



STANFORD UNIVERSITY MEDICAL CENTER

STANFORD, CALIFORNIA 94305 • (415) 321-1200

STANFORD UNIVERSITY SCHOOL OF MEDICINE
DEPARTMENT OF RADIOLOGY

MALCOLM A. BAGSHAW, M.D., *Professor & Chairman*
RICHARD C. PLACONE, M.A., *Administrator*

Diagnostic Radiology

F. FRANK ZBORALSKE, M.D., *Professor & Director*

Nuclear Medicine

JOSEPH P. KRIS, M.D., *Professor & Director*

Radiation Therapy

MALCOLM A. BAGSHAW, M.D., *Professor & Director*

Radiobiology Research

ROBERT F. KALLMAN, Ph.D., *Professor & Director*

March 13, 1974

The Sheen Award Committee
American Medical Association
535 North Dearborn Street
Chicago, Illinois 60610

Gentlemen:

Professor Joshua Lederberg and I take pleasure in nominating Henry Seymour Kaplan, Maureen Lyles D'Ambrogio Professor, for the Dr. Rodman E. Sheen and Thomas G. Sheen Award. The accomplishments in basic science, radiobiology, and radiotherapy noted in the summary following, briefly outline the contributions made by Dr. Kaplan during his long and successful tenure as Chairman of the Department of Radiology at Stanford University, from 1948 through 1972. It is difficult to identify his single most important contribution; however, his long-term studies on the mechanism of induction of murine leukemia probably rank as the most important in basic research. These experiments demonstrated that murine leukemia induction by radiation is an indirect effect produced by the unmasking of an otherwise latent virus.

From the standpoint of clinical medicine, the most significant contribution has been in improving the treatment of Hodgkin's disease. Dr. Kaplan and his colleagues have led an almost universal international movement which has modified the potential for cure during the past decade from approximately 25% to 85%. While the improvement in cure rate has been the most immediately obvious result, this came about by the application of rigidly controlled, randomized trials that have changed much clinical research from anecdotal mediocrity to well-planned prospective programs.

A more detailed summary of his contributions follows.

Cellular and Molecular Radiobiology. Kaplan has made significant contributions in the identification of DNA as the sensitive target for lethal radiation injury. He demonstrated the increased lethality in bacteria by pre-irradiation incorporation of halogenated pyrimidine and purine analogs in the DNA of bacteria. He correlated the base composition of DNA with X-ray sensitivity and demonstrated that both single and double-stranded scissions are produced by exposure to X-rays,

and that single-strand scissions are repaired, whereas double-stranded are not.

Leukemogenesis. Beginning in 1940 and continuing to the present, Kaplan and associates demonstrated that the murine leukemia induced by radiation is an indirect effect produced by the unmasking of an otherwise latent virus. This was the first evidence that the action of external leukemogenic agents may be mediated by viruses. The radiation leukemia virus has been partially purified, demonstrated by electromicroscopy, in the irradiated thymus and characterized by identification of tumor-specific antigens. The members of this research team, under Kaplan's continuing direction, are now engaged in a new investigation of the possible causal agents (viral?) for Hodgkin's disease and human lymphosarcoma.

Linear Accelerator Development. In the early 1950's, Dr. Kaplan recognized that the considerable development in microwave technology at Stanford, especially in the area of linear accelerator design and construction for nuclear research, might be applied in medicine. Thus, Kaplan, Ginzton and Mallory conceived of the design of a small linear accelerator which could be used as a megavoltage X-ray source for radiation therapy. They supervised the successful construction of a medical linear accelerator which was handmade in the Stanford Department of Physics and installed for radiation therapy in 1956 at the Stanford Hospital in San Francisco. This was the first linear accelerator in the Western Hemisphere and was the prototype for the commercial production of linear accelerators for medical use. Since that time, linear accelerators have become the dominant equipment for sophisticated high energy radiation therapy. This episode is now being repeated some 20 years later by the collaboration of Kaplan and Bagshaw from the Radiation Therapy Division, and Fairbank and Schwettman from High Energy Physics in the design and fabrication of a new radiation source. This new machine will consist of two parts: one, a linear electron accelerator which operates at extremely low temperatures in order to achieve a high output beam which, in turn, two, activates a target assembly which will produce negative pi mesons and focus these negative pi mesons at any prescribed depth within the human body for the treatment of cancer. There is considerable physical and biological evidence to indicate that beams of negative pi mesons will dramatically increase the potential for curing many types of localized cancer in humans.

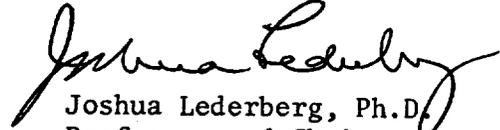
Hodgkin's Disease. Kaplan's greatest clinical contribution has been in the application of radiotherapy for the cure of Hodgkin's disease. Prior to the comprehensive study of Hodgkin's disease launched at Stanford by Kaplan and co-workers in the early 1960's, Hodgkin's disease was generally considered to be a fatal disease. By the introduction of a number of well-designed prospective clinical protocols, this team was able to demonstrate that (a) individual foci of Hodgkin's disease could be completely cured if irradiated to doses in the easily-tolerated range of 4,000 to 4,500 rads, and that the critical issue in developing appropriate therapeutic programs for individual patients revolved around precise pre-treatment staging of the disease prior to the institution of therapy. As the program evolved, it became clear that identification of potential areas of involvement was so important that the use of lymphangiography and, indeed, exploratory laparotomy and splenectomy became mandatory prerequisites for appropriate treatment planning in nearly all cases. During the past decade, the potential for cure has risen from

approximately 25% to 85%. Although less well known during this same interval, Kaplan and co-workers have made significant advances in the radiation therapy of a number of other types of cancer, including retinoblastoma, a rare malignancy of the eyeball occurring in infants, carcinoma of the urinary bladder, carcinoma of the laryngopharynx, non-Hodgkin's lymphomas, mycosis fungoides, and carcinoma of the prostate.

Sincerely yours,



Malcolm A. Bagshaw, M.D.
Professor and Chairman
Department of Radiology



Joshua Lederberg, Ph.D.
Professor and Chairman
Department of Genetics

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