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GERALD DONALD AURBACH
1927—1991

A Biographical Memoir by

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Biographical Memoir

GERALD DONALD AURBACH

March 24, 1927–November 4, 1991

BY IRA PASTAN

GERALD D. AURBACH REVOLUTIONIZED OUR understanding of bone metabolism and calcium homeostasis.

Gerald D. Aurbach was born in Cleveland, Ohio, on March 24, 1927, but grew up in Washington, D.C. After spending one year in the U.S. Army-Air Force at the end of World War II, he entered the University of Virginia, where he received his bachelor's degree in 1950 and his M.D. in 1954. These years at the University of Virginia were some of the happiest days of Gerry's life and he remained devoted to the University of Virginia for the remainder of his life. He received the singular honor of being named the Centennial Alumnus of the university in 1988. Ironically it was during a visit to the university on November 4, 1991, that he was fatally injured in a senseless act of violence.

Gerry began his studies on parathyroid hormone early in his career while a medical student at the University of Virginia in the laboratory of Dr. William Parson. Dr. Parson was chief of medicine and a professor of medicine at the University of Virginia. A renowned endocrinologist, Parson had worked with Dr. Fuller Albright, a leader in the field of endocrinology and metabolism, while training at the Massachusetts General Hospital. After graduation from medical school, Gerry took an internship at the New England Medical

Center and a residency at the Boston City Hospital. In 1956 he joined the laboratory of Ted Astwood as a research fellow at Tufts Medical School, where he was able to continue his studies on parathyroid hormone. This area of research occupied most of his research career. At that time only a few polypeptide hormones had been characterized. It was known that injection of an extract of parathyroid glands into test animals raised calcium levels in the blood, but the nature of the active substance was not known. Many investigators had already tried to purify this factor without success. Gerry thought of the novel idea of using phenol extraction to remove the hormone from proteins with which it was associated and to inactivate proteases causing its degradation. This approach was very successful and a paper published in 1959 established Gerry as the leader in the field.

Despite his early success Gerry felt he needed further training in research and applied to a new, prestigious training program at the National Institutes of Health in Bethesda, Maryland. Gerry was selected for the Research Associate Training Program and in 1959 joined the laboratory of William Jakoby, where he received training in enzyme biochemistry. In 1961 he accepted a research associate position in the Metabolic Diseases Branch of the National Institute of Arthritis and Metabolic Diseases and established his own research group. He spent his entire career in the branch, eventually becoming its chief in 1973.

When Gerry started his own laboratory, he returned to the parathyroid hormone field. His first goal was to obtain sufficient amounts of highly purified protein to determine its sequence. This was a challenging problem because the amount of hormone in each parathyroid is very low; parathyroid glands are small and protein purification techniques were in their infancy. Aurbach and colleagues were able to overcome these obstacles and they obtained sufficient

amounts of highly purified bovine and human hormone to fully characterize the protein. In addition, they were able to chemically synthesize a biologically active form of the protein. These studies opened up the field of parathyroid hormone research, eventually leading to the understanding and treatment of several important diseases, including osteoporosis.

The availability of purified parathyroid hormone enabled Gerry to investigate several new areas of research. One of these was to develop a radioimmunoassay that could measure parathyroid hormone levels in the blood and other body fluids. This assay became a valuable tool in the diagnosis of hyperparathyroidism. A second was to radiolabel parathyroid hormone and determine its pharmacokinetic behavior. And a third was to investigate the mechanism of parathyroid hormone action. Influenced by the classic studies of Earl Sutherland, Gerry reasoned that parathyroid hormone acted on its target tissues, kidney and bone, by raising cyclic adenosine monophosphate (AMP) levels. To study this process in animals and humans he and his fellow, Lew Chase, developed a highly sensitive assay for cyclic AMP. They then used this assay to show that parathyroid hormone activated adenylate cyclase and elevated cyclic AMP levels in target cells and in the urine. The cyclic AMP in the urine could be used to assess the parathyroid hormone status of patients, an invaluable clinical tool. He was also in the position to investigate some hereditary diseases of calcium metabolism. Fuller Albright had described pseudohypoparathyroidism as the first example of a disease of hormone resistance rather than hormone deficiency. Gerry and Lew Chase discovered that patients with pseudohypoparathyroidism failed to elevate cyclic AMP levels in the urine in response to parathyroid hormone and showed that the biochemical basis of this was a defect in the ability of parathyroid hormone to activate renal adenylate

cyclase. And later, with Allen Spiegel, Gerry showed that the specific defect in adenylate cyclase was a deficiency in the guanine nucleotide binding protein Gs.

Gerry's contributions extended outside the parathyroid hormone field and had broad implications for the entire field of hormone action. One very important contribution was the design and synthesis of radiolabeled iodohydroxybenzylpindol. This compound was used as a marker of specific binding to the beta-adrenergic receptor, and enabled Aurbach and colleagues to study in detail a critical initial step in hormone action.

Gerry was a fine physician and his groundbreaking research in the parathyroid hormone field resulted in many patients being referred to the National Institutes of Health from community hospitals as well as large medical centers in the United States and abroad. Gerry being a compassionate person and physician kept in close touch with his patients over the years. In collaboration with John Doppman, a radiologist from the Clinical Center, and many endocrine surgeons, including Sam Wells, Murray Brennan, and Jeff Norton, Gerry's team achieved an extraordinary success rate in treating patients with hyperparathyroidism who had previously had unsuccessful neck exploration; thus, making the NIH Clinical Center the leading referral center for the treatment of hyperparathyroidism.

Additionally, studies by his group, and particularly with Steve Marx, led to the characterization of several hereditary forms of hyperparathyroidism (multiple endocrine neoplasia Type 1, familial hypocalciuric hypercalcemia, hyperparathyroidism-jaw tumor syndrome) and the eventual identification of the genetic basis for each of these diseases. One striking example of Gerry's impact on clinical medicine is the current excitement about using parathyroid hormone to treat osteoporosis.

Gerry's reputation as an outstanding researcher and a superb mentor and clinician encouraged young physicians to come to NIH to work and train in his laboratory. Many are now leaders in the endocrinology and biomedical communities; these include Lew Chase (chief of medical service, Veterans Affairs Medical Center, Washington University, St. Louis), Allen Spiegel (director of the National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK]), Steve Marx (chief of the Metabolic Diseases Branch at NIDDK), Ed Brown (Endocrine/Hypertension Division at Brigham and Women's Hospital in Boston), Maria Luisa Brandi (professor in the Endocrine Section at the University of Florence in Italy), and John Bilezikian (chief of the Endocrine Division at Columbia University Medical Center in New York).

Gerry's contributions were recognized by many awards, some of which included the John Horsely Memorial Award from the University of Virginia in 1960, the Andre Lichiwitz Prize from France in 1968, the William F. Neuman Award of the American Society for Bone and Mineral Research in 1981, the Gairdner Foundation International Award in 1983, the Edwin B. Astwood Award from the Endocrine Society in 1985; and the Distinguished Service Medal of the Public Health Service in 1988.

Perhaps one of the most meaningful awards was the Edwin B. Astwood Award of the Endocrine Society. This was because Gerry began his research career in Dr. Astwood's laboratory and was very active in the Endocrine Society, holding positions on various committees and serving as its president from 1998 to 1999. Since his death, both the Endocrine Society and the American Society for Bone and Mineral Research have established memorial lectures in his honor. The University of Virginia Medical School established the Gerald D. Aurbach Professorship in Endocrinology in 1998 in recognition of his scientific contributions and his

service, and in 2002 the university named their new medical research building "The Gerald D. Aurbach Medical Research Building" in his honor.

Gerry was a member of many prestigious medical societies, including the American Society for Clinical Investigation, the American Society for Biochemistry and Molecular Biology, and the Association of American Physicians. He was a founding member of the American Society for Bone and Mineral Research. He served as president of the Endocrine Society. In 1986 he was elected into the National Academy of Sciences.

Gerry was a fourth generation Washingtonian. His mother's family arrived in Washington in 1859. He attended the Lafayette Elementary School and graduated from Wilson High School in 1945. Part of his reason for joining the NIH staff was to return to the city he loved. Gerry was a devoted husband to Hannah, whom he married in 1960, and he was a wonderful father who set a fine example for their daughters, Elissa and Pamela. Yearly family vacations at North Shores in Rehoboth Beach, Delaware, and in Virginia Beach, Virginia, were always looked forward to. Winter trips to Colonial Williamsburg, Virginia, through New Year's Eve were also a favorite, especially since Hannah was from the Tidewater area.

A lover of classical music, Gerry was also an accomplished pianist who enjoyed sitting down at his Steinway Grand (which he had played since age 6) upon returning home from work no matter what the hour. He could often be seen jogging in Great Falls Park close to his home in Potomac, Maryland. He was an avid Redskins fan through both the good and bad times. He and his dad seldom missed attending the Senators baseball games. He was a collector of old maps, and any John Wayne movie was his favorite. He and Hannah visited all new art exhibitions in Washington and found local art

museums when traveling; the Smithsonian National Air and Space Museum was Gerry's favorite because of his love of flying. Gerry also enjoyed traveling. Trips to Asia (especially Singapore), Israel, and Europe, often combined with meetings and speaking engagements, were always very special to both Gerry and Hannah.

I met Gerry in Boston when he was a fellow in the laboratory of Ted Astwood and I was a medical student. We came to the National Institutes of Health the same year and were both interested in the mechanism of action of polypeptide hormones. Because we lived in the same general area, we often drove home from work together. He was a wonderful friend and colleague, as well as a gentle, wise, and supportive person loved and respected by his colleagues and family.

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