

Edward Herbert: 1926–1987



The ability of higher organisms to adapt to environmental changes or to maintain dynamic, intrinsic biological rhythms with precise metabolic modulation reflects a remarkable diversity of molecular and cellular signals. Understanding how these signals are endowed with temporal and cell-type specificity fascinated Ed Herbert.

Edward Herbert was born in Hartford, Connecticut, on January 28, 1926. His parents, Orthodox Jews from eastern Europe, were prototypes, hard working and motivated to make a better life for their children. Ed's father had run away from home in Poland as a young man, finding his way to Ellis Island only to be sent back and to reenter America in 1914. He was married ten years later. The Herberts settled in Hartford's close-knit Jewish neighborhood, where Ed's father established his own business, a small bakery, from which he profited enough to support his family, buy a modest apartment building as an investment, and bring his wife's sister to live with them. Ed was the younger of two boys. Although Ed's parents stayed in Hartford, the rest of the family eventually moved to the relatively new upscale suburbs of West Hartford.

Ed attended Weaver High School in Hartford, aspiring to be either a sports coach or M.D. After graduating, Ed entered the local Trinity College. However, World War II interrupted his education and Ed enlisted in the Navy. Assigned as a hospital apprentice, Ed aspired to be a pharmacist's mate but he flunked the required formal test for "bedmaking." Then he was sent to Camp Pendleton for training as a fleet marine, but hurt his knee in a fall and was discharged from the service. After the war, Ed used the G.I. bill to attend the University of Connecticut in Storrs, and was an excellent student. From childhood and throughout his life, Ed was an avid sports fan and athlete. At UConn, he excelled in several sports. As a member of the track and field team, Ed performed the shot-put and discus throw. He was the starting defensive end for the football team, and started as guard for UConn's nationally recognized basketball team that played in the Eastern finals against St. Johns in Madison Square Garden. Majoring in zoology, ostensibly for pre-med, Ed took an inorganic chemistry class that included students from several science disciplines. From the back row where he sat, Ed admired a young engineering major who always sat in the front row. Inquiries about her resulted in an introduction through a common acquaintance and an intense courtship ensued.



Sydney was from Stratford, Connecticut, and in January of 1946, they were engaged. Ed approached Sydney's father for permission to marry his daughter. He was asked if he had a job, which he did not; if he had a way to support Sydney, which he did not; or even "a plan," to which he answered that he did not. Permission was denied, and the couple promptly eloped to New Hampshire. Upon returning to Connecticut, Sydney assumed they would immediately tell her parents they had married, while Ed assumed they would not. Although Ed did not yield, his wallet somehow found its way onto a bench in her parents' household, open and showing the marriage license. After some discussion, Ed was welcomed into their family; the marriage lasted happily for the rest of Ed's life.

The couple graduated together. Ed applied to medical school, one of many among the flood of returning vets, and did not get accepted. Instead, Ed opted to attend graduate school, studying general physiology at the University of Pennsylvania. Throughout his life, Ed was not comfortable in big groups, and this led him to join the smaller laboratory of Merkel Jacobs, the noted red-cell physiologist. The relationship between student and mentor was at once healthy and formal; Jacobs always referred to Ed as "Mr. Herbert," and Ed did not depart from "Dr. Jacobs." Yet Dr. Jacobs had a profound influence on Mr. Herbert, instilling in Ed an appreciation for science as well as the enthusiasm and drive to pursue his goals to the end. During these particularly formative years, Ed also fashioned several lifelong friendships, especially among the five other graduate students with whom he taught the General Physiology laboratory, a cathartic experience. One member of that group was a medical student, Nelson Gelfman, who would always remain proud of the bump on his nose acquired from an encounter with Ed's elbow during a basketball game.



The Herberts had a son, Ed Jr., born in July of 1952 while they lived hand to mouth as Ed was preparing his thesis. Upon graduating, Ed became a full instructor at Penn, a position which compensated for the poor salary by eligibility for faculty parties. Ed began comparative studies with red blood cells, and they bought a duck to supply Ed with erythrocytes. Occasionally the young couple would tie a string to the duck's leg and take it for a swim.

By 1953 Ed began work with Van Potter at Wisconsin and became involved in the emerging field of RNA synthesis; this was a good time in the Herberts' lives. His professional motivations led him to apply for an instructor position in the Biology Department at MIT. Despite an embarrassing job talk, highlighted by spilling his cue cards, MIT offered Ed the position, and he taught biology. Ed's career began to bloom as MIT was at the hub of RNA biology. Ed was promoted first to assistant professor and

then to associate professor. Despite Sydney's objections, the Herberts bought a house in the suburb of Sudbury, and Sydney renewed her education, entering the master's program in social work at BU.

Although this was a successful period, and it seemed they would settle for the long term, it was a surprise to Sydney when Ed announced they were leaving—for Oregon. Ed often referred to MIT as "a good place to be from." The newly established Centers of Excellence program had made a generous award to Ed to start a program in the Chemistry Department at the University of Oregon. The Herberts bought a new car and took 30 days to drive across the country. After arriving in Eugene in 1963, along with several members of the lab from MIT who had decided to join Ed in Oregon, they found that the labs were not yet ready. Ed took the whole group camping all over Oregon for several weeks; not a serious word was spoken and they had a special initiation into life in the West.

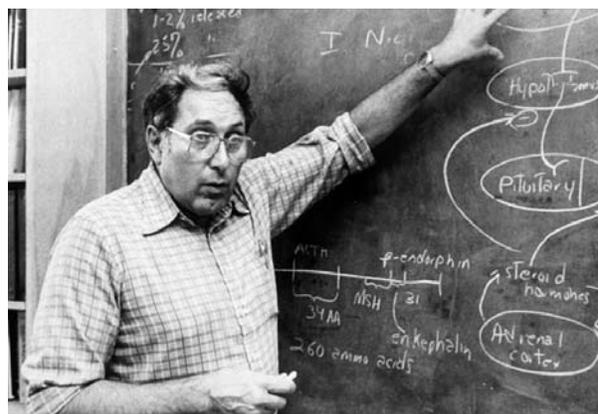
The early years in Oregon were difficult ones for Ed. There was resentment of "the big bucks guy," he was not a chemist but was in the Chemistry Department, and this excluded him from the biology department. He didn't seem to fit. One colleague complained that "items in chemistry department laboratories should not carry molecular biology inventory numbers." Yet the science took off, grants came in, the program grew, and Ed became a Professor in the Chemistry Department. His work brought him national and international recognition. The Herberts enjoyed a wonderful, comfortable life in Eugene. Sydney spent a year in Seattle completing her degree and was active on social issues, particularly environmental and justice issues. Together they raised their son; Ed was an attentive and caring father. Ed's success allowed the family to travel to many places.

In 1983 Ed was selected as the founding director of the Vollum Institute, a research institute established as part of the Oregon Health Sciences University in Portland, Oregon, through a donation by Howard Vollum, the founder of Tektronix, and government funding obtained by Senator Mark O. Hatfield. The mission of the Vollum was to become a world-class neuroscience research institute. Ed saw this as a new frontier and final challenge. By 1985 the new Institute was almost completed. The lab moved from Eugene, at first to temporary space in the biochemistry department. There was great anticipation and excitement, and again resentment of the "the big bucks guy." Yet Ed had another concern: he had become physically uncomfortable and soon learned of his pancreatic cancer. Since his death on February 19, 1987, the Vollum Institute has fulfilled the founders' aspirations, and stands today as a testimony to Ed's vision.

The two most influential people in Ed's development were probably his Ph.D. advisor, Dr. Jacobs, and a high school physics teacher, Mr. Parks. Jacobs taught Ed the importance of asking the right questions, and instilled in Ed an aesthetic appreciation for the techniques he used. He taught Ed to be comfortable with not knowing, to share experiences and thereby gain knowledge. The contribution by Mr. Parks was appreciated after their time together, when Ed realized he had not been a good student, inattentive and scattered, but that Mr. Parks had never given up on him, and told him to be serious. Ed appreciated this so much that he returned to Hartford to thank the then aging Mr. Parks, still teaching physics. Parks listened to Ed's generous comments and then told Ed he had come at just the right time because, for the first time, he was just about to give up on some of his students.

PROFESSIONAL CHRONOLOGY

Ed Herbert's professional life rested on the cutting edge, not just technically although he was always seeking to advance the methods, but also conceptually. Ed's first publication, one year after the work of Watson and Crick, concerned the phosphorylation of nucleotides to di- and triphosphate derivatives, and launched a series of manuscripts examining the biosynthesis and modification of nucleotides. These papers were followed by several years of steady contributions to understanding RNA synthesis using cell free systems. Ed discovered the enzyme that adds the CCA sequence to tRNA and showed that this enzyme regulates tRNAs amino acid acceptor activity. He also demonstrated an important translational level of control for protein synthesis in which hemin regulates the initiation of globin synthesis by modulating the activity of an initiation factor.



Ed's career took a pivotal turn in 1969–1970 when he took a sabbatical at Harvard. The result was a transition from classical biological chemistry into neurochemistry and neuroscience. In his usual manner, Ed was quietly yet completely dedicated and committed to this change, despite the consequent struggles for new grants and a paucity of students. But in 1977, Ed's work culminated in a profound scientific breakthrough with the discovery of pro-opiomelanocortin (POMC), a polyprotein that contains ACTH, β -endorphin and several other stress hormones. Using cultured pituitary cells, he went on to show that the processing of the bioactive peptides from the POMC precursor is coordinate. He defined the glycosylation and proteolytic cleavage steps involved in POMC processing and most importantly, showed that processing of the POMC prohormone into bioactive derivatives is different in the neighboring cell types of the anterior and posterior pituitary. These results led Ed to propose that POMC tissue specificity is controlled by differences in protein processing rather than by alternative mRNA splicing or expression of distinct POMC genes in the different cell types. Ed investigated this novel principle for the opioid peptides. Using the emerging techniques of synthetic DNA probes to isolate clones encoding precursor proteins, Ed demonstrated that the sixteen opioid peptides are all derived from three different precursor proteins: POMC, pro-enkephalin A, and pro-enkephalin B.

Ed received numerous honors and awards, some of which are listed with the selected bibliography that follows. It is somehow pleasing to know that mixed with and obscured by his everlasting gentleness and kindness, Ed also derived real satisfaction from these acknowledgments. He was proud of his contributions. He was nominated three times for membership in the National Academy prior to his posthumous selection. He once confided, "I'll get a Nobel Prize before they let me in."

It is only appropriate to finish by reiterating Ed's commitment to the people with whom he worked, especially his students. Ed had a gift for recognizing those with potential talent even when others were at best unsure. His lab always had an eclectic dimension, one that all of us appreciate still. Always kind, Ed was unfailingly principled and in a quiet effective manner he was forceful. Ed was an outspoken advocate for academic freedom and, together with Sydney, championed women's rights and environmental causes. Above all, Ed was a scholar and a teacher. He was gentle and quiet which was in some ways misleading because he was also thoroughly committed and compelled to succeed. Ed was the best of mentors. He was not easy. He was always there for you, but students had to make it on their own. You could fail in Ed's lab because the standards were high, and he taught us the importance of complete intellectual honesty. Everyone who learned from Ed, who spent time under his guidance, all of us who earned degrees or were postdoctoral fellows with him, and the faculty and staff he recruited to the fledgling Vollum Institute, gave him our love and respect; he earned it. It was, and remains for all of us, the proudest of honors to be a part of the Herbert lab.

—John Adelman, on behalf of all who had the privilege to know Ed.

AWARDS AND LECTURESHIPS

- 1978 Pfizer award for Fundamental Contributions to Endocrinology, Clinical Research Institute of Montreal and McGill University
- 1981 Rosetta Briegel Lectureship Award for pioneering work in biochemistry, University of Oklahoma
- 1982 Leslie Bennett Award and Lectureship in Endocrinology, University of California, San Francisco
- 1983 First Mark O. Hatfield Award and Lectureship, the Oregon Health Sciences University, Portland
- 1984 McKnight Foundation Distinguished Research Award and Lectureship in Neurobiology
- 1984 Lamport Lectureship in Physiology, University of Washington, Seattle
- 1984 New York University Honors Program Lecturer
- 1987 Posthumous election, National Academy of Sciences

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