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HERBERT EDMUND CARTER
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A Biographical Memoir by
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Biographical Memoir

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H. Carter

HERBERT EDMUND CARTER

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BY ROBERT K. YU AND JOHN H. LAW

HERBERT EDMUND CARTER, whose outstanding research early in his career led to his election to the National Academy of Sciences at the age of only 43, died in Tucson, Arizona, at the age of 97. He pioneered the field of sphingolipids and made major contributions to understanding the structure of other lipids, particularly the glycolipids of plants, and of amino acids and antibiotics. He was an outstanding administrator at the University of Illinois and the University of Arizona. He also served in leadership roles in many national organizations, most notably as president of the American Society of Biological Chemistry (now the American Society for Biochemistry and Molecular Biology) and as chair of the National Science Board. He inspired a large number of students and postdoctoral associates, many of whom followed in his footsteps as teachers, research leaders, and university administrators.

EDUCATION AND EARLY LIFE

Herb Carter was born to a Quaker family in Mooresville, Indiana, in 1910, was reared with his brother and three sisters on a small farm, and attended a one-room school through sixth grade. His father farmed and invented, among other things, a color photography process. His mother was a school

teacher who encouraged her children to read extensively, even at the expense of carrying out farm chores. Herb reported that he liked history and mathematics, but he disliked art.

Herb developed an interest in chemistry in high school, from which he graduated at the age of 15. He furthered his education in chemistry at DePauw University in Greencastle, Indiana, graduating in 1930 with a bachelor of arts degree. That same year he entered the graduate school to pursue chemistry at the University of Illinois in Urbana-Champaign. His supervisor, Professor Carl S. Marvel whose primary topic of research was the chemistry of amino acids, fostered Herb's strong interest in biochemistry. Even before completing his doctoral thesis in 1934, he was made an instructor at the University of Illinois by Professor William C. Rose, head of the division of biochemistry in the chemistry department. Herb began his important and productive career, rising to professor in 1945. He remained in that position for 26 years until he moved to the University of Arizona in 1971. He continued working there until he was 94.

RESEARCH ACCOMPLISHMENTS

When Professor Rose offered a post to Herb, he asked him to help with the isolation and synthesis of a new amino acid, essential in the diet of rats, which after Rose and his colleagues determined its structure, became known as threonine. Recalling this time in his career, Herb said, "I owe much of my research career to Dr. Rose and to the wonderful opportunity he gave me to participate in the threonine story."¹

His work on threonine chemistry set the course for his future work. His synthesis of thiothreonine proved similar to synthetic routes to penicillamine, a degradation product of penicillin, and led to an invitation from Hans T. Clarke to participate in the penicillin program during the Second

World War. This involved frequent train travel under difficult wartime conditions to help coordinate research programs between universities and pharmaceutical companies, including Upjohn in Kalamazoo, Michigan, and Eli Lilly in Indianapolis, Indiana.

Many family stories grew from this project. Betty sometimes told the story of the night Herb walked home from the train station in Urbana, half frozen, arriving at 2 a.m. to announce that he thought he was going to prison. He had fallen asleep while waiting hours for a train from Mattoon to Urbana. The station master, who had come to recognize him after many trips, shook him awake. He managed to dash onto the train just in time, only to realize later that he had left his briefcase—full of top-secret research reports—at the station. To his immense relief the station master retrieved it and sent it on the next day.

Threonine chemistry also led Herb to investigate the structure of sphingosine, known to be a hydroxyamino compound. Sphingosine was first described by J. L. W. Thudichum (1829-1901) as a component of brain lipids such as cerebrosides and sphingomyelins. The term “sphingosine” is from the Greek for “to bind tight” and also connotes “sphinx” because discovering the correct structure of sphingosine was elusive after its initial description. Earlier investigators showed that the compound had a C-18 chain that contained a double bond, two hydroxyl groups, and an amino group. The structural enigma was finally resolved by Herb, who showed that the N-benzoyl derivative of the reduced dihydrosphingosine was not cleaved by periodate under a variety of conditions. Periodate specifically oxidizes vicinal diols, so the two hydroxyl groups had to be further separated. Dihydrosphingosine itself was oxidized to formic acid, ammonia, and formaldehyde in equal proportions, and palmitaldehyde. That analysis established dihydrosphingosine

as 1,3-dihydroxy-2-amino-octadecane and sphingosine as 1,3-dihydroxy-2-amino-octadecene-4. Later studies established the absolute configuration of both compounds.

At this time, the term "lipide" rather than the shorter "lipid" was used, and Herb coined a new term, "sphingolipides" (1947). "Among the lipide constituents there are at least three, the cerebrosides, sphingomyelins and gangliosides, which are derivatives of the base sphingosine. Sphingosine also may be present in other compounds. As a matter of convenience it is proposed that the term sphingolipides be used to designate these substances." Thus was born a new field of lipid research. Herb was then able to establish the structure of ceramides (fatty acid amides of sphingosine bases) and the glycolipids of nerve tissue, galactocerebrosides and glucocerebrosides (compounds in which the 1-hydroxy group of the ceramide is glycosylated).

Herb took up the study of glycolipids of plants. He discovered a new base, phytosphingosine, and investigated the structure of its parent compounds, which he named "phytoglycolipids." The core of these compounds is a ceramide phosphorylinositol. Similar compounds have been shown to be major components of yeast membranes. He then described the structures of phytosphingosine (1,3,4 trihydroxy-2-amino-octadecane) and dehydrophytosphingosine (with an 8-trans double bond). Further variations of the sphingolipid base repertoire were followed by his discovery of branched-chain sphingolipid bases (with an isopropyl terminus). In addition, he and his students discovered a new class of glycolipids from plant tissues, the galactosylglycerides, and also the diol lipids from beef lung.

Among his other scientific contributions, he studied the structure of the lipid A component of the lipopolysaccharides of Gram-negative bacteria as well as of the polyene antibiotic, filipin. He collaborated with Professors David Gottlieb and

Kenneth Rinehart at the University of Illinois to isolate and determine the structures of chloramphenicol, levomycin, neomycin, streptomycin, and streptothricin.

Herb's contribution to the concept of prochirality is relatively little recognized. He examined the reactions at a prochiral carbon atom (which he termed a "*meso*-carbon atom") with an asymmetric reagent that yielded unequal amounts of diastereoisomers. It was known that enzyme-catalyzed reactions at a prochiral center yielded complete stereoselectivity. Carter argued that this result was caused by a distinct difference in the two identical groups at the prochiral center. This conclusion was vigorously disputed by another distinguished chemist, but this work was fully verified by others who generalized the concept of a *meso* carbon atom to a prochiral center.

PERSONAL LIFE

In 1933 Herb married Elizabeth W. DeWees, whom he met during his years at DePauw University. Betty's Quaker background contributed to her generous nature and great compassion for her immediate family, qualities she extended to Herb's students and colleagues. Herb and Betty were married for 72 years, an extraordinary, lifelong love affair that ended only with her death in 2005. They had two daughters, Anne, who became a highly successful bookstore manager in Tucson, Arizona, and Jean, who has had a distinguished career in anthropology and education at the University of California, Berkeley. Betty and Herb traveled extensively after Anne and Jean were grown: through Europe, the former Soviet Union, Australia, New Zealand, India, and Japan. They spent their summers from 1945 through 2001 at the Congregational Summer Assembly in Frankfort, Michigan, where they had a dearly loved summer cottage overlooking Lake Michigan.

Herb was an enthusiastic sportsman, winning an athletic letter at DePauw for his contribution to the track team as a long-distance runner. He excelled at squash. He was a pillar of the local bowling league in Urbana (the cottage decor includes a collection of his little silver-painted plastic bowling trophies). But most notably he was obsessed with the game of golf. One time, arriving on a dark and rainy night at a city hosting a scientific meeting, Herb insisted upon visiting the local golf course, where he got out in the downpour and tested the greens—*before* going to the hotel. He once won a prize, also at the cottage, for hitting a hole in one in a contest at a driving range in Palo Alto.

His sense of humor was legendary. A gifted raconteur, he sometimes needed to be reined in by Betty when the jokes turned ribald. He could not resist a pun, and was especially fond of limericks. He once sponsored an international contest for the composition of limericks in which the third and fourth lines were, “If research isn’t fun, it shouldn’t be done.” Those lines also were his motto.

A famous incident in the chemistry department at the University of Illinois illustrates both his humor and his compassion. Fires in the laboratories were not uncommon, but one broke out in a locked closet in the middle of the night. Herb, then head of the department, arrived at his office early the next morning to find two very unhappy graduate students. “You look like a couple of firebugs,” he joked as he passed them on the way to his office. After a long pause there was a knock on his door, the two entered his office, were seated, and then confessed that they had caused the fire. It seems that they were entertaining themselves by spraying a flammable liquid at enormous cockroaches, followed by throwing lighted matches at them. One of the flaming victims had run under the door of the locked closet. The damage was minimal. Herb found the culprits intensely

amusing. But in his administrative position he had to maintain serious decorum. He finally said, "I'd hate like hell to be the head of a department where the students never got into trouble, but I sure wish you two would find something sensible to get into trouble about." He then dismissed them without punishment.

SERVICE AND HONORS

On the retirement of Professor Roger Adams in 1954 Herb became head of the department of chemistry and chemical engineering at the University of Illinois. He later served as acting dean of the graduate college and as vice chancellor for academic affairs. In 1971 he moved to the University of Arizona where he served as coordinator of interdisciplinary programs. He was asked to bring together biochemists in various parts of the university to form a new Department of Biochemistry, which he then headed from 1977 until 1981. After he retired, Herb continued with advisory roles in many parts of the university.

Herb was a member of the Council of the National Academy of Sciences, and he chaired a committee on election procedures that established the current method of selecting members. As mentioned earlier, he became president of the American Society of Biological Chemistry in 1957 and was chair of the National Science Board from 1970 to 1974. He served on or chaired many committees of the American Chemical Society, the National Research Council, the National Institutes of Health, and the American Association for the Advancement of Science. He founded *Biochemical Preparation* and served on the editorial boards of several major scientific journals.

Herb received the Eli Lilly Award in Biochemistry in 1943. As indicated earlier, he was elected to the National Academy of Sciences in 1953 at a relatively early age, and later to the

American Academy of Arts and Sciences. He received the Nichols Medal, the Kenneth A. Spencer Award, the Alton E. Bailey Award, and honorary degrees from DePauw University, the University of Illinois, Indiana University, Thomas Jefferson University, and the University of Arizona. Carter's Ridge, a wild-looking grey and snowy peak in Antarctica, was named for him in recognition of his service as chair of the National Science Board.

Herb Carter is considered the father of the fields of sphingolipids and glycolipids. Although he was not the first to tackle the "enigma of the Sphinx," he advanced the field to a much greater degree than his predecessors. While many of his contemporaries failed to recognize the importance of these compounds, Herb never lost his enthusiasm for them, and he lived to see the present understanding of their great significance in cell biology. In addition to his remarkable accomplishments as a scientist and administrator, he was above all a great mentor. We were privileged to have him as a friend and adviser.

THE AUTHORS ARE GREATLY INDEBTED to Professor Jean Carter Lave for much personal information about her father and his family.

NOTE

1. H. E. Carter. Identification and synthesis of threonine. *Fed. Proc.* 38(1979):2684-2686.

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