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DEWITT STETTEN, JR.

1909—1990

A Biographical Memoir by
J. EDWIN SEEGMILLER

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Biographical Memoir

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May 31, 1909–August 28, 1990

BY J. EDWIN SEEGMILLER

DEWITT STETTEN, JR., made significant contributions to science as a biochemist, as an unusually talented mentor in the training of young scientists, and as an inspiring and dedicated administrator of educational and research programs. Through his pioneering use of heavy isotopes as labels of various molecules, Stetten was one of the first investigators to obtain quantitative assessment of the dynamic relationship of interconversions between various molecules in intact biological systems. He extended these studies to include assessment of aberrations of relevant metabolic pathways in human diseases, including the first demonstration of an impaired synthesis of fatty acids in patients with diabetes and the causes of hyperuricemia in patients with gouty arthritis. In addition, Stetten's standards of integrity, his contagious excitement about science and life, his honesty, his warm personal concern for his friends, and his pervasive humor are well remembered by his many scientific associates and personal friends.

EARLY LIFE AND SCHOOLING

DeWitt Stetten, Jr., was born in New York City on May 31, 1909, to DeWitt Stetten, Sr., a prominent young surgeon,

and his wife, Magdalena Ernst Stetten. A German nursemaid caring for his older sister Margaret disliked the name DeWitt and so she gave Stetten the affectionate name of "Haensel" and Margaret the German contraction "Gretel." Thus, Stetten was known as "Hans" to all visitors, and the name persisted among family and friends throughout his life.

As children, Stetten and his sister attended the Horace Mann School, an experimental school associated with Columbia University in New York City. While still a young boy in the Horace Mann Boy's School, Stetten's parents sought to help him overcome his excessive shyness by arranging for him to receive special instruction in performing magic from one of his teachers who had this as a hobby. He then entertained family and friends, as well as audiences on steamships during family vacation travels to and from Europe, as an amateur magician. The same teacher also taught a wood-working class at school—thus started two of Hans's lifelong hobbies.

Another hobby was his construction at age 12 of a radio receiver using a galena crystal as a detector and a coil of wire wrapped around a wooden rolling pin as a tuner—all from instructions he found in the journal *QST*, the official publication of the American Radio Relay League. Stetten then progressively increased the performance of succeeding radios over the years as vacuum tubes became available. His resulting hobby of electronics was helpful to him later when he participated in the construction of two mass spectrometers used at different times in his research career.

Stetten received an A.B. degree magna cum laude from Harvard College in 1930, along with membership in Phi Beta Kappa. Although he knew by this time that his first love was biochemistry, he was encouraged by his surgeon father as well as by his tutor and mentor at Harvard, Frank

Fremont-Smith, to attend medical school before embarking on a laboratory career. He therefore received his M.D. in 1934 from the College of Physicians and Surgeons of Columbia University.

EARLY RESEARCH TRAINING

After his internship and residency at Bellevue Hospital in New York City, Hans was convinced that, even with the best of medical care then available, the effectiveness of treatment was severely restricted by lack of knowledge of the normal human body and the changes induced in it by each disease process. Some years earlier Hans had spent part of a summer vacation in the laboratory of Dr. Rudolf Schoenheimer in Freiburg, Germany, and had become fascinated with Schoenheimer's brilliant mind and his approach to science. Since Dr. Schoenheimer had recently arrived on the faculty at Columbia University as a refugee from Germany, Stetten selected him as his mentor for his Ph.D. degree in biochemistry, which was awarded in 1940. For his dissertation, published with Schoenheimer, Stetten used the then newly developed technique of isotopic labeling with deuterium to follow the biological conversion of labeled palmitic acid to stearic and palmitoleic acid and the conversion of aliphatic alcohols to fatty acids in intact rats, published in two papers in the *Journal of Biological Chemistry*. He then continued his research by studying the origins of the extra fat in various types of fatty liver using ^{15}N labeling to show the dynamic relationships of choline, ethanolamine, and related compounds, as well as the role of lipotropic methyl groups in the synthesis of choline in rats. It was in 1941 that he married fellow graduate student Marjorie Roloff, known as Marney, and thus began both a scientific and a domestic partnership of over four decades, until her sudden death from a heart attack in 1983. They had four chil-

dren—Gail, Nancy, Mary, and George. A year later at Woods Hole, Massachusetts, where their two families had spent many summer vacations as friends, Stetten married Jane Lazarow, widow of Dr. Arnold Lazarow.

ACCOMPLISHMENTS IN BIOMEDICAL RESEARCH

Stetten was a superb teacher with a contagious enthusiasm for scientific research. From 1938 to 1947 he taught biochemistry and continued his research at Columbia University. One of his early students in research was Juan Salcedo, who on returning to his homeland eliminated the nutritional disease beri beri from Bataan province and subsequently held many high scientific offices in the Philippines. During a subsequent two years of teaching and research at Harvard University's Peter Bent Brigham Hospital, Stetten taught a course on the clinical aspects of biochemistry. One of his students was an undergraduate, Gordon Tompkins, who credited Stetten's course as being the decisive event contributing to his own decision to make a career in biochemistry and medicine, eventually becoming chief of the Laboratory of Molecular Biology at the National Institute of Arthritis and Metabolic Diseases, from which he became a professor of biochemistry and biophysics at the University of California, San Francisco. Stetten's research on gouty arthritis began in Boston with his use of heavy isotope labeling of uric acid to determine the pool size and turnover of uric acid in gout.

In 1948 Stetten moved back to New York for his appointment as chief of the Division of Nutrition and Physiology of the Public Health Research Institute of the City of New York. He described this six-year period as one of the most productive times of his life. Among the bright young physicians attracted to his laboratory as a postdoctoral fellow was James Wyngaarden, later a director of the National Insti-

tutes of Health. Among the achievements of this general period was Stetten's demonstration of the marked expansion above normal of the miscible pool of uric acid in gouty humans and the role of overproduction of uric acid as the cause of hyperuricemia in at least a portion of gouty patients. For this and other major contributions of his laboratory during this period, Stetten was honored with election to the National Academy of Sciences.

In 1954 Stetten was appointed associate director in charge of the intramural program of research at the National Institute of Arthritis and Metabolic Diseases of NIH. During his eight years in this position, he recruited a number of outstanding young scientists to the program, including Marshall W. Nirenberg, who became the intramural program's first Nobel laureate for his identification of the DNA code for specific amino acids. Stetten was also coauthor of the first two editions of *Principles of Biochemistry* with Abraham White, Phillip Handler, and Emil L. Smith, which was designed for graduate and medical students and widely adopted as the standard textbook of biochemistry. The authors spent summer vacations together in Woods Hole, Massachusetts, for the book's development and revisions. Stetten felt strongly the importance of formal teaching programs as an important symbiotic component of an optimal research environment. He therefore worked with other NIH researchers of like minds to aid in the establishment of the Foundation for Education in the Sciences, a nongovernmental teaching institution located adjacent to the NIH campus, and later served as its president.

DEAN OF RUTGERS UNIVERSITY MEDICAL SCHOOL

In 1962 Stetten left NIH to serve as the founding dean of the Rutgers University School of Medicine soon to be launched in Nutley, New Jersey. He used his considerable

skills as a negotiator to help establish a first-class medical school, complete with a strong program, excellent faculty, and a handsome medical sciences building. After much hard work on Stetten's part, the two-year medical school was up and running and the four-year medical school was ready to be launched; however, the state legislature decided to separate the medical school from the university in order to integrate it with the recently acquired Seton Hall Medical School. The merger was opposed by faculty, students, and administrators alike, but they were overruled by the legislature. When the merger took place, Stetten tendered his resignation.

NIH ADMINISTRATION

Stetten returned to Bethesda, Maryland, in 1970 to head the National Institute of General Medical Sciences. From 1974 to 1979 he was NIH's deputy director for science, guiding the intramural research activities of a vast number of researchers. During this time he also served as chairman of the recombinant DNA advisory committee. In response to concerns in the scientific community about potential dangers in biotechnology research, Stetten's committee drafted guidelines for scientists using the new techniques.

In 1978 Stetten asked to be relieved of his duties as deputy director because of his deteriorating eyesight, caused by macular degeneration. Donald Fredrickson, then NIH director, appointed him senior scientific advisor to the director. From an office in Stone House, Stetten took up a number of new projects. He wrote a widely cited letter to the editor of the *New England Journal of Medicine* suggesting that ophthalmologists learn more about advising their visually handicapped patients on services available for the blind. Some years later the Library of Congress recognized Stetten's efforts on behalf of blind and low-vision people by asking

him to pose for a poster promoting its Talking Books program.

At this time, in 1979, Stetten found the opportunity to do something about his long-held perception of the principal drawback facing each scientific director upon moving to the administration building: isolation from the research he hoped to foster. To counter this, Stetten established a Friday morning seminar series that became an honored forum for scientists to tell about their laboratory and clinical research activities. He also initiated the Museum of Medical Research, which now bears his name, during NIH's centennial observance. In the museum's collection is a gavel made by Stetten for NIH Director Robert Q. Marston and passed to his successors. An avid woodworker, Stetten made the gavel on his own lathe. For the head he used wood from the plane tree, found on the Aegean island of Cos and associated with Hippocrates, the father of medicine. The handle was made of all-American cherry wood. In another project, carried out in collaboration with William T. Carrigan, Stetten edited a book on the NIH intramural program, *NIH: An Account of Research in Its Laboratories and Clinics*.

LEADERSHIP POSITIONS

Always in demand as a leader, Stetten served as chairman of the Roche Institute of Molecular Biology's Scientific Advisory Committee from 1966 to 1970. In 1971 he was president of the Foundation for Advanced Education in the Sciences and from 1977 to 1979 headed the Society for Experimental Biology and Medicine.

Long before his election to the National Academy of Sciences in 1974, Stetten served on many of the Academy's advisory committees. After his election, he served on the Academy's council, was a member at large for the Division of Medical Sciences, and served three terms on the Execu-

tive Committee. He also served two terms as a representative of the American Society of Biological Chemists.

This long and event-filled list of accomplishments cannot convey Hans Stetten's humor, his care for and facility with language, and his refusal to be slowed down in his later years even by blindness. He was an amateur magician and a professional mediator, whose ability to guide and smooth the way brought him many positions of leadership during his sixty years in the service of science.

HONORS AND DISTINCTIONS

EDUCATION

- 1930 A.B., Harvard College
1934 M.D., Columbia University
1940 Ph.D. (Biochemistry), Columbia University

SPECIAL TRAINING OR EXPERIENCE

- 1934-37 Intern, Resident, Bellevue Hospital, New York City
1947-49 Associate in medicine, Peter Bent Brigham Hospital,
 Boston
1952-53 Study Section on Nutrition and Metabolism, National
 Institutes of Health, Public Health Service, Bethesda,
 Md.

EMPLOYMENT

- 1938-47 Assistant, Instructor, Assistant Professor, Department of
 Biochemistry, Columbia University
1947-48 Assistant Professor, Department of Biochemistry,
 Harvard University
1948-54 Chief, Division of Nutrition and Physiology, Public
 Health Research Institute of the City of New York
1954-62 Associate Director in Charge of Research and Chief,
 Section on Intermediary Metabolism, National Institute
 of Arthritis and Metabolic Diseases, National Institutes
 of Health, Bethesda, Md.

- 1962-70 Dean, Rutgers University School of Medicine, and
Director, Medical Center
- 1970-74 Director, National Institute of General Medical Science,
National Institutes of Health
- 1974-79 Deputy Director for Science, National Institutes of
Health
- 1979-85 Senior Scientific Advisor, Office of the Director,
National Institutes of Health

MEMBERSHIPS

American Academy of Arts and Sciences
American Association for the Advancement of Science (fellow);
Vice-President, 1962
National Academy of Sciences, 1974
American Society of Biological Chemists
Harvey Society
Phi Beta Kappa
Alpha Omega Alpha
Sigma Xi

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1930

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1941

Biological relationships of choline, ethanolamine and related compounds. *J. Biol. Chem.* 140:143.

1943

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1944

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1947

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1948

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1949

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1950

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1952

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1953

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1954

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1955

With B. Bloom. The fraction of glucose catabolized via the glycolytic pathway. *J. Biol. Chem.* 212:555.

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With J. E. Seegmiller and L. Laster. Incorporation of 4-amino-5-imidazolecarboxamide-4-C¹³ into uric acid in the normal human. *J. Biol. Chem.* 216:663.

1956

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1971

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1981

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1982

The DNA disease. *Nature* 297:260.