

(b.p. 102°/6 mm.; 84 per cent yield). Ethyl *bis* (dimethylamino)-phosphonite (III),  $(\text{NMe}_2)_2\text{PO}(\text{OEt})$ , was made by reaction of II with an equimolecular amount of sodium ethoxide in alcohol (b.p. 93·5°/8 mm.; 88 per cent yield). When II and III were heated together in equimolecular amounts in boiling xylene for 20 hours, ethyl chloride was evolved and, after fractionation, *bis* (*bis*-dimethylamino)-phosphonous anhydride,  $(\text{NMe}_2)_2\text{P}(\text{O})\text{O}(\text{NMe}_2)_2$ , was obtained in 81 per cent yield as a colourless, almost odourless liquid, b.p. 98°/0·002 mm., 102°/0·003 mm., or 106°/0·004 mm. Analysis gave C, 33·9; H, 8·5 and N, 19·8, while the formula  $\text{C}_8\text{H}_{24}\text{N}_4\text{P}_2\text{O}_3$  requires C, 33·6; H, 8·4 and N, 19·6 per cent.

**Biological tests with *Aphis fabae*.** For the biological tests the material, prepared as above, was diluted to a 10 per cent v/v solution in distilled water and stored to be diluted further as required.

Broad beans were infested with *Aphis fabae* and kept in a greenhouse at 16–26° C. The relative humidity and light conditions varied greatly. The results of the observations made to date may be summarized as follows.

**Contact action.** The day after the plants have been dipped in a 0·05 per cent v/v solution of the insecticide containing 0·1 per cent 'Teepol' as a wetting agent, the colonies of aphids are very much reduced in numbers. The young die first; but the plant is not entirely free from aphids for about three or four days. A 0·1 per cent solution acts rather more quickly and a 0·025 per cent solution more slowly. The leaves retain their toxicity to new infestations of aphids for about three days only. The action is slow on aphids arriving on the third day and the colonies take about six days to die out. Necrotic areas develop on the leaves after about fourteen days with concentrations of 0·05 per cent and more. 'Teepol' alone, at the stated concentration, is somewhat toxic to aphids, but the colonies survive and no necrotic areas develop on the plants.

**Absorption from the roots.** When applied to potted plants about six inches high in quantities ranging from 0·2 to 0·05 c.c. per 400 gm. soil, there is little apparent effect for three to five days, depending on the dose, but all aphids are killed in six to eight days. The plants are still toxic three weeks later, but at doses of 0·05 c.c./400 gm. soil and more, necrotic areas develop after about ten days.

In culture solutions, a 0·5 per cent concentration of insecticide frees the plant from all aphids in twenty-four hours, but necrotic areas develop in five days. A 0·05 per cent solution produces the same effect in four days, and necrotic areas appear about the fourteenth day. A 0·005 per cent solution kills the aphids in about nine days, and necrotic areas only begin to appear about the twentieth day. At this time the plants are still toxic to aphids.

If the plants are allowed to absorb 6–10 c.c. of a culture solution containing 0·1 per cent v/v of the insecticide, they remain toxic to aphids for at least twenty-one days. They develop necrotic areas after about fourteen days.

**Concentration in the plant necessary to kill the aphids.** A dose of 1 c.c. of a 0·1 per cent v/v solution gives a 99 per cent kill of aphids in two days when absorbed totally and rapidly (about three hours) by the cut main root of a plant weighing 10–15 gm. If it is assumed that the insecticide is absorbed and translocated unchanged, this dose would represent a concentration of insecticide of about 60–100 mgm./kilo in the plant tissue. When the absorption is

slower (several days), the kill is delayed and may be incomplete.

**Absorption from the leaves.** When 0·5 c.c. of a 0·2 per cent v/v solution of the insecticide is applied to the upper surface of a pair of bean leaves, the aphids feeding on the lower surface are killed, but on the other parts of the plant they are unaffected. Absorption and translocation does not follow applications made to the undersurfaces of the leaves, either.

**Mode of action on the insects.** It is reasonable to suppose that the insecticide is absorbed by the roots and carried in the transpiration stream, and that the sap on which the insects feed becomes poisoned. Experiments in which the transpiration of certain leaves is depressed by enclosing them in a saturated atmosphere tend to confirm this. There is no evidence with this material that any vapour action is involved.

**Tests against other insects.** The material does not appear to be highly toxic to the stored-product insects *Ptinus tectus* and *Tribolium confusum*, which have been placed on surfaces treated with it. In this respect it is less toxic than O, O-diethyl O-*p*-nitrophenyl thiophosphate (E605).

It is hoped to publish a more detailed account of this work at a later date.

<sup>1</sup> Martin, H., and Shaw, H. Developments in methods and materials for the control of plant pests and diseases in Germany. Rept. No. 1095. British Intelligence Objectives Sub-Committee. (London, 1948.)

<sup>2</sup> Schrader, G. Rept. No. 714, *ibid.* (1948.)

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## PROGRESS OF CANCER RESEARCH

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THE British Empire Cancer Campaign (11 Grosvenor Crescent, S.W.1) has now supported cancer research for a quarter of a century. The twenty-sixth annual report, edited by Sir Heneage Ogilvie, is a weighty volume of 320 pages where the reader will find that the Campaign finances, wholly or in part, nine centres of research in London and twenty-eight in the provinces, and co-ordinates, or is affiliated to, other centres in Canada, Australia, New Zealand and South Africa; that the Campaign's income was more than £300,000 in 1948, and that it is administered by more than a score of committees and sub-committees. The Campaign supports three types of investigation and development, namely, radiological, clinical, and a composite group, mainly biochemical.

The accompanying table shows the subject and number of investigations which are described in the report:

Radiology; biophysics	26
Carcinogens; carcinogenesis	12
Chemotherapy	8
Biochemical	7
Hormones	6
Clinical (excluding the Clinical Committee Report)	5
Pathology	4
Genetics; mutation	3
Virus tumours	3
Cytology	2
Tissue culture	2
Social incidence	2
Effect of diet on growth of tumours	1
Milk factor for mouse mammary carcinoma	1

The ever-increasing prominence of physics-inspired research and development expresses not only the

urgent needs of the therapy of cancer, but also the remarkable evolution of physical and optical instruments, such as the synchrotron, the phase-contrast and ultra-violet and electron microscope, Geiger counters and the infra-red spectrometer.

With regard to researches of biochemical type, space will allow something to be said about only a few lines of advance. Sir Ernest Kennaway and his collaborators are compiling a bibliography of carcinogenic compounds and the tumours produced by them. The literature of the most sensational discovery in cancer work now has an author index referring to more than three thousand papers, which have appeared in a quite overwhelming number of journals (340) in several languages, representing the growth of the subject up to 1947. (The first paper on pure carcinogenic compounds quietly made its appearance in 1930 under the title, "Further Experiments on Cancer Producing Substances" by E. L. Kennaway, *Biochem. J.*, **24**, 497; 1930).

Sir Ernest is continuing the statistical studies from the Registrar General's reports on cancer of the lip and other tissues (see below).

New carcinogens are still being added to a long catalogue of more than 300. These latest compounds, discovered by Haddow and colleagues, are, in fact, the notorious nitrogen mustards; for example, methyl-di(2-chloroethyl) amine, which produces lung carcinoma, and lympho-sarcoma and sarcoma at the site of injection in mice; in the aromatic series, NN-di(2-chloroethyl)- $\beta$ -naphthylamine induces sarcoma at the site of injection in rats. These examples again illustrate Haddow's original postulate that carcinogenic and inhibitory potentialities are due to a common property of the molecule.

Carr and Harris have been working out the technique for obtaining Rous virus in a purified condition, when it can be put to further analysis by the electron microscope and by chemical and serological methods. Their very active preparations show that only  $10^{-13}$  gm. nitrogen is present in a tumour-producing dose.

An investigation, attractive in more ways than one, has been pursued by Horning and George, who spent three months at the cosmic ray laboratory on the Jungfrauoch at 12,000 ft.; Figge, in the United States, had claimed that intensification of the cosmic ray incidence, by favourable screening with lead sheet, stimulated the carcinogenic effect of methylcholanthrene in mice. At 12,000 ft. the cosmic ray showers are substantially improved by a factor of five. However, the Figge effect of cosmic rays on the carcinogenic process could not be confirmed.

Of particular interest is the work of Ludford, who has used the phase-contrast and ultra-violet microscope to some purpose in the study of the widely different cytological structures present in even a small fragment of tumour, and of the nucleotide characteristics of rapidly growing and regressing tumour cells.

At Leeds, Passey and co-workers are making progress in the investigation of the transmissible milk factor for mouse mammary carcinoma. The agent will survive extraction of fat in a Soxhlet with petrol ether, and its activity is paralleled by electron microscope estimations of particle yield. Of great interest is the discovery that the mouse breast cancers initiated by treatment with methylcholanthrene show no evidence of containing the milk factor, provided the process is carried out in a strain of mice which are naturally free from milk factor, that is, in

low breast cancer strains, thus showing that breast cancers are clearly of two types.

Clinical work is represented chiefly by statistical surveys and therapeutic trials. The task of collecting basic data concerning the natural history of various forms of cancer is a formidable one, involving the study of incidence, and changing incidence in relation to social habits, racial, economic and occupational factors. These data are being added to year by year, and in the present report figures relating to cancer of skin and lip and of the uterus are given.

A fascinating analysis of the mortality, between 1911 and 1944, of cancer of the skin, and especially cancer of the lip among the males of three occupational groups (agricultural, mining, professional), representing a population of more than  $2\frac{1}{2}$  million, shows that while the agricultural worker is about three times more likely to die of cancer of some part of the skin than the professional man, he is twelve times more likely to die of cancer of the lip. It may be supposed that greater exposure to sunlight in the case of the agricultural worker increases his susceptibility; but the similar incidence among miners in whom such exposure is largely absent shows that some other factor is involved. The low mortality among professional men may not, however, be related to morbidity in the same ratios as in the other occupations, earlier and therefore more successful treatment preventing many deaths among them. Material from many parts of the world indicates that Jewish women are about three times less likely to develop uterine cancer than are non-Jewish women. This is apparently related to the Jewish practice of abstinence from intercourse during the first twelve days of the menstrual cycle. The incidence of uterine cancer increases in both single and married women with descent in the economic scale.

In at least six centres concerted efforts are being made to obtain precise evidence concerning the value of sex hormones in the treatment of mammary carcinoma. The most ambitious of these efforts is that in which the British Columbia Cancer Institute is taking part as one out of forty-eight clinics in Canada and the United States. Six different oestrogens, natural and synthetic, and testosterone propionate in dose schedules ranging from 75 to 600 mgm. per week are being tested.

At several centres measurements of 17-ketosteroid and oestrogen excretion before, during and after such treatment are being carried out, and at Guy's Hospital this work is being done concurrently with a long-term survey of cases of mastitis, in which it is hoped to establish more precisely the relationship between mastitis and breast cancer, an issue which is still controversial after a century of study by clinicians and pathologists.

At St. Bartholomew's Hospital the differential excretion of individual 17-ketosteroids separated by chromatography is being studied with special reference to prostatic disease. The abnormal excretion of aetiocholanolone, which had been previously reported by Dobriner as occurring particularly in malignant disease, has now been shown to occur in cases of benign prostatic hypertrophy. In cases of prostatic cancer, the pattern of excretion changes under oestrogen therapy. This is being fully investigated, together with the changes in wave form obtained by polarographic examination of serum.

Other studies include detailed analyses of nearly four hundred cases of ovarian cancer, and of more than a hundred of cancer of the vulva, and several

series reporting the results over a number of years of surgical and X-ray treatment of cancer of uterus and breast. Million-volt therapy appears to have no inherent advantages over 200 kV. therapy, though for technical reasons it may sometimes be more efficient.

On the physical side the report shows that considerable effort is being made in a number of centres to provide the facilities and equipment necessary for the clinical use of radioactive isotopes, which have been available from the Medical Research Council for therapeutic purposes since September 1948. Among the new instruments for detection and measurement of radioactive isotopes on which work is being carried out is the scintillation counter. Several centres report investigations on the possibilities of cobalt-60 as a replacement for radium in various therapeutic applications.

A survey is given in the report from St. Bartholomew's Hospital on the clinical results with the million-volt plant over the last eleven years. Measurements that have been made on very high energy X-radiations are reported from the Royal Cancer Hospital, where a 30-million volt synchrotron is now being installed.

Three centres report on the investigations on dosage and protection requirements with 10-gm. radium units. Of particular interest is the report from the Leeds General Infirmary, where the shielding of the unit is provided by uranium metal.

Critical studies of problems in dosage measurement are reported from several centres, particularly with regard to the energy absorption occurring in or near bone. Geometrical methods of estimation of dosage within patients appear to be giving way to some extent to methods of direct measurement on the patient during treatment, and the design and construction of various instruments for this purpose are reported on.

The chemical effects of radiation are being further investigated. A report from the Christie Hospital and Holt Radium Institute describes continued work on 'protection' phenomena, and at the Royal Victoria Infirmary, Newcastle, further investigations have been carried out to test the free radical theory. As a result of this latter study it has been possible to develop methods of dosage measurement based on chemical effects which may be of considerable importance in dosimetry studies with radioactive isotopes.

Related to these experiments on the chemical effects of radiation, a report from Mount Vernon Hospital states that it has been demonstrated that the sensitivity of the broad bean root to X-radiation is very dependent on the oxygen concentration of the water in which the root is immersed.

In the field of experimental radiology, reports on whole body irradiation of mice and localized irradiation of rat tumours show that in each case the effects of the radiation depend on the protein diet of the animals.

Possibilities of the therapeutic applications of microwaves of wave-lengths 1-100 cm. are reported from two centres. The work done so far has been on the absorption and dielectric properties of water and various types of tissue.

The report from the Dominion X-Ray and Radium Laboratory, Christchurch, gives an interesting account of the development of a radio-physical advisory centre in New Zealand, and of the particular problems involved in such a country with a small and relatively scattered population.

## INSTITUTION OF ELECTRONICS (N.W. BRANCH) JH FOURTH ANNUAL EXHIBITION

**A**FTER a modest beginning, the exhibition of the Institution of Electronics (N.W. Branch) now appears to be firmly established as an annual affair. Each succeeding year has seen a widening in scope and variety of the apparatus exhibited, until this year there were sixteen firms represented, the floor space occupied being considerably greater than at any of the previous exhibitions. On show this year, in addition to the standard measuring and communications apparatus, were several instruments of improved design, and others in which new features were incorporated.

Dawe Instruments, Ltd., showed a Swiss product which is now being manufactured in Great Britain under licence. The apparatus measures the moisture content of warps and fabrics and affords a continuous drying control over the entire width of the material. The measuring principle is based on the fact that the magnitude of the electrostatic charges which develop on fibrous material in motion depends to a large extent upon the degree of moisture of the material. These charges are collected by means of small insulated concave riders, which act as brushes, and are transferred to a measuring instrument of new design which is capable of detecting extremely small electrostatic charges.

A high-power stroboscope for use in the examination of heavy machinery operating at speeds within the range 20-3,000 r.p.m. was also shown by the same firm. The instrument, which can be operated remotely, has a variable-phase control so that any required part of the machine can be examined.

W. Edwards and Co., Ltd., showed a new relay for vacuum control in which variation in conductivity of the gas with pressure causes a long heated filament to operate electrical contacts. The ranges of pressure are between 0.001 and 10.0 mm. mercury, with differential according to requirements. New types of rotary pumps and a range of oil diffusion pumps were also exhibited.

A novel feature demonstrated by Everett Edgumbe and Co., Ltd., was a valve demonstration panel for educational purposes. It is designed for laboratory use to facilitate the plotting of valve characteristics with direct potentials, and comprises an a.c. power pack with voltage controllers, voltmeters and ammeters in each electrode circuit. A mimic diagram embraces the controllers, indicators and external terminals.

Ferranti, Ltd., showed two new instruments: a cold-cathode voltage stabilizer having a running voltage of 60.5 volts with a current-range from 2.5 m.amp. to the unusually low value of 120  $\mu$ amp., and an electronic impulse counter. In the counter, a photoelectric cell amplifier is connected either directly or by way of a frequency-dividing network to a mechanical recording counter. Light flashes at rates of up to 8,000 per minute can be accurately observed.

Marconi Instruments, Ltd., demonstrated their six-channel electroencephalograph, which has proved reliable over a period of three years. The direct-coupled mains amplifiers have a gain of  $10^6$  with less than 2 per cent distortion on full gain. The same firm was one of several exhibiting meters for the determination of the moisture content of timber and