# Cancer Research.

By DR. J. A. MURRAY.

DURING the last twenty or thirty years the above title has been very frequently the text for reviews, summaries and editorial articles, and might in other circumstances be regarded as covering an over-written subject. The wide interest taken in cancerous diseases—an interest stimulated by the apparently increasing toll of this malady which the mortality figures of the Registrar-General reveal—suggests that the editorial request for a further article on the same theme should not be neglected. Recently the general Press has contained the announcement of Lord Atholstan's offer under certain conditions of a prize of 22,000*l*. for the discovery of a medical cure for cancer, whilst this has been followed by Sir William Veno's prize of 10,000*l*. The final form in which these sums will be applied to the stimulation, and perhaps the subvention, of cancer research has probably not yet been definitely decided, but both gifts can be looked upon as concrete examples of the importance which men attach to a solution of the problem of cancer.

At the present time we have in this country two important and outstanding diseases, namely, cancer and tubercle, both of which are great destroyers of human life. The latter is certainly the more important in an economic and social sense for it attacks people at a much earlier age, but nevertheless it does not seem to have the same hold as cancer on the imagination of the public. It would almost seem as if the *spes phthisica*, the illusory hope of recovery often entertained by the almost moribund consumptive, had spread from the victim to his fellow-man. The prime cause of tuberculosis has been known for forty years, yet treatment is still very unsatisfactory; in cancer the cause is still unknown, and a wider field for investigation is presented, as well as one offering the attraction of the unknown.

Physicians and surgeons are not alone in entertaining the interest thus awakened, but share it with a wider army of pathologists, physiologists and biologists, who may regard cancer as a perverted form of growth perhaps induced by an aberrant type of metabolism. If we restrict our survey to the period of the war and the following years, we find that although research was greatly curtailed, especially in Europe, it did not cease entirely; since the war, work has been resumed and certain progress made. To-day, work is being done even in impoverished Austria, and from Japan in the East to the United States in the West, from Denmark to the Argentine Republic. Investigation into the nature of cancer is almost as widespread geographically as the disease itself.

It is at no time easy to formulate a working hypothesis for attacking a biological problem, and it is especially difficult in the case of the ill-defined one we are considering; but if the attempt be made to analyse the different lines of inquiry adopted, this might profitably be done by arranging them according to their bearing upon the theory that cancer is caused by an extraneous parasite. The parasitic theory has been in the field for many years, but from the opening of the present century it did not claim so many adherents until about ten years ago, when its advocates had their view strengthened by the discovery of a peculiar sarcoma in fowls which could be transmitted by a porcelain candle filtrate, and presumably contained one of the filterable viruses. The exact relation of this chicken sarcoma to the true neoplasms is still a matter of uncertainty, but the failure to repeat this experiment with tumours from other animals leads one to suppose that their nature is essentially different. A similar comment applies to the infective venereal tumour of dogs, a sarcoma-like growth transmitted by coitus, especially amongst bull-dogs. Here, again, it is no easy matter to define the relationship with the infective granulomata on one hand, or with the true neoplasmata on the other.

A great many of the opponents of the parasitic theory of cancer believe in the efficiency of "chronic irritation" as an actual inducer of the cancerous transformation of a tissue. By chronic irritation they usually mean a prolonged succession of chemical or physical insults to a group of cells, these insults being of a degree which does not destroy the vitality of the cells but serves to excite their powers of growth and reproduction. That cancerous disease may supervene in tissues maltreated in this way is shown in a wide variety of cases, of which there may be cited chimney-sweeps' cancer, "kangri" cancer, the cancer of X-ray workers, and the cancer developing at the site of a long-standing ulceration.

All these instances lead directly to the attempt to produce cancer experimentally, but it is only within the last few years that any measure of success has attended the experiments. The production of cancer has been most successful in rabbits and mice in which a small skin area has been painted for a period of six to twelve months with coal tar. About half the animals thus treated show tumour growth at the treated site, and the method promises to be exceedingly useful for studying the conditions affecting tumour origin. Another method of producing cancer experimentally is less straightforward than the preceding, but about equally efficacious. In this a chemical or physical agent is not applied but the irritation produced by the presence of a gross parasite is employed. The artificial infection of rats by a species of nematode, *Gongylonema neoplastica*, leads to the overgrowth of the squamous portion of the stomach and in a fair percentage of cases to the development of cancer. Sarcoma of the liver of rats can also be produced with ease by the simple expedient of infecting the animal with ova of the cat tapeworm, *Taenia crassicollis*. All three methods seem likely to further our knowledge of the etiology of the disease.

The search for the cause of cancer in a developmental (embryonic) abnormality does not appear now to command many followers; it is at best a very fatalistic line of thought, and discouraging to all but the most robust-minded.

Starting from an already established tumour, much work has been done upon observing the characters of 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.

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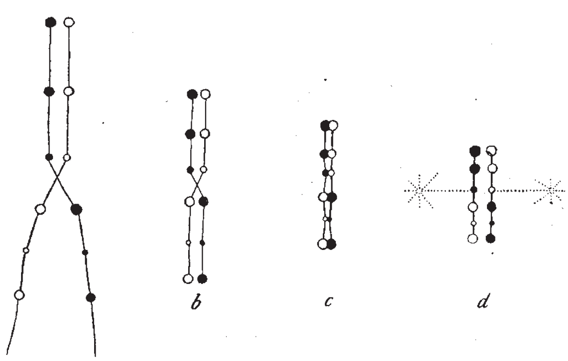
## The Mechanism of Heredity.[1]

By Prof. T. H. MORGAN, Columbia University, New York City, U.S.A.

### 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



a b c d

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.

[1] Continued from p. 278.

*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