This elegy is written on the occasion of the sudden death, on April 15, of Steven C. Hebert, MD, the C.N.H. Long Professor of Physiology and Medicine, Chairman of the Department of Cellular and Molecular Physiology at Yale School of Medicine, and Treasurer of the ISN. This elegy is all the more poignant because Steve, although remarkably successful, had not yet reached his full potential as a brilliant investigator, chairman, and teacher and because he was clearly a person cherished by his family, his friends, and the academic community. Here I pay tribute to the man and mention briefly his exceptional scientific achievements.

Steve was destined for greatness. He skipped two grades in high school, finished college in 3 years and, in 1966, entered the University of Florida College of Medicine, Gainesville. There he became interested in the work of Thomas Maren on carbonic anhydrase and in the work of Robert Cade, who developed Gatorade. A third individual who stimulated Steve’s intellect enormously was the famed Lester Dragstedt, who did the first truncal vagotomy at the University of Chicago before retiring to Gainesville. Steve was awed by Dragstedt’s intellect.

I first met Steve in 1970, having arrived at the University of Alabama School of Medicine, Birmingham, as Director of Nephrology, and Steve arrived, at the same time, as a Medicine intern. I was fortunate to recruit him to Nephrology, and after his residency, he served as a Fellow in the Division of Nephrology, 1973 through 1975, then served in the military and rejoined my laboratory again in 1977, working together with James Schafer, now Professor Emeritus of Physiology at UAB, and Michael Culpepper, now Director of Nephrology at the University of South Alabama College of Medicine, Mobile. Our Saturday laboratory meetings, including Steve, Jim, Mike, and me were clearly a high point of the week. The meetings were genuine intellectual jousts of high order, always carried out in a spirit of warmth and friendship. After the laboratory meeting, Steve and Jim, in particular, would dissipate the heat of intellectual exchange with games of racquetball, also intensely competitive and friendly between the two of them, followed by long sessions of beer-drinking.

In the laboratory, Steve’s productivity was dazzling. He learned isolated tubule perfusion of cortical collecting tubules from Jim Schafer. That work culminated in explaining the disparity between osmotic and diffusional effects of ADH on apical membrane water transport. Hebert and Schafer argued that the ADH-dependent water channels inserted in apical membranes transported water by single-file diffusion, thus excluding urea. The work coincides precisely with the description of the aquaporin water channels by the Nobelist Peter Agre.

Steve then began what turned out to be a life-long interest in the medullary thick ascending limb (mTAL). First, Steve and Mike Culpepper showed that ADH augmented salt and water absorption in mTAL segments. They also found that there was functional nephron heterogeneity, because the response to vasopressin was limited to medullary but not cortical thick limbs.

Steve also supervised, meticulously so, a dialysis unit at the Birmingham VA Hospital. There he took exceptional interest in staffing patterns, patterns of dialysis, and meticulous patient care.

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singly cordial place in which to learn the principles of dialysis, and Steve was universally regarded as a splendid teacher.

In 1979, Steve and Mike joined me at the University of Texas Medical School, Houston, where I had been appointed Chair of Internal Medicine. There Steve assumed full responsibility as a clinician on our Nephrology consult service. He earned the strong respect of fellows, students, and house staff and distinguished himself as an excellent clinical teacher and nephrologist. He also developed the Mechanisms of Disease Course for the Department of Internal Medicine, providing a course for sophomore medical students that was of the highest scientific caliber.

Our laboratory in Houston consisted of Steve, as the senior collaborator, and co-investigators Mike Culpepper and Peter Friedman, now Professor of Pharmacology at Pittsburgh. Peter amplified the notion of functional heterogeneity by showing that $CO_2$ augmented the rate of NaCl absorption in cortical but not medullary thick limbs, a finding consonant with the fact that the renal cortex has a high $pCO_2$. In subsequent years, W. Brian Reeves, now Professor and Director of Nephrology at Penn State University, and Donald A. Molony, now Professor of Medicine at the University of Texas Medical School at Houston, joined the lab. Brian and Don, after Steve’s departure, showed that ADH increased basolateral $Cl^-$ conductance by raising cytosolic calcium, a finding again consistent with the fact that ADH exerted an admittance effect on NaCl entry in the mTAL. Our lab meetings, occupying the better part of all of Saturday, were again intellectual free-for-alls combined with great personal warmth. Steve’s brilliance dominated, to a very great extent, these felicitous and productive encounters.

In 1984, he joined the faculty at Harvard Medical School and Brigham and Women’s Hospital in the Department of Medicine, Division of Nephrology. In a short time, he rose to the rank of Professor.

At Harvard, he maintained his consistent interest in the mTAL but shifted his approach to analyzing mTAL transport events to molecular renal physiology. Among other contributions, he cloned ROMK, the ATP-sensitive $K^+$ channel, which was, at the time, the first channel discovered with only two membrane-spanning domains; the thick limb Na$^+$/K$^+$/2Cl$^-$ apical (NKCC) salt transporter and the thiazide-sensitive apical NaCl salt transporter.

It may be that, in the long run, his greatest contribution was his discovery, together with Ed Brown, of the calcium-sensing receptor (CaSR), which senses changes in extracellular fluid calcium. CaSR is the first known sensing mechanism for the concentration of ions in extracellular fluid. Steve and Ed Brown also described calcimimetic agents, which can down-regulate the activity of CaSR independent of the level of serum calcium.

In 1997, he became the Ann and Roscoe R. Robinson Professor of Medicine, Physiology and Cell Biology and Director of the Division of Nephrology at Vanderbilt University School of Medicine. In 2000, he assumed his current position as the C.N.H. Long Professor of Physiology and Medicine and Chairman of the Department of Cellular and Molecular Physiology at Yale School of Medicine. At Yale, Steve, together with John Geibel, described suppression of cholera-mediated fluid secretion in intestinal crypts of rat small intestine by activating CaSR with calcimimetic agents. The latter set of observations may be Steve’s greatest legacy, because they hold open the possibility of curing cholera and other secretory diarrheas with a simple pill.

Steve was widely honored, including his receipt of the Homer Smith Award from the American Society of Nephrology, the Carl W. Gottschalk Award of the American Physiology Society, the Alfred Newton Richards Award from the International Society of Nephrology, and, most recently, his election to the National Academy of Sciences.

Steve’s activities were not limited to dazzling renal physiology, superb clinical medicine, and elegant teaching. He also launched a biotech company, MariCal, based in Portland, ME, concerned with enhancing the growth rate of maturing salmon. As a second development, he formed the Pearl Development Group, a pearl-culturing venture in the South Seas. Both of these activities derived from his interest in the interrelations between calcium and magnesium. As it happens, at a celebration in 2004, Steve presented my wife, Elizabeth, with a lovely pair of black pearl earrings, a product of the Pearl Development Corp., which she cherishes.

Steve had a remarkably felicitous marriage with his charming wife Pat for 38 years and a singularly principled and intelligent son, Steve, Jr. Steve was a devoted family person, a wonderful friend, a scholar with an exceptional sense of humor, and, to close the loop in an unexpected way, a vigorous manual worker who reveled not only in racquetball but also in carpentry, home remodeling, and painting. He found a genuine joy in these heavy manual chores on weekends.

This is an elegy lamenting our loss, but we should celebrate Steve the man and his exceptional contributions, and we should remember fondly this remarkable scholar and friend with cherished memories.