

## OBITUARY

### Myron R. Karon—A Tribute (1932–1974)

On November 16, 1974, Dr. Myron R. Karon died of a cerebral hemorrhage at the age of 42. With his passing, we have lost one of the most outstanding, innovative, and effective pediatric oncologists. Perhaps it is incorrect to classify Dr. Karon so narrowly, since his interests and talents ranged broadly over the fields of pediatrics, oncology, pharmacology, molecular biology, chemotherapy, experimental design, and hematology. Most important, he brought a broad perspective, a profound humanism, and an intense compassion to all of these areas and their application to human disease. This was manifest in the unique and affectionate relationship Dr. Karon had with his patients. Furthermore, his incisive and uncompromising intellectual honesty with himself and with others was in the highest tradition of science and academic medicine. His forthrightness and integrity were absolute and made one proud to be in his company and numbered among his friends and colleagues. These qualities also gave him the sense of humor and the sense of the absurd that allowed him to cut to the heart of the matter and to put it in a unique and proper perspective.

Dr. Karon was born in Los Angeles on February 27, 1932. In addition to a conventional education in the public schools of Los Angeles, he received intensive training in and exposure to all aspects of the arts and music, which remained important to him throughout his life. Deciding that his humanistic impulses would be best expressed in the field of medicine, he entered premedical studies with a Kerr scholarship at Reed College in Portland, Oregon, in 1951 and was graduated Phi Beta Kappa in 1954. He continued this achievement during his medical training at the University of Chicago, being graduated Alpha Omega Alpha in 1957. After an outstanding performance in internship and residency in pediatrics at U.C.L.A., Dr. Karon served with distinction as Chief Resident in pediatrics at the University of Wisconsin. During these years he manifested a strong drive to develop a career both as a clinician and a laboratory scientist.

From 1960 to 1965, while a Senior Investigator at the Medicine Branch of the National Cancer Institute, Dr. Karon's national and international reputation was established. His interest in basic pharmacology and molecular biology was established during his collaboration with Dr. Sherman Weissman, and his interest in clinical pediatric oncology, leukemology, and chemotherapy was established through his work with Dr. Emil J Freireich and Dr. Emil Frei, III. Also, during this period he developed a deep and abiding interest in the psychiatric well-being of the child with cancer and in the relationship between patient, parent, and physician-therapist. Research in virology and hemoglobin metabolism rounded out his multifaceted activities.

After leaving the National Cancer Institute in 1965, Dr.

Karon spent 1 year in molecular biology research at the laboratory of Professor François Gros in Paris and 2 years as Associate Professor of Pediatrics and Chief of the Section of Applied Molecular Biology at the University of Texas, M. D. Anderson Hospital and Tumor Institute, at Houston. Subsequently, he was Director of the Division of Hematology-Oncology at the Children's Hospital of Los Angeles, Professor of Pediatrics at the University of Southern California School of Medicine, and Coordinator of the Pediatric Oncology Program of the University of Southern California Cancer Center. In Los Angeles he worked closely with Dr. Denman Hammond, both at the Children's Hospital and in development of the University of Southern California Cancer Center program. He was a major guiding influence to the clinical investigators of the Children's Cancer Study Group, of which he was Associate Chairman for Leukemia Studies.

The themes of molecular biology, basic pharmacology, chemotherapy, and emotional support of the cancer patient dominated Dr. Karon's career and resulted in some critically important contributions at the basic and clinical levels. In the area of chemotherapy, Dr. Karon established the efficacy, toxicity, and ideal therapeutic schedule of vincristine in acute leukemia of childhood. His studies form one of the major foundations of the curative therapy of this disease that have been developed since 1965. In addition, his observations on vincristine contributed to the wide application of this agent to many human cancers. More recently, he established the use of 5-azacytidine in the management of advanced refractory myelogenous leukemia in children. In addition, he played an important role in the development of the theory and application of experimental design in leukemia chemotherapy and, indeed, in all cancer chemotherapy research. Dr. Karon's leadership roles in these areas were recognized in recent years by the appointments mentioned previously.

Dr. Karon's contributions to the areas of molecular biology and basic and applied pharmacology are well known. In collaboration with the molecular biology group at the National Cancer Institute, he described the characteristics of pseudouridine metabolism in leukemia and contributed much important information to our understanding of the ineffective nucleic acid synthesis in this disease as well as in certain nonmalignant conditions, such as gout and psoriasis. These studies formed the basis of his subsequent work in molecular pharmacology.

Dr. Karon's major contributions to our understanding of the molecular biology and pharmacology of cytosine arabinoside include the characterization of the effects of the drug on macromolecular biosynthesis and on chromosome structure and function. He also studied the locus of action in, and the mechanism of action on, the cell cycle, the

mechanism of drug-induced lethality, and the reversal of this lethality by inhibition of DNA synthesis. The pharmacology of the drug was also studied in patients by using labeled compounds. The results of this research had a profound impact on the use of this agent in acute leukemia in terms of drug dose and schedule, and these applications have played a major role in the potentially curative role of the drug in this disease in adults.

Dr. Karon's great humanity and compassion led him to recognize the need for honesty and forthrightness in the tripartite relationship among pediatric patient, physician, and parent. He recognized that patient and parental fear and anxiety, based on ignorance, were harmful to patient management and the patient's response to treatment, while hopeful honesty and education of those involved were highly beneficial. These observations, made according to the highest principles of medical research, were reported in a series of research papers and publications for the involved layman. This work has revolutionized the way that we deal with all cancer patients and has greatly benefited cancer treatment in general.

Recently, Dr. Karon became progressively more involved in the design of clinical trials and the theoretical and practical problems in the design of experimental therapy in pediatric leukemia, in which the response to therapy is already very good. He struggled successfully with the problem of developing experimental designs based on host variability and prognostic factors so that progress can be made relatively quickly in sequential nonrandomized studies even in a disease in which the median duration of remission approaches 5 years. This led to a series of special lectures and manuscripts, the publication of which, tragically, must be posthumous.

It is relatively easy to summarize the concrete achievements of a productive individual and to indicate the loss to

mankind when such productivity is terminated by an unexpected early death. While social scientists tell us that the flow of history and the development of science are related to factors beyond the individual and that the "great man theory" of history is wrong, the impact of Dr. Karon's personality, life, and work on his friends and colleagues would suggest otherwise. The leading edge of oncology research consists of a network of individuals, each with his or her own unique creativity and contribution. The loss of one diminishes the whole, particularly in the areas of Dr. Karon's contributions. The best testament to Dr. Karon's achievement is the profound impact he had on his family, friends, and colleagues. All those whose lives he touched have been enriched. His students and colleagues will surely carry on his work, as will those who are inspired by the permanent legacy of his research papers, reviews, and other commentaries. We hope that this untimely and unfortunate passing will emphasize his work and further inspire us to build upon his achievements.

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