

Thus it is possible that capillary irradiation is responsible for or contributes to the selective death of basal cells. This possibility will be studied, using a boron-10 colloid that is retained intravascularly. The time course of the boron concentration in the blood following intravenous injection will be determined in pigs. The skin of animals containing a known concentration of circulating boron colloid will be irradiated. The effects of the resulting  $B^{10}(n,\alpha)Li^7$  reaction on the capillaries and indirectly on the skin will be evaluated, using electron and light microscopy. Other parameters will include the determination of dye extravasation, tissue blood volumes and circulation times, and skin temperature regulation.

If intravenous injection of the colloid to the intact animal results in loss of colloid because of phagocytosis by the R.E. system, then suitable organ or isolated limb perfusion methods will be employed.

✓ JIC 2066 USE OF ANTIBODIES AS CARRIERS OF RADIOACTIVITY FOR THERAPY OF CANCER. William F. Bale (Rochester, N. Y. Univ. School of Medicine and Dentistry). Contract W-7401-eng-49.

This project in cancer immunology seeks to produce radioactive antibodies that after parenteral administration can serve to carry therapeutic amounts of radioactivity to primary and metastatic cancer lesions. Studies in human patients have been largely with  $^{131}I$ -labeled antibody to human fibrinogen. In many instances, diagnostic doses have been useful in locating tumors (primarily brain metastases) for radiation therapy or surgery. This antibody accumulates with such considerable specificity and concentration in some malignant tumors that in cases in which surgery or conventional radiation therapy were contraindicated, single doses of  $^{131}I$  up to 170 mc attached to antibody have been given. Although there were examples of clinical remission and objective evidence of tumor size reduction or disappearance, no permanent cures have been obtained. Research and clinical groups from other departments of this medical center and from other institutions are collaborating in this work and allied studies with this preparation, such as locating peripheral thrombi.

Associated animal work is directed at finding means of increasing the rate, magnitude, and permanence of antibody deposition to make it a more widely useful clinical diagnostic and therapeutic tool. Effects of plasmin, plasminogen inhibitors, agents effecting fibrinogen-fibrin conversion, chemotherapeutic agents and artificial fever are among those under study. Other work is directed at the production and isolation of specific antibodies to animal tumors with localizing properties, and of labeled components of complement. Laboratory studies are directed at improved methods of antibody isolation and labeling.

JIC 2254 EXTERNAL TOTAL-BODY IRRADIATION FOR LEUKEMIA AND RELATED DISEASES. G. A. Andrews (Oak Ridge Inst. of Nuclear Studies, Inc., Tenn.). Contract AT(40-1)-Gen-33.

The objective is to improve the use of total-body irradiation in leukemia and other diseases by the best selection of patients, radiation dose, dose rate, and to achieve permanent homologous bone-marrow grafts after total-body irradiation in patients with acute leukemia. Total-body irradiation as palliation has not been used to its full effectiveness because of insufficiently uniform technique and inadequate follow-up. The USAEC and NASA need information on irradiation effects in man and these studies will help provide it.

Most patients selected for the low dose have chronic leukemia, lymphosarcoma, or polycythemia vera. Treatment is given in the total-body irradiation and hematologic and biochemical values are measured in a follow-up of at least 6 weeks. A few patients are given high doses (300 r or more) to produce remissions in acute leukemia.

In the 50 r series, 1 of 4 had mild radiation sickness. Only 4 of 13 in the 100 r group had no nausea, vomiting, or anorexia. Two had considerable subjective improvement, 9 moderate and 1 no improvement. Benefits of low-dosage total-body irradiation are comparable to conventional therapy in chronic leukemia and lymphosarcoma. The patient with polycythemia apparently had

the same response from 100 r total-body irradiation as would have been expected from 4 or 5 millicuries of intravenous  $^{32}P$ . The response of the patient with reticulum cell sarcoma (100 r) was particularly gratifying in significant reduction of lymphadenopathy.

JIC 2269 EXPERIMENTAL TELETHERAPY. F. V. Comas (Oak Ridge Inst. of Nuclear Studies, Inc., Tenn.). Contract AT(40-1)-Gen-33.

The objective is to find methods of improving the radiocurability of cancer.

Many ideas require clinical trial including fundamental questions on the mechanism of radiation injury. Advances in radiation therapy offer one of the major hopes for salvage of certain kinds of cancer. Transplantable rat tumors are used for accumulating basic evidence such as the relative radiosensitivity of tumors and normal tissue treated under anoxia. Clinical trials with  $^{60}Co$  teletherapy will be made in selected cancer patients. For example, probably the first patient ever irradiated with willful interference with the blood supply was one with extensive squamous cell carcinoma of the left maxillary antrum. To achieve anoxia of the tumor, Jacobson cuffs were applied around each external carotid artery and were inflated during each treatment. The tumor showed good immediate response, but several complications occurred during treatment. Even so this trial showed that the procedure is feasible. A second example concerns the mechanism of effects of local splenic irradiation in patients with chronic myelogenous leukemia, which has never been explained. Does irradiation directly destroy or inhibit the proliferation of the many leukemic cells in the spleen, or is something peculiar to the spleen (hormal) activated by irradiation? Two patients have been given 500 r to spleen and liver. One patient showed no hematologic changes when the liver was irradiated, but a profound fall in circulating white blood cells occurred after irradiation of the spleen. The other patient responded to liver irradiation in a way undistinguishable from the changes occurring after spleen irradiation; in both instances the peripheral white count went from about 100,000 to 20,000 with a fast return to pretreatment levels.

## K SELECTED BENEFICIAL APPLICATIONS

This category includes projects to foster and encourage new and unique applications of radiations and radioisotopes in medicine, as in the diagnosis and characterization, treatment and control of diseases other than cancer, and in basic studies of organs and organ systems in health and disease; also in agriculture to control and eliminate insects, weeds and diseases, improve farm animal productivity and increase knowledge of animal diseases.

### K1A MEDICAL RESEARCH

This subcategory consists of studies on the unique applications of radioisotopes and special radiation sources in diagnosis and therapy, such as:

1. Treatment and control of diseases other than cancer;
2. Diagnosis and characterization of disease states such as blood dyscrasias, cardiovascular-renal disturbances and endocrine disorders;
3. Basic biological studies on metabolism and synthesis as related to disease, and better understanding of the transportation of metabolites between intracellular spaces, cells, organs and organ systems in health and disease;
4. Development and use of whole-body counting facilities and scanning devices for study of metabolic processes having diagnostic potential.

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