Robert H. Wasserman

1926–2018

BIOGRAPHICAL *Memoirs*

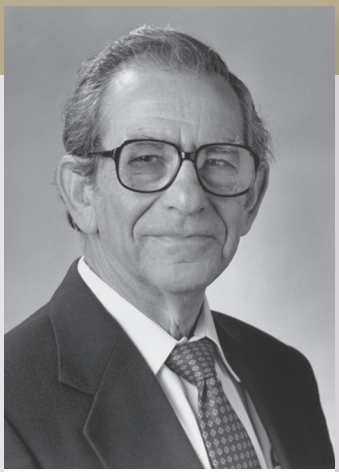
A Biographical Memoir by
Robert J. Cousins
and Sylvia Christakos

NATIONAL ACADEMY OF SCIENCES

ROBERT HAROLD **WASSERMAN**

February 11, 1926–May 23, 2018

Elected to the NAS, year 1980



By Robert J. Cousins and Sylvia Christakos

Robert H. Wasserman was a true "Cornellian" for over a half century, from his days as an undergraduate after WWII to becoming Chair of the Department of Physical Biology and Section of Physiology (1983–1987) and the James Law Professor of Physiology Emeritus in 1998. Wasserman passed away at ninety-two in Ithaca, New York. Known to friends and colleagues as "Bob," he made a lasting impression on the nutrition field with seminal studies on mineral ion transport, specifically, the molecular mechanism of absorption of calcium from the diet and discovery of calcium binding protein. After four years conducting nuclear studies at Atomic Energy Commission facility of the University of Tennessee, in 1957 he would return to Ithaca and Cornell for his long and renowned career as an academic and researcher in physiology and mineral metabolism.

Early Years

Wasserman was born in Schenectady, New York, on February 11, 1926 to Joseph and Sylvia Wasserman. His education through high school was in that city in upstate New York. He credited his older brother, Ernest, with stimulating his interest in biology. Starting in June 1943, he studied at Union College in Albany, New York, and after three months, he joined the Army Specialized Training Corp based at Cornell University in Ithaca, New York. After this training, he entered the U.S. Army and received basic training at multiple sites in the United States. His division was sent overseas in October 1944, entering European Theater combat near Aachen, Germany, where he participated in operations of the Battle of the Bulge that December. Most of his division was captured by the German army and were released by American military forces in May 1945.

College Years

After military service in WWII, he spent a year working on a farm in upstate New York. Thereafter, he enrolled at Cornell University and received a bachelor's of science in June

1949. During his undergraduate years, he washed glassware and did analyses for animal nutritionist Thomas Reid, who served as another role model for Wasserman. Next, he matriculated at Michigan State University for a master's degree, where his research was on rumen microbiology. After the masters was awarded in August 1950, he returned to Cornell, for similar research studies in animal science and microbiology, with the Ph.D. degree awarded in June 1953.

Early Academic Career

Wasserman's first academic position was at the University of Tennessee-Atomic Energy Commission at Oak Ridge, Tennessee. There he worked with Dr. Cyril L. Comar, a well-known radiation biologist, who served as director of the program. This would turn out to be a twenty-one-year professional relationship. In the spring of 1958, Wasserman returned to Cornell as an associate professor in the newly created Laboratory of Radiation Biology at the New York State College of Veterinary Medicine. Comar, who had moved to Cornell the year before, was director of that laboratory. In this new position, Wasserman would initiate his studies on vitamin D and calcium and phosphorus metabolism—these would eventually gain him international professional recognition. In 1960, he was merged into the newly formed Department of Physical Biology, with Comar as chair. Wasserman was awarded the full professor rank at Cornell in 1963.

Early Research at Cornell and Oak Ridge

Wasserman's earliest published research was in ruminant animal husbandry, many in collaboration with J. "Jack" K. Loosli. These were derived from his doctoral research. The transition to Oak Ridge led to his first studies in radiobiology. There he published a paper on effects of feeding dogs meat from cattle and sheep that had been lethally irradiated. The paper was published in *Science* (1955). Other studies with radio-isotopes followed, including studies with strontium (^{90}Sr) and calcium (^{45} Ca) and the interactions of these two metals. ^{90}Sr was of great health concern because of the abundance of this radio-isotope in atomic fission products and, like calcium, it was incorporated into bone leading to radiation damage. At this time, there was great concern that the contamination of foods with radionuclides produced by atomic weapons testing posed a major health risk. Some of these published studies were with human subjects at the medical division at Oak Ridge, but most of these early studies were with ruminants or rats and chickens. This research provided him with the opportunity to conduct his first studies on calcium absorption. Wasserman was early to realize that the growing chick, particularly those that were rachitic due to vitamin D deficiency, was an excellent research model

system. The response of the rachitic chick to repletion with vitamin D and the subsequent enhancement in calcium absorption served as a system that was widely used in the Wasserman lab and by others interested in calcium absorption and utilization. Most of these studies utilized tracing calcium transport with ^{45}Ca, the most widely used radioisotope of calcium for research.

Discovery of Calcium Binding Protein (Calbindin-D)

The rachitic chick model and repletion with vitamin D_3 allowed Wasserman and his research associates, including Alan N. Taylor and Francis A. Kallfelz, the system with which to measure calcium fluxes across the chick duodenum. They characterized the active transport of calcium, its sensitivity to pH and non-essentiality of sodium ion, in the early 1960s. Thereafter, they discovered a vitamin D_3 –stimulated factor in intestinal homogenates. An exciting series of very productive experiments followed and led to the identification of an intestinal calcium binding protein (CaBP) that was induced by vitamin D. These studies led to the identification of this protein in other calcium utilizing systems, e.g. the uterus of the laying hen. The purification and characterization of CaBP was described in 1968. The method of detection was an elegant in vitro assay that used ^{45}Ca and its competition between CaBP and Chelex -100 ion exchange resin devised by the Wasserman lab. The method allowed for the detection of calcium binding activity in biological fluids and tissue extracts. They used the ^{45}Ca-binding assay to follow the purification process for CaBP in tissue extracts from numerous species.

In 1964, Robert E. Olson hypothesized that fat-soluble vitamins might act through regulation of gene expression. Shortly thereafter, others showed that the stimulation of calcium absorption by vitamin D was inhibited by administration of actinomycin D, an inhibitor of RNA-directed protein synthesis. Soon through experiments done by Robert A. Corradino in the Wasserman lab, CaBP production in response to vitamin D was demonstrated to be blocked by prior administration of actinomycin D. Moreover, they showed that CaBP inhibition was coincident with elimination of the stimulatory effect of vitamin on calcium absorption. These classic studies led to a model wherein the vitamin induced an RNA that led to CaBP production and a subsequent physiologic effect. This model was quickly adopted by the vitamin D and calcium research communities as CaBP provided a unique product to integrate into studies of calcification, calcium transport and vitamin D function. After the active form of vitamin D, i.e. 1,25-OH_2 vitamin D_3 (calcitriol) was identified by Hector DeLuca and others, calcitriol was shown to induce CaBP in the intestine and that pathway was integrated into a model for vitamin D-induced calcium absorption. The identification of the calcium binding protein (CaBP,

Robert H. Wasserman, Robert J. Cousins and Malden C. Nesheim (l to r) at the inaugural Prichard Lecture in Nutrition for the Division of Nutritional Sciences at Cornell University, September, 2016 (Photo by Patrick J. Stover.)

later named calbindin-D (-D9k, 9,000 Mr in mammals and –D28k, 28,000 Mr in chicks) as the first known target of vitamin D action (its induction is still one of the most pronounced effects of 1,25(OH)2D_3 in the intestine) was a seminal discovery. It provided the foundation for the studies which led to our basic understanding of the molecular mechanism of 1,25(OH)2D_3 action. In addition to rats and chicks as experimental models, the Wasserman group went on to integrate the concept of CaBP-mediated calcium transport into the nutrition of production animals including cattle and swine as well as horses. They completed the sequence for bovine intestinal CaBP in 1975.

In the mid-1970s, Wasserman developed an interest in the hypercalcemic effects of extracts of the Solanum malacoxylon. This plant is common to South American countries, where calcinosis, including tissue calcification, and associated pathology, that can be lethal, occurs in grazing cattle. This calcinogenic plant was demonstrated to produce the hypercalcemic effect through production of 1, 25-dihydroxyvitamin D_3-glycoside. Wasserman purified this water-soluble botanical in 1976. They also identified a similar calcinogenic plant, Cestrum diurnum, that is found in the southern United States. They established this plant also produced these effects of calcium metabolism via the same glycoside.

In the 1990s, his studies using ion microscopic imaging of calcium were pioneering and suggested the presence of a vitamin D induced calcium channel in the intestine (later identified as the vitamin D regulated epithelial calcium channel, TRPV6). He was also one of the first to identify the regulation by vitamin D and calcium deficiency of the intestinal baso-lateral localized plasma membrane calcium pump.

Wasserman was recognized as an outstanding, innovative, thoughtful, and internationally well-respected scientist. He was also a generous and supportive mentor not only to those in this lab but also to others in the field, always interested in new findings and willing to give helpful suggestions and encouragement. We have greatly benefited not

only from Wasserman's pioneering contributions but also because he is a role model who has provided a standard of excellence for all of us. Bob Cousins recalls that the vitamin D-Calbindin model developed in the Wasserman lab was important in the early days of his research on trace element absorption and transport.

Productive and Honored Scientist and Communicator

Robert Wasserman published over 360 research articles by the time he was appointed James Law Professor of Physiology in 1989. This includes eighty-nine major reviews and over 155 peer-reviewed research papers. He has a total of fourteen papers in *Science* and seven papers in *Nature*, which is an impressive record for a single principal investigator (unlike today's large research groups where output is generated by the collective contributions of numerous investigators and laboratories.)

Honors for Professor Wasserman include: Mead Johnson Award in Nutrition (1969) from the American Society for Nutrition; Burroughs Lectureship at Iowa State University, 1974 and 1987; Prix Andre Lichtwitz Prize from Institut National de la Santé et de la Recherche Médicale-Paris, 1982; MERIT Award from the National Institute for Diabetes and Digestive and Kidney Diseases, 1989; William F. Neuman Award of the American Society for Bone and Mineral Research, 1990; Fellow, American Society for Nutrition, 1992; Guggenheim Fellowships, with H. H. Ussing, 1964–65, and with A. D. Care, 1972. Honorary society inductions included Phi Kappa Phi, Sigma Xi, Phi Zeta, and Gamma Sigma Delta.

Due to his many achievements and fundamental discoveries, he was inducted into the National Academy of Sciences in 1980, and was a member of the Applied Biology and Agricultural Sciences section. He was the first and only faculty member of the College of Veterinary Medicine at Cornell to receive this recognition.

Cornell honored Wasserman as the James Law Professor of Physiology in 1989.

Sabbatical leaves were at the University of Copenhagen 1964–65, University of Leeds (1972), Woods Hole Marine Biological Laboratory (1981), and National Institute of Aging (1982–83).

Professional Service

Service to the profession included: NIH General Medicine B Study Section; Editorial Boards of the -Proceedings of the Society for Experimental Biology and Medicine,

Cornell Veterinarian, Journal of Nutrition and Calcified Tissue Research; committees of the American Institute of Nutrition (now ASN); Chair of Gordon Research Conferences; NAS/NRC Food and Nutrition Board membership; and Chair of the NRC Committee on the Scientific Basis of Meat and Poultry Inspection. He participated in over 40 international conferences on calcium metabolism, bone health, calcification, and vitamin D.

A Warmly Remembered Colleague

Curtis S. Fullmer, a Cornell University-based scientist who worked with Wasserman for 30 years, recalls his mentor's "quiet thoughtfulness and unending interest in learning. He never gave up. He would teach courses in a variety of subjects so he could stay abreast in those fields. He was one of the best people I ever knew. You don't continue working for someone for 30 years if they're not remarkable."

Francis A. Kallfelz, emeritus professor of veterinary medicine at Cornell University, worked with Wasserman as a veterinary student and Ph.D. candidate. Kallfelz stated, "He was a good boss, patient in his directives, forgiving and encouraged interest. He never failed to credit his students. He was a brilliant, generous, supportive, and enabling mentor, and had a modest and gentle nature—personality traits that are very rare in scientists that have reached his level."

Jesse P. Goff, professor of veterinary medicine at Iowa State University, stated, "He was such a legend to us as a scientist, but I remember how impressed I was at how genuinely modest he was and interested in what us young scientists were doing!"

Sylvia Christakos, distinguished professor at Rutgers, New Jersey Medical School, stated, "I have kept in touch with Bob ever since I was a post-doctoral fellow studying the function and regulation of calbindin (a main focus of my research throughout my career). Bob was always supportive of my work and provided outstanding advice and perspective. One year before he died, I was invited speaker at Cornell. Bob attended my presentation. He went to dinner with us where he discussed findings in the current literature still providing excellent perspective and thoughtful insight. We have lost a great scientist. I have been most fortunate to have known Bob as a friend and mentor."

Douglas McGregor wrote as part of a Cornell tribute: "Wasserman was recognized as a gifted teacher and role model for individuals who aspired to a career in science." He had "a passion for accuracy and a penchant, whenever possible, to quantify the kinetics of chemical and biological reactions."

Family and Personal Life

Robert Wasserman was married to Marilyn Joyce Mintz on June 11, 1950, in Ithaca. They met while Marilyn, a native Ithacan, was a home economics major at Cornell, where she graduated in 1950. They had three daughters: Diane Jean Herrup (Pittsburgh, Pennsylvania), Arlene Lee Wasserman (Ithaca) and Judith Rose Wasserman (Morgantown, West Virginia), born in 1952, 1954, and 1958, respectively. He has four grandchildren in whom he had shown endless interest. Robert is also survived by his sister Lois Bluestein. He is remembered by many friends as having an unwavering devotion to his family.

Wasserman loved to design and build furniture, create welded steel structures, sail on Cayuga Lake, play poker with a regular group, appreciate music of all types, root for the New York Yankees, and sip Danish beer.

Wasserman passed away peacefully on May 23, 2018, in Ithaca, New York. Funeral services were held at Temple Beth-El in Ithaca.

ACKNOWLEDGMENTS

The authors acknowledge that sources of the material to this memoir included obituaries from the Ithaca Journal and Cornell Chronicle and Douglas McGregor, biographical information provided to the NAS by Professor Wasserman in the form of a curriculum vitae with full bibliography. Scientific descriptions and interpretations were derived from analysis of the literature by RJC and SC.

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