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WILLIAM J. DARBY
1913—2001

A Biographical Memoir by
NEVIN S. SCRIMSHAW

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Biographical Memoir

William J. Darby

Historical Collection, Eskind Biomedical Library, Vanderbilt University.

WILLIAM J. DARBY

November 6, 1913—June 6, 2001

BY NEVIN S. SCRIMSHAW

WILLIAM JEFFERSON DARBY, who was one of the leaders in the 20th century responsible for the recognition of nutrition as a disciplinary and interdisciplinary science of major importance for human health and welfare, died on June 6, 2001, at his home in Nashville, Tennessee. He had been suffering the results of multiple strokes. He was the last survivor of a remarkable group of nutrition pioneers, including Conrad Elvehjem, Joseph Goldberger, Grace Goldsmith, Paul Gyorgy, Glen King, Henry Sherman, Tom Spies, Heinrich von Dam, George Whipple, and a number of others, who in the early and mid-20th century identified the individual vitamins and essential amino acids.

FORMATIVE YEARS

William Darby, known to everyone as "Bill," was born in Galloway, Arkansas, in 1913. His mother, a school teacher, contributed importantly to his early education. His high school chemistry teacher, Miss Ora Parks, recognized his exceptional promise and encouraged his interest in science. After finishing high school in 1930, Darby planned to study chemical engineering. However, circumstances required him to find a job, which he did, as a Fuller Brush salesman.

That autumn he encountered Miss Parks who was surprised that he wasn't at the university. By a fortunate coincidence a few days earlier, Paul Day, professor and chair of the Department of Physiological Chemistry at the University of Arkansas Medical School, had asked her whether she knew a high school graduate whom he could employ "to help with animal maintenance, and cleaning in the laboratory." Miss Parks sent Darby to see Day, who found him an "intelligent and diligent worker" and soon launched him on a lifetime career in nutrition science.

Day not only included Darby on his research team as an "assistant in physiological Chemistry" but also encouraged him to enroll part-time in college as a premedical student and then to enter the medical school at the University of Arkansas in 1930. He graduated with a B.S. in 1936 and an M.D. in 1937. He served as instructor in physiological chemistry at the Arkansas School of Medicine part-time during 1935-1939. While a medical student, he courted and, in 1935, married Elva Louise Mayo, whom he first met in the high school orchestra, where she played violin and he the clarinet.

In 1940 Bill and Elva moved to Ann Arbor where he was a Horace Rackam fellow and a graduate student of Professor H. B. Lewis in the Department of Biological Chemistry at the University of Michigan. He was greatly influenced by Lewis, who instilled in him a lifelong interest in the scientific literature of the past as well as high standards for lectures and research. He completed an M.S. in biological chemistry in 1941 and spent the academic year 1941-1942 as a National Research Council fellow in the Department of Biochemistry of Columbia University College of Physicians and Surgeons. He was awarded a Ph.D. in biochemistry from the University of Michigan in 1942.

He then became a special fellow in nutrition of the International Division of the Rockefeller Foundation assigned to the Vanderbilt University School of Medicine for a year. He next accepted a one-year appointment as assistant research professor in nutrition at the University of North Carolina School of Public Health and director of medical education for the North Carolina State Board of Public Health.

As Darby describes it in an autobiographical article (*Annu. Rev. Nutr.* 5[1983]:1-6), the excitement of new discovery was intense in the 1930s and 1940s with the "rapidly growing evidence and identification of new essential nutrients and related metabolic phenomena, water soluble vitamins, fat soluble vitamins, essential amino acids, trace elements, and emerging metabolic cycles and biologic phenomena relating food and nutrition to human disease."

SERVICE TO VANDERBILT UNIVERSITY

Darby returned to Vanderbilt in 1944 with dual appointments as assistant professor in the departments of Medicine and Biochemistry and was promoted to associate professor in 1946. For the rest of his life he remained devoted to Vanderbilt. In 1948 he became director of the Division of Nutrition in the Vanderbilt University School of Medicine and served in this capacity until 1971. The following year he was appointed chair of the Department of Biochemistry in the School of Medicine. During this period he modernized the Department of Biochemistry by recruiting over a dozen outstanding biochemists to the faculty, one of whom went on to win a Nobel Prize. He also established the Division of Nutrition and Toxicology within the department.

Darby was appointed professor of nutrition in the Vanderbilt School of Medicine in 1964 and in the following year also professor of medicine in nutrition. He held both appointments until 1979 even while he was on leave to serve

as president of the Nutrition Foundation. From 1979 until his death he was professor emeritus of biochemistry (nutrition) in the Vanderbilt School of Medicine.

CONTRIBUTIONS TO THE FOOD AND NUTRITION BOARD AND ITS FOOD PROTECTION COMMITTEE

Darby was a long-term member of the Food and Nutrition Board of the National Research Council and the driving force in the creation and activities of its Food Protection Committee (FPC); he chaired its steering committee with energy and vision for 17 years beginning in 1954. The reports of this committee were based on critical study of all available evidence objectively assessed and ended with specific conclusions. Their objective was recommendations assuring maximum public benefit with minimal risk. He promoted the concept that there is no such thing as "absolute safety" and established guiding principles for acceptance or exclusion of proposed food additives followed by specialized subcommittees of the program. When the committee began its work, there was no comprehensive list of substances approved as food additives, and the FPC undertook successfully the task of developing one.

Over three decades the FPC served the public by evaluating specific categories of food additives such as surfactants and sweeteners. Bill was instrumental in the production of two classical monographs on naturally occurring toxic materials present in foods, and in developing the *Food Chemical Codex*. This was not only the first official codex of food chemicals in the United States but also became the model for many other countries and eventually for the *Codex Alimentarius* of the Food and Agriculture Organization and the World Health Organization.

PRESIDENT OF THE NUTRITION FOUNDATION

From 1972 to 1982 Darby served as president of the Nutrition Foundation, founded by Charles Glen King. As its first director, in 1942 King had made it the leading private supporter of nutrition research for the next 21 years, mainly with funds raised from industry. Paul Pearson then carried on this tradition for an additional 9 years. When Darby was offered the presidency, he saw in it an irresistible opportunity to contribute to research and training in nutrition and turned down concurrent offers to head the Nutrition Unit of the World Health Organization in Geneva and the Institute for Arthritis and Metabolic Disease of the National Institutes of Health.

His goals, as he described them when he accepted responsibility for the foundation, included greater emphasis on public education and information and establishment of national nutrition priorities. He moved the foundation from New York to Washington, D.C., better to fulfill them. Its governance was changed from a board of directors in which 15 of 17 members were representatives of supporting companies to one in which 12 of 21 represented the public.

During Darby's tenure as president, the foundation sponsored many international meetings on nutrition issues, supported young investigators, financed nutrition research projects nationally and internationally, and published 16 monographs on nutrition as well as the highly regarded monthly Nutrition Reviews. The latter was the leading source for authoritative summaries and interpretation of current nutrition topics. It summarized and interpreted research on nutrition topics at a time when the science of nutrition was emerging rapidly. However, unrestricted industry support weakened and in 1982 he returned to his professorship at Vanderbilt.

MAJOR SCIENTIFIC CONTRIBUTIONS TO NUTRITION

Darby's earliest research, while working for Paul Day, was the finding that *L. casei* factor, later designated folic acid, cured anemia and leucopenia in monkeys fed an experimental diet. He was a coauthor on the publication. He and his coworkers then demonstrated that this factor was effective in the treatment of patients with nontropical sprue. He then went on to demonstrate that it was efficacious for macrocytic anemia and nontropical sprue. With Calvin Woodward he demonstrated a relationship between folic acid and vitamin C. He also showed that the newly discovered vitamin B_{12} was not efficacious in correcting the "pernicious anemia" of pregnancy, but the latter could be corrected by folic acid. In this prolific period in the 1950s, he described the renal toxicity of pteroylglutamic acid and the efficacy of folic acid for megaloblastic anemia in infants. With William Pearson he developed an ultramicromethod for determining pteroylglutamic acid. In 1961 he and coworkers published estimates of human dietary needs for tocopherol, retinal, niacin, pyridoxine, and vitamin B_{12}. In 1963, with James Dinning and others, he described vitamin E and coenzyme Q_4 metabolism in infants with severe protein-energy malnutrition. This was followed in 1966 by measurement of B_{12} requirements and its metabolism in human adults.

A pioneering 1953 paper showed that excess sodium fed to rats caused renal vascular injury and hypertension. This provided the basis for others to determine the role of sodium, potassium, and other minerals in human hypertension and its association with diet. As early as 1947 he conducted a survey of iron deficiency in a rural community in North Carolina and measured iron absorption in children. In 1961 he published a paper describing iron absorption in pregnant women.

From 1953 to 1958 Darby with a number of others—including several students who later became well-known nutritionists—orchestrated a comprehensive study of nutrition in pregnancy, seeking a clue to the cause of preclampsia, eclampsia, and other complications of pregnancy. The prevailing nutritional hypothesis at the time was an association with protein deficiency, but the results did not confirm this. The findings were published in nine papers that described the diets and nutritional biochemical characteristics of over 2,000 women during pregnancy. An interesting finding was that there was no change in caloric intake during pregnancy in these women despite the increased uterine, fetal, and placental weight and metabolism because they were compensated for by reduced physical activity.

In 1945 he completed a nutrition and health survey of Tennessee school children for the State Department of Health. In 1950 he collaborated with Grace Goldsmith and others in a comprehensive nutrition survey in families in Norris Point, Newfoundland. In 1955 with William McGannity, Harold R. Sandstead (father of Harold H.), and Edwin Bridgeworth he carried out the first comprehensive nutrition and health survey of the Navajo Indians. It revealed widespread malnutrition in this native U.S. population group.

This experience with clinical surveys led to his key role in the organization in 1955 of the International Committee on Nutrition for National Development (ICNND) and membership on the editorial board of *Manual for Nutrition Surveys*. This publication guided the studies that were carried out in 32 foreign countries. The ICNND was established to assess the nutrition status and problems of developing countries and how the countries' own resources could be used to solve them. Darby described his work with the ICNND as "personally rewarding, uniquely productive scientifically, and of remarkable humanitarian benefit."

INFLUENCE ON NUTRITION AND HEALTH PUBLICATIONS

Just as Darby contributed so much to the nutrition community in so many other ways his editorial activities were extensive. He was the chair of the Publications Management Committee of the American Institute of Nutrition (1959-1970). He edited the *Monograph Series on Basic and Applied Nutrition* published by Academic Press (1978-1990). He served as editor of the *Annual Review of Nutrition* from 1980 to 1984 and continued on its editorial board. He also served on the editorial boards of the *Journal of Nutrition* (1949-1952), *Nutrition Today* (1965-1972 and 1986-until his death), *Journal of Clinical Investigation* (1950-1954), and *Dialogues in Nutrition* (1976-1979).

INTERNATIONAL CONTRIBUTIONS TO NUTRITION

Some of his most important international contributions came through his chairing or participating in World Health Organization (WHO) and Food and Agriculture Organization (FAO) expert committees and consultations. He chaired the first joint FAO/WHO Expert Committee on Food Additives (1956) and the WHO Expert Committee on Nutrition in Pregnancy and Lactation (1964). He was a long-term member of the WHO Expert Advisory Panel on Nutrition. From 1961 to 1965 he was a founding member of the WHO/FAO/UNICEF Protein Advisory Group. He was a member of the FAO/WHO Joint Expert Committee at its meetings in 1954, 1961, and 1966 and chaired the meeting in 1957. From 1961 to 1965 he served on the National Institutes of Health (NIH), International Advisory Committee for Medical Research that supervised NIH-supported research centers in San Jose, Costa Rica; Cali, Colombia; Lahore, Pakistan; and Calcutta, India.

He also served as a member of the U.S. National Committee for the International Union of Nutrition Sciences (1985-1988) and was chair in 1986. He chaired a food science mission to Europe for the U.S. Department of Agriculture in 1963. He was a member of the Nutrition Advisory Committee of the U.S. Agency for International Development (1968-1972).

THE VANDERBILT NAMRU-3 COLLABORATIVE NUTRITION PROJECT

As a consultant investigating pellagra in Yugoslavia and Egypt for the World Health Organization in 1949, Darby became acquainted with the Naval Medical Research Unit (NAMRU-3) in Cairo. He revisited it following a 1960 ICNND survey in Ethiopia and at the invitation of its commanding officer, Capt. John Seale, a pioneer in the treatment of cholera, who agreed to collaboration with Vanderbilt that would enhance the capabilities of NAMRU-3 for addressing nutrition problems. The resulting successful and highly productive research collaboration continued for nearly 25 years.

Supported by a series of major NIH grants, this project provided exceptional research opportunities to a series of younger scientists who have since made important contributions to nutrition knowledge, training, and leadership in the United States. They included James Carter, Charles Halsted, Harold H. Sandstead, and Carol Waslien, among others. Darby brought Ananda Prasad from Iran to NAMRU-3 and—after a visit to a village near Cairo where Prasad showed him 16- to 18-year-old boys who appeared to be 6 to 9 years old—changed research plans so as to test Prasad's hypothesis that zinc deficiency was the cause of the dwarfism and hypogonadism. A series of studies at NAMRU-3 and in Iran characterized human zinc deficiency for the first time.

This discovery of zinc deficiency in humans was the basis for subsequent worldwide research demonstrating the many functions of zinc throughout the life cycle and the high prevalence of zinc deficiency in impoverished populations. Later, Darby expressed deep satisfaction with his critical role in this pioneering work.

Darby's participation in the activities of the Vanderbilt Research Group in NAMRU-3 included an interest in nutrition in both modern and ancient Egypt. He encouraged and collaborated with the young nutritional anthropologist Louis Grivetti at a time when involvement of this discipline with nutrition was rare. With the Egyptian endocrinologist Paul Ghalioungui and Grivetti he coauthored a definitive two-volume monograph on the history of food in Egypt, *Food: The Gift of Osiris* in 1977. When V. N. Patwardhan, a former director of the National Institute of Nutrition, Hyderabad, India, retired from his position as head of the nutrition unit of WHO in 1964, Darby greatly strengthened the Vanderbilt Research Group in Cairo by putting him in charge.

INSTITUTE OF NUTRITION OF CENTRAL AMERICA AND PANAMA

In 1948 Fred Soper, director of the Pan American Health Organization (PAHO), offered Darby the directorship of the proposed new Institute of Nutrition of Central America and Panama (INCAP) to be established in Guatemala with support from member country quotas, the Kellogg Foundation, and PAHO. The Government of Guatemala was to provide the building. Darby was then in the middle of the major study of nutrition in pregnancy already described and was not ready to leave Vanderbilt. However, this study was concurrent with ones initiated by the director of the Children's Fund of Michigan, Icie Macy Hoobler, and at the School of Medicine of the University of Rochester that I had initiated as a young postdoctoral fellow.

The three study directors had been meeting periodically to discuss and compare their findings. I had interned in Gorgas Hospital in the Panama Canal Zone and, like Darby, had a Ph.D. in a basic science. Darby not only recommended me to be the director of INCAP but also made a commitment to help in its development. As a key member of the Technical Advisory Committee (TAC) during its formative years, he had a major impact on its successful development.

Darby chaired the first TAC meeting in Costa Rica in 1950 and many of its annual weeklong meetings for the next 12 years. This committee with Antonio Pena Chevaria, Paul Gyorgy, Glen King, Leonard Maynard, and Henry Sebrell as core members was of critical importance to the scientific success of INCAP. During the 1959 TAC, the President of Guatemala was to personally present Darby with the country's highest decoration for a scientist, the *Order of Rodolfo Robles*. At a grand reception in the National Palace Darby's name was called to come forward to receive his medal, but he was still finishing the TAC report at INCAP several miles away with Maynard, already a National Academy of Sciences member, who was to be similarly honored.

Another time I was returning from a trip to the Guatemalan highlands with Darby and Maynard, their wives and mine in my 1947 Plymouth by way of the highest pass in Guatemala on a very steep unpaved, rutted, and boulder-strewn road that damaged the crankcase. When the oil ran out, the engine stopped. After a long time a truck passed with a load of large rocks. On them was a layer of very large bags of onions and on top of them a layer of people. The truck agreed to tow the car and made room for Elva Darby and Helen Maynard with the driver, but Darby and Maynard had to sit on the onions with the rest of the people. My wife, Mary, stayed with me. At several of the steep hairpin turns

the rope snapped and needed to be retied. When the high point of the pass was reached, the truck returned its extra passengers and left our car to coast, with uncertain brakes and no engine compression, down the steep switchback 5 miles to the village below. They were good sports about it, but it became a frequent topic of future conversation.

HISTORIAN FOR NUTRITION

Day had instilled in Darby the necessity of disciplined study of the scientific literature, including early papers. He continued this practice throughout his life. After retiring from the Nutrition Foundation and returning to Nashville, he dedicated his energies to building a collection on the history of nutrition as his legacy to Vanderbilt, and scoured the world for the original texts of relevant publications. At his death he contributed his own extensive personal collection.

The Vanderbilt library also became the historical archive for the American Institute of Nutrition (AIN), and until his death he served as its official historian. He was also responsible for establishing an AIN committee on the History of Nutrition and for establishing a tradition of History of Nutrition Symposiums at the annual FASEB meetings.

For many years he and his wife, Elva, personally presented a fascinating exhibit on the history of nutrition at the annual AIN meetings held as part of the FASEB meetings. These became legendary. He was a very active honorary curator for the Historical Collection of the Eskind Biomedical Library of Medicine at Vanderbilt University. His collection of works on the classical nutritional diseases of goiter, pellagra, scurvy, anemia, marasmus, and kwashiorkor was probably unequaled.

A little-known late contribution of Darby was as adviser with me and Irwin Rosenberg to a project to make electronically readable the medical records of U.S. Civil War veterans from recruitment until death. The project was led by the Nobel Prize-wining economic historian Robert Fogel. The challenge was to provide feasible guidelines for nonmedical data entry staff in the National Archives to code the data from the often arcane handwritten nineteenth-century medical records. Darby's knowledge of medical history and terminology and the resources of his library were invaluable to our overcoming the seemingly insurmountable difficulties. The resulting data tapes have already resulted in four books and over 160 scientific papers, book chapters, and reviews, many of them groundbreaking.

EDITORIAL CONTRIBUTIONS

His influence on nutrition publications was extensive. He served as chair of the Publications Management Board of the American Institute of Nutrition (1959-1970). He edited the *Annual Review of Nutrition* (1980-1984) and remained on its editorial advisory board until 1988. He was associate editor of *Nutrition Reviews* (1944-1950) and editor of the Monograph Series, *Nutrition, Basic and Applied for Academic Press* (1978). He served on the editorial boards of *Nutrition Reviews* (1944-1950), *Journal of Nutrition* (1949-1952), *Nutrition Today* (1965-1972), *Journal of Nutrition Education* (1971-1975), *Present Knowledge of Nutrition* (1976-1984). *Dialogues in Nutrition* (1976-1979), *Annual Review of Nutrition* (1984-1988), and *Journal of Clinical Investigation* (1950-1954). From 1966 he was a corresponding editor of the *Journal of Nutrition and Dietetics* (India).

OTHER PROFESSIONAL CONTRIBUTIONS

Darby's impact on U.S. nutrition policy can be judged from the many committees, panels, and commissions that he chaired. For NIH alone these included Biochemistry and Nutrition Study Section (1948-1951), Metabolism and Nutrition (1951-1953), General Medicine Study Section (1956-1959), Nutrition Study Section (1959-1961).

Additional advisory groups he chaired included Scientific Advisory Committee, Samuel Roberts Nobel Foundation (1955, 1958, 1961, 1978); Advisory Committee to the Surgeon General (1959-1972); Council on Food and Nutrition of the American Medical Association (1960-1962, 1967-1970); Advisory Committee on Nutrition, American Health Foundation; Advisory Committee on Nutrition, Office of the Surgeon General (1959-1972); Panel 6, White House Conference on Nutrition and Health (1969); Secretary's Commission on Pesticides, Department of Health, Education, and Welfare (1970-1971); Hazardous Materials Advisory Committee, Environmental Protection Agency (1971-1974).

It is not possible to list all the nearly 60 additional committees, commissions, and panels of which he was a member. Worth noting are, Scientific Advisory Board, National Vitamin Foundation; U.S. Public Health Service; Commission on Nutrition Research; Division of Indian Health, U.S. Public Health Service; National Academy of Sciences Panel on Nutrition, Space Science Board; NIH Advisory Group on International Health; Visiting Committee, Department of Nutrition and Food Science, MIT; Environmental Health Advisory Committee, Environmental Protection Agency; and Board of Trustees, International Life Sciences Institute.

It is not necessary to list the more than 15 societies in which he was a member and often played a significant role.

For example, he deserves much of the credit for ensuring that when the American Society of Clinical Nutrition was founded in 1951, it was the clinical division of the American Institute of Nutrition and not a separate society.

HONORS

Darby took greatest pride in his election to the National Academy of Sciences in 1972. He began accumulating honors in the early stages of his career and continued to receive them throughout his life, beginning with Phi Beta Kappa and Alpha Omega Alpha at Vanderbilt University and Phi Lamba and Sigma Xi at the University of Michigan. He also received the Mead Johnson Award (1947), outstanding Alumnus Award from Little Rock Junior College (1951); Distinguished Alumnus Citation, University of Arkansas (1957); Serbian Academy of Science (1959); American Institute of Nutrition (AIN); Osborne-Mendel Award, AIN (1962); Star of Jordan, Jordan (1963); Joseph Goldberger Award in Clinical Nutrition, American Medical Association (1964); Thomas Jefferson Award, Vanderbilt University (1964); Order of Cedars of Lebanon, Lebanon (1972); Spencer Award, American Chemical Society (1972); Conrad Elvehjem Award, AIN (1972); the Robert Herman Award, American Society for Clinical Nutrition (1983); and the Underwood Prescott Award, Massachusetts Institute of Technology (1979).

His honorary memberships include the Colegio Medico de Guatemala (1950); Austrian Public Health Association (1951); Philippine Dietetic Association (1957); Serbian Academy of Science (1959); National Medical Society of Panama (1951); American Dietetic Association (1975); Institute of Nutrition of Egypt (1976); International Association of Bioorganic Chemists (1977).

He received honorary degrees from the University of Arkansas (1984), the University of Michigan (1966), and Utah State University (1973).

He presented many named lectures, some of them unique for their historical perspective on the topic. These included the Charles Franklin Craig Lecture, American Society of Tropical Medicine (1950; Herbert Smith Carter Lecturer (1965); Kempner Lecture, University of Texas, Galveston (1961); Margaret King Lecture, Henry Ford Hospital (1965); Lydia Robert Lecture University of Puerto Rico (1966); Sydney Negus Lecture, Medical College of Virginia (1972); W. O. Atwater Lecture, U.S. Department of Agriculture (1975); Underwood Prescott Lecture, Massachusetts Institute of Technology (1979); Brooks James Lecture, University of North Carolina (1980); Joseph Garland Memorial Lecture, Boston Medical Library (1984); and the Culpepper Lecture, University of Texas, Medical Branch, Galveston (1987). Similar recognition included Centennial Visiting Lecture, University of California, Davis (1967); American Chemical Society Lecturer (1973); FASEB General Session Lecturer (1984); Distinguished Summer Lecturer, Utah State University (1984); and Visiting Professor for the Centennial Year University of California, Davis (Sept.-Dec. 1967).

EPILOGUE

An outstanding personal characteristic was his generosity in encouraging and supporting younger investigators, and helping them to get established in their careers. As a teacher and mentor he influenced the lives and careers of several generations of graduate students in this manner. He also willingly served actively and wholeheartedly on review boards, panels, and editorial and advisory committees related to both national and international nutrition. His positive, critical, constructive, and multifaceted approach to nutrition issues

worldwide combined with an enthusiastic and charismatic personality made him an inspiring leader.

Throughout his professional life he received strong support from his wife, Elva, who provided continuity to the family and whose calmness was an important counterpoint to his sometimes frenetic pace. He was very proud of his three sons, William J. III, James Richard, and Thomas Douglas.

THE INVALUABLE HELP OF Harold H. Sandstead, Darby's former student and close long-term friend and colleague is gratefully acknowledged. This memoir also draws heavily on the autobiographical article by W. J. Darby, "Some Personal Reflections on a Half Century of Nutrition Science: 1930s-1980s," in *Annu. Rev. Nutr.* 5(1985):1-24, and the biographical article "William J. Darby 1913-2002" by H. H. Sandstead and C. Wagner in *J. Nutr.* 132(2002):1103-1106.

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