



Edward Herbert

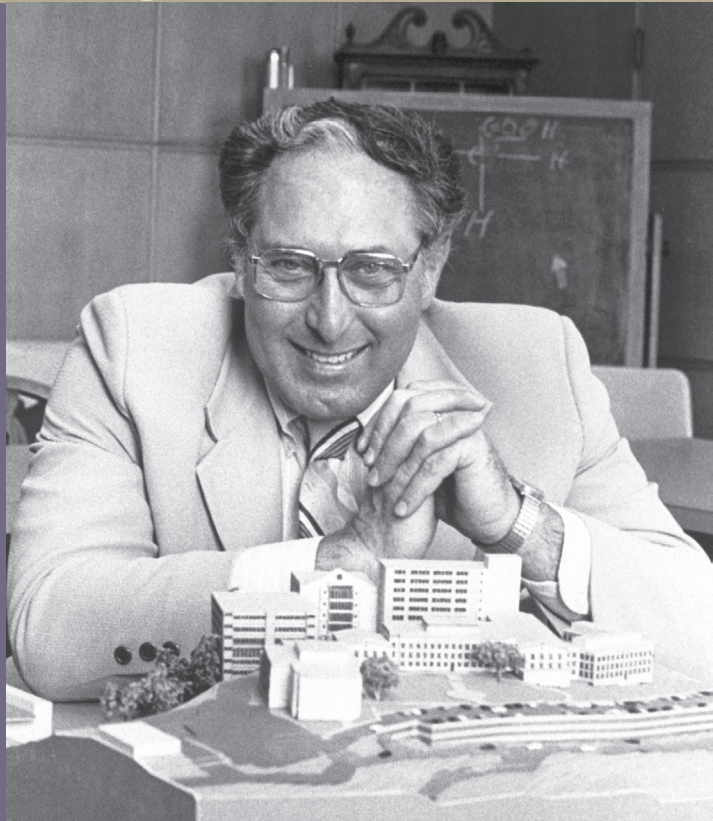
1926–1987

BIOGRAPHICAL

Memoirs

*A Biographical Memoir by
John P. Adelman*

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NATIONAL ACADEMY OF SCIENCES

EDWARD HERBERT

January 28, 1926–February 19, 1987

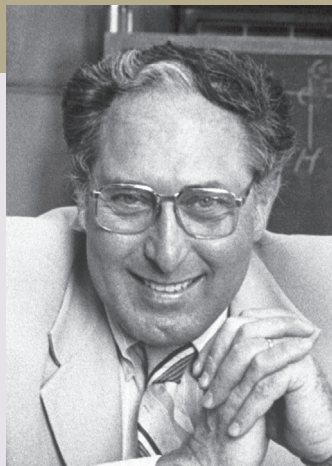
Elected to the NAS, 1987

Edward Herbert was a pioneering neurochemist who specialized in researching the ability of higher organisms to adapt to environmental changes or to maintain dynamic, intrinsic biological rhythms with precise metabolic modulation thanks to a remarkable diversity of molecular and cellular signals. Understanding how these signals are endowed with temporal and cell-type specificity fascinated Herbert. He had begun his career as a biochemist, but beginning in 1960 his interest shifted to neurochemistry, toward which he devoted the rest of his life. In 1977 his work culminated in a profound scientific breakthrough with his discovery of pro-opiomelanocortin (POMC), a polypeptide that contains adrenocorticotropic hormone (ACTH), β -endorphin, and several other hormones whose serum levels may be altered by emotional or physical stress.

Herbert earned a bachelor's degree in zoology in 1949 from the University of Connecticut, followed by a Ph.D. in physiology from the University of Pennsylvania and a position as an instructor at Penn. In 1955 he moved to MIT, starting as an instructor and advancing to associate professor. In 1963 he moved to the University of Oregon and in 1985 became the founding Director of the Vollum Institute at the Oregon Health and Science University in Portland.

Edward Herbert was born in Hartford, Connecticut, on January 28, 1926. His parents, Jews from Eastern Europe, were hard-working immigrants motivated to make a better life for their children. The Herberts settled in Hartford's close-knit Jewish neighborhood, where Ed's father opened a small bakery, from which he earned enough to support his family, buy a modest apartment building as an investment, and bring his wife's sister to live with them. Ed and his older brother, were the Herberts' offspring.

Ed attended Weaver High School in Hartford, aspiring to be either a sports coach or a physician. After graduating, he entered the local Trinity College. World War II inter-



Photograph courtesy of the Vollum Institute.

Edward Herbert

By John P. Adelman

rupted his education, and Ed joined the Navy. Assigned as a hospital apprentice, he aspired to be a pharmacist's mate—the Navy's name for a medical corpsman during the war—but he flunked the required formal test for “bedmaking.” He was then sent to Camp Pendleton for training as a marine but injured his knee in a fall and was discharged from the service. After the war Ed attended the University of Connecticut (UConn) on the G. I. Bill and was an excellent student.

Throughout his life he was an avid sports fan and athlete. At UConn, he excelled in several sports. As a member of the track-and-field team, he performed the shot put and discus throw. He was the starting defensive end for the football team, and started as guard for UConn's outstanding basketball team, which made it to the NCAA Eastern Regional finals 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 his seat in the back row he admired a young engineering major, Sydney, 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 1946, they became 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 if he had “a plan,” which he did not. Permission was denied, so 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.

Professional advancement

The couple graduated together in 1949. Ed applied to medical school, one of many among the flood of returning vets, but was not accepted. He then 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 small laboratory of Merkel Jacobs, a noted red-cell physiologist. The relationship between student and mentor was simultaneously healthy and formal; Jacobs always referred to Ed as “Mr. Herbert,” and Ed did not depart from “Dr. Jacobs.” Yet Jacobs had a profound influence on Ed, instilling in him an appreciation for science as well as the enthusiasm

Despite an embarrassing job interview, highlighted by Ed's spilling his cue cards, MIT offered him the position, and he took up teaching there in 1955.

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.

Ed and Sydney had a son, Ed, Jr., born in July 1952 while they lived hand to mouth as Ed was preparing his dissertation. Upon earning his Ph.D.,

he became a full instructor at Penn, a position that compensated for a low salary by giving him access to faculty parties. Ed began comparative studies with red blood cells, and he and Sydney 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.

In 1953 Ed began work in the emerging field of RNA synthesis with Van Rensselear Potter, a noted biochemist who was a professor of oncology at the University of Wisconsin. This was a good time in the Herberts' lives. His professional ambitions led him to apply for an instructor position in the Biology Department at MIT. Despite an embarrassing job interview, highlighted by Ed's spilling his cue cards, MIT offered him the position, and he took up teaching there in 1955. Ed's career began to bloom, as MIT was at the hub of RNA biology. He 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 resumed her education, entering the master's program in social work at Boston University.

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 at the University of Oregon had made a generous offer to Ed to start a program in the Chemistry Department. 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 enjoyed a special initiation into life in the West.

The early years in Oregon, however, turned out to be difficult ones for Ed. There was resentment because he was “the big bucks guy,” he was not a chemist but was in the Chemistry Department, and this status excluded him from the Biology Department. 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. 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 the environment and justice. Together they raised their son; Ed was an attentive and caring father. His success allowed the family to travel to many places.



Ed Herbert with a model of the Vollum Institute campus.

(Photo courtesy of the Vollum Institute.)

In 1983 Ed was selected to become the founding director of the Vollum Institute, a research facility that opened in 1986 as part of the Oregon Health Sciences University, in Portland. The institute was funded with a donation by Howard Vollum, the founder of Tektronix, and government appropriations 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 facility 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 begun to feel unwell and soon was diagnosed with pancreatic cancer. Although he put up a stiff fight, Ed died on February 19, 1987. Despite this tragedy, the Vollum Institute has fulfilled the founders’ aspirations, and stands today as a testament to Ed’s vision.

Biochemical discoveries

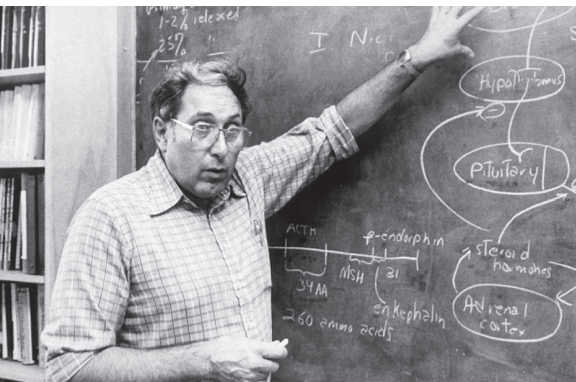
The two most influential people in Ed’s development were probably his Ph.D. advisor, Dr. Jacobs, and a high school physics teacher named Parks. Jacobs taught Ed the importance of asking the right questions, and instilled in him an aesthetic appreciation for

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, inattentive and scattered, later realized he had not been a good student but that Mr. Parks had never given up on him and persuaded him to be serious. Ed came to appreciate this so much that he returned to Hartford to thank the then aging Mr. Parks, who was 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, the teacher was just about to give up on some of his students.

Ed's professional life rested on the cutting edge, not just technically but also conceptually. His first publication, issued one year after the DNA work of Watson and Crick, concerned the phosphorylation of nucleotides to di- and triphosphate derivatives and launched a series of Herbert manuscripts examining the biosynthesis and modification of nucleotides. Ed followed these papers with several years of steady contributions to understanding RNA synthesis using cell-free systems. He discovered the enzyme that adds the cytosine-cytosine-adenine (CCA) sequence to transfer ribonucleic acid (tRNA) and showed that this enzyme regulates tRNA's 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 when he spent a sabbatical year at Harvard: he made a transition from classical biological chemistry into neurochemistry and neuroscience. In his usual manner, he became quietly yet completely dedicated and committed to this change, despite facing struggles for new grants and a paucity of students. But in 1977 his work culminated in a profound scientific breakthrough with his discovery of pro-opiomelanocortin (POMC), a polyprotein that contains adrenocorticotrophic hormone (ACTH), b-endorphin, and several other hormones whose serum levels may be changed, for better or worse, by emotional or physical stress.

Using cultured pituitary cells, Ed 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



At the blackboard.

(Photo courtesy of the Vollum Institute.)

propose that POMC tissue specificity is controlled by differences in protein processing rather than by alternative messenger RNA (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, he demonstrated that the 16 opioid peptides are all derived from three different precursor proteins: POMC, pro-enkephalin A, and pro-enkephalin B.

Summing up

Ed received numerous honors and awards, including: the Pfizer award for Fundamental Contributions to Endocrinology, from the Clinical Research Institute of Montreal and McGill University (1978); the Rosetta Briegel Lectureship Award for pioneering work in biochemistry, University of Oklahoma (1981); the Leslie Bennett Award and Lectureship in Endocrinology, University of California, San Francisco (1982); the first Mark O. Hatfield Award and Lectureship, the Oregon Health Sciences University, Portland (1983); the McKnight Foundation Distinguished Research Award and Lectureship in Neurobiology (1984); the Lamport Lectureship in Physiology, University of Washington, Seattle (1984); the New York University Honors Program Lecture; and, posthumously, election to the National Academy of Sciences.

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 of Sciences 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 about them. His lab always had an eclectic

dimension, one that all of us appreciated. Always kind, he was unfailingly principled and in a subtle but effective manner he was forceful. He 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 you had to make it on your own. You could fail in Ed's lab because the standards were high, and he taught his students the importance of complete intellectual honesty. 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. It was, and remains for all of us, the proudest of honors to be a part of the Ed Herbert lab.

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

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