the growth exhibited and the nature of the differentiations displayed by the tumour cells. The discovery of the transplantability of tumours of the lower animals has provided much material for this line of research, but the many attempts made to fix on any one outstanding character of tumour cells differentiating them sharply from normal cells have been unsuccessful. As before, we are confronted with the unexplained and unco-ordinated powers of proliferation shown by the tumour cells. The discovery that animals could be rendered resistant to transplanted tumours raised hopes that it might be possible to elicit an immunity towards cancer in an animal affected spontaneously, but these hopes are now considerably abated.

A start has also been made to ascertain the food requirements, general and special, of the tumour cells, but these experiments are still too slightly advanced for us to know whether any result of positive value will be obtained.

Research into the treatment of cancer other than surgical has produced many empirical experiments and observations, but, apart from the extended knowledge of radio-therapy, nothing of importance has come to light. In the field of radio-therapy, the manner of action of the rays used, and the way in which they induce destruction of cancerous cells, still offers an unsolved problem of high importance. In conclusion, it may be predicted that progress in cancer research will in large measure be closely co-ordinated with that in the ancillary sciences.

The Mechanism of Heredity.[1]

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III.

Further Relations between Chromosomes and Heredity.

IN examining the chromosomes for a stage when "crossing-over" might be possible, we turn naturally to the time when the members of each pair come together. This occurs once in the history of every germ-cell. In many accounts it has been shown that the members of each pair come to lie side by side throughout their length. Even more interesting is the fact that just prior to this union the chromosomes have spun out into long, thin threads. There are also

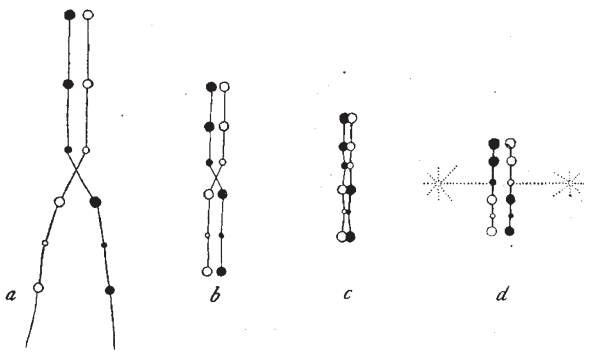

FIG. 16.

several detailed accounts showing that at this time the two chromosomes of each pair may actually twist about each other in one or more turns (Fig. 16). They then come to lie side by side and appear as a single thread that shortens preparatory to entering upon the first maturation division. Here, apparently, we find realised a condition that might make interchange possible between the members of a pair of chromosomes, for if the threads fuse where they cross each other and the ends on the same side unite, the interchange of pieces will be accomplished. From the nature of the case it would be almost impossible to demonstrate that the twisted threads do break and make new unions at the crossing point. It is true that there are certain later stages that lend, perhaps, some support to the view that breaking and reunion have occurred, as Janssens has pointed out, but it cannot be claimed that this evidence does more than give, on such an assumption, an account consistent with certain configurations he describes. Here the case must rest for the present. The genetic evidence is clear and far in advance of what the cytologist is able to supply. But, nevertheless, it is very important to find that, so far as the cytological evidence goes, it furnishes a great many of the facts essential to the kind of process that the genetic evidence calls for.

The Number of the Linkage Groups and the Number of the Chromosomes.

When Sutton in 1902 directed attention to the fact that in the behaviour of the chromosomes at maturation there was supplied a mechanism for Mendel's two laws, it was evident that the number of independently assorting hereditary characters would be limited to the number of the chromosome pairs characteristic of each species of animal and plant, provided the chromosomes remain intact from generation to generation. The integrity of the chromosome was held, in fact, by a few leading cytologists at that time, notably by Boveri, on evidence which, if not complete, was the best then obtainable. In the circumstances, the later discovery of the agreement between the number of chromosome *pairs* of *Drosophila melanogaster* and the number of its linkage groups was of paramount importance for the chromosome theory. In this species the number of known hereditary characters is so large (more than 300 in all) that this relation can scarcely be due to a coincidence, especially when the whole evidence concerning chromosomes and heredity is taken into account.

It is true, with the possible exception of the garden pea (where there appear to be as many independently

[1] Continued from p. 278.

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Mendelising pairs as there are chromosome pairs, namely, seven), that this relation has as yet been established only for species of Drosophila. But it is also true that not a single animal or plant has yet been found in which the number of known hereditary groups of genes is greater than the number of chromosome pairs. It is to be anticipated that some one will before long announce such a discovery, for it is very probable that if two linked genes happen to be so far apart as to give 50 per cent. of crossing-over, they will appear to be in different groups. But such a situation need cause no alarm when (or if) it arises, and will not, of course, refute the correspondence of linkage and chromosomes, unless it can be shown that each such member belongs to a different linkage system. Furthermore, it is to be anticipated that where compound groups of chromosomes exist, such as have been described in some grasshoppers and bugs, peculiar relations are likely to be found.

The evidence from two species of Drosophila other than *D. melanogaster* should also be taken into account. In *D. obscura* Lancefield has shown that there are five pairs of independently assorting characters. There are also five pairs of chromosomes. In *D. virilis* Metz has found six pairs of chromosomes, and up to the present at least five independent loci. The fact that no crossing-over takes place in the male makes the evidence for the independence of the pairs practically certain.

Origin of Mendelian Genes.

Mendelian heredity is sometimes slightingly referred to as a particular kind of heredity dealing with characters that are due to losses of wild-type *characters*. This view ignores some significant facts and considerations. To argue that because a *character* is lost or modified there must be a corresponding loss in the *germ-plasm* is clearly a *non sequitur*. Each organ of the body is the end result of a long series of stages in embryonic development. Any change in any one of the stages would be expected to alter the end product. There are no grounds for assuming that such changes must necessarily be losses, although losses also might sometimes produce such effects. The argument has all the earmarks of reasoning by analogy.

However, the discussion need not rest any longer on philosophical grounds, since we have crucial experimental data which show that loss of a character is not necessarily due to loss of a gene. One case will suffice. In addition to the white-eyed mutant of Drosophila there are ten other eye colours that lie in the same locus. Obviously there cannot be ten kinds of absences. The only other possible explanation of ten absences would be that there were ten genes here so close together that crossing-over does not take place. Hence they appear to be in the same locus. Now, fortunately, the origin of these ten mutations is known, and shows—if they were really a closely linked nest of genes—that when the last one appeared there must have been at the same time mutation in nine other genes in order to get the results. The rareness of mutation precludes such an interpretation. Attempting to save the interpretation of recessive characters as due to absence of genes, it has been argued that perhaps only a part of the wild-type gene is *lost* when a new recessive character appears. It is, however, not obvious why the hypothesis needs to be saved. It is simpler and suffices to cover our ignorance to say that a change has taken place.

There is another question connected with these multiple allelomorphs—changes in the same locus—that is very important. Any given individual may normally have at most any two of the genes (one derived from the father, and one from the mother), but never more than two. When there are two such mutant genes present they behave towards each other in the same way as does any mutant gene towards its wild-type allelomorph. It follows that the Mendelian behaviour is not a peculiar relation of a mutant gene to a wild-type gene. It would seem, therefore, highly probable that wild-type genes behave in this way towards each other, and, in fact, where two wild types exist in Nature that differ in a single allelomorph, they are found to give a Mendelian segregation when brought together.

The discovery of a large number of mutants in the same species may be expected in time to furnish some idea of the number of hereditary genes that exist in a species, or, in other words, to tell us how many different kinds of genes *plus* the cytoplasm constitute a species. At present, even in the case of Drosophila, we are far from being able to make such a calculation. There are, however, one or two rough estimates which seem to indicate that the number of genes is more than several thousands. The upper probable limit cannot even be guessed.

How the genes bring about their effects, which are shown as modifications of the protoplasm (or by-products of it), is entirely unknown. If it seems desirable at present to limit the definition of heredity to cover only the distribution of the genes in successive generations, the result of their effects on the protoplasm becomes a problem of embryology. To many geneticists, however, no such limitation seems desirable, because it may appear that the ultimate constitution of the genes themselves can be discovered only by working backwards, through the effects produced, to the nature of the material that furnishes the first stage in the elaboration. With this pious hope I heartily agree, but in the meantime I do not think it desirable to let premature attempts in this direction interfere with clear-cut methods of research that Mendelian results supply.

Finally, the question as to whether all hereditary characters arise, or have arisen, through mutational changes in the germ-plasm similar to those found occurring to-day, can be settled only by future evidence. Guessing is scarcely worth while. One point, however, seems fairly well established—namely, that in several cases where differences in wild species have been subjected to the experimental analysis employed by geneticists for variation arising by mutation, they give the same kind of results.

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