



**David A. Karnofsky**  
1914 – 1969

## OBITUARY

David A. Karnofsky

On August 31, 1969, the field of cancer research lost one of its outstanding practitioners, Dr. David A. Karnofsky.

In 1940, while he was a resident at the Colis P. Huntington Memorial Laboratory for Cancer Research of Harvard University, Dave began clinical investigation in cancer under Dr. Joseph Aub. Under a contract from the Office of Scientific Research and Development, in 1942, he began working with Dr. Homer Smith at New York University and at the Mt. Desert Island Biological Laboratory on the biological activities of the mustard gases—studies which he continued both in the laboratory and later in the field after joining the Army Chemical Warfare Service. It was there that an incident occurred which was typical of Dave's constant questioning of unproved medical and scientific tradition. During the planning of a field trial in which a small number of goats were to be subjected to mustard gas, Dave, a first lieutenant, suggested that more significant data might be obtained using several hundred mice placed at strategic intervals instead of a few goats. When the colonel in charge replied that mice were too small and goats, being larger, were naturally much better, Dave proposed that perhaps one should carry this theory further by dispensing with the goats entirely and using one elephant instead. Two days later he received orders to report to Camp Bushnell in Florida where he spent months tethering goats in appropriate locations. Again it was characteristic of Dave that, after the plane with the mustard gas had finished spraying, he was usually the first to return to the gassed area to assess the biological effects. He often carried the intoxicated goats out of the testing area himself.

While still in the Army, Dave became interested in the antineoplastic activity of nitrogen mustard and was subsequently assigned on temporary duty to Memorial Hospital to study this drug clinically. When Dr. Rhoads was planning the new Memorial Hospital-Sloan-Kettering Institute unit, where biochemical and animal studies could be immediately translated to practical application in the patient, he chose Dave as one of the original, essential core to help realize his exciting vision. On his discharge from the Army, therefore, Dave returned to Memorial to continue his clinical investigations. The wisdom of Dr. Rhoads' choice became more and more apparent as Dave continued to play a vital and indispensable role in the Center as it developed in scope and complexity.

Dave's distinguished career in the chemotherapy of cancer included the development and clinical evaluation of numerous chemotherapeutic agents, among them being the first oral alkylating agent triethylene melamine, as well as the purine antagonists, the glutamine antagonists, azaserine and DON, various pyrimidine antagonists, and the more recently discovered antibiotic, Daunomycin. His last clinical study was the evaluation of L-asparaginase, the first chemotherapeutic agent to take advantage of a metabolic requirement unique to certain cancer cells—in this case a requirement for the amino acid asparagine. He masterminded this study

on some 400 patients, which demonstrated the value of this form of therapy, particularly in acute lymphoblastic leukemia.

Shortly after his arrival at the Institute, Dave began studying the effects of drugs against mouse tumors growing on the chorioallantoic membrane of the developing chick embryo. Since he had had considerable predoctoral training in embryology, he also closely observed the toxic effects of anticancer agents on the embryo itself. His investigations in this area were classic, and over the next 20 years he described several agents with high specific toxicity for both the chick and rat embryo. These distinguished studies may yet provide answers to some of the problems of population control. In studying the effects of chemical and physical agents on proliferating cells, he correlated their effects on tumor and embryonic growth and thus, as a by-product of cancer research, contributed greatly to the field of teratology. In the summers he returned to his beloved Maine where, at the Mt. Desert Island Biological Laboratory, he studied the effects and mechanism of action of various antimetabolites on the developing sand dollar embryo.

Dave was particularly well known in his early days at Memorial Hospital for his emphasis on the meticulous clinical evaluation of drugs, combining just the right amount of enthusiasm with careful and critical judgment. He did much to change the reporting of cancer chemotherapeutic results from the anecdotal to the truly objective. His creation in 1948 of the performance status to evaluate subjective improvement of patients, his system of record keeping, and his development of a biennial chemotherapy course, which has been training classes of approximately 100 chemotherapists every 2 years for the past 14 years, all did much to raise Medical Oncology to the status of a scientific discipline.

Because of his outstanding position in the field of Medical Oncology, Dave was frequently called abroad for lectures or consultations. He loved international travel, and his home was filled with souvenirs of these trips. Even as recently as December 1968 he flew to Iran to give a series of lectures at the invitation of the Empress.

He was the recipient of many awards, including the Lucy Wortham James Award of the James Ewing Society in 1967, the Order of Merit from the Italian Government in 1968, the Katharine Berkan Judd Award in 1968, the Shahbanu Medal for Cancer Research from the Government of Iran and the Lila Motley Foundation in 1968, and the Guy H. Heath and Dan C. Heath Memorial Award in 1969.

Dave was a fountain of ideas, stimulating all those around him to new and better research while constantly helping them with wise counsel to be critical of their own results. One of his most important contributions to cancer research was in the training of young investigators in the science of chemotherapy, thereby improving immeasurably the stature

of Medical Oncology. Literally hundreds of physicians in this country and abroad are following the precepts he taught them. We at Memorial have been immensely fortunate to have had more than 2 decades of association with him as a friend, a distinguished and truly creative scientist, a careful and exact clinical investigator, a wise counselor, and, most important of all, a great and dedicated physician. I believe that Shakespeare best expressed what his associates feel about Dave:

“His life was gentle and the elements  
So mix’d in him that Nature might stand up  
And say to all the world, ‘This was a man.’ ”

Joseph H. Burchenal  
*Sloan-Kettering Institute for Cancer Research*  
*New York, New York*