
LEGENDS IN UROLOGY

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When *The Canadian Journal of Urology* (CJU) asked me to contribute an autobiographical article to the Legends in Urology section of the CJU, I was at first reticent and concerned that I may be providing my own obituary. They asked me to discuss my contributions to urology from a personal perspective, and what motivated me to the career that I pursued and continue to pursue. They also wished me to address the accomplishments that I am most proud of and to provide a motivational message to young urologists. Those who know me, know that I would never have thought of such a project on my own. However, after reading previous contributions to this series, I was honored, flattered, and humbled to be included.

Wilbur Wright who is credited with inventing, building, and flying the world's first successful airplane, said, "If I were giving a young man advice as to how he might succeed in life, I would say to him, pick out a good father and mother, and begin life in Ohio." I was not born in Ohio, but rather in New York City, and indeed, my first mentor was my father, David Weiss who was a general surgeon. After he returned from a tour in New Guinea during WWII, we moved to Forest Hills where I attended high school. Although I cannot say that I was a great athlete, I can say that I was captain of a team - the math team - which included Lubert Stryer who wrote the Biochemistry textbook that many burgeoning urologists have used.

I spent 3 years at Franklin and Marshall College in Lancaster, PA. I was scheduled to go to Columbia, but here my mentor, my father, made sure that I leave NYC and go to a small school, as long as it was not coed. No distractions. Franklin and Marshall College focused on science and there I interacted with Stan Dudrick, who subsequently put hyper-alimentation on the map. F & M required a course in public speaking which proved important to a compensated introvert, destined for a career in academics. Serendipity!

I discontinued my studies of mathematics to enter medical school in 3 years. I believe mathematics and urology have much in common. In both, an organized thought process leads to a correct plan of action. At the State University of New York, Downstate Medical Center, I worked in the Department of Pharmacology with Dr. Kwang Soo Lee, a biochemist, studying cardiac muscle. An important early mentor. In his lab I studied glycerinated heart muscle. Little did I realize that the study of muscle would be the foundation for my future career. Serendipity! Dr. Robert Furchgott who subsequently received a Nobel Prize for identifying a factor in the endothelium that led to vascular smooth muscle relaxation, ie., nitric oxide, was the Chair of Pharmacology. In the future I would be PI of a NIH grant directed at the role of nitric oxide in inflammation. Not planned, but fortuitous.

In medical school we were brainwashed that Internal Medicine was for those who were smart. I thus spent a year as an intern on the Cornell Division of Internal Medicine at Bellevue Hospital. The strong resident group included Joe Fraumeni from the Li-Fraumeni Syndrome. Adversity, however, was near by. Uncle Sam wanted me. My approach was to plead with the head of the draft board to let me finish my residency. He refused, which in retrospect was the best thing he could have done for me. It gave me time to decide on a career in urology, and increased my desirability to the top departments in the country, since I had already completed my service commitment when others were being taken to serve in Vietnam. I have always considered this episode in my life to parallel the story of the Siberian

sparrow who left the warmth and security of the nest to fly in the arctic air. Frozen, he fell to the snow-covered ground and surely would have died if not for the chance passing of a cow that dropped a large cow-dung on top of him. Its warmth resuscitated the sparrow who began to twitter, which drew the attention of a homeless cat that pulled the sparrow out of the dung and devoured him. The moral is that “he who shits on you is not necessarily your enemy and he who pulls you out of it is not necessarily your friend.”

Fifty percent of my tour of duty was in Camp Century Greenland, “The City under the Ice”, a nuclear powered base 50 feet under the surface of the icecap, 138 miles northeast of Thule, and 800 miles from the north pole. On awaking each morning I would quote Voltaire, “All is for the best in this best of all possible worlds” and use my time to read urology, listen to Mahler and Bartok, play chess, and drink martinis. The other half of my tour was in Fort Belvoir, Virginia, where Art Peck, a young urologist who had recently finished residency at Walter Reed, became another serendipitous and important mentor. He shared with me his insight that many of the leaders of urology had built their careers by becoming experts in a small circumscribed area. Within months I had applied to urology residencies and accepted Dr. John Lattimer’s offer to join the program at Columbia.

Dr. Lattimer was someone to emulate. He earned his reputation by becoming the leading expert in a very circumscribed field, GU tuberculosis. In addition, he was one of the founding fathers of pediatric urology, my future clinical area of expertise. Shortly after beginning my residency, Dr. Lattimer received one of the first NIH sponsored training grants. Having failed to fill the slots with fully trained urologists, he turned to his most junior resident, me, and told me that I was to spend the next year in the lab. I pleaded that I had just spent approximately 2 years in the service, and it was time for me to become a clinician. Dr. Lattimer would not take no for an answer, and off I went to the lab and the best and most important year of my training. Here, again, what I conceived as adversity turned out to be the biggest favor he could have done for me. The consequence of apparent adversity has been a strong mantra for me: as Marcus Aurelius said, “Our actions may be impeded.....but there can be no impeding our intentions or dispositions.....the impediment to action advances action, what stands in the way becomes the way.” Or in the words of the Cathaginian general, Hannibal Barca - *inveniamus viam aut faciemus* (we will find a way or we will make one).

Remembering my previous training I approached Dr. Brian Hoffman, David Hosack Professor and Chair of Pharmacology at Columbia. David Hosack was the physician who cared for Alexander Hamilton after he was shot. Dr. Hoffman was a cardiac electro-physiologist who had previously been at Downstate. When I entered his office I told him that I wanted to study glycerinated ureteral smooth muscle. Dr. Hoffman grunted, as was his way, turned to his drawer of reprints, and pulled out an electrical tracing that had been published by Orbelli and von Brucke in the German literature in 1910. Although it looked like an electrocardiogram (EKG) it was an electromyogram from ureteral smooth muscle. Dr. Hoffman had been impressed by how much the ureter resembled the heart. Brian Hoffman proved to be an important mentor and thus began a collaboration lasting over 25 years. I ultimately achieved the rank of Adjunct Professor of Pharmacology at Columbia. Although my planned studies of glycerinated ureteral smooth muscle did not pan out, I did publish a paper in *Nature* on the electrical potentials in glycerinated cardiac muscle. Predicated on the similarities between the heart and the ureter, I published papers on the localization of the ureteral pacemaker, Wenckebach phenomenon in the ureter, and the effect of cardiac glycosides on ureteral contractility.

Upon completing my residency I made the most important decision of my career. I decided on academics even though there was a several-fold difference in financial compensation from private practice. I also took the correct fork and joined Bernard Lytton at Yale who was supportive of my career and has been a life-long friend.

Academia offered a dynamic and interesting career. Over the years I was selected as a member of the American Urological Association and American Board of Urology Exam Committee, an Associate Editor of the Investigative Urology Section of the *Journal of Urology*, a member or chair of numerous NIH and DOD study sections, a Trustee of the American Board of Urology, and numerous Visiting Professorships and Invited Lectureships in North America, Europe and Asia. In addition, I was elected to membership in a number of prestigious academic societies including the American Association of Genito-urinary Surgeons, the Clinical Society of Genito-urinary Surgeons, and the American Surgical Association. Along the way I served as Chief of Urology and Interim Chair of the Department of Surgery

at Yale. I also was President of the New England Section of the American Urological Association, President of the Clinical Society of Genito-urinary Surgeons and President of the American Association of Genito-urinary Surgeons.

My research career was marked by navigating a series of forks in the road. As Ralph Waldo Emerson prudently guides us, “Do not go where the path may lead, go instead where there is no path and leave a trail.” My first years focused on studies of the electrophysiologic and contractile properties of ureteral smooth muscle. During that time I was fortunate to collaborate with Arthur Bassett, a physiologist, Piero Biancani, a biomedical engineer, and Michael Rosen a cardiac electrophysiologist.

In 1975 my studies took a more biochemical direction. As a surgeon-scientist this was an important change that permitted me to split my time between the lab and the clinic. I spent a sabbatical with Dr. Joel Hardman, Professor of Physiology and subsequently Chair of Pharmacology at Vanderbilt. He was a pharmacologist and biochemist who wished to increase his knowledge of smooth muscle physiology, and I was a smooth muscle physiologist who wished to learn a more biochemical approach to the function of smooth muscle - a great collaboration and friendship which was renewed at annual Gordon Signal Transduction Conferences. Joel had taken over the lab of Earl Sutherland who received the Nobel Prize for cyclic AMP, and my research became directed to the role of cyclic nucleotides in smooth muscle function. Jamshid Latifpour, a receptor pharmacologist, and Marcia Wheeler, a biochemist, joined me in the lab and we had a fruitful collaboration in the study of uretero-vesical smooth muscle. During that time we mentored numerous international fellows and residents. Training future clinicians and scientists is our future.

In the early 90s, we reached another fork in the road and our focus changed to the role of nitric oxide in urinary function. We showed that nitric oxide was involved in urethral relaxation and were the first to show the presence of inducible nitric oxide synthase (iNOS) in human polymorphological leukocytes. This was possible because we, as urologists, studied urine, whereas basic scientists had not. The most recent fork occurred when in collaboration with Dr. W. Mark Saltzman, Chair of Biomedical Engineering at Yale, we functionalized nano-particles to transport agents into bladder smooth muscle. The most successful aspects of these studies turned out to be the administration of siRNAs and chemotherapeutic and diagnostic agents for the localization and treatment of bladder and prostate cancers. Darryl Martin, a molecular pharmacologist, recruited from Newfoundland, Canada, was instrumental in these studies. When we reached each fork in the road we took it.

The CJU asked what honors I was most proud of. I was the first urologist to receive an NIH Merit Award, received a Lifetime Achievement Award from the Urodynamics Society in recognition of significant contributions and leadership in the field of Neurourology, the Keyes Medal awarded by the American Association of Genitourinary Surgeons for “outstanding contributions in the advancement of Urology”, (this is recognized as the greatest individual citation from that society and has been awarded sparingly), the John W. Duckett, MD Pediatric Urology Research Excellence Award, and in 2018 I will receive the Pediatric Urology Medal from the American Academy of Pediatrics. Although I have received many awards for my research and clinical contributions, I look back with most pride to maintaining and advancing an excellent Section of Urology at Yale that had previously been lead by Clyde Deming, B. Marvin Harvard and Bernard Lytton, and turning an excellent program over to Peter Schulam who has lead the expansion from a section to a department. But, perhaps the greatest pleasure has been to mentor many young investigators and clinicians who are the future of our specialty. Beyond all the prestigious awards I was most honored in reading a faculty review by the Yale Urology residents, which stated, “Dr. Weiss is the kindest best teacher a resident can ask or hope for. Overall [he] continues to be one of the best surgical and medical instructors in the field. He cares about the residents, he cares about the patients. If I end up one tenth the man or the physician Dr. Weiss is, I will have led a wonderful life.” We need collaborators, we need mentors, and in turn we need to mentor the next generation. I also take great joy in knowing that my two children considered me a positive mentor and are both in academic medicine – Erik is double boarded in radiology and nuclear medicine in the VA system in Phoenix and Dana is a pediatric urologist at the Children’s Hospital of Philadelphia– and most importantly they both have suffered with me as New York Jet fans.

My career and happiness were shaped by mentors and friends, the ability to collaborate with others in different fields of expertise, serendipity, the ability to gain from rather than be defeated by adversity, picking an important yet focused area of study, and remembering Yogi Berra’s aphorism “When you come to a fork in the road, take it”

– and there were many forks. Most important was selecting the ever changing excitement of an academic career. I never forgot the First Law of the Arctic which pertains to the dog sled, “Only the lead dog has an interesting and changing view, to the others the view is rather monotonous”. I realize and appreciate that this career, with the added time commitment and decreased financial compensation, required a supportive spouse. Ilana has been that.

To end it is important to remember the Percy Bysshe Shelley poem of Ozymandias.

“I met a traveller from an antique land,
Who said—“Two vast and trunkless legs of stone
Stand in the desert.....
And on the pedestal these words appear:
My name is Ozymandias, King of Kings;
Look on my Works, ye Mighty and despair!
Nothing besides remains.

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