On the Passing of Thomas E. Andreoli

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The death of Tom Andreoli deprives American medicine of a gifted scholar and an academic leader.

A creative renal physiologist committed to biomedical research at the most basic level, he simultaneously dedicated himself to patient care and teaching, thereby constituting a model of the clinical scholar. As a chairman of medicine, he was able to discharge formidable financial and administrative responsibilities without impairing the cultivation of scholarship as it interacts with clinical medicine and student teaching. At the time of his death, he was busily engaged in ward rounds, morning report, and the editing of the eighth edition of Cecil Essentials of Medicine.

Tom Andreoli was born on January 9, 1935, in a poor Italian neighborhood in the borough of Bronx, NY. His mother and two aunts raised him in an extremely devout Catholic household. At their insistence, augmented by priestly support, he enrolled in a small Benedictine college, St. Vincent College, in Pennsylvania, where he graduated cum laude in 1956. He then attended Georgetown University for his MD degree, graduating magna cum laude in 1960.

In 1960, Tom left for Duke, where, after housestaff training, he rose to faculty rank of associate professor of medicine by 1970. Two individuals left a profound imprint on Tom’s subsequent career. Eugene Stead, the Chairman of Medicine at Duke, was revered by Tom as the ultimate expression of an academic leader. The tradition of morning report, ward rounds with meticulous attention to individual patients, and research, were instilled into Tom as necessary ingredients for a career as an academic leader. Stead, in turn, early identified Tom’s intellectual gifts and provided him with special opportunities. His progress as a house officer and fellow was so arranged as to allow for a period of training at the National Institutes of Health and then as a research fellow in Dan Tosteson’s laboratory. This latter activity was the second formative influence at Duke. Tom brought with him an easy mastery of mathematics and physics, and these talents were channeled in Tosteson’s laboratory into a life-long study of the biophysical properties of cell membranes in the analysis of the transport of water and electrolytes.

In July 1970, Tom left Duke to assume the position of director of nephrology at the University of Alabama. There his talents as an academic leader began to emerge. He quickly developed programs of hemodialysis and nephrology consultation and was awarded research grants from the National Institutes of Health, the American Heart Association, and the John Hartford Foundation. A distinguished faculty, consisting of new recruits or previous trainees, was assembled: Don DiBona, Steve Hebert, Gabby Navar, David Ploth, Jim Schafer, Steve Rostand, Ed Rutsky, and others. Under his leadership, the research program flourished. Extensive editorial work on a variety of journals and books was undertaken, aided by Clementine Whitman, his personal secretary, who remained with him throughout his subsequent career in Houston and Arkansas.

In recognition of his academic leadership and outstanding investigations, Tom became an attractive candidate for chairmanship of a department of medicine. In 1979, he assumed such a post at the University of Texas School of Medicine in Houston. His teaching, clinical, and research activities flourished; a distinguished faculty was assembled, consisting of Steve Hebert, Ed Weinman, Brian Reeves, and others. He worked tirelessly to form a department organized after the program established at Duke by Stead; however, the academic autonomy of the medical faculty was challenged by the hospital administration, demanding far more extensive commitment to clinical service. Seven of the department chairmen, including Tom, left their positions.

Offers of other chairs in medicine were not long in coming, and in 1988 he accepted an appointment as chairman of internal medicine at the University of Arkansas School of Medicine, a position he held until his death on April 14, 2009. There, too, he plunged tirelessly into the task of forging a distinguished academic department, installing morning report, ward rounds, individual patient care, and scientific research—all welded together in the manner he had inherited long ago from Stead. There, too, distinguished faculty such as Robert Safirstein, Hugo Jasins, and others were appointed. Tom’s death—a legacy, no doubt, in part from smoking, hamburgers, and French fries—was the consequence of a cerebral hemorrhage associated with dicumaral therapy.

This review of Tom’s career does scant justice to the diversity of his accomplishments and interests. It seems appropriate to call attention to his achievements in the several areas that define an academic career: After training with Tosteson...
at Duke University, Tom launched an independent research career in which he became a major force in the characterization of the basic mechanisms by which epithelia in general and renal tubules in specific transport solutes and water. After initially working in lipid bilayers, by which he examined the effect of unstirred layers on transport rates, Tom was one of the early investigators to adopt the use of the in vitro perfused renal tubule. Whereas many other investigators in the field used this technique merely to determine which physiologic functions were performed by which segments, Tom and his group were the first to address the question of the biophysical mechanisms for transport. In an initial in-depth analysis of proximal tubule NaCl transport, which included numerous publications, Tom and his colleagues determined the various components of NaCl transport that were due to active transcellular NaCl transport, active rheogenic transcellular Na transport with passive paracellular Cl transport, passive paracellular NaCl diffusion driven by chemical gradients, and solvent drag. Their meticulous approach to defining these mechanisms set a standard for analyzing transport in perfused renal segments, which has now been followed by many subsequent investigators.

A second area that Tom and his group addressed was the mechanism responsible for water transport in the proximal tubule. Although lateral intercellular space hypertonicity had been the accepted mechanism for this process, a number of mathematical models had found that this explanation was not feasible. Tom and his group developed the theory that luminal hypotonicity rather than peritubular hypertonicity provided the osmotic driving force for water movement. Subsequent studies by their group and by other groups have lent strong support to this theory. A key point in this regard was the development of methods by Tom to measure the water permeability of the proximal tubule, which is extremely high.

Tom’s next major contribution was in his studies investigating the mechanism by which ADH increased water permeability of the collecting tubule. Using his biophysical background, he first determined the unstirred layers in series with the cell membranes to characterize water movement. These studies demonstrated that the rate-limiting step for water movement was the apical membrane of the collecting tubule and that this was the membrane whose permeability was increased by ADH. This conclusion subsequently was verified by numerous studies. In addition, on the basis of a large set of observations, Tom and his group concluded that water crosses the apical membrane of the collecting tubule by single-file diffusion through narrow aqueous channels.

Finally, he applied the same meticulous and thorough approach toward examining cellular mechanisms by which the thick ascending limb transports NaCl, as well as the mechanisms by which these processes are regulated. When Tom and his group entered this area, the mechanism responsible for the lumen-positive voltage and NaCl absorption in the thick ascending limb of the loop of Henle was unknown. Tom’s group was one of two major groups that helped to develop a cell model and prove this model was indeed correct. After helping to define the transporters responsible for NaCl absorption in the thick ascending limb, Tom and his group made the very important finding that ADH, in addition to increasing water movement in the collecting tubule, helped to generate medullary hypertonicity by directly increasing NaCl absorption in the medullary thick ascending limb. His investigations into the medullary thick ascending limb used standard tubular microperfusion but in addition involved technically innovative approaches such as preparation of membrane vesicles from this segment, puncturing of thick ascending limb cells with microelectrodes, and the study of ion channel activity by insertion of channels into lipid bilayers.

These probing, meticulous studies, extending all the way from organ physiology to molecular biology, constitute a major foundation for the explanation of the concentrating and diluting powers of the kidney. In recognition of the high quality of his research, he received the most distinguished awards in his discipline: The Homer W. Smith Award of the American Society of Nephrology in 1995, the David M. Hume Award of the National Kidney Foundation in 1977, and the Robert W. Berliner Award of the American Physiologic Society in 2000.

Tom also enjoyed greatly editorial activities. He was a senior editor of leading textbooks in medicine—Cecil Textbook of Medicine and Cecil Essentials of Medicine—and in physiology—Physiology of Membrane Disorders. He held editorial board positions on multiple journals, two of which deserve special mention. From 1976 through 1983, he was the editor-in-chief of the renal section of the American Journal of Physiology. When Ike Robinson retired as editor of Kidney International in 1983, Tom was a logical successor. This appointment had to be approved by the council of the International Society of Nephrology, especially its president. Tom was laggard in appearing for an interview and received a stinging presidential rebuke at the council meeting. After he was cautioned about the importance of due deference to Napoleonic figures, he appeared 30 min early for his second interview. The council received a glowing report of Tom’s reformation, and his appointment as editor-in-chief of Kidney International followed quickly. He served from 1984 through 1997 and forged a major unification of basic renal physiology with clinical nephrology.

Despite the sophistication of his research program, Tom delighted in clinical medicine. Morning report was not only a review of clinical admissions but also a congenial interchange with house officers, often involving bets and contests. Ward rounds were conducted in a personal manner and included intimate contact with individual patients as a basis not only of medical care but also of clinical teaching. The cultivation of promising students along academic lines was a particular joy, and the successful careers of important figures in academic medicine that emerged from his programs are eloquent testimony to the rich rewards of such relationships.

Tom was completely dedicated to academic clinical medicine. It is fascinating to note that although his research was conducted at a very fundamental level, basic scientists were not his heroes. There is little doubt that Stead formed the model for
his academic career. No matter how important the research, his special joy was interaction with students and house officers about clinical problems. In a genuine sense, he viewed himself as a clinical scholar and sought to emulate the distinguished figures in that domain. Tom was a model for Flexner’s view of the academic clinician, and it is no surprise he was elected president of both the American Society of Nephrology and the International Society of Nephrology.

Personally, Tom was an individual dedicated to the highest standards of quality. Despite his remarkable intellectual abilities, he was warm and generous—readily appreciative of the performance of individuals who were less gifted than he and perhaps working in disciplines remote from his own. It is true that he was intense and hard driving; however, these qualities were embraced in an overall context of humane warmth and rich appreciation for the multifaceted requirements of clinical medicine and academic work.

Nevertheless, Tom was something of an enigma. His conservative dress was wedded to a somewhat stylized manner. His speech was sometimes precious, loaded with adjectival qualifiers such as “elegant,” “felicitous,” etc., yet at the same time, his interests were probing and penetrating. It is not surprising that a son of the Bronx would love the Yankees, Joe DiMaggio, Frank Sinatra, Italian opera, and dogs, but it is especially revealing that he was profoundly moved by great painting and collected carefully a group of small works of high quality. He particularly prized a Modigliani drawing and several small works by French impressionists, but his deepest fascination was with Caravaggio. How a murderer and a thief could create the great paintings such as the Beheading of St. John in Malta or the St. Matthew Cycle in the church of San Luigi dei Francesi in Rome was an unfathomable mystery. Clearly, the rational calculus could not explain everything. In committing himself to a love of the mystery and profundity of painting, no less than a love of medicine, the depths of Tom Andreoli are revealed.

Along with Elizabeth, we too shall miss him.