

Cancer Problems.

THE International Conference on Cancer arranged by the British Empire Cancer Campaign was held in London on July 16-20. The mornings were devoted to sectional meetings and discussions at the house of the Royal Society of Medicine and at the College of Nursing next door; in the afternoons visits were paid to various hospitals and other institutions, where more practical demonstrations were given. More than a hundred delegates came from the British Empire, most European countries, the United States, China, and Japan, and more than two hundred from British institutions. The whole occasion went off very well. It is impossible to give any complete account of the proceedings: we deal only with a few topics of more general interest.

More than twenty years ago, Bashford and Murray showed that a malignant tumour of epithelium (carcinoma), propagated by being transplanted from mouse to mouse, might occasionally cause the normal connective tissue in contact with it to take on the characters of a malignant tumour and become a sarcoma with the characteristic capacity for indefinite and independent growth. It seemed evident that some substance must pass out from the carcinoma cells to influence the adjacent connective tissue cells. All attempts, however, to demonstrate such a substance by inoculating extracts of carcinomata and similar experiments were uniformly unsuccessful until, in 1912, Rous and Murphy found several sarcomata of fowls in which this carcinogenic substance was so stable that it could be extracted and studied at leisure. A number of similar tumours have since been found in fowls by other observers. With most tumours transmission from animal to animal can be effected only by the transference of live cells; these Rous tumours can be transmitted by ground-up cells, dried cells, and by extracts which have been filtered through porcelain so that they contain no recognisable remains of cells at all.

The activity of these extracts, in which the active agent has a limited stability and persistence, in inducing malignant tumours in fresh fowls is conditioned by a number of factors which are not clearly defined and about which there has been a good deal of difference of opinion and experience in recent years, since Gye revived interest in the matter by his fresh interpretation. Acidity, alkalinity, mechanical and chemical injury, etc., have been found to influence the result; particular interest attaches to the action of extracts of other tissues which, it appears, may have either a favourable or an inhibitory effect.

Whether the active agent in these extracts can fairly be called a virus depends to a considerable extent on what 'virus' means. If it connotes an organism capable of independent life and multiplication of the same order as is enjoyed by most ordinary bacteria, the evidence is distinctly against the Rous tumour being a 'virus' disease, and at the Conference, Dr. J. B. Murphy, of New York,

brought forward further observations which make it scarcely possible to believe in a 'virus' interpretation of the facts. He showed that by differential precipitation of Rous tumour extracts by electro-dialysis (or simply by acidifying the extracts) the whole of the active agent could be separated. It appears to be mainly or wholly a nucleoproteid and can be dissolved and reprecipitated repeatedly without losing its activity: it still produces tumours in fowls with great regularity, and can also be found in the blood of fowls with developed tumours.

The isolation of this active agent is the logical sequel to Bashford and Murray's experiments. It has been possible because these particular fowl tumours contain the agent in such a form that it will tolerate experimental manipulation.

Such experiments involve the use of materials derived from an existing cancer: they may explain how a tumour involves neighbouring cells in its mad career, but they do not necessarily throw any light on how a tumour originates *de novo*. All the available evidence is against the idea that the active agent spreads from one individual to another, and it is in connexion with the popular idea that cancer may be 'catching' that the use of the word 'virus' is practically undesirable. The outstanding piece of progress in respect of our knowledge of the origin of fresh cancers, which was dealt with in a variety of ways at the Conference, is the cumulative realisation of the importance of chronic irritation and injury and the progressive implication of the products of burnt coal as the most effective irritants known.

Clinically and epidemiologically, instances of the relation have multiplied steadily during the last fifty years: the kangri cancers of the belly wall in Kashmir, the cancers arising in X-ray burns, and the appearance of mule-spinners' cancer in Lancashire, are practically human experiments on a big scale. The recent increase in cancer of the lung was the subject of a special discussion at the Congress, and everyone looked for the explanation in some new sort of irritant—the influenza of 1918-19, tarred roads, motor fumes and oil, cigarette smoking, and what not. It is becoming easier to understand why the great majority of human cancers occur in a limited number of places in the body—uterus, breast, lips and mouth, stomach, large intestine and rectum.

While, therefore, the importance of irritation was fully recognised, the influence of the qualities of the irritated tissues (*i.e.* of the constitutional factor) was illustrated by Miss Maude Slye's account of her mice in Chicago. By selective inbreeding she has on one hand so intensified the tendency to develop cancer in a given environment, and on the other hand so eliminated it, that she has two groups of animals in which almost all, and scarcely any respectively, develop tumours. By a unique piece of devoted work she has shown that the incidence of fresh cancers is partly dependent on heritable

qualities. Mating which is selective *qua* cancer is at present not practised by man, and in human experience heredity is negligible. But with the same inducement in the way of irritation, some people are no doubt more liable to develop tumours than others.

No one succeeded clearly in reproducing this experience about irritation experimentally until, in 1914, Yamagiwa and Ichikawa showed that cancers of the skin could be produced fairly regularly by the patient and persistent application of tar to mice. In other animals it is more difficult, and we owe one great advance in our knowledge of cancer to this peculiar susceptibility of mice just as we owe another to the exaggeration of the active agent by the Rous tumours. General principles are often revealed by special instances.

This great discovery is important in many ways. It put into the hands of experimenters a method of producing new cancers at will. Using it to test the carcinogenic properties of various irritants, they have found that coal products have an efficacy which seems to be unique: tar and soot and mineral oils and various preparations made from them all contain something (which has not yet been precisely identified) which causes cancer more or less readily in mice. We have here the experimental verification of the association recognised long ago in chimney-sweep's cancer of the scrotum, and in such statistico-geographical inquiries as those of Mr. C. E. Green, who clearly worked out the connexion between cancer and burnt coal with a layman's enthusiasm and common sense. The case against soot has come to be a very strong one.

If cancer can be produced by irritation, it is reasonable to assume that the active agent has originated in the irritated tissues. It is known from a variety of evidence that the products of the autodigestion which dead cells undergo in the body stimulate the growth of cells, and that the tissues of embryos are particularly rich in these growth-promoting substances. The implantation of embryonic cells into the body of an animal of the same species does not give rise to a tumour. But, as Carrel showed, a positive result may occasionally be obtained if to the mashed-up embryo a little arsenic or indol is added, which also by itself would be ineffective. The next step in this sequence also

came from Dr. Murphy at the Conference. He announced that by treating the testicles of normal fowls by the same technique that resulted in the separation of the active agent from fowl tumours, he had obtained a preparation which caused malignant tumours when inoculated into fowls. Dr. Leitch also stated that he had found that extracts of pancreas were singularly effective in aiding the action of tumour extracts, and that on one occasion he had succeeded in producing a tumour with an extract of normal pancreas by itself.

These remarkable results of course require confirmation, but they are not unexpected, and follow naturally from our previous knowledge. They suggest that tar, for example, unmasks an active agent which is normally present in an ineffective form or is held in check by the resistance of the tissues. It may be that the active agent arises (or is let loose in an effective form) in the body as the result of cell injury and degeneration much more often than we commonly suppose, and that it fails to give rise to an obvious cancer either because ancillary substances are absent or because inhibitory substances or processes are present. The practical problem of cancer prevention may perhaps be more fruitfully phrased as, Why does not everybody have cancer? rather than as, Why do some people have cancer?

The only other point requiring mention which came out clearly at the Congress is the substantial practical advance which has been made in treatment by radium. By dispersing the radium throughout the substance of the tumour and in its neighbourhood, and by using small doses for long times rather than large doses for short times, there is no doubt that a good many cases of cancer can be cured, and most material alleviation can be secured in cases which have progressed too far to stop. At the same time, there is no justification for any talk about surgery being eliminated. The present price of radium seems to need some justification. How it operates is still not understood. The radiations may act better than other differential killing agents because of their nature or because they impinge continually upon the tissues without being too concentrated at their point of origin: like other harmful agents, they kill the cells of tumours more easily than those of normal tissues.

The International Research Council.

THE fourth General Assembly of the International Research Council was held at Brussels on Friday, July 13. M. Picard, president of the Council, presided, and the meeting was attended by delegates from most of the countries adhering to the Council. A meeting of the executive committee had been held on the previous Wednesday. The report of the general secretary, Sir Arthur Schuster, was presented, and a number of resolutions adopted. The report showed that at the conclusion of the extraordinary general meeting in June 1926, the secretary had taken

steps to inform the nations concerned of the unanimous decision to invite Germany, Austria, Hungary, and Bulgaria to join the Council and the Unions attached to it.

Austria, Hungary, and Bulgaria each possess an Academy, which is the recognised authority in scientific matters, and invitations were sent to each of these; at the same time their diplomatic representatives in London were informed. In the case of Germany there is no single representative Academy. The Foreign Office in London was consulted, and by its advice an invitation to join was