

STANFORD UNIVERSITY
STANFORD, CALIFORNIA 94305-2060

OFFICE OF THE PRESIDENT

MEMORIAL RESOLUTION
SUMNER MYRON KALMAN
(1918 - 1992)

Sumner Myron Kalman, professor emeritus of pharmacology, died on January 11, 1992 at the age of 73 after a long illness. He had served as an active member of the faculty for 34 years until his retirement in 1988.

Kalman was born in Boston, where he attended the Boston Public Latin School. He received his undergraduate degree at Harvard in 1940, and then enlisted in the U.S. Navy during World War II. He served below decks for five years in the Atlantic destroyer fleet, finally as Engineering Officer with the rank of Lieutenant Commander. After the war he came to Stanford to study medicine and received the M.D. degree in 1950. Four years later, after clinical training at Mount Zion Hospital, and postdoctoral fellowships here and abroad, he joined the faculty of the Stanford Department of Pharmacology. For the next four years he performed a major and indispensable service to his department by directing its teaching activities in San Francisco while new faculty were establishing themselves on the Stanford campus in preparation for the move of the entire medical school in 1959.

In 1953 he traveled to Copenhagen, where he spent a year in the laboratory of the biochemist Linderstrom-Lang, followed by a half year with the physiologist Ussing. These two experiences shaped much of his subsequent research career. On returning to Stanford, his early research interests were in the newly blossoming field of allosteric enzymes, and he studied the mechanisms by which various substances (including drugs) modified enzyme structure and function. These interests coincided with a shift in the disciplinary basis of pharmacology during the sixties and seventies, from physiology to biochemistry and eventually molecular biology. Kalman joined his colleagues Avram Goldstein and Lewis Aronow in writing a new kind of pharmacology textbook, stressing principles, with a strong biochemical, genetic, and molecular biologic flavor, rather than categorical listings of drug families and their medical applications. The book, *Principles of Drug Action*, was first published in 1968; a second edition appeared in 1974. Kalman made major contributions to this book, especially the chapters on drug toxicity, which was rapidly becoming his principal research interest.

Around 1970, adequately sophisticated and reliable analytic techniques for therapeutic drug monitoring were only just being developed, and Kalman took up the challenge eagerly. This effort was truly a pioneering one. With increasing ability to measure drugs in blood and other body tissues, researchers noted that people varied in drug blood levels after a single dose much more than anyone had supposed. This fact introduced a new necessity into pharmacotherapy, namely, that response to dosage be monitored by regular analytic measurements, so that it could be individualized. This was especially important for drugs with a narrow therapeutic range; *i.e.*, drugs that were highly toxic even at slightly excessive levels. The prototypic example was digoxin, the mainstay of treatment in cardiac failure and the drug to which Kalman turned his attention first, establishing digoxin plasma level assays. This was followed shortly by assays for the antiepileptic drugs such as diphenylhydantoin and phenobarbital.

Seeing the need for a full service facility to carry out such assays, which would obviously be essential for rational drug therapy, Kalman established a Drug Assay Laboratory at Stanford. It was later incorporated into the administrative structure of the Stanford Hospital, but at the peak of its autonomous existence under Kalman's direction, this facility had twelve employees and operated seven days a week, twenty-four hours a day.

The same kinds of analytic technique also proved essential in diagnosis and treatment of drug toxicity, especially in initial screening for victims of poisoning. Soon Kalman's laboratory was regularly receiving samples for assay from hospital emergency rooms and physicians over the entire Bay Area and beyond. His interests in drug toxicity led him to a deep concern about environmental toxicity, initially lead poisoning, then other toxic hazards.

In 1979 Kalman published (with Dennis Clark) *Drug Assay, The Strategy of Therapeutic Drug Monitoring*. This elegant manual embodies the principles he established in the Drug Assay Laboratory. Kalman had a remarkable gift for combining basic research with clinical applications. Data from patients would often suggest to him the need for further understanding of biologic mechanisms, and findings in his laboratory would suggest new clinical applications. Ian Irwin, who managed the Drug Assay Laboratory for him, said: "In a remarkable way Dr. Kalman brought the spirit of science into a service facility."

At that same time, the ALZA Corporation was being founded, with a novel focus on drug delivery systems. It was natural for Kalman to become a consultant to ALZA, to assist them in choosing drug candidates that would benefit from more rational delivery, and to identify areas of pharmacology for them to explore. One of ALZA's scientists wrote: "Dr. Kalman was instrumental in establishing ALZA's Medical Review Board and was one of its original members. In this capacity he provided insight in defining ethical standards for the conduct of clinical trials."

Kalman's interest in digoxin and other cardiac glycosides provoked the question of whether there was any deeper meaning to the extraordinary response of the failing heart to these substances of plant origin. Might a similar chemical, acting as a regulator of cardiac function, be present normally in the animal body? Kalman embarked on a long search for such a substance, obtaining functional evidence that it did exist, but never succeeding in isolating the substance so as to determine its chemical structure. This was a great disappointment; but the attempt was a pioneering one, which stimulated other researchers to seek endogenous mimics of known drugs.

At Stanford, Kalman was always generous with his time, not only in advising his own postdoctoral fellows and graduate students, but in his willingness to help any colleague who knocked on his door. Several professors in the clinical disciplines recall warmly how, during their early days as trainees, Kalman would devote himself unstintingly to assisting them with technical advice, always treating them as colleagues. He also served as a faculty advisor to minority students during the early days of affirmative action, when significant numbers were first being recruited to the medical school.

Kalman embodied qualities of idealism, concern for community, uncompromising honesty, and courageous independence. These are no better illustrated than in the controversial medfly episode. Kalman's scientific judgment led him to conclude that spraying malathion indiscriminately from helicopters over heavily populated Santa Clara County was unwise and posed a potential toxic hazard to the population. He and others continued to speak out on this issue, though unsuccessfully, despite vigorous public support of the spraying by the president of the University. When it became apparent that powerful forces could not be overcome, Kalman proposed that at the very least a well planned study on the long-term consequences of the spraying for human health be undertaken; but his suggestion was ignored.

Deeply committed to environmental concerns, Kalman served on Stanford's Committee on Environmental Information and the Administrative Panel on Safety and Health. He was a consultant to the federal Food and Drug Administration. Population control was also a concern close to his heart, and he was a member of the Board of Directors of the Santa Clara County Planned Parenthood Association. As a consultant and also as an activist, he pointed out dangers in the use of riot control agents like Mace, especially as they were being used in an unrestrained way on prisoners. After his retirement and before he became ill, he was working on a textbook of environmental toxicity; but unfortunately, this was never completed.

Kalman had an endearing, somewhat quixotic, sense of humor, which extended to technical matters as well as to his personal relationships. A lifelong devotee of physical fitness, Kalman was committed to running and cycling, and he

took a serious interest in karate; he was a proud wearer of the black belt, which—remarkably—he earned at the age of 64.

Kalman enjoyed a 40-year-long marriage to Anneliese Korner, a distinguished research professor of psychiatry at Stanford, who survives him. Their daughter, Susan Persico, could be said to have followed in her father's footsteps; she is a molecular biologist searching for novel and less toxic methods of agricultural pest control. He also leaves a grandson, Joseph Sumner Persico.

Stanford has lost a respected colleague, who contributed to science, to medicine, to the University, and to the community in many ways over many years.

Avram Goldstein, Chair
John I. Brauman
Charlotte D. Jacobs
Lincoln E. Moses