

CANCER RESEARCH IN GREAT BRITAIN

TWO annual reports which have recently been published, those of the Imperial Cancer Research Fund* and of the British Empire Cancer Campaign†, record the slow but steady progress that has been made in cancer research during the past year. The report for 1948 of the Imperial Cancer Research Fund gave first place to an account of certain investigations which lent weighty support to the virus theory of cancer, in that it was thought that what had been done since the classical work of Peyton Rous in 1911 on the chicken tumour could be reproduced on a mammalian tumour. It had been shown in the Fund's laboratories that mouse tumours could be frozen and dried, yet could still be successfully transplanted into mice. Freeze-drying kills cells but not viruses, and so it is considered that mouse tumour is transmitted by a virus liberated from the killed tumour cells.

The assumption of this essential condition did not survive tests at some other centres of cancer research. It was soon shown that freeze-drying, if carried to a more-or-less advanced stage, still leaves some viable cells which can be demonstrated by their growth in tissue culture. The positive results on inoculation can therefore be explained without invoking a virus as the agent for transmitting the tumour.

In the present report, the director of the Fund, Dr. James Craigie, frankly states that the mammalian virus hypothesis of tumour transplantation can no longer be considered. He has found, however, that the cells of a mouse tumour contain, in addition to the usual neoplastic cells, another type of cell characterized by being highly resistant to freeze-drying and by its high refractility. It can only be recognized by phase-contrast microscopy. He suggests that the cells of some tumours can assume the refractile state and that these cells can also change back into "normal tumour cells". The analogy with spore formation of micro-organisms is obvious.

The refractile cells are very potent tumour-carriers; only seventy-five cells are required to produce a tumour on inoculation into mice. "It has been found possible to obtain them (refractile cells) in considerable quantity for study, either by fractionating suitable suspensions prepared from subcutaneous tumours or by collecting them from the fluid which accumulates when tumour growth is produced by intraperitoneal inoculation . . . it was found that the refractile bodies were not stable *in vitro* but might change into recognizable tumour cells. . . . The discovery that the cells of some tumours assume this resistant state raises a number of questions. . . . Clearly, these observations are of great importance and their development should do much to stimulate the biology of cancer.

Other studies at the Fund's laboratories at Mill Hill include those of L. Foulds on the responsiveness of some mouse mammary tumours to the hormonal influences which operate during parturition and lactation. An attempt is being made by P. C. Williams to induce similar effects by supplying hormones artificially to female mice bearing this type of tumour.

* Forty-Eighth Annual Report of the Imperial Cancer Research Fund, 1950-1951. (Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2.)

† British Empire Cancer Campaign. Report for 1950. Edited by Sir Heneage Ogilvie. (11 Grosvenor Crescent, London, S.W.1.)

H. G. Crabtree has as yet found no straightforward relationship between the liver cancer inducing potency and the chemical structure of a series of azo-carcinogens. Reduction fission of the azo-compound yields a diamine moiety which selectively inhibits enzymes the activity of which is dependent upon intact sulphhydryl groups; however, the correlation between carcinogenicity and potential inhibition shows some discrepancies.

E. Vazquez-Lopez finds that administration of thiourea to virgin mice of cancer-labile strains causes a significant decrease in the incidence of mammary cancer. After treatment by thiourea the oestrogenic secretion is re-established and mammary tumours begin to appear. These experiments suggest that "oestrogens are active carcinogenic agents independently of their primary morphogenetic functions".

Of the scores of researches described in the report for 1950 of the British Empire Cancer Campaign, the most attractive is by Sir Ernest Kennaway. Sir Ernest, who has recently celebrated his seventieth birthday, is too well known for his achievements in cancer research to need reiteration; the enigma of neoplasia has been compared to an uncharted ocean, and on this basis he could be called its Columbus. One of the reasons for the extraordinary interest of his essay is that it does squarely face the problem of the cause of cancer.

Cancer of the lung has undergone an immense increase of incidence in recent years—four times as high in an interval of fifteen years. Is this multiplication due to an increase in the inhalation of carcinogens, benzpyrene in town smoke or of arsenic in tobacco smoke? The analysis of twenty-seven brands of cigarettes shows that British, Canadian, American and Norwegian cigarettes contain the largest amount of arsenic (24-106 $\mu\text{gm./gm.}$), and Bulgarian the least, 0-1.2; Turkish tobacco contains little arsenic, 0-4.3. Nevertheless, the incidence of lung cancer is very high in Istanbul, for in 1946-48 the percentage of cancer of lung was thirty per cent of all cancer autopsies in males. In autopsies at St. Bartholomew's Hospital, London, the comparable figure was 41.17 per cent. Although no simple relation can be thus shown between lung cancer and arsenic in tobacco, the possible synergistic effect of this carcinogen cannot be ignored; a smoker can volatilize half a milligram of arsenic a day. Certain occupations have a low lung-cancer incidence, namely, agriculture, coal mining and mule spinning. The workers in the two last-named cannot smoke for a third of the day, and, in the first, atmospheric benzpyrene from town smoke is at a minimum. The aeration and temperature of the glowing tip of a cigarette is such as to render the production of benzpyrene negligible. In town smoke this carcinogen is due to the agglomeration of active domestic chimneys, for it is not emitted by properly working industrial furnaces or generating stations. The part played by other associated factors has still to be investigated—for example, the size of the particles in smoke containing the benzpyrene and the chances of these being retained in the bronchi and lungs, and secondly, the carcinogenic effect, if any, of components in the exhaust gases of motor vehicles.

"The finely divided carbon (in human lungs) . . . represents the intake of a lifetime. . . . The carbon itself may be innocuous, but from the study of atmospheric pollution . . . one can form some idea of the amount of benzpyrene which would accompany

it. The small amounts of radioactive material, and of arsenic, which have been found in the dust of towns incline one to attach more importance to benzpyrene in this respect, but one must remember that: (a) we have no data upon the minimum effective dose of any carcinogen in man; and (b) we do not know whether the effects of different carcinogens upon the same tissue can summate."

Cancer of the larynx has increased of late years but not so rapidly as lung cancer, and this disease also shows a sex difference. Sir Ernest, in explanation, advances the stimulating idea that: "The differences in the anatomical, social and geographical distribution of cancer of the larynx in men, and in women, show that these two must be regarded as, to a large extent, different diseases; any statistics in which they are pooled are of no value. The larynx is a secondary sexual organ, hence such differences are not surprising. The adoption of smoking by women, and the increased consumption of tobacco and especially of cigarettes, by both sexes, has not affected the absolute numbers of cancers of the larynx in recent years; there has been no uniform change in either sex since 1930. As recently as 1929 the numbers of cancers of the larynx, and of the lungs, in males was about equal . . . since then, the deaths attributed to the latter have increased enormously".

After these examples of scientific thought and language, the approach to the rest of the report requires some little mental readjustment; most of the material presented is very technical and will be of great interest, and of course is mainly intended, for research workers engaged on closely allied branches of work.

Specialization is inevitable; but it carries with it a danger for cancer research, for each step in development implies more refined technique and more recondite treatment, and consequently there sometimes arises a tendency to encourage the pursuit of the means rather than the end.

A long report from the Clinical Cancer Research Committee on cancer of the lip, mouth and tongue is concerned chiefly with the compilation of abundant data rather than the extraction of generalizations.

Apart from the investigations mentioned so far, the principal themes of research have been threefold: physics and radiology (developments in radio-therapy, and changes in tissue brought about by X-rays); 'model experiments', that is, the study of changes induced in genic material and structures; and carcinogens and carcinogenesis.

The attention devoted to chemotherapy is rather less than in previous years; much more emphasis is being laid on the lines of the 'model experiments'. The agents used for investigation have been radiations, mitotic poisons, nucleotoxins, carcinogens and mutagens; the test objects have been cells in tissue culture, chromosomes, genes and nucleoproteins. The precise relation of this voluminous work to cancer is perhaps not obvious to the uninitiated. It depends upon the thesis that cancer is an aberration of growth, development, repair and differentiation, that these four features of cells and tissues depend in turn on the nucleus of the cell, that the dynamics of the cell are an expression of the structure, metabolism and influence of the nucleoproteins, and, finally, that genes and viruses have largely the same type of chemical nature.

J. F. Danielli and collaborators have succeeded, using microdissection, in transplanting the nuclei of two amoebæ giving an *Amœba proteus* nucleus living

in an *Amœba discoides* cytoplasm. The next step is plain: these investigators should now try to transplant the nucleus of a tumour cell into the enucleated cytoplasm of a normal cell.

The histological alterations in the epidermal tissue of the mouse after X-radiation has been examined by A. Glücksmann, who found that destruction of the epidermis, hair follicles and superficial parts of the derma is followed by regeneration, scarring, a breakdown of the scar tissue and a repetition of the whole process, without further radiation, which finally gives rise to squamous cell cancer.

J. W. Orr and co-workers have transplanted mouse skin, which had previously been painted with methylcholanthrene, on to some other part of the mouse; the striking fact has been revealed that the decisive pre-cancerous change has been effected in the sub-epithelial tissues although the methylcholanthrene-induced cancer arises in the epithelial cells: ". . . when the stroma has been adequately prepared by carcinogenic treatment it is not necessary that the epithelium growing on it should have been itself exposed to a carcinogen before carcinoma can occur. It also appears that carcinogen-treated epithelium may not become neoplastic when transferred to a healthy bed."

Two items dealing with cancer of the liver are also included: the report from the South African Cancer Association refers to the extreme susceptibility of the Bantu to liver cancer (forty times as high as in Europeans); C. Berman has now published his admirable studies in this field of cancer research in the form of a monograph, "Primary Carcinoma of the Liver" (H. K. Lewis, London).

ROYAL GREENWICH OBSERVATORY ANNUAL REPORT

THE report of the Astronomer Royal to the Board of Visitors of the Royal Greenwich Observatory*, presented at the annual visitation held on June 2, covers the period May 1, 1950–April 30, 1951, and exhibits the state of the Observatory on the last date. Only some of the more outstanding matters of general interest can be mentioned here.

Many will regret the fact that Flamsteed House, including the Octagon Room, is no longer under the jurisdiction of the Royal Observatory, as it has been converted into two flats for naval officers of the Royal Naval College. The Wren Building, taken over by the Ministry of Works, will be treated as an ancient monument, and repair work is now in progress. At Herstmonceux no work has yet started on the sites of either the meridian group or the equatorial groups, but the exact locations for the individual meridian instruments have been selected. Work has not proceeded as anticipated in the previous year's report, which stated that the building for the Cooke reversible transit circle was not expected to be completed before the spring of 1951; that the building for the photographic zenith tube was planned to be com-

* Report of the Astronomer Royal to the Board of Visitors of the Royal Greenwich Observatory read at the Annual Visitation of the Royal Observatory, 1951 June 2. Pp. ii+29. (Greenwich: Royal Observatory, 1951.)