Tobacco Station[11] resulted in abnormal physiological symptoms in tobacco if the amounts of manganese in the soil exceeded a certain optimum.

Boron, in the form of salts of boric acids, especially borax, has been known for some time to be very toxic to farm crops if in concentrations of more than three parts per million in the nutrient medium. But in less concentrations (the optimum being about 1:1,500,000) it has been found by Lipman and his associates[3] at the University of California, by Brenchley[12] in England and by Warrington[13] in Sweden to be absolutely indispensable for satisfactory growth of many crop plants. Both Miss Brenchley and Miss Warrington report that insufficient supplies of boron in the nutrient medium result in definite anatomical abnormalities in the plants, particularly retardation of the development of meristem tissue, with certain specific discolorations in the stems of the plants which are recognizable as definite diagnostic symptoms for the boron-deficiency.

Zinc has been shown, by Sommer,[14] by Brenchley[1] and by McHargue and Shedd[15] to be a specific necessary nutrient for certain types of crops, but apparently not so, at least in the same degree, for others. The macroscopic evidence of zinc-deficiency is cited as an alteration of the normal proportion of straw and grain, but this is of course only a final result of some disturbance in the plant's metabolism or physiological processes the nature of which has not yet been studied.

These examples are probably adequate to indicate the basis for my assumption of a series of phenomena and principles of plant nutrition parallel to or at least comparable with the vitamin function in animal nutrition.

Fortunately for the proposed experimental study of this hypothesis, the elements to which these specific nutritional functions are apparently attached are presumably well-known chemical entities, for which qualitative and quantitative methods of testing are already available, thus making unnecessary one type of investigation which is essential in vitamin studies. But there does remain to be done a large amount of experimental study of the conditions and limitations of the requirements for these accessory factors of plant nutrition, and of the forms of compounds and conditions of protoplasm under which they exert their specific effects, together with a wide range of studies of the actual ill effects, physiologically and anatomically, of deficiencies in the diet of different types of farm crops of these plant "vitamins." For this latter type of studies, a new technique will probably have to be developed, as was the case with the animal vitamins. I believe, however, that this is a very promising field of research, and, as I said, I hope to have an opportunity soon to enter upon a definite program of investigations in it. It is to possible cooperation in this undertaking that I invite the attention of interested agronomists, chemists and plant physiologists.

[11] H. G. M. Jacobsen and T. R. Swanback, "Manganese Toxicity in Tobacco," SCIENCE, 76 (No. 1812): 283–284. 1929.

[12] Winifred E. Brenchley, "Investigations on the Effect of Boron on Plant Life," *Agr. Prog.* (*Agr. Ed. Assn., London*), 3: 104–105. 1926.

[13] Katherine Warrington, "The Changes Induced in the Anatomical Structure of *Vicia faba* by the Absence of Boron from the Nutrient Solution," *Ann. Bot.* (*London*), 40 (No. 157): 27–42. 1926.

[14] A. L. Sommer, "Further Evidence of the Essential Nature of Zinc for the Growth of the Higher Green Plants," *Plant Physiology*, 3 (No. 2): 217–221. 1928.

[15] J. S. McHargue and O. M. Shedd, "The Effect of Manganese, Copper, Zinc, Boron, and Arsenic on the Growth of Oats," *Jour. Am. Soc. Agron.*, 22 (No. 8): 739–746. 1930.

THE RISE OF GENETICS. II

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INFLUENCE OF THE GENES ON THE CYTOPLASM

IF another branch of zoology that was actively cultivated at the end of the last century had realized its ambitions, it might have been possible to-day to bridge the gap between gene and character, but despite its high-sounding name of *Entwicklungsmechanik* nothing that was really quantitative or mechanistic was forthcoming. Instead, philosophical platitudes were invoked rather than experimentally determined factors. Then, too, experimental embryology ran for a while after false gods that landed it finally in a maze of metaphysical subtleties. It is unfortunate, therefore, that from this source we can not add, to the three contributory lines of research which led to the rise of genetics, a fourth and greatly needed contribution to bridge an unfortunate gap. I say this with much regret, for, during that time and even now, I have not lost interest in this fascinating field of embryological experimentation. It is true that a great deal of factual evidence came to light, and it is true that many misleading ideas were set aside, but the upshot was negative so far as the formulation of any of the factors of development, whether mechanistic or otherwise, are concerned. This may be because the work was pioneer and largely qualitative. Perhaps my disappointment at the outcome of the work has led me to an overstatement of its failures. Something did emerge that the future may show to be of fundamental importance for genetics. I mean the experimental demonstration that the immediate factors in the differentiation of the embryo are, at the time of their activity, already in the cytoplasm of the cell. Second only in interest was the discovery that, within certain limitations, the already determined specificity may be reversed, or rather, shall I say, the initial steps already taken are reversible by factors extraneous to the individual cells.

These statements call for further elaboration, because they are unconsciously in the background of much of our thinking about genetic problems, and should if possible be more sharply formulated.

That the form of cleavage of the egg is determined by the kind of chromosomes it contained before the egg reached maturity has been sufficiently proven; and since the foundations of all later differentiation are laid down at this time, the demonstration is of first-rate importance for genetics, because it shows that we are not obliged to suppose the genes or chromosomes are functioning at the moment of the visible appearance of characters.

This is demonstrated by introducing into the egg foreign sperm of a species having another type of development. Although the chromosomes from the sperm are present from the first cleavage onward, they produce at first no effect on the cleavage; only after a time do they succeed in bringing about changes in the embryo. This evidence is, as I have said, important for our genetic analysis, for it serves as a warning that the time relations between gene and cytoplasm may have a relation different from that of an immediate dynamic change in the cytoplasm. The preparation for the effect may have taken place long before the actual event.

The second inference is no less significant. I need not labor the point at this late date that the characters of the individual are the product both of its genetic make-up and its environment. The earlier, premature idea, that for each character there is a specific gene—the so-called unit-character—was never a cardinal doctrine of genetics, although some of the earlier popularizers of the new theory were certainly guilty of giving this impression. The opposite extreme statement, namely, that every character is the product of all the genes, may also have its limitations, but is undoubtedly more nearly in accord with our conception of the relation of genes and characters. A more accurate statement would be that the gene acts as a differential, turning the balance in a given direction, affecting certain characters more conspicuously than others. But let us not forget that the environment may also act as a differential, intensifying or diminishing, as the case may be, the action of the genes.

The best illustration of this double relation is seen in the determination of sex. When an unpaired chromosome is present, in one or in the other sex, its genes determine, as a rule, whether a male or a female develops from each egg. Under environmental conditions which, as we say, are normal, the differential acts almost perfectly; but under other unusual conditions and in a few special cases its power may be partially overcome and even a reversal may take place. These unusual environmental conditions may be external agents, such as temperature or light. They may also be internal factors, such as hormones. Even "age" itself may bring about a reversal of sex in certain types. These statements are commonplaces to-day. The only differences of opinion concern the emphasis that one theorist places on the environment, and another on the genic composition.

In passing, a word may be said about the genes as sex factors or differentials. All through the 32 years of the present century there have been attempts to isolate (in a genetic sense) the sex-determining factors. At first, when the chromosome mechanism was discovered, the idea prevailed that one X, let us say, made a male, and two X's a female. The sex-chromosome itself was then taken as the differential. Very soon after this the idea that the sex chromosome was the carrier of a gene for sex suggested itself, and a search was started to locate such a gene or genes in this chromosome. More recent work on translocations has shown the probable futility of such an interpretation. The tendency at present is rather to look upon all the genes, or at least many of them, as sex-determining in exactly the same sense, as all or many of the genes have an effect on the development of each character. It may well be, however, that certain genes in the sex-chromosome (as in other chromosomes) are more influential than others in turning the balance one way or the other, but even so, it does not at the present moment—in the light of recent evidence—seem probable that a single gene for sex-determination is to be found in the X-chromosome any more than, in the contrary sense, there is a single gene for sex in any special autosome. Here again, some one or a few genes may be more influential than others, but this is also true to varying degrees of the gene for any other character. The theory of balance between the intracellular products of the genes is the most direct contribution to physiology that modern genetics has made. It is an idea familiar to classical physiology as applied to organ systems, but a distinctly new contribution to cellular physiology. It may be a long time before these intracellular genic substances are isolated and purified (since there may be many steps between the actual primary substances and the end-product of such substances in the cell-plasm); nevertheless as a point of view the presence of genic materials rather than a dynamic action of the nucleus is supported by some analytical evidence. Already there is afoot in several quarters, and by methods partly genetic, partly physiological, partly embryological, partly physical and chemical, a decided effort to approach this problem.

If we could obtain these substances in pure condition we might then be in a position to speak more confidently of a quantitative study of gene-activities in the sense that chemistry is quantitative. Meanwhile there are other more practical methods by which we may construct provisional hypotheses as to the nature of the intracellular substances that are the products of the genes, namely, through a study of triploids, trisomic types, fragments of chromosomes and by analysis of crosses between different species. These openings do not, of course, exclude the possibility of the discovery of entirely new methods of approach.

Let us not forget that the idea of balance, as seen in the character, is really an old and familiar one to geneticists. For example, the intermediate character of the F_1 hybrid was generally interpreted as due to a conflict between the old and the new gene. Again, the familiar statement that characters are often affected by modifying gene-action that enhances or diminishes the effect of the primary gene, is another example of the intracellular balance of the activity of the genes.

What has been said so far relates to the action of the gene on the cytoplasm of its own cell—its intracellular action. Those of us working with insects or plants are apt to think of genetic problems in this way, and are inclined to consider mainly the effects that do not reach beyond the cells in which they are produced. But in other groups, especially birds and mammals, the effects of the genes are not always so limited. We are on the threshold of work concerned with the isolation of the so-called sex-hormones, the end-products of the thyroid gland, the pituitary, the thymus, and the substances isolated from the suprarenal bodies. All these substances produce their effects outside of the cells that manufacture them. In themselves they are far removed from the primary action of the genes.

In this connection certain work carried out by experimental embryologists should not be overlooked, beginning with the early experiments of Lewis in 1904 and culminating in the more recent work of Spemann. Here it appears as the result of grafting experiments that certain organs of the body develop in response to the vicinity of other organs, as when, for example, the lens of the eye of the frog is shown to be a response to the presence beneath the skin of the optic lobe. Similar and more far-reaching effects have been recently found for other organs of the embryo. The simplest interpretation, perhaps, is the setting free of a hormone by an embryonic organ or group of cells that calls forth a response in neighboring regions.

This and other evidence goes to show that gene-activity may produce results outside of the cells in which the first steps are initiated. The problem at present is one of immediate importance in the study of gynandromorphs, mosaics and intersexes.

EVOLUTION

Sooner or later every geneticist is asked what bearing this work has on the theory of evolution. In the early years of the century when genetics was new, some of us tried to sidestep the question, partly on the grounds that genetics was not ready to discuss the bearing of the new work on evolution, but mainly because it seemed unfortunate to compromise the precise results of the new procedure with the evolution doctrine which, because it dealt with a historical problem, was largely speculative. After 32 years of activity, caution may still be the wiser course to pursue; yet, on the other hand, we are now prepared, I think, to make a more definite commitment. It is, of course, obvious that only those characteristics that are inherited can take part in the process of evolution. The only characters that we know to be inherited are those that arise first as mutants, *i.e.*, discontinuously, or, as we say, by a change in a gene. Here genetics has made a very important contribution to evolution, especially when it is recalled that it has brought to the subject an exact scientific method of procedure. If we compare our present status in this respect with the discussions of the old school of evolutionists concerning variability, there can be no question but that genetics has contributed valuable information.

In the second place, the objection has been not infrequently made that geneticists are dealing only with aberrant or abnormal characters—hence their results, however accurate, can have nothing to do with the kind of progressive changes that have made evolution of new types possible. Such objections have come largely from those who ignore what geneticists have done and are doing. The same objections have also come from those whose minds are closed to new evidence, or who can not distinguish between the value of tested and verifiable theories and vague views or juvenile impressions with a teleological background or bias.

Without elaborating, I wish to point out briefly that there is to-day abundant evidence showing that the differences, distinguishing the characteristics of one wild-type or variety from others, follow the same laws of heredity as do the so-called aberrant types studied by geneticists.

Even this evidence may not satisfy the members of the old school because, they may still say, all these characters that follow Mendel's laws, even those found in wild species, are still not the kind that have contributed to evolution. They may claim that these characters are in a class by themselves, and not amenable to Mendelian laws. If they take this attitude, we can only reply that here we part company, since *ex cathedra* statements are not arguments, and an appeal to mysticism is outside of science.

There remains still the question of the causal origin of mutations. Here also some progress has been made, but the subject is admittedly by no means on the same footing as is our knowledge of the laws of inheritance. It behooves us, then, to be careful, for our progress in this respect has been slow and to some extent erratic. I mean by this that we have not yet found a method of producing specific results—*i.e.,* a method by which particular genes can be changed in a particular way.

Even here, however, something has been done. In the work with x-rays and heat the same mutants appear that are already known, and that have come up without treatment. In addition, new mutants appear, as they do also without treatment. If it can be shown on a large scale that the same ratio for known mutations holds for x-ray and for spontaneous mutations, we may have found an opening for the further study of the causes of certain types of mutation.

I have been challenged recently to state on this occasion what seemed to be the most important problems for genetics in the immediate future. I have decided to try, although I realize only too well that my own selection may only serve to show to future generations how blind we are (or I have been, at least) to the significant events of our own time.

First, then, the physical and physiological processes involved in the growth of genes and their duplication (or as we say their "division") are obviously phenomena on which the whole process of reproduction rests. The ability of the new genes to retain the property of duplication is the background of all genetic theory. Whether the solution will come from a frontal attack by cytologists, geneticists and chemists, or by flank movements, is difficult to predict, although I think the latter more promising.

Second: An interpretation in physical terms of the changes that take place during and after the conjugation of the chromosomes. This includes several separate but interdependent phenomena—the elongation of the threads, their union in pairs, crossing over, and the separation of the four strands. Here is a problem on the biological level, as we say, whose solution may be anticipated only by a combined attack of geneticists and cytologists.

Third: The relation of genes to characters. This is the explicit realization of the implicit power of the genes, and includes the physiological action of the gene on the rest of the cell. This is the gap in our knowledge to which I have referred already at some length.

Fourth: The nature of the mutation process—perhaps I may say the chemico-physical changes involved when a gene changes to a new one. Emergent evolution, if you like, but as a scientific problem, not one of metaphysics.

Fifth: The application of genetics to horticulture and to animal husbandry, especially in two essential respects; more intensive work on the physiological, rather than the morphological, aspects of inheritance; and the incorporation of genes from wild varieties and species into strains of domesticated types.

Should you ask me how these discoveries are to be made, I would become vague and resort to generalities. I would then say: By industry, trusting to luck for new openings. By the intelligent use of working hypotheses (by intelligence I mean a readiness to reject any such hypotheses unless critical evidence can be found for their support). By a search for favorable material, which is often more important than plodding along the well-trodden path, hoping that something a little different may be found. And lastly, by not holding genetics congresses too often.

OBITUARY

RALPH HOFFMANN

RALPH HOFFMANN, director of the Santa Barbara Museum of Natural History, met sudden death in a fall from a cliff on San Miguel Island, California, on July 21.

He was born in Stockbridge, Massachusetts, in 1870, was educated at Williston Academy, and graduated from Harvard University in 1890. After graduating he taught at the Browne and Nichols School in Cambridge. In 1910 he became head master of the Coun-