

THOMAS H. MORGAN

The relation of genetics to physiology and medicine

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The study of heredity, now called genetics, has undergone such an extraordinary development in the present century, both in theory and in practice, that it is not possible in a short address to review even briefly all of its outstanding achievements. At most I can do no more than take up a few outstanding topics for discussion.

Since the group of men with whom I have worked for twenty years has been interested for the most part in the chromosome mechanism of heredity, I shall first briefly describe the relation between the facts of heredity and the theory of the gene. Then I should like to discuss one of the physiological problems implied in the theory of the gene; and finally, I hope to say a few words about the applications of genetics to medicine.

The modern theory of genetics dates from the opening years of the present century, with the discovery of Mendel's long-lost paper that had been overlooked for thirty-five years. The data obtained by De Vries in Holland, Correns in Germany, and Tschermak in Austria showed that Mendel's laws are not confined to garden peas, but apply to other plants. A year or two later the work of Bateson and Punnett in England, and Cuénot in France, made it evident that the same laws apply to animals.

In 1902 a young student, William Sutton, working in the laboratory of E. B. Wilson, pointed out clearly and completely that the known behavior of the chromosomes at the time of maturation of the germ cells furnishes us with a mechanism that accounts for the kind of separation of the hereditary units postulated in Mendel's theory.

The discovery of a mechanism, that suffices to explain both the first and the second law of Mendel, has had far-reaching consequences for genetic theory, especially in relation to the discovery of additional laws; because, the recognition of a mechanism that can be seen and followed demands that any extension of Mendel's theories must conform to such a recognized mechanism; and also because the apparent exceptions to Mendel's laws, that came to light before long, might, in the absence of a known mechanism, have called forth purely fictitious modifications of Mendel's laws, or even

seemed to invalidate their generality. We now know that some of these "exceptions" are due to newly discovered and demonstrable properties of the chromosome mechanism, and others to recognizable irregularities in the machine.

Mendel knew of no processes taking place in the formation of pollen and egg cell that could furnish a basis for his primary assumption that the hereditary elements separate in the germ cells in such a way that each ripe germ cell comes to contain only one of each kind of element: but he justified the validity of this assumption by putting it to a crucial test. His analysis was a wonderful feat of reasoning. He verified his reasoning by the recognized experimental procedure of science.

As a matter of fact it would not have been possible in Mendel's time to give an objective demonstration of the basic mechanism involved in the separation of the hereditary elements in the germ cells. The preparation for this demonstration took all of the thirty-five years between Mendel's paper in 1865, and 1900. It is here that the names of the most prominent European cytologists stand out as the discoverers of the role of the chromosomes in the maturation of the germ cells. It is largely a result of their work that it was possible in 1902 to relate the well-known cytological evidence to Mendel's laws. So much in retrospect.

The most significant additions that have been made to Mendel's two laws may be called linkage and crossing-over. In 1906 Bateson and Punnett reported a two-factor case in sweet peas that did not give the expected ratio for two pairs of characters entering the cross at the same time.

By 1911 two genes had been found in *Drosophila* that gave sex-linked inheritance. It had earlier been shown that such genes lie in the X-chromosomes. Ratios were found in the second generation that did not conform to Mendel's second law when these two pairs of characters are present, and the suggestion was made that the ratios in such cases could be explained on the basis of interchange between the two X-chromosomes in the female. It was also pointed out that the further apart the genes for such characters happen to lie in the chromosome, the greater the chance for interchange to take place. This would give the approximate location of the genes with respect to other genes. By further extension and clarification of this idea it became possible, as more evidence accumulated, to demonstrate that the genes lie in a single line in each chromosome.

Two years previously (1909) a Belgian investigator, Janssens, had described a phenomenon in the conjugating chromosomes of a salamander,

Batrachoseps, which he interpreted to mean that interchanges take place between homologous chromosomes. This he called chiasmotypie - a phenomenon that has occupied the attention of cytologists down to the present day. Janssens' observations were destined shortly to supply an objective support to the demonstration of genetic interchange between linked genes carried in the sex chromosomes of the female *Drosophila*.

Today we arrange the genes in a chart or map. The numbers attached express the distance of each gene from some arbitrary point taken as zero. These numbers make it possible to foretell how any new character that may appear will be inherited with respect to all other characters, as soon as its crossing-over value with respect to any other two characters is determined. This ability to predict would in itself justify the construction of such maps, even if there were no other facts concerning the location of the genes; but there is today direct evidence in support of the view that the genes lie in a serial order in the chromosomes.

What are the genes?

What is the nature of the elements of heredity that Mendel postulated as purely theoretical units? What are genes? Now that we locate them in the chromosomes are we justified in regarding them as material units; as chemical bodies of a higher order than molecules? Frankly, these are questions with which the working geneticist has not much concern himself, except now and then to speculate as to the nature of the postulated elements. There is no consensus of opinion amongst geneticists as to what the genes are - whether they are real or purely fictitious - because at the level at which the genetic experiments lie, it does not make the slightest difference whether the gene is a hypothetical unit, or whether the gene is a material particle. In either case the unit is associated with a specific chromosome, and can be localized there by purely genetic analysis. Hence, if the gene is a material unit, it is a piece of a chromosome; if it is a fictitious unit, it must be referred to a definite location in a chromosome - the same place as on the other hypothesis. Therefore, it makes no difference in the actual work in genetics which point of view is taken.

Between the characters that are used by the geneticist and the genes that his theory postulates lies the whole field of embryonic development, where the properties implicit in the genes become explicit in the protoplasm of the

cells. Here we appear to approach a physiological problem, but one that is new and strange to the classical physiology of the schools.

We ascribe certain general properties to the genes, in part from genetic evidence and in part from microscopical observations. These properties we may next consider.

Since chromosomes divide in such a way that the line of genes is split (each daughter chromosome receiving exactly half of the original line) we can scarcely avoid the inference that the genes divide into exactly equal parts; but just how this takes place is not known. The analogy of cell division creates a presumption that the gene divides in the same way, but we should not forget that the relatively gross process involved in cell division may seem quite inadequate to cover the refined separation of the gene into equal halves. As we do not know of any comparable division phenomena in organic molecules, we must also be careful in ascribing a simple molecular constitution to the gene. On the other hand, the elaborate chains of molecules built up in organic material may give us, some day, a better opportunity to picture the molecular or aggregate structure of the gene and furnish a clue concerning its mode of division.

Since by infinite subdivisions the genes do not diminish in size or alter as to their properties, they must, in some sense, compensate by growing between successive divisions. We might call this property autocatalysis, but, since we do not know how the gene grows, it is somewhat hazardous to assume that its property of growth after division is the same process that the chemist calls autocatalytic. The comparison is at present too vague to be reliable.

The relative stability of the gene is an inference from genetic evidence. For thousands - perhaps many millions - of subdivisions of its material it remains constant. Nevertheless, on rare occasions, it may change. We call this change a *mutation*, following De Vries' terminology. The point to emphasize here is that the mutated gene retains, in the great majority of cases studied, the property of growth and division, and more important still the property of stability. It is, however, not necessary to assume, either for the original genes or for the mutated genes, that they are all equally stable. In fact, there is a good deal of evidence for the view that some genes mutate oftener than others, and in a few cases the phenomenon is not infrequent, both in the germ cells and in somatic tissues. Here the significant fact is that these repetitive changes are in definite and specific directions.

The constancy of position of genes with respect to other genes in linear

order in the chromosomes is deducible, both from genetic evidence and from cytological observations. Whether the relative position is no more than a *historical accident*, or whether it is due to some relation between each gene and its neighbors, can not be definitely stated. But the evidence from the dislocation of a fragment of the chromosome, and its reattachment to another one indicates that accident rather than mutual interaction has determined their present location: for, when a piece of one chromosome becomes attached to the end of a chain of genes of another chromosome or when a section of a chromosome becomes inverted, the genes in the new position hold as fast together as they do in the normal chromosome.

There is one point of great interest. So far as we can judge from the action of mutated genes, the kind of effect produced has as a rule no relation to location of the gene in the chromosome. A gene may produce its chief effect on the eye color, while one nearby may affect the wing structure, and a third, in the same region, the fertility of the male or of the female. Moreover, genes in different chromosomes may produce almost identical effects on the same organs. One may say, then, that the position of the genes in the hereditary material is inconsequential in relation to the effects that they produce. This leads to a consideration which is more directly significant for the physiology of development.

In the earlier days of genetics it was customary to speak of unit characters in heredity, because certain contrasted characters, rather clearly defined, furnished the data for the Mendelian ratios. Certain students of genetics inferred that the Mendelian units responsible for the selected character were genes producing only a single effect. This was careless logic. It took a good deal of hammering to get rid of this erroneous idea. As facts accumulated, it became evident that each gene produces not a single effect, but in some cases a multitude of effects on the characters of the individual. It is true that in most genetic work only one of these character effects is selected for study - the one that is most sharply defined and separable from its contrasted character - but in most cases minor differences are also recognizable that are just as much the product of the same gene as is the major effect. In fact, the major difference selected for classification of the contrasted character-pairs may be of small importance for the welfare of the individual, while some of the concomitant effects may be of vital importance for the economy of the individual, affecting its vitality, its length of life, or its fertility. I need not dwell at length on these relations because they are recognized today by all geneticists. It is important, nevertheless, to take cognizance of them,

because the whole problem of the physiology of development is involved.

The coming together of the chromosomes at the maturation division, and their subsequent movement apart to opposite poles of the meiotic figure, insures the regular distribution of one set of chromosomes to each daughter cell and the fulfilment of Mendel's second law. These movements have the appearance of physical events. Cytologists speak of these two phenomena as *attraction* and *repulsion* of the members of individual chromosomes, but we have no knowledge of the kind of physical processes involved. The terms attraction and repulsion are purely descriptive, and mean no more at present than that like chromosomes come together and later separate.

In earlier times, when the constitution of the chromosomes was not known, it was supposed that the chromosomes come together at random in pairs. There was the implication that any two chromosomes may mate. The comparison with conjugation of male and female protozoa, or egg and sperm cell, was obvious, and since in all diploid cells one member of each pair of chromosomes has come from the father and one from the mother, it must have seemed that somehow maleness and femaleness are involved in the conjugation of the chromosomes also. But today we have abundant evidence to prove that this idea is entirely erroneous, since there are cases where both chromosomes that conjugate have come from the female, and even where both have been sister strands of the same chromosome.

Recent genetic analysis shows not only that the conjugating chromosomes

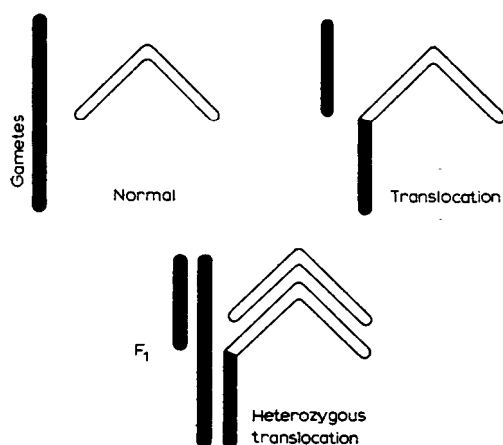


Fig. 1. Diagram to illustrate the case when a piece of one chromosome (*black*) has been translocated to another chromosome (*white*). In the lower part of the figure the method of conjugation of these chromosomes is shown.

are like chromosomes, i.e., chains of the same genes, but also that a very exact process is involved. The genes come together, point for point, unless some physical obstacle prevents. The last few years have furnished some beautiful illustrations showing that it is genes rather than whole chromosomes that come to lie side by side when the chromosomes come together. For example: occasionally a chromosome may have a piece broken off (Fig. 1 above) which becomes attached to another chromosome. A new linkage group is thus established. When conjugation takes place, this piece has no corresponding piece in the sister chromosome. It has been shown (Fig. 1 below) that it then conjugates with that part of the parental chromosomes from which it came.

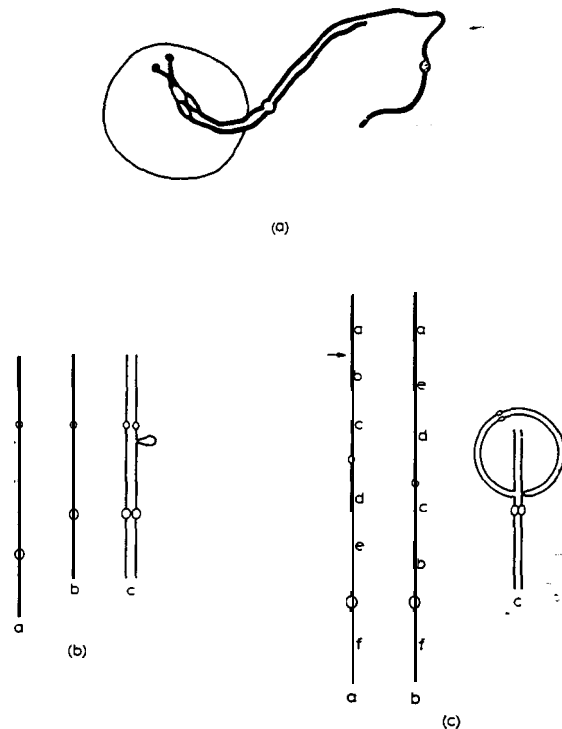


Fig. 2. (a) Two conjugating chromosomes of Indian corn (after McClintock). One chromosome has a terminal deficiency. (b) Two chromosomes of Indian corn, one having a deficiency near its middle. When these two chromosomes conjugate there is a loop in the longer chromosome opposite the deficiency in the other one. (c) Two chromosomes of Indian corn, one having a long inverted region. When they conjugate they come together as shown in the figure to the right (after McClintock), like genes coming together.

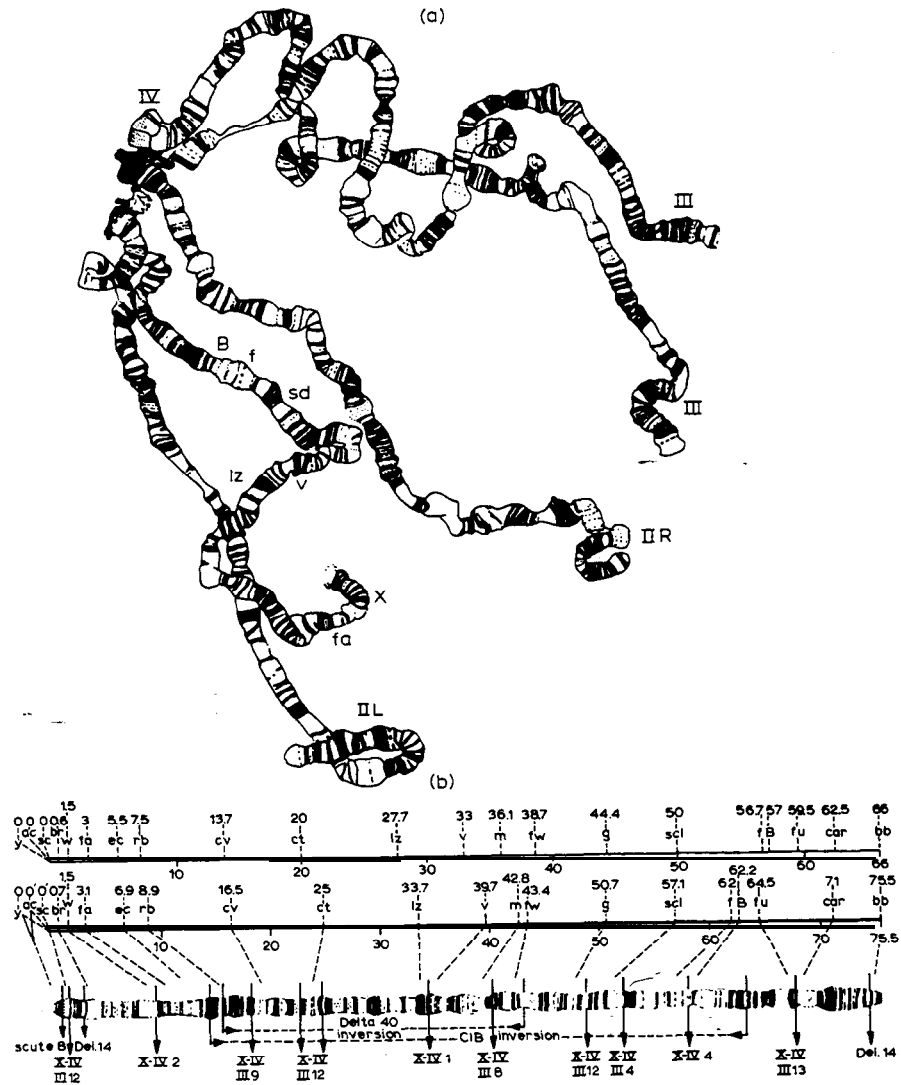


Fig. 3. (a) The chromosomes of the salivary gland of the female larva of *Drosophila melanogaster* (after Painter). The two X-chromosomes are fused into a single body. This chromosome is attached at one end to the common chromidial mass at its "attachment end". The 2nd and 3rd chromosomes have the attached point near the middle and are fused with the common chromidial mass at this point, leaving two free ends of each chromosome. Like limbs of each of these free ends are fused, giving four free ends in all. (b) The banded salivary X-chromosome of *Drosophila melanogaster* is below, with the genetic map above (after Painter). Oblique broken lines connect the loci of the genetic map with corresponding or homologous loci of the salivary chromosome.

When a chromosome has lost one end, it conjugates with its mate only in part (Fig. 2a), i.e., where like genes are present. When a chromosome has lost a small region, somewhere along its length, so that it is shorter than the original chromosome, the larger chromosome shows a loop which is opposite the region of deficiency in the shorter chromosome as shown in Fig. 2b. Thus like genes, or corresponding loci, are enabled to come together through the rest of the chromosome. More remarkable still is the case where the middle region of a chromosome has become turned around (inversion). When such a chromosome is brought together with its normal homologue, as shown in Fig. 2c, like regions come together by the inverted piece reversing itself, so to speak, so that like genes come together as shown to the right in Fig. 2c. In this same connection the conjugation of the chromosomes in species of *Oenothera* furnish beautiful examples of the way in which like series of genes find each other, even when halves of different chromosomes have been interchanged.

The very recent work of Heitz, Painter, and Bridges has brought to light some astonishing evidence relating to the constitution of the chromosomes in the salivary glands of *Drosophila melanogaster*.

The nuclei of the cells of the salivary glands of the old larvae are very large and their contained chromosomes (Fig. 3) may be 70 to 150 times as large as those of the ordinary chromosomes in process of division. Heitz has shown that there are regions of some of the chromosomes of the ganglion cells - more especially of the X- and the Y-chromosomes - that stain deeply, and other regions faintly, and that these regions correspond to regions of the genetic map that do not and do contain genes. Painter has made the further important contribution that the series of bands of the salivary chromosomes can be homologized with the genetically known series of genes of the linkage maps (Fig. 3a, b), and that the empty regions of the X and Y do not have the banded structure. He has further shown that when a part of the linkage map is reversed, the sequence of the bands is also reversed; that when pieces are translocated they can be identified by characteristic bands: and that when pieces of linked genes are lost there is a corresponding loss of bands. Bridges has carried the analysis further by an intensive study of regions of particular chromosomes, and has shown a close agreement between bands and gene location. With improved methods he has identified twice as many bands, thus making a more complete analysis of the relation of bands and gene location. Thus, whether or not the bands are the actual genes, the evidence is clear in showing a remarkable agreement between the

location of genes and the location of corresponding bands. The analysis of the banded structure has confirmed the genetic evidence, showing that when certain alterations of the order of the genes takes place, there is a corresponding change in the sequence of the bands which holds for the finest details of the bands.

The number of chromosomes in the salivary nuclei is half that of the full number (as reported by Heitz) which Painter interprets as due to homologous chromosomes conjugating (Fig. 3a). Moreover, the bands in each of the component halves show an identical sequence which is strikingly evi-

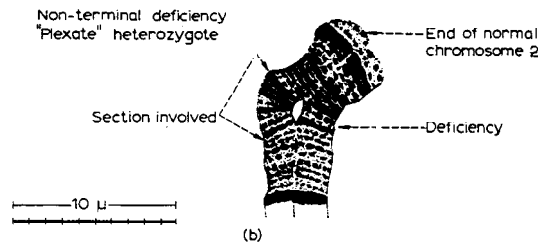
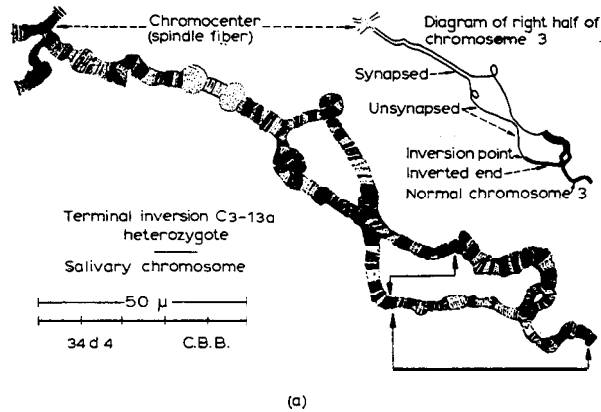


Fig. 4. (a) Salivary gland preparation of the right half of the third chromosome. The two components are united through a part of their length (above left). One component had a terminal inversion. This part conjugated with the corresponding normal chromosome by turning back on itself, as shown in the small diagram above (*to the right*). (b) Salivary gland preparation showing a part of chromosome 2; one component is "deficient". At the level of the deficiency the other component is bent outward so that above and below these level like bands meet. (After Bridges.)

dent when the halves are not closely apposed. It has been suggested by Bridges and by Koltzoff that homologous chromosomes have not only united, but that they have each divided two or three times, giving in some cases as many as 16 or 32 strands (Fig. 4 a, b). The bands may then be said to be composed each of 16 or 32 genes; or, if this identification of the bands as genes is questioned in so far as the genes are concerned, the bands are multiples of some kind of unit of which the chromosomes are composed.

A few examples may serve to illustrate the way in which the banded chromosomes confirm the genetic conclusions as to occasional changes that have taken place in the serial order of the genes. In Fig. 4a the right half of chromosome 3 from the salivary gland is represented. In part the two components are fused, in part are separate. In the lower part of the figure a reversed piece of one component is present (terminal inversion). Like bands conjugate with like and, as shown in the smaller diagram above, in Fig. 4a, this is made possible by the end of one component turning back on itself. In Fig. 4b is drawn a short region of chromosome 2. One component has a deficiency for certain genes; the opposite normal chromosome forms a bulge in the region of the deficiency, allowing like bands to come together above and below the deficiency level.

The physiological properties of the genes

If, as is generally implied in genetic work (although not often explicitly stated), all of the genes are active all the time; and if the characters of the individual are determined by the genes, then why are not all the cells of the body exactly alike?

The same paradox appears when we turn to the development of the egg into an embryo. The egg appears to be an unspecialized cell, destined to undergo a prescribed and known series of changes leading to the differentiation of organs and tissues. At every division of the egg, the chromosomes split lengthwise into exactly equivalent halves. Every cell comes to contain the same kind of genes. Why then, is it that some cells become muscle cells, some nerve cells, and others remain reproductive cells?

The answer to these questions seemed relatively simple at the end of the last century. The protoplasm of the egg is visibly different at different levels. The fate of the cells in each region is determined, it was said, by the differences in different protoplasmic regions of the egg.

Such a view is consistent with the idea that the genes are all acting; the initial stages of development being the outcome of a reaction between the identical output of the genes and the different regions of the egg. This seemed to give a satisfactory picture of development, even if it did not give us a *scientific explanation* of the kind of reactions taking place.

But there is an alternative view that can not be ignored. It is conceivable that different batteries of genes come into action one after the other, as the embryo passes through its stages of development. This sequence might be assumed to be an automatic property of the chain of genes. Such an assumption would, without proof, beg the whole question of embryonic development, and could not be regarded as a satisfactory solution. But it might be that in different regions of the egg there is a reaction between the kind of protoplasm present in those regions and specific genes in the nuclei; certain genes being more affected in one region of the egg, other genes in other regions. Such a view might give also a purely formal hypothesis to account for the differentiation of the cells of the embryo. The initial steps would be given in the regional constitution of the egg.

The first responsive output of the genes would then be supposed to affect the protoplasm of the cells in which they lie. The changed protoplasm would now act reciprocally on the genes, bringing into activity additional or other batteries of genes. If true this would give a pleasing picture of the developmental process. A variation of this view would be to assume that the product of one set of genes is gradually in time overtaken and nullified or changed by the slower development of the output of other genes, as Goldschmidt, for example, has postulated for the sex genes. In the last case the theory is dealing with the development of hybrid embryos whose sex genes are assumed to have different rates of activity.

A third view may also be permissible. Instead of all the genes acting in the same way all the time, or instead of certain kinds of genes coming successively into action, we might postulate that the kind of activity of all the genes is changed in response to the kind of protoplasm in which they lie. This interpretation may seem less forced than the others, and in better accord with the functional activity of the adult organ systems.

We must wait until experiments can be devised that will help us to discriminate between these several possibilities. In fact, geneticists all over the world are today trying to find methods that will help to determine the relation of genes to embryonic and adult characters. The problem (or problems) is being approached both from a study of chemical changes that take

place near the final steps in organ formation, especially in the development of pigments, and from a study of the early differentiation of the cell groups of the embryo.

We have come to realize that the problem of development is not as simple as I have so far assumed to be the case, for it depends, not only on independent cell differentiation of individual cells, but also on interactions between cells, both in the early stages of development and on the action of hormones on the adult organ systems. At the end of the last century, when experimental embryology greatly flourished, some of the most thoughtful students of embryology laid emphasis on the importance of the interaction of the parts on each other, in contrast to the theories of Roux and Weismann that attempted to explain development as a progressive series of events that are the outcome of self-differentiating processes, or as we would say today, by the sorting out of genes during the cleavage of the egg. At that time there was almost no experimental evidence as to the nature of the postulated interaction of the cells. The idea was a generalization rather than an experimentally determined conclusion, and, unfortunately, took a metaphysical turn.

Today this has changed, and owing mainly to the extensive experiments of the Spemann school of Germany, and to the brilliant results of Hörstadius of Stockholm, we have positive evidence of the far-reaching importance of interactions between the cells of different regions of the developing egg. This implies that original differences are already present, either in the undivided egg, or in the early formed cells of different regions. From the point of view under consideration, results of this kind are of interest because they bring up once more, in a slightly different form, the problem as to whether the organizer acts first on the protoplasm of the neighboring region with which it comes in contact, and through the protoplasm of the cells on the genes; or whether the influence is more directly on the genes. In either case the problem under discussion remains exactly where it was before. The evidence from the organizer has not as yet helped to solve the more fundamental relation between genes and differentiation, although it certainly marks an important step forward in our understanding of embryonic development.

The physiological action of the genes on the protoplasm, and reciprocally that of the protoplasm on the genes, is a problem of functional physiology in a very profound sense. For it is a problem that involves not only the irreversible changes of embryonic development, but also the recurrent changes in the organ systems of the adult body.

Genetics and medicine

That man inherits his characters in the same way as do other animals there can be no doubt. The medical literature contains hundreds of family pedigrees, in which certain characters, usually malformations, appear more frequently than in the general population. Most of these are structural defects; a few are physiological traits (such as haemophilia); others are psychopathic. Enough is already known to show that they follow genetic principles.

Man is a poor breeder - hence many of these family pedigrees are too meagre to furnish good material for genetic analysis. When an attempt is made to combine pedigrees from different sources in order to insure sufficient data, the question of correct diagnosis sometimes presents serious difficulties, especially in the older materials; but with the very great advances that have been made in medical diagnosis in recent years this difficulty will certainly be less serious in the future.

The most important contribution to medicine that genetics has made is, in my opinion, intellectual. I do not mean to imply that the practical applications are unimportant, and I shall in a moment point out some of the more obvious connections, but the whole subject of human heredity in the past (and even at the present time in uninformed quarters) has been so vague and tainted by myths and superstitions that a scientific understanding of the subject is an achievement of the first order. Owing to genetic knowledge, medicine is today emancipated from the superstition of the inheritance of maternal impressions: it is free from the myth of the transmission of acquired characters, and in time the medical man will absorb the genetic meaning of the role of internal environment in the coming to expression of genetic characters.

The importance of this relation will be seen when it is recalled that the germ plasm or, as we say, the genic composition of man is a very complex mixture - much more so than that of most other animals, because in very recent times there has been a great amalgamation of many different races owing to the extensive migration of the human animal, and also because man's social institutions help to keep alive defective types of many kinds that would be eliminated in wild species through competition. Medicine has been, in fact, largely instrumental in devising means for the preservation of weak types of individuals, and in the near future medical men will, I suggest, often be asked for advice as to how to get rid of this increasing load of

defectives. Possibly the doctor may then want to call in his genetic friends for consultation! The point I want to make clear is that the complexity of the genie composition of man makes it somewhat hazardous to apply only the simpler rules of Mendelian inheritance; for, the development of many inherited characters depends both on the presence of modifying factors and on the external environment for their expression.

I have already pointed out that the gene generally produces more than one visible effect on the individual, and that there may be also many invisible effects of the same gene. In cases where a condition of susceptibility to certain diseases is present, it may be that a careful scrutiny will detect some minor visible effects produced by the same gene. As yet our knowledge on this score is inadequate, but it is a promising field for further medical investigation. Even the phenomenon of linkage may some day be helpful in diagnosis. It is true there are known as yet in man no certain cases of linkage, but there can be little doubt that there will in time be discovered hundreds of linkages and some of these, we may anticipate, will tie together visible and invisible hereditary characteristics. I am aware, of course, of the ancient attempts to identify certain gross physical human types - the bilious, the lymphatic, the nervous and the sanguine dispositions, and of more modern attempts to classify human beings into the cerebral, respiratory, digestive and muscular, or, more briefly, into asthenics and pycnics. Some of these are supposed to be more susceptible to certain ailments or diseases than are other types, which in turn have their own constitutional characteristics. These well-intended efforts are, however, so far in advance of our genetic information that the geneticist may be excused if he refuses to discuss them seriously.

In medical practice the physician is often called upon for advice as to the suitability of certain marriages where a hereditary taint is present in the ancestry. He is often called upon to decide as to the risk of transmitting certain abnormalities that have appeared in the first-born child. Here genetics will, I think, be increasingly helpful in making known the risk incurred, and in distinguishing between environmental and hereditary traits.

Again, a knowledge of the laws of transmission of hereditary characters may sometimes give information that may be helpful in the diagnosis of certain diseases in their incipient stages. If, for example, certain stigmata appear, whose diagnosis is uncertain, an examination of the family pedigree of the individual may help materially in judging as to the probability of the diagnosis.

I need scarcely point out those legal questions concerning the paternity of an illegitimate child. In such cases a knowledge of the inheritance of blood groups, about which we now have very exact genetic information, may often furnish the needed information.

Geneticists can now produce by suitable breeding, strains of populations of animals and plants that are free from certain hereditary defects; and they can also produce, by breeding, plant populations that are resistant or immune to certain diseases. In man it is not desirable, in practice, to attempt to do this, except in so far as here and there a hereditary defective may be discouraged from breeding. The same end is accomplished by the discovery and removal of the external causes of the disease (as in the case of yellow fever and malaria) rather than by attempting to breed an immune race. Also, in another way the same purpose is attained in producing immunity by inoculation and by various serum treatments. The claims of a few enthusiasts that the human race can be entirely purified or renovated, at this later date, by proper breeding, have I think been greatly exaggerated. Rather must we look to medical research to discover remedial measures to insure better health and more happiness for mankind.

While it is true., as I have said, some little amelioration can be brought about by discouraging or preventing from propagating well-recognized hereditary defects (as has been done for a long time by confinement of the insane), nevertheless it is, I think, through public hygiene and protective measures of various kinds that we can more successfully cope with some of the evils that human flesh is heir to. Medical science will here take the lead - but I hope that genetics can at times offer a helping hand.