THE BRITISH EMPIRE CANCER CAMPAIGN

ANNUAL REPORT

IN the introduction to the twenty-first annual report of the British Empire Cancer Campaign, the honorary secretary, Mr. J. P. Lockhart-Mummery, says that "it is a matter of satisfaction that, at the end of five years of war, cancer is being studied in this country with even greater intensity than before". It is indeed remarkable that so much progress should be made. Soon the work should be accelerated.

When proposing the adoption of the report, Prof. F. L. Hopwood directed attention to the possibility of introducing radioactive elements in non-toxic compounds into the body. In this way local concentrations of radioactive material in particular organs or tissues might be achieved. Such a new technique would require expensive equipment for the preparation of radioactive elements, and the work would not be without risks for the operators; but interesting results should be obtained.

Therapy. The treatment of cancer of the prostate with œstrogens has been developed during the past year. The present report gives further evidence of the effectiveness of this treatment. The benefits of therapy have been maintained for long periods in many cases. Cancer of other organs has also been treated with œstrogens. Thirty-six cases of late cancer of the breast have been treated with trichloroethylene or stilbœstrol at the Royal Cancer Hospital and the Christie Hospital, Manchester. Of these cases, fifteen showed temporary retardation of the growth, although the effects were in general less than could be expected from local palliative X-irradiation. Of twenty-nine cases of advanced cancer of organs other than prostate and breast, only one (a case of carcinoma of the bladder) showed undoubted partial retrogression. Triphenylmethylethylene was less effective than either stilbœstrol or triphenylchloroethylene.

Experiments on chemotherapy of cancer carried out by Dr. A. Haddow and Prof. G. A. R. Kon have been concerned with the action of symmetrical diphenylethylene derivatives. Two of these compounds are especially active in checking tumour-growth in animals.

Carcinogenesis. Studies in carcinogenic action during the past year appear to have been concerned with the elucidation of the action of known carcinogenic agents rather than with the search for new compounds. Carcinogenic agents inhibit body-growth, but this inhibition is most unlikely to be solely due to deprivation of cystine, as had been suggested by American workers.

2-Acetylaminofluorene has been further investigated by Prof. H. N. Green and Dr. F. Bielschowsky. This substance induces liver tumours and a few mammary tumours in rats. Liver damage is probably the primary change, and as a result œstrogens in the body are not metabolized and so may cause an increase in the number of mammary tumours. 2-Acetylaminofluorene does not normally induce tumours of endocrine glands, but in an experiment in which rats were treated with the carcinogen and allylthiourea to stimulate the thyroid, adenomata of the thyroid were induced. Allylthiourea itself induces hyperplasia of the thyroid but is not carcinogenic. Thus acetylaminofluorene is able to induce tumours in hyperplastic thyroid tissue but not in the normal gland. No liver tumours have apparently been induced in mice treated with acetylaminofluorene in the Sheffield laboratories. Aminofluorene has pronounced bacteriostatic action *in vitro* and this action is inhibited by blood and tissue extracts. Mouse liver gives a much more potent antagonizing extract than does rat liver. 2-Acetylamino-7-hydroxyfluorene has been isolated from the urine of rats as a metabolism product of the carcinogen.

There is considerable variation in the response by different species or even by different strains to carcinogenic agents. Thus, although coal tar will produce tumours on the skin of mice and rabbits, many hydrocarbons that induce skin tumours in mice will not do so in rabbits. Dr. I. Berenblum has now found that the potent carcinogen, 9 : 10-dimethyl-1 : 2-benzanthracene, will produce skin carcinomas on the ears of rabbits. Experiments are proposed to determine if this compound will also induce skin tumours in rats and guinea pigs, which are resistant to most carcinogenic agents.

Dr. A. Glücksmann suggests that the sensitivity of mouse skin varies with the density of the hair coat. The hair follicles act as germinative centres, and the onset of ulceration and papilloma formation coincide with certain phases of the normal hair cycle.

Examination of lubricating oils for carcinogenic activity had made it possible for the Manchester Committee on Cancer to recommend oils which would be expected to be non-injurious from an examination of physical properties. Owing to war conditions, however, the safer oils were not available for some time and there was an increased amount of illness and even death due to epitheliomata of the skin of mule spinners and other workers in cotton mills.

Œstrogenic substances. The possible carcinogenic effects of a number of œstrogenic stilbene derivatives on the skin of mice have been investigated at the Middlesex Hospital. Of thirteen substances tested only one, α-ethyl-β-*sec*-butylstilbene, induced skin tumours. This compound is but feebly carcinogenic to skin, as only two tumours occurred in twenty-one mice that survived a year of treatment. Attempts to find water-soluble œstrogens have led to the synthesis of sodium hexœstrol phosphate and stilbœstrol potassium sulphate. The biological action of aqueous solutions of both these products is being explored both *in vivo* and *in vitro*.

Tumours in pure-line mice. The occurrence of spontaneous cancer in pure-bred strains of mice may be related to other characters of the mice. Thus Dr. F. L. Warren has confirmed the American findings of lowered hæmoglobin in the blood of female mice of strains liable to mammary cancer. The strain of *CBA* mice kept at the Royal Cancer Hospital has a low incidence of mammary cancer, and the mice appear to live longer than mice of strains in which mammary cancer is common. The ovaries and adrenals of mice of this strain have distinct histological differences from corresponding organs of other strains, in which mammary cancer is often seen. The mean concentration of ascorbic acid in the livers of mice of strains with a low incidence of mammary cancer is often lower than the concentration in the livers of mice from high cancer strains.

Dr. G. Bonser, of Leeds, has induced testicular tumours in mice of a number of strains by treatment with œstrogens. The milk factor, or mammary tumour inciter, appears not to influence the incidence of these tumours, but no testicular tumours were

obtained in the *CBA* strain (a low mammary cancer strain) while all the treated mice of the Strong *A* strain developed tumours. Other strains gave intermediate responses: the 'white label' and *IFS* strains gave a few tumours, and the *R*III strain a moderate number of testicular tumours if the mice lived long enough.

The British Empire Cancer Campaign has been concerned with research for twenty-one years and is now taking on the additional duty of advising medical practitioners as to the value of any new form of treatment about which the Campaign has knowledge.

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GENETICAL ASPECTS OF THE CANCER PROBLEM

A "PRELIMINARY Report on a Survey of the Situation in Cancer", by Dr. Fritz Blank, appears in the *Archives of Surgery, Chicago* (49, No. 5, 301; 1944). The general interest of the study warrants a digest showing the limits of the field surveyed and the findings. In his foreword, Prof. F. A. E. Crew points out that this survey of the biological background in cancer is the first major attempt by the Bureau of Human Heredity (115 Gower Street, London, W.C.1) to present the results which can be achieved through the 'clearing-house method'. It has been made possible by international collaboration between the Institute and the Department of Medical Genetics of Ohio State University, both of which are foci of much friendly co-operation between individual workers and numerous institutes.

The Bureau of Human Heredity has been developing the mechanism for such work as this since it opened in 1936. The method by which the cross-reference index is made is best compared to a great sorting machine. The desiderata were outlined early on by Profs. R. A. Fisher and J. B. S. Haldane in consultation. It works well; three thousand sections on constitution and traits were already available when Dr. Blank began the cancer collection; points in the present survey can be set against a further 1,500 or so. This preliminary survey covers most of the literature between 1900 and 1941, with data from about four thousand papers.

The summarized genetical findings are not the less important for presenting no surprises. The myth of hereditary cancer is disposed of. Geneticists are more and more aware in other fields of the fact that hereditary make-up controls type of constitution; in other words, individual variations in physiological function. There is evidence from many sources that carcinogenic agents react differently on various types of constitution. This would be expected from physiological genetics. An illuminating point may be gleaned here, namely, that certain types respond quickly to diverse kinds of irradiation. In another series it appears to be mainly hormone imbalance which prepares the body for growths and/or malignancy. Fortunately, data give at least a rough guide as to means of differentiating between these two major sources of the disease.

It is significant to learn that certain diseases of hereditary type appear frequently as precursors of neoplastic growth and malignancy. Here the clearing-house method may have special importance. Practitioners, by contributing their observations to the Centre, will do much to accelerate accumulation of knowledge of practical value to their colleagues and to humanity.

Dr. Blank's survey is set out in chapters dealing with those aspects in which research was sufficiently advanced in 1940 to show a bearing on the biological background; no reference is therefore made to the data on nuclear division, including polyploidy and extrachromosomal factors, on which researches are now in progress. Statistics come first: of high genetical interest are comparative figures for different parts of the world and different races. These show that for all those areas and peoples for which reliable figures are available, the general incidence of cancer is practically the same, although site and type of the disease vary greatly; and there is a hint in the Dutch East Indies that hereditable racial characteristics underlie this fact where Malays and Chinese working side by side demonstrate racial incidence comparable to that of their home areas.

Detailed studies in Norway (Waaler, 1931), later repeated by Wassink in Holland, throw light on the question in general and show the complexity of the problem. Greenwood's analysis is as follows: (1) "some forms of cancer (e.g. lip cancer) are produced quite independently of any inheritable *anlagen*; extrinsic factors have greater, perhaps exclusive, influence upon males; (2) the heritable factors show two independent factors, both of which occur with a frequency of about 16%". These, according to Wassink, are the existence of a general predisposition and also a tendency to certain localization.

'Cancer families' are reviewed, beginning with studies in 1856; it has been shown that simple statistical study here is unreliable (Cramer, 1937), since in large families where sibs survive to thirty-five years, the expectation will be approximately that of the general population. Twin studies are mentioned, but since none conforms to the criteria set up by von Verschuer and Kober, the findings are omitted from the general argument.

The work on rodents receives notice proportionate to its importance and covers spontaneous tumours and the reaction of different strains to transplantation and induced tumours. In each series sharp differences in incidence and reaction are noted between stocks within any given species or variety: there are immune, partially immune or tumour-prone. There remains an unresolved problem here in a change of average incidence in experiments with foster suckling (the so-called milk factor). But here also a variation in resistance of the stocks persists; recent work on agglutinogens in milk were not available at the date to which the survey is carried.

Carcinogenic agents are surveyed in detail; the organic type, the viruses, have been the focus of the search for a possible causative factor or prime agent. Occupational cancers stimulated research on chemical agents, and these are reviewed. Work with hormones proceeding over the same period is not unrelated to those investigations; of these, œstrin has given important results, namely, the production of mammary cancer in 100 per cent of male mice in a cancer-prone stock. Cramer and Horning relate this to a heritable faulty metabolism shown as 'brown degeneration of the adrenals'.

Of great practical interest are the data on those diseases with genetic background which are frequent precursors of cancer. These are spoken of as the internal carcinogenic environment. In addition to