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HUBERT BRADFORD VICKERY
1893—1978

A Biographical Memoir by
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Biographical Memoir

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HUBERT BRADFORD VICKERY

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BY ISRAEL ZELITCH

VICKERY AND I SAW each other almost daily for more than twenty-five years; with such constant exposure one could not help learning a great deal about science—and about him. He came right to the point of any matter, with no time for trivia; although his brusque exterior sometimes intimidated younger colleagues, he was in fact kind and sentimental. Above all else, he demonstrated high professional standards, whether in the manner he criticized research work that failed to meet his high expectations, when apologizing publicly for an error in one of his papers, or in correcting shoddy scholarship in the literature.

He was extremely skillful with his hands and enjoyed doing laboratory work and designing laboratory gadgets. He appreciated precise carpentry, respected fine handtools, and was proud of the guesthouse he built at his summer retreat. His manual dexterity was at its finest, however, when he played Bach on the piano. He once boasted that although there were better pianists than he in New Haven, there were few who could sight read music as well. He was a collector of things, such as catalogs, chemical samples that filled a vault, reprints, photographs of friends, and letters. Some of the correspondence he saved has recently become valuable to scholars of the history of biochemistry. He was unusually energetic, in perpetual motion, and a chain-smoker.

Vickery, a self-confessed "chemist among plants," and a Canadian by birth, took his doctorate at twenty-nine from Yale University and spent the remainder of his professional life at The Connecticut Agricultural Experiment Station in New Haven. It was Professor Treat B. Johnson, his director of graduate studies at Yale, who one February day walked with Vickery to the Station to introduce him to the famed Dr. Thomas B. Osborne, who was in need of an assistant to work on a problem in progress on plant protein chemistry. Thus began an active association with the Station that lasted through graduate school, and continued on through his tenure as a staff member from 1922 until Vickery's retirement in 1963, at the age of seventy.

Following his official retirement, he continued at the Station as scientist emeritus. He maintained an active office where he did historical research and consulted with and assisted colleagues until his death fifteen years later. His publications span a period of sixty years. One of his last papers, published in 1972 in *Advances in Protein Chemistry*, begins: "In the forty years that have elapsed since the publication in 1931 of the review of the protein amino acids by Vickery and Schmidt (1931), a surprising number of new amino acids have been found in hydrolyzates of proteins."

Vickery took special interest in his forebears and had, in his personal records, voluminous notes that began with the first Vickery in America, a George Vickery who lived in Marblehead, Massachusetts, in 1637. Members of his family on both sides attained prominence as shipwrights, ship owners, makers of marine instruments, businessmen, and ministers in Congregational and Episcopal churches. Among these were Thomas Wetmore (1615–1681), who came to America in 1635 and was one of the three founders of Middletown, Connecticut, and Dr. Comfort Starr (1590–1659), who practiced medicine in Newe Town (Cambridge)

and Boston, Massachusetts, and whose property in Cambridge is now part of the Harvard Yard. One of the great pleasures of Vickery's life was the purchase in 1931 of a summer property, "Toleration," in Scotland, Connecticut, in the part of the state associated with some of his ancestors.

Hubert Vickery's father, Edgar Jenkins Vickery, was born in Yarmouth, Nova Scotia, in 1861. He was orphaned at an early age and shipped out to sea as a cabin boy at age fourteen. At age twenty-five he set up a book and stationery store in Yarmouth, and later owned a bookstore in Halifax. In 1888 he married Mary Katherine Dudman, who was also descended from New England people; Hubert was the second son and child in a family of four children born to the couple. The family lived prosperously by local standards in a commodious home that had been originally built by Mrs. Vickery's father.

Years later Vickery was able to precisely pinpoint the beginning of his interest in chemistry; it was the Christmas when he was twelve and his father had given him a present of Steele's *Fourteen Weeks in Chemistry*. He eagerly learned the symbols for the elements and immediately began carrying out his first experiments.

The following year, while in the eighth grade, Hubert successfully passed the examinations for entrance into the Academy, as the high school was then called, and settled down to the study of serious courses—beginning Latin and French, English, algebra, geometry, science, botany, physics, and chemistry! For most students, high school ended upon completion of the eleventh grade. Those who planned to teach, as Hubert did, continued for a twelfth year in the so-called "A" course. So in 1910 Vickery, and about a dozen others, began: two courses in Latin, one being six books of Caesar and five of Virgil, the other Latin composition; two courses in English, one in reading, the other in history of the

language; one each in French, plane and spherical trigonometry, plane and spherical geometry, higher algebra, botany, and chemistry. This was a formidable course of study for a young man who turned seventeen in February of 1911. Because his parents held to the opinion that he was too young to begin university, he took a job for one year as a senior teacher in a two-department school in a village named Brooklyn, three miles from home, and continued to live with his family.

Vickery entered Dalhousie University as a sophomore in the fall of 1912. There were unusually able men on the faculty: MacMechan in English, MacKay in chemistry, and Bronson in physics. President A. Stanley MacKenzie had known Hubert's father from Halifax days, and was especially kind to Vickery, reviewing his course of study and advising him on the courses necessary for admission to the chemistry honors course. The first year went well, and following a summer school of science in Halifax, Vickery began his second year at Dalhousie in the chemistry honors course. He was, indeed, the *only* student accepted into this course comprised entirely of chemistry and physics, with lectures and laboratory work all day, each school day. There he sat, the lone student in a large lecture room, while Professor MacKay delivered lectures in the history of chemistry and, later, in physical chemistry with the same formality he would show had the classroom been filled with students. In contrast, Professor Bronson taught Vickery the course in thermodynamics at his roll-top desk. He was assigned a small laboratory, and his professors would look in from time to time to see how the one chemistry honors student was progressing.

It was during Vickery's second year at Dalhousie that Professor Nickerson requested a determination of ammonia in a urine sample that one of the doctors at the hospital

needed as part of a diagnosis. The results were satisfactory and for this service Vickery received \$10, which he promptly spent for a new pair of shoes. This payment of cash for services rendered provided great satisfaction because it signified to him that he had become a chemist. He published two papers during his undergraduate career, his first an analysis of the stone used in building the new chemical laboratory. He read the paper at a meeting and in the audience was the premier of the province, another friend of his father's, who was present, Vickery said, "to see how I carried myself."

After graduation from Dalhousie, he taught high school chemistry and physics for three years and simultaneously worked with Professor MacKay on his master's thesis on the isochlor lines in natural waters of the peninsula of Nova Scotia. Vickery spent 1917–1919 working as an analytical chemist with Imperial Oil Ltd., and later taught science at the Provincial Normal School. Because of the sudden death of Professor MacKay, he was asked to step in and teach chemistry I and II at Dalhousie; this experience resulted, in the summer of 1920, in an invitation to accept an 1851 Exhibition Scholarship to do further graduate work. This scholarship was a most prestigious award; only three were then available in all of Canada. This unexpected opportunity allowed him in the fall of 1920 to begin graduate school in chemistry at Yale University, where he went on the advice of Professor Bronson. There he began initially under the direction of Treat B. Johnson.

Early in 1921 it happened that one of Thomas B. Osborne's assistants in the Biochemistry Department of the nearby Connecticut Agricultural Experiment Station left for another position. Osborne chanced to meet Johnson and inquired if he knew of a student who would come to the Station to fill the vacancy and pursue research there. A few days later, Johnson introduced Vickery to Osborne, who

asked if he would be willing to do research under his direction. Vickery wrote later: "To a young and impecunious student, the chance to work in a large, well-equipped, and comfortable laboratory under a man of international reputation, with no fees or charges for reagents or apparatus, offered a choice to which there was only one answer." A few days later he began work in the laboratory where he was to spend the remainder of his professional life.

Osborne was then working on the chemistry of proteins and on animal nutrition. Vickery attended lectures at Yale and did all of his laboratory work at the Experiment Station. His thesis research was on the stability to acid hydrolysis of the amide nitrogen of the wheat protein gliadin. It was accepted and he received his Ph.D. from Yale University in 1922.

Vickery soon learned that among his other qualities, Osborne was a tough critic of the use of the English language, and drafts of manuscripts were scrutinized laboriously word by word with the author. Vickery later remembered, "If one could get the first sentence worked at each day past him, things went more smoothly." It was this method, obviously learned from Osborne, that Vickery later duplicated in dealing with papers written by his colleagues. Vickery's patience in going over a manuscript was inexhaustible. Sitting beside the author, every word was examined and debated, and every alternative explored before a sentence was considered satisfactory. These long sessions were interrupted only long enough for Vickery to sharpen his pencil or to light up another cigarette.

In the early twenties the staff of the Biochemistry Department consisted of about four professional scientists, occasional visiting scientists and graduate students, several technicians, and a secretary. The Experiment Station, founded in 1875, was then, and still is, largely supported by the State of

Connecticut. The number of people in the Biochemistry Department remained essentially the same throughout Vickery's career. Osborne invited Vickery to join the staff after he received his Ph.D. degree, and although his beginning salary was only a little more than he had earned as a teacher in Nova Scotia, he felt the opportunity to continue a life of research in a laboratory directed by such an outstanding scientist was far too good to be missed. He said that he never regretted his decision.

His first work was an attempt to account for as much of the nitrogenous constituents in alfalfa as possible, but after three years of study he could account for about only 55 percent of the nitrogen. In the course of these first investigations he identified the presence of adenine (no information then existed in the literature to suggest any possible function in metabolism for this compound) and the methylated bases, choline and betaine. By 1927 it had become clear that the methods available for the analysis of extracts of plant tissues were hopelessly inadequate, and he turned to a study of the methods for the determination of the basic amino acids of proteins, something he believed to be a simpler problem. Gravimetric methods to determine arginine and histidine, using flavianic acid for arginine and the insoluble salt of 3,4-dichlorobenzenesulfonic acid for histidine, were developed. He also had the personal pleasure in the course of this work of preparing lysine as a free base in crystalline form for the first time. Crystalline compounds prepared in the laboratory appealed greatly to his esthetic sense, especially those seen for the first time, as I observed years later when Vickery first produced shimmering crystals of monopotassium isocitrate in the laboratory.

Vickery began an association with Yale University as a lecturer in the Department of Physiological Chemistry in 1924. In the beginning he gave a graduate course on protein

chemistry, but later the subject matter shifted to amino acid chemistry. For a number of years his course was used as the main departmental hurdle to screen graduate students in biochemistry. He used to chuckle when telling about his tough reputation among Yale graduate students. Nevertheless, a red-eyed student was once observed leaving his office after an interview, and it later turned out that a few tears and an extra written paper had convinced Vickery to change a failing grade to a passing one.

On Osborne's retirement in June, 1928, Vickery was appointed chief biochemist. He assumed responsibility for the chemical work and continued the animal nutrition work in collaboration with Professor Lafayette B. Mendel of Yale, as Osborne had. Vickery had little interest or knowledge of the nutrition work and gave it up entirely in 1934. The Osborne rat colony was continued, however, and nutrition research continued in the Department until the sixties under a succession of staff members: Helen Cannon, Rebecca Hubbell, and Lester Hankin. During this period the rat colony was maintained by George R. Smith.

Under Osborne's influence Vickery soon became aware of and interested in research on the proteins of green leaves. Osborne had used spinach leaves as a source of vitamins for the rats, and his early efforts to isolate spinach leaf proteins attracted a young British graduate student, A. C. Chibnall, who joined the Department in the fall of 1922. He stayed for two years preparing and studying proteins from leaves of a number of species. Vickery and Chibnall became good friends, and Vickery was later instrumental in arranging Chibnall's famous 1938 Silliman Lectures at Yale, which resulted in the publication of his book, *Protein Metabolism in the Plant*. In 1928 Vickery started investigations on the tobacco plant because it had large leaves and plants were available in Connecticut during the summer for the acquisi-

tion of leaf proteins. His biochemical studies with this species, many in collaboration with George Pucher, who joined the staff in 1928 and worked closely with Vickery, are among his best known.

Their collaborative work was characterized by great analytical precision and attention to detail. Studies on the metabolism of organic acids were Pucher's main responsibility, and those on the chemistry of nitrogen compounds were largely Vickery's. Vickery wrote all their joint papers. If the subject was organic acids, the authorship was Pucher and Vickery; if it was nitrogen chemistry, it was Vickery and Pucher. They worked productively for eighteen years until Pucher's sudden death in 1947. Their greatly improved technique of ester distillation enabled them to determine the organic acids of the tobacco leaf and to identify the so-called "crassulacean malic acid" of *Bryophyllum* as isocitric acid, an accomplishment that led to extensive studies of the organic acid metabolism of this and related plants. Their development of an accurate method for the determination of citric acid was widely used by other workers. In particular it helped Krebs develop the tricarboxylic acid cycle hypothesis as the explanation of respiration in pigeon breast muscle, for which he later received a Nobel Prize.

Vickery's interest in the organic acids of tobacco leaves was enhanced by the observation made in the laboratory in the early 1930s that citric acid increases dramatically when leaves are cultured in water in darkness, thus indicating that the organic acids are extremely reactive metabolites in the cell system. The analytical problems of measuring changes in organic acid concentration were made much simpler by the development of precise methods of separation and determination of organic acids by use of anion exchange chromatography. These methods were perfected by James K. Palmer, who joined the staff in 1952.

With the availability of improved analytical methods and of organic acids labeled with ^{14}C , Vickery undertook an examination of the behavior of the components of the tricarboxylic acid cycle as well as a number of other acids when fed to tobacco leaves cultured in darkness. Enzymatic assays were also used, for example, to determine isocitrate concentration. The metabolism of malate, succinate, citrate, fumarate, glycolate, malonate, tartrate, bicarbonate, pyruvate, isocitrate, glutamate, and asparagine were studied in considerable detail. Evidence was accumulated to support the view that the organic acids are the central metabolites for the systems involved in carbohydrate and protein chemistry, in the phenomena of photosynthesis and respiration, and in many more functions of the life processes of plants. I was hired by Vickery in 1952 to work on plant enzymes associated with organic acid metabolism, and was encouraged by him to work on the metabolism of glycolate in leaves. This led to the discovery of the importance of photorespiration on net photosynthesis.

Studies on tobacco leaf metabolism and curing resulted in several major publications. These consisted of a series of *Station Bulletins*, of which the most important are: No. 352, 1933; No. 374, 1935; No. 442, 1940; No. 569, 1953; and No. 640, 1961. In 1933 Vickery's contributions to plant biochemistry were recognized by the award of the prestigious Stephen Hales Prize by the American Society of Plant Physiologists. He wrote, "I had had no inkling that our work with leaves had been noticed by colleagues in this discipline." He took the occasion of the award address to emphasize the importance of a training in fundamental chemistry, especially analytical chemistry, for all students of plant physiology who hoped to learn to account for the behavior of plants in terms of recognizable and general physical laws.

Investigations by Harold E. Clark, a postdoctoral fellow

studying the metabolism of the tomato plant, resulted in the isolation of glutamine from the stalk tissue of plants grown with ammonium salts as a source of nitrogen. This led to a long series of investigations on glutamine. Large quantities of this then rare substance were isolated from beets grown in the greenhouse and watered with ammonium sulfate solution. James Melville, who had taken his degree under Chibnall in 1932, was working in the laboratory at the time and succeeded in obtaining "beautifully pure glutamine crystallized" in large quantities. Within a few years glutamine became an article of commerce.

In all of the papers published in the early thirties on amide metabolism, Vickery emphasized that nothing was known of the precursor of either asparagine or glutamine. There was evidence, however, that the precursors were non-nitrogenous in nature. It turned out, as first suggested by Chibnall, that the precursors of the amides were oxaloacetic and α -ketoglutaric acids produced from the Krebs tricarboxylic acid cycle through normal enzymatic transformations of the organic acids.

Plants of the family Crassulaceae exhibit the fascinating phenomenon of diurnal variation of acidity to an extreme degree. During the night the concentration of organic acids, mainly malic acid, increases at the expense of starch, while during the day it decreases again and starch accumulates. The study of Crassulacean metabolism occupied Vickery and his colleagues for many years. They investigated the effect of prolonged exposure of *Bryophyllum* leaves to both light and darkness and the capacity of the leaves to recover from stresses, as well as the effect of temperature on the transformation of starch to malic acid in darkness. The interdependence of malic acid and starch concentrations on their transformations was demonstrated. Isocitrate is present in high concentrations in these species but undergoes little

diurnal change. Attila Klein, a postdoctoral fellow in 1962, supplied ^{14}C -isocitrate prepared by Vickery to *Bryophyllum* leaves and showed it was metabolized. This demonstrated the existence in leaves of metabolic pools that are removed from the activity of enzyme systems.

From time to time Vickery's scholarly interest led him into historical research. Early in his career he became curious about the history and development of the Kjeldahl method to determine nitrogen. Samuel W. Johnson, the first director of the Experiment Station, invented the type of apparatus universally used for this determination, and there was a set of early equipment still in use in the Department of Analytical Chemistry. Vickery was able to track down and write a paper describing the discovery of the use of mercury as a catalyst, the idea of adding potassium sulfate to the digestion, the combination of mercury and copper as the most effective catalyst, and the devising of the type of apparatus that is commonly used today. Another of his historical researches concerned the matter of the origin of the word protein. Although it was generally assumed that the term was invented by Mulder in the late 1830s, further investigation led to the publication of a note on the origin of the word that revealed that Berzelius had suggested the use of the word "protein" in an 1838 letter to Mulder because it was derived from the Greek word meaning "to be in the first place."

Late in the thirties Vickery was elected to the Editorial Committee of the *Journal of Biological Chemistry*, and in 1942 he joined the Editorial Board. The editorial offices were housed at Yale University, where Rudolf Anderson was managing editor. For several years Vickery dealt with more papers than Anderson did, often from 120 to 130 yearly. In 1949, Anderson, Joseph S. Fruton, and Vickery edited 329 papers of the 1176 submitted. This load was maintained

until about 1954 when the Board was enlarged and the load was distributed more evenly. He also served as managing editor during Anderson's vacation for one month each summer.

Vickery adopted a principle, faithfully observed throughout his professional life, of returning all papers received for review within twenty-four hours. "It does not seem decent to keep someone's manuscript for more than a day or two," he wrote. Even when he occasionally sought the advice of a colleague about the merits of a paper submitted to the *Journal of Biological Chemistry*, he demanded—and received—the manuscript back within twenty-four hours. He was an associate editor of the *Journal of the American Chemical Society* and had a term on the Editorial Board of *Plant Physiology*.

His experiences as an editor led him to try to lessen the confusion existing in the nomenclature of the amino acids. He prepared a proposal for the nomenclature committee of the American Chemical Society for the complete reform of the nomenclature based on the use of the small capital letters D and L as prefixes, and this system came into general use in 1952 when it was approved by The International Union of Pure and Applied Chemistry. The rules, however, failed to deal satisfactorily with the difficult problem of naming the isomers of amino acids that have more than one center of asymmetry. He resolved this problem, at least temporarily, by appropriating the prefixes of carbohydrate nomenclature to the names of the more complex amino acids in order to define the configurational relationship, and this rule was officially approved in 1963. An outgrowth of Vickery's interest in nomenclature was to stimulate the direction of the work of Kenneth R. Hanson, who joined the Biochemistry Department in 1960. In 1966, Hanson first introduced the concept of prochiral centers and a method of naming

individual stereoheterotopic groups at such centers that is now in general use.

Vickery had a long friendship with Edwin Cohn at the Harvard Medical School based on their common interest in protein chemistry. During World War II Cohn led a team at Harvard carrying out the fractionation of blood serum to prepare albumin by low-temperature alcohol precipitation. Cohn was most anxious to get this method into large-scale application for the armed forces, and Vickery was named associate director of the Plasma Fractionation Laboratory. Through 1942 and much of 1943 he spent from two to five days a week at Harvard supervising the production and evaluation of the serum albumin, and Saturday morning directing the work of the laboratory at the Station in New Haven. It was while at Harvard that he was notified of his election to the National Academy of Sciences in 1943.

Vickery was married three times. At age twenty-three he married Vera Claire Heustis, who died nineteen years later. In 1936 he married Mildred Raye Hobbs, who died in 1968. He married Dr. Jeanette Opsahl in 1971, and she survived him for less than a year.

Among his honors: he was elected a fellow of the American Academy of Arts and Sciences, 1948; President of the American Society of Biological Chemists, 1950; Charles Reid Barnes Life Membership Award of the American Society of Plant Physiologists, 1956; Samuel W. Johnson Distinguished Scientist Emeritus by the Experiment Station, 1969. He received honorary degrees from Yale University, 1948, and Dalhousie University, 1973. The citation for the latter includes, "for the contributions of this gifted scholar."

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