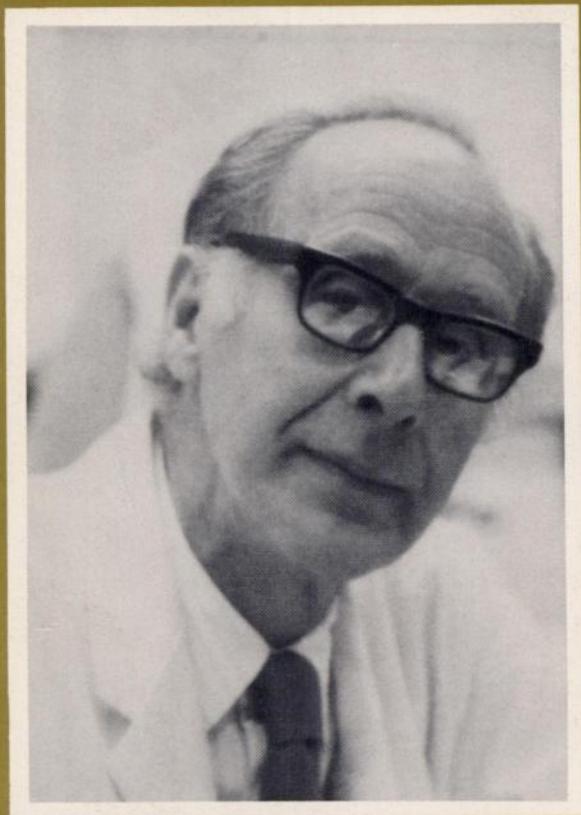


Cancer Research

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“**T**he marked effects of the mustards on lymphoid tissue, coupled with the finding that actively proliferating cells are selectively vulnerable to the cytotoxic action of the mustards, suggested the therapeutic use of these compounds in the treatment of neoplasms of lymphoid tissue. Because of its undesirable physical properties and extreme chemical reactivity, sulfur mustard does not lend itself to parenteral administration. However, nitrogen mustards in the form of their hydrochloride salts are water-soluble, crystalline compounds, which can be readily dissolved in sterile saline for intravenous administration. Experiments on transplanted lymphosarcoma in mice revealed that dissolution of such tumors could be rapidly effected although the dose required bordered on the toxic, and the tumor invariably returned. The first clinical trial of the nitrogen mustards was conducted on a group of six patients in the terminal stages of various neoplastic diseases. In two cases of lymphosarcoma in which X-ray therapy had been discontinued, a rapid dissolution of large tumor masses followed a course of injections. The results were sufficiently encouraging to warrant further clinical experimentation.

.....

Although some patients receiving nitrogen mustards have been observed for a period of 28 months, the evaluation of the clinical status of this group of compounds will require many more years of careful study. At present there is no basis for assuming that the therapeutic efficacy of the nitrogen mustards is any greater than that of X-ray.

It is possible that the potential value of the nitrogen mustards in the treatment of neoplastic diseases will be fully realized only when the opportunity to explore the relationship between chemical constitution and pharmacodynamic action has been exhausted. At present only two of the nitrogen mustards have been investigated clinically, namely, tris(β -chloroethyl)amine and methyl-bis(β -chloroethyl)amine. These have been the product of a screening program designed for the evaluation of toxic chemical warfare agents rather than of compounds of therapeutic interest. Literally hundreds of congeners remain to be synthesized and evaluated. Thus, a series of compounds which can reproduce in many ways the cellular effects of X-rays is available for chemical and biological investigation. It may be hoped that the previous successes which have characterized the evolution of chemotherapeutic agents by chemical alteration of a parent compound may be duplicated in the case of the β -chloroethyl amines. The result would be a compound having a sufficiently specific toxic action for certain types of proliferative cells to possess therapeutic value.”

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COVER LEGEND



The journal *Cancer Research* and the American Association for Cancer Research, Inc. salute Frederick Stanley Philips on this month's cover.

For four decades Dr. Philips has been active in research on cancer therapeutic drugs. He was born in 1916 in Mt. Vernon, New York. He was educated at Columbia University and the University of Rochester, obtaining his Ph.D. from the latter in 1940. In 1942, he was invited to join the laboratory of Drs. Alfred Gilman and Louis Goodman where he became interested in the effects of chemical warfare agents on neoplasms. From 1943 to 1946 this secret research on war gases was conducted at the Yale University School of Medicine and at the Medical Research Laboratory, Edgewood Arsenal, Maryland, from which he emerged as "Captain Philips." The text on the cover summarizes the early work on the introduction of nitrogen mustard as a chemotherapeutic agent against leukemia and lymphoma (A. Gilman and F. S. Philips, *Science*, 103: 409-415, 1946). It also marked the beginning of a lifetime career in the pharmacology of cancer chemotherapeutic agents.

After a one-year fellowship at the Massachusetts

Institute of Technology, Dr. Philips joined the Dr. Cornelius P. Rhoads "magic bullet" team at the Memorial Hospital/Sloan-Kettering Institute in New York where he authored or coauthored almost two hundred research papers. He collaborated effectively with colleagues interested in both laboratory and clinical experimentation. Covering a broad spectrum of agents, these papers assess the therapeutic potential and limiting toxicological events associated with alkylating agents, antipurines, antipyrimidines, antifolates, hydroxyurea, and various nucleosides and anthracyclines. In 1956, he became a full Member of the Sloan-Kettering Institute for Cancer Research. He became head of the pharmacology section of the experimental chemotherapy program organized by Dr. Rhoads. In 1957, he was made Professor of Pharmacology, and since 1969, he has held the position of Associate Director of the Sloan-Kettering Division of the Cornell Graduate School of Medical Sciences.

Dr. Philips has contributed immeasurably to the national effort against cancer by serving on many advisory committees of the National Cancer Institute, the American Cancer Society, the NIH General Medical Services Division, and the National Research Council. The journal *Cancer Research* has, in particular, benefitted by Dr. Philips' work and dedication to high standards as a member of the Editorial Board and Associate Editor (1958-1960, 1963-1965).

Dr. Philips has served the American Association for Cancer Research in several capacities: Director (1982-1985) and Director *ex officio* (1977-1982). Currently he is a nominee for Vice President of the Association (1983-1984). Most importantly, he was elected Secretary-Treasurer in 1977, a post he held with distinction for five years. As Secretary-Treasurer, his contributions to the Association and its members, and to its official publication outlet, *Cancer Research*, cannot be overestimated. The Editors and the entire editorial staff are indebted to Dr. Philips for his insightful guidance of the financial affairs of the journal and for his genuine concern and interest in the journal's operation.

Dr. Philips is shown in a recent photograph on the cover. Dr. Charles J. Kensler, a long-time friend and colleague, kindly provided the material for this cover.