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OAK RIDGE INSTITUTE of NUCLEAR STUDIES

Medical Division

Midyear Report

For The Period Ending December 30, 1955



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CLINICAL STUDIES

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STUDIES WITH IODINE-131

Previously reported studies on the destruction of the thyroid gland with iodine-131 are being continued. A series of new histologic specimens is available on patients with multiple myeloma who are given large doses of iodine-131 and whose thyroid glands showed varying degrees of radiation damage.

The long-range study of thyroid carcinoma continues, with increased use of the scintiscanner and improved external-counting methods in an effort to understand more clearly the behavior and distribution of radioiodine. Histologic specimens and autoradiograms showing the distribution of the isotope in the lesions are obtained wherever possible. Two unusual cases in children of thyroid carcinoma, showing a peculiar clear cell transformation after removal of the normal thyroid, have been carefully studied and a report on them is in preparation.

Selected patients with hyperthyroidism and with heart disease are being treated with radioiodine. Several types of special studies have been done on these patients. One of these is to follow the protein-bound radioiodine in the plasma at daily intervals for periods of ten days after each tracer and therapeutic dose; this is being done in an effort to determine whether or not the therapeutic dose will produce a significant abnormal release of protein-bound iodine material and, if so, whether the quantity of this material released into the blood stream can be used as an index of the effectiveness of the therapeutic dose.

A series of patients who had received radioiodine were studied for the salivary iodine excretion over a period of many days after each dose; this program was chiefly carried out by Zeth Gabrielsen, a visiting resident physician from Norway. The concentration of the isotope in the saliva was compared with the free and protein-bound isotope in the plasma. All of the data, which are being prepared for publication, indicate that the concentration of the isotope in the saliva derives entirely from the unbound form in the plasma. No evidence has been produced to support the theory that the salivaries play an important role in breaking down iodine-

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containing organic compounds.

The effort to treat multiple myeloma with large doses of radioiodine has, in general, been unsuccessful. Slight temporary improvement in some patients has been seen, but has not been considered of sufficient degree or duration to justify recommendation of this form of treatment. Detailed autopsy studies with radioassays and autoradiograms on several patients have failed to indicate any tendency for the myeloma lesions to concentrate the radioiodine. It appears that any benefit obtained is a result of the rather generalized radiation produced.

Special external-counting studies (see section on Medical Physics) on the thyroid with the scintiscanner and with various uptake-measuring devices have been continued. The old type of scintiscanner with a simple cylindrical collimation and a small crystal has proved to be of distinct value in studying certain types of isotope-distribution patterns. Perhaps its greatest single usefulness has been in evaluating the location of areas of functioning tissue in the neck of patients with thyroid carcinoma. The scintiscanner has frequently made it possible to differentiate between residual normal and areas of carcinoma. We have been unable to confirm, however, the reports of success in delineating small hyper- and hypofunctioning lesions in the thyroid gland. It appears that the old type of scintiscanner is considerably less discriminating than has been reported. We have seen examples of adenomas showing distinct differences in function from normal tissue, but not detected by the scintiscanner. There has been some success in delineating the criteria for evaluation of scintiscan records, and in describing the cause of artifacts. The instrument has been found useful with many isotopes other than radioiodine.

An improved scintiscanner developed by P. R. Bell, J. E. Francis, Jr., and C. C. Harris of Oak Ridge National Laboratory has been given limited trial and shows great promise. Its chief virtues are a high degree of sensitivity, relative freedom from inverse-square-law effect, and fine discrimination.

Another instrument developed largely by P. R. Bell and the group working with him is a probe counter for surgical procedures. This has been found to be of distinct value, chiefly with radioiodine.

ROSE BENGAL TAGGED WITH IODINE-131

Work has begun, and is continuing, on the evaluation of rose bengal tagged with iodine-131 as a liver-function test. This program is being carried out by Warren Glaser, resident physician in experimental medicine, and other members of the staff. The experiment has been divided into two parallel and simultaneous determinations:

accumulations as a result of metastatic neoplasms. Efforts have been made to determine the therapeutic usefulness of yttrium-90 and lutecium-177 as isotopes for intracavitary injection, in close cooperation with Granvil Kyker and other members of the Medical Division staff who are making basic biochemical and animal studies. Complete evidence has been collected indicating that these isotopes remain well localized in the region of the cavity, and from a point of view of metabolism and distribution are highly suitable for this type of therapy. It is not yet possible to state their relative merits in comparison with colloidal gold-198 or chromic phosphate (phosphorus-32). Neither do we know the doses of yttrium and lutecium necessary to produce an adequate radiation effect. Continued research on this problem is in progress.

Studies of plasma disappearance and distribution after intravenous administration of these materials have also been performed. A preliminary report on this work was given at the rare-earths conference held in Oak Ridge on October 27, 28, and 29, 1955.

STUDY AND TREATMENT OF HEMATOLOGIC DISORDERS

In addition to continued use of phosphorus-32 for certain patients with polycythemia vera and the continued study of intravenous colloidal gold-198 in chronic granulocytic leukemia, certain selected patients have been studied with iron-59 and chromium-51 in an effort to gather more information about isolated clinical cases of interesting blood disorders. One of these patients, studied in great detail, is a man with aplasia of the erythrogenic elements of the marrow, without much disturbance of granulopoiesis or thrombocyte formation.

TRAINING PROGRAM

The clinical staff of the Medical Division continued to assist in the teaching of the basic courses given by the Special Training Division of the Institute. During most of the one-month basic isotope-techniques courses, a clinical program involving three or four afternoons plus one lecture was carried out. There were also special lectures in other Special Training Division courses, including a regular lecture in the veterinary radiological health courses by Arthur L. Kretchmar.

The clinical staff of the Medical Division has maintained an active training program. For the first time, the one-year approved residency in internal medicine (experimental clinical medicine) has been filled. There are now two residents on this program, one who began in July and one who began in October.

1. The first part of the work has involved injecting rose bengal iodine-131 intravenously into selected patients admitted to the clinical service; the surface of the liver is then surveyed with the medical spectrometer and a permanent record has been obtained on a Brown or Esterline-Angus recorder. Correlation is made of data obtained with the liver chemistries and the clinical condition of the patient at the time of testing.
2. The second part of the work has involved injecting rose bengal iodine-131 into adult rats and sacrificing them at appropriate intervals. The livers are assayed for iodine-131 activity, and gross and microscopic autoradiograms are made. Other tissues, as the gastrointestinal tract and spleen, are also assayed.

At this time it is too early to attempt to make a direct correlation between the curves obtained on liver survey and the various diseases of the liver. There are, however, definite indications that the shape of the curve (time necessary to reach maximum activity, the absolute height of the curve, the plateau and slope of the excretion portion) is altered by both intrinsic and extrinsic hepatic disease.

The technique for microscopic autoradiography of the liver is still to be refined. However, preliminary data suggest that the radioactivity does diffusely locate in the hepatic cells and is not concentrated in the Kupffer cells. More careful resolution is necessary before a final evaluation can be made.

BONE-SEEKING ISOTOPES AND OSTEOGENIC SARCOMA

A study of osteogenic sarcoma has been continued and a considerable number of patients have been followed throughout the course of the disease. The use of gallium has not been continued during the last six months, but P-32 and other isotopes have been given for the purpose of the study of their distribution in lesions. Several patients have been subjected to repeated surgical procedures by George Minor of the University of Virginia for removal of pulmonary metastases, although this appears to be a rather discouraging therapeutic approach. Because of the multiplicity of metastases in most cases, several patients have shown evidence of significant palliation, and further study of the operation appears worthwhile. One of the unusual findings in the group of patients currently being studied is that metastases in the chest wall occur rather frequently. The mechanism of their production is obscure.

STUDY OF COLLOIDS AND RARE-EARTH ELEMENTS

A continuous study has been made of patients having fluid