitutes a mammal, and if the former makes only an amoeba-like cell and the rest collectively a man, it scarcely seems necessary to postulate fewer genes for an amoeba or more for a man.

Are Genes of the Order of Organic Molecules?

The only practical interest that a discussion of the question as to whether genes are organic molecules might have would relate to the nature of their stability. By stability we might mean only that the gene tends to vary about a definite mode, or we might mean that the gene is stable in the sense that an organic molecule is stable. The genetic problem would be simplified if we could establish the latter interpretation. If, on the other hand, the gene is regarded as merely a quantity of so much material, we can give no satisfactory answer as to why it remains so constant through all the vicissitudes of outcrossing, unless we appeal to mysterious powers of organization outside the genes that keep them constant. There is little

hope at present of settling the question. A few years ago I attempted to make a calculation as to the size of the gene in the hope that it might throw a little light on the problem, but at present we lack sufficiently exact measurements to make such a calculation more than a speculation. It seemed to show that the order of magnitude of the gene is near that of the larger-sized organic molecules. If any weight can be attached to the result it indicates, perhaps, that the gene is not too large for it to be considered as a chemical molecule, but further than this we are not justified in going. The gene might even then not be a molecule but only a collection of organic matter not held together in chemical combination.

When all this is given due weight it nevertheless is difficult to resist the fascinating assumption that the gene is constant because it represents an organic chemical entity. This is the simplest assumption that one can make at present, and since this view is consistent with all that is known about the stability of the gene it seems, at least, a good working hypothesis.