

11/1/76

CENTER FOR HUMAN RADIOBIOLOGY

Fact Sheet on

Mechanisms of Tumor Induction

The purpose of this work is to investigate the mechanisms of tumor induction by radiation in order to predict the effects of irradiation to large populations at low doses. If the induction of a bone tumor by radiation necessarily involves the suppression of one of the systems of the immune response or the release of a virus, a linear dose response would no longer be a physiological possibility. Thus by learning more about how radiation transforms cells in culture and by studying the viral and immune status of our radium patients we stand a chance of uncovering the key to the shape of the dose-response curve at low dose levels—probably the most important practical issue in radiobiology.

Irradiation

(a) Transformations—As far as we know we are the first to have produced transformations of cells in vitro using alpha-particle irradiation. We have irradiated a layer of well-characterized mouse cells using 5.6 MeV alpha particles from a Tandem Van de Graaff and shown increasing frequency of transformations with increasing dose.

(b) Cell killing—We have found the surprising result that the mean lethal dose (~100 rads) for flattened cells, such as those lining bone surfaces, corresponds to a passage of about twenty alpha particles through the nucleus and not one or two as has previously been supposed. This suggests new concepts for mechanisms of cell killing and carcinogenesis giving further information about the location and dimensions of the critical sites.

Viruses

The experimental work done in collaboration with Dr. J. F. Loutit at Harwell showing viruses in osteosarcomas induced by <sup>226</sup>Ra in mice has now been published (over). Further studies have also shown viruses in tumors produced by <sup>239</sup>Pu; however, the most surprising result was the increased incidence of tumors other than osteosarcoma in the animals injected with the lower doses of <sup>239</sup>Pu. This work is ready for publication.

Immune Responses—Early Tumor Detection in the Radium Patients

Lymphocytes and sera from the high-level radium patients are being tested for cell mediated immunity and for sarcoma antibodies against osteosarcoma cells in culture. In the patients studied so far, no differences have been observed between the controls and the radium patients, as was to be expected, since none of the radium patients developed osteosarcomas. Samples from tumor patients by contrast showed positive reactions. These tests, therefore, appear promising as methods for the early detection of tumors.

REPOSITORY Cigarette/CHR  
COLLECTION Records Related to Industrial/Medical  
BOX No. Exposure to Radium, Box 121 A-H  
FOLDER Folder #33 - CHR Fact Sheets  
Review Committee  
History of CHR from ANR Reports

### Publications

Viruses in Osteosarcomas Induced by Ra-226: A Study of the Induction of Bone Tumors in Mice

E. L. Lloyd, J. F. Loutit, and F. Mackevicius  
*Int. J. Radiat. Biol.* 28, 13-33 (1975).

Cell Mediated Immunity as an Early Diagnostic Test for Osteosarcoma in Human Radium Cases

E. L. Lloyd, M. Menon, and J. L. Mitchen  
Radiation and the Lymphatic System, National Technical Information Service, Springfield, Virginia, pp. 165-168 (1975)

Immunodiagnostic Test for Osteosarcoma in Patients with a High Body Burden of Radium

E. L. Lloyd, M. Menon, and J. L. Mitchen  
Critical Factors in Cancer Immunology, Eds. J. Schultz and R. C. Leif, Proc., Miami Winter Symposium, January 13-17, 1975, 10, Academic Press, New York, p. 328.

Immunological Studies in the Human Radium Population

E. L. Lloyd and M. Menon  
Workshop on the Biological Effects and Toxicity of Pu-239 and Ra-226, Sun Valley, Idaho, Oct. 6-9, 1975. Health Effects of Plutonium and Radium, W. S. S. Jee, Ed., J. W. Press, Salt Lake City, pp. 485-496 (1975).

Immune Status of the Radium Patients

E. L. Lloyd and M. Menon  
Neoplasm Immunity: Mechanisms, University of Illinois 3rd Annual Chicago Symposium, September 11-12, 1975, in press.

### Papers in RER Annual Reports

Differences in the Characteristics of Cell Cultures Established from Seven Human Osteosarcomas

E. L. Lloyd, C. B. Henning, and F. Mackevicius  
Radiological and Environmental Research Division Annual Report, Center for Human Radiobiology, July 1974-1975, Argonne National Laboratory Report ANL-75-60, Part II, p. 43.

Cell-Mediated Immunity in Patients with Osteosarcoma

E. L. Lloyd and C. B. Henning  
Radiological and Environmental Research Division Annual Report, Center for Human Radiobiology, July 1974-June 1975, Argonne National Laboratory Report ANL-75-60, Part II, p. 149.