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# NEOPLASMA

SEPARATUM

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## Review of the Research Work Carried on at the Institute of Oncology in Poland

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Scientific work at the Institute of Oncology in Poland started under particularly difficult post-war conditions, after the total devastation of the building and the equipment and with a very limited research staff. In January 1947, when the Institute resumed its activities after the interval caused by the war, the training of the staff and the organization of the work were its foremost preoccupations.

Research work was undertaken as the next step. Scientific investigations became one of the chief tasks of the Institute apart from the services or the activities dealing with the organization and cancer control in this country.

The evaluation of the present status of research work at the Institute of Oncology in Poland is not an easy matter in view of the varied and multiple lines of research. The Institute of Oncology is namely a scientific research institution embracing various branches of specialization such as pathomorphology, radiotherapy, surgery, experimental oncology and applied physics in the field of radiotherapy, with its proper scientific topic. Moreover, research is in progress along the lines of chemotherapy and radiobiology. I shall begin this review of the research work of the experimental oncology which is running at the present in the Institute.

The essential line of research of the Department of Tumour Biology is the problem of the mechanism of the morphogenetic action of estrogens. This is not only a theoretical question, but it is closely related with the hormonal therapy of the tumour, because the elucidation of the hormone-dependence of the neoplastic tissue is of a great clinical importance. In order to evaluate the response to estrogens, a test consisting of determination of alkaline phosphatase activity in the cells of the vagina epithelium was applied. Comparing the response of the normal vagina epithelium with that of the transplantable tumours of the vagina G93 and G94 in mice it was established that the neoplastic tissue is 10 000 times less responsive to estrogens than the normal epithelium. The papers dealing with this problem present the first attempt of a qualitative evaluation of the differences in response of the normal and the neoplastic tissues in the literature.

Investigations on the problem of the response of neoplasms to hormones constitute the basis for collaboration of the Department of Biology with the clinic. Endocrinological examinations of patients with breast cancer, treated by surgical methods (oophorectomy, adrenalectomy) lead to interesting conclusions. It was revealed that certain operations of endocrine glands proved to be ineffective in regard to the hormonal balance of the organism. This discovery makes a thorough endocrinological examination of patients with breast cancer imperative before undertaking surgical treatment. There are reasons to hope that following this trend of research it will be possible to formulate appropriate indications for the hormone-therapy in breast cancer after careful endocrinological investigations.

Another line which traces the research in the Department of Tumour Biology represents the problem of changes in the antigenic properties of neoplasms as demonstrated by immunological methods. A durable change in the antigen structure of Guerin's epithelioma in rats was obtained by its temporary transplantation to mice.

In another work the presence of an additional antigen in the transformed neoplasms was detected. A new subject of investigations is open at the present, namely work on the mechanism of antigenic transformation of tumours. It was demonstrated that the new genetic properties in Guerin's rat tumour can be induced by the DNA extracted from lymphatic tissues in mice. These studies are going on. The preliminary results indicate the possibility of the genetic transformation of the somatic cells of higher organisms (analogous to the well known phenomenon of transformation in bacteria).

There are three main lines in the research studies at the Department of Biology of Tumours at Gliwice: biochemical, histochemical and cytochemical. Biochemical studies have been carried on on the incorporation of the labelled DNA by means of biosynthesis in the cells of Ehrlich ascites carcinoma. The other problem dealing with the transaminase activity has been investigated in homogenates of some tumours and particularly of the hepatoma in comparison to the normal liver tissue. A drop in the transaminase enzymes activity in the liver of hosts has been demonstrated in the majority of cases after inducing neoplastic growth in an animal.

Histochemical studies included the investigation dealing with the activity of various enzymes (leucyaminopeptidase, dehydrogenase, phosphorylase) in the organs and in the neoplastic tissues. Cytochemical methods have been employed to determine the distribution of enzymes (among others of ATP-ase) in the particular fractions of cells.

The lack of studies concerning the virological trend in the Polish experimental oncology requires attention. There is no laboratory in this country working systematically on tumour viruses, while in other countries this problem is considered as of paramount importance in the experimental oncology.

Pathomorphology is another field of the research work at the Institute of Oncology. It is generally accepted that histopathology is the most valuable and reliable diagnostic method regarding oncology. This does not mean, however, that it involves no gaps and obscurities. There exists namely in the field of oncology a number of pathological entities requiring further study and investigation and the establishment of a close relation between the microscopic structure, the clinical symptoms and the biological behaviour of tumours. One of the most important lines which pathology should trace in research work is the study of the histoclinical features of the neoplastic process. This consists in the confrontation of the microscopic picture with the biological course and the clinical symptoms of tumour growth: this work at the oncological clinic is intrinsically linked with the pathology.

Pathology involves another trend of investigation i. e. nosology, the purpose of which is to establish and to describe pathological entities so far unknown and to give their exact morphological, biological and clinical characteristics. It is worth mentioning that in the last few years, 10 so far unreported pathological entities have been established such as: tumours of the ovary (interstitioma ovarii), of the testicle (folliculoma lipiticum testis), of the thyroid gland (carcinoma hyalinicum glandulae thyreoideae) and others. This year a paper on sarcoma aponeuroticum with specific microscopic and clinical features has been published. In collaboration with the laboratory of X-ray diagnosis a detailed evaluation of calcifications in tumours of the soft somatic tissues has been made, supplying thus a basis for tissue diagnostics both in non-neoplastic processes as well as in tumours originating in the soft somatic tissues.

Finally work is being carried on along diagnostic lines. This trend in oncological pathomorphology is extending the register of microscopic diagnostics to oncological entities unknown in Poland or so far erroneously identified. This refers particularly to the newly noteworthy skeletal tumours.

The Department of Pathology at the Kraków branch of the Institute of Oncology, has finished studies on pathomorphology of gastric mucosa in the peptic ulcer and cancer of the stomach. These studies, based upon 377 operative specimens, have revealed, that in the gastric mucosa which shows no macroscopic abnormalities, typical changes either of inflammatory or of metaplastic character take place in the microscopic picture. Very advanced regenerative changes constitute morphologic evidence of the patient being exposed to the danger of a malignant metaplasia. Pathomorphology of the ulcer — cancer lesions has also been studied on the material of 351 cases: in 8,5 per cent of the cases the typical pattern of cancer was ascertained in the ulcer wall and in 8 per cent of the cases there was found that the advanced gastric carcinoma had developed from the preexisting peptic ulcer. Significant, from the pathoclinical point of view, features of carcinomas, ulcer — cancers and gastric ulcers have been also established. Scientific work at the Department of Pathology of the Institute of oncology, Gliwice Branch, has also been carried on along the histoclinical and diagnostic lines.

A large scale research work on the cytology of cancer has been developed at the Institute of Oncology in Gliwice with special reference to the cancer of the uterine cervix and to the bronchial cancer. In the cancer of the uterine cervix under study there were not only problems as for the diagnosis, but also as for the evaluation of advantages and disadvantages of the treatment based on observations of postirradiation changes in cancer cells and in the normal epithelium of the cervix. The study of the extensive group of patients with cancer of the lung and other pulmonary lesions (bronchiectasis) enables to establish precise criterions for the cytologic differential diagnosis.

As for clinical oncology, research is conducted chiefly in the sphere of tumour surgery, radiotherapy, hormone- and chemotherapy. The main task of the oncological surgery is the development of new methods of operative treatment of neoplasms, based on their pathology, dynamics and clinical behaviour as well as improvement of methods of combined treatment with radiotherapy, hormonal therapy and chemotherapy. New surgical methods of treatment are induced on the basis of well verified clinical data. In this way the usefulness of the following surgical methods of treatment has been proved: radical and paliative surgery of cardiac-oesophageal carcinoma, combination of preoperative irradiation with high X-ray doses and radical surgery in breast cancer or so-called extended mastectomy including the parasternal lymph-nodes dissection in cancer located in the median quadrants or the central area of the breast. Further experiences are being collected in the hormonal treatment of advanced cases of breast cancer and in the surgical-chemotherapeutical procedure in particularly malignant growths in prognostically unfavourable cases. This concerns primary malignant tumours of the bone, cancer of the stomach and malignant melanomas.

Experimental work on regional perfusion was performed. For the purpose of perfusion a de Wall oxygenator was constructed. In 12 experimental perfusions of the extremities on dogs various cytotoxic drugs were applied, as: Endoxan, Trenimon, Thio-tepa in increasing concentrations. The optimal doses were finally established and methods were developed for reducing the toxicity of the cytostatic substances.

Large scale team-work carried on at the Kraków Branch on the problem of the cancer of the stomach deserves particular attention. In this center many materials which provide a basis for evaluation of the end-results of treatment have been collected. Metabolic

studies in the cases of gastric carcinoma have also been carried out by investigation of the behaviour of the metabolism of sodium, potassium, glico- and lipoproteins and by investigation of the liver function in patients with cancer of the stomach. Biochemical analysis of cases of gastric carcinoma revealed that fatt-tissues and also the tissues metabolically active (muscular and nervous system and parenchymatous organs) account for the weight loss in the patients.

The Department of Surgery, Gliwice Branch, has worked on the evaluation of the efficacy of operative technics in the treatment of gastric cancer, cancer of the rectum and of malignant melanomas. Moreover, diagnostics of neoplasms located in the chest, particularly of cancer of the bronchus have been improved.

Chemotherapy is the youngest branch of tumour therapy in the Institute of Oncology. The lack of a laboratory serving as base and the lack of adequately trained personal makes it impossible to undertake experimental work within the scope of the „preclinical program“ (term used by the Cancer Chemotherapy National Service Center Program). As for the clinical experiment, i. e. the clinical evaluation of the efficacy of a drug after establishing its properties, the mode of application, the dosage, the toxicity etc. the work is, however, progressing. Particular attention is devoted to the application of chemical therapeutics in the treatment of primary lung cancer. In 70 histopathologically verified cases benzoquinone derivatives, phosphoramides, nitrogen mustard and actinomycin K were tested.

The relation between the microscopic structure of the neoplasm and the improvement of the condition of the patient is the subject of detailed analysis. In ovarian tumours mainly benzoquinone derivatives (E-39, Trenimon) were applied intravenously or intraperitoneally. The best results were obtained after intraperitoneal administration of benzoquinone in cases of ovarian tumours with ascites.

In the treatment of tumours of the lymphatic system mostly alkylating agents (Dopan, Sarcoclysin, Degranol, Mitomen) and in some cases adrenal hormones were used.

The study of the extensive material of patients receiving various chemical drugs in combined chemotherapeutic treatment in the course of the last few years will enable to establish more accurate medical indications and to evaluate the method.

Radiotherapy played from the very beginning an important role in the development of research in the Institute.

At the present in all Institutes of Oncology special attention is drawn to the clinical problems related to the radiation treatment of cancer of the uterus, ovaries, urinary bladder, larynx, breast, thyroid gland and cancer of the oesophagus. In addition to the classical forms of curie- and static conventional X-ray therapy, new methods of radiotherapy were applied: the rotation technique in the treatment of cancer of the oesophagus and the cobalt-60-teletherapy in cases of cancer of the urinary bladder, larynx and in tumours of other localizations. Our own experience is collected in the clinical application of isotopes: I-131, metallic and colloidal Au-198 and P-32.

In the last years a great deal has been done on working out the basis for applied physics in the radiotherapy and to introduce the precise physical principles of treatment.

A team-work with the Department of Surgery is in progress. The main subject of investigation is the combined radiotherapeutic and surgical treatment, particularly in cancer of the breast, uterus and ovaries.

The problem of the hormonal therapy of the breast cancer has been investigated in all Institutes. At the clinical departments of the Institute, studies on etiology and improvement of the diagnostic methods of tumours have been carried on continuously. These studies have dealt in particular with the relation between tobacco smoking and carci-

carcinoma of the bronchus, larynx, lower lip, mouth and oesophagus (Gliwice). The present results obtained in large scale investigations on the possible relation between tobacco smoking and cancer of the bronchus and oesophagus deserve particular attention also in foreign cancer centers.

Concluding my report I should like to add some words on the research work in the radiobiology. The main problems investigated at the Isotope Department of the Institute of Oncology in Warsaw are the calcium metabolism in man and the comparative biological efficiency of radiations and cytostatics. These investigations are carried on at the Clinical Ward and at the Radiobiological Laboratory of the Department.

The radioactive isotope — calcium-47 is used as a tracer of the calcium metabolism in normal people and in patients with primary and secondary bone tumours. The analysis of data collected during a period of 2 years enables to construct the model of calcium-47 turn-over in men; an original mathematical method of data-analysis has been applied and on this base several hypothetical compartments have been quantitatively characterized. The problem of the late exchange of the isotope between the „inaccessible“ bone calcium and the body fluids was also investigated. At the same time the metabolism of scandium, a daughter element of calcium-47 has been studied in men and in animals.

The Radiobiological team is interested since several years in the comparison of the effects exerted by radiations and cytostatics on the biological systems in vitro. Shortterm culture of the bone-marrow cells in rats and mouse Ehrlich carcinoma cells has been used; the biosynthesis of nucleic acids has been investigated, using labeled NA precursors (thymidine-C-14 and orotic acid-C-14). The obtained dose response curves show that the mechanism of action of the agents under investigation (radiation and radiomimetic drugs) is different.

The respective clinical and research units at the Institute of Oncology in Gliwice are specially interested in the use of radioactive iodine in the treatment of the cancer of the thyroid gland, in the use of strontium-85 as a diagnostic tool in bone tumours and in the role of the oxydative process in the radiation effects. The clinical material of the thyroid cancers amounts to more than 100 cases treated and followed-up during the last five years. The use of strontium-85 is a new development and our own experience is rather scarce. The influence of the oxygen on the radiation response of the cells and the consumption of oxygen by the irradiated cells and tissues is a main part of the radiobiological programme of the Gliwice Institute.

The scientific programme of the five Cancer-Congresses, which took place in the post-war period, consisted chiefly of the studies performed by means of the common effort of various departments of the Institute of Oncology. At the Congresses many topics were discussed in detail; there were the following problems among them: cancer of the breast and uterus, precancerous conditions, the methods of work in the field of oncology, tumours of the soft somatic tissues, hormone therapy of cancer, application of isotopes in the oncology. A great majority of the research papers from the Institute have been published in the periodical „Nowotwory“, which is the organ of the Polish Cancer Society and the Institute of Oncology. This year the printing of the XII-th volume of this periodical has been started.

This review gives no idea of the difficulties and the conditions under which research work is carried out in the Institute of Oncology. All the work is done by a small group of research workers, who in addition are burdened with an excess of organisation- and service duties resting on the Institute and its workers.

In view of the overcome difficulties of the Institute, its research achievements (about

600 papers published since 1948) should be appreciated. They inspire the hope that in the forthcoming years further scientific results will be achieved in accordance with the Institute's research programme.

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