LEGENDS IN UROLOGY

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I received a flattering request from Dr. Gabriel Haas, Editor of The Canadian Journal of Urology. It was his idea to publish articles on recollections of senior urologists (old dinosaurs) with what he described as "stories of interest to the readership" in a new section to be called Legends in Urology. As I frequently do, I had to consult my faithful Standard College Dictionary,[1] where a legend is defined as "*an unauthenticated story from earlier times, preserved by tradition and popularly thought to be historical*". An alternative definition was "*a romanticized or popularized concept of a person*". Ummm…I thought that my involvement with the treatment of bladder cancer might qualify for the former, although such involvement has been *authenticated* in the medical literature. The other, the *romanticized* thing, certainly would not qualify. I agree to put down on paper a story of earlier times because it contains several lessons that, in my view, could be profitable for young urologists of both private as well as academic plumage.

Let me rush to explain that below you will find nothing that comes close to a legend; rather personal ruminations and faded memories of events in the life of a urologist. I would like to start by quoting Alan Alda of M*A*S*H* fame who in his unique style, described flattery as the door to embarrassment.[2] Having overcome my embarrassment, here is my story or perhaps, more appropriate, my "single case report".

Upon my appointment in Urology at Queen's University in the 1970s I found myself full of enthusiasm for an academic career. A few years back great strides were made in the field of tumor immunology with the development of syngeneic mice and the ability to transplant tumors for study of immunological mechanisms. Immunotherapy appeared to be promising.

Let's recall the exciting if simpler, state-of-the art of cancer immunology in those days. In the late 1960's researchers at NIH had established the criteria for successful Bacille Calmette-Guerin (BCG) immunotherapy in guinea pigs (small tumors, direct contact between tumors and BCG, an immunocompetent host, an immunogenic cancer and an adequate dose of BCG). On reading these studies, it became obvious to me that non-muscle invasive (NMIBTs) or superficial, as we used to call them, bladder tumors would be the ideal target for immunological manipulation. An application to the National Cancer Institute of Canada was soundly rejected with a reviewer commenting that BCG was not only ineffective and dangerous but "a throw back from the stone age of tumor immunology". Pretty discouraging comments from some faceless but, in my imagination, knowledgeable individual. Discouraged but not defeated, I decided to apply to the Cancer Research Institute of New York (CRINY) for support. The reason being that the CRINY was founded by Mrs. Helen Coley Nauts, the daughter of W. B. Coley, a New York City cancer surgeon, who first reported on the use of a bacterial preparation to treat cancer in the early 20th century. She was determined to prove her father's theories right. The application was successful. If I may digress for a moment… those were the days when Richard M. Nixon had, with great hyperbole but also great naivety, announced his determination to "conquer cancer" as his more visionary but better informed predecessor, JFK, had successfully put in motion the resources to put a man on the Moon "within a decade". Nixon's vision certainly made a remarkable amount of funds available for the fight against cancer. But let's refocus…with a team of basic and clinical researchers, at Queen's, we conducted the initial studies showing a decrease in the recurrence rate of NMIBTs which were published in 1976[3] and 4 years later the first successful experience in the treatment of carcinoma-in-situ with the intracavitary administration of BCG.[4] The remarkable thing here is that the total number of patients for both open-labeled, single arm trials was just about 20. They were, however, followed closely and their progress recorded carefully. Years later controlled, randomized studies (conducted by others) with hundreds of patients, extraordinarily close duplicated our initial observations. As it is often said, "the rest is history".[5]

Progress in oncology is rather slow and tedious. Clinicians are, frequently, at a disadvantage in competing for support with our colleagues in the basic sciences. Therefore, without completely abandoning my commitment to oncology, I diverted some of my free time to other interests: sexual medicine/andrology. In those pre-intracavernosal injections and, certainly, pre-Viagra years, the choices were limited but the field for research was widely open. Our team did a number of studies in diagnostic techniques (from psychological assessments to complex sleep studies) for ED (a.k.a impotence, then) and developed the first central acting erectogenic drug for oral use (the fact that it was not approved by the FDA is another story). My incursion into the field of Andrology proved to be a rich and rewarding experience.

Of late, I have returned to my old interest in urological oncology and am currently involved in a number of trials of compounds, hopefully as effective and safer than BCG. Time will tell. This multivariate approach to my professional career is a powerful testimony to the rich opportunities that Urology offers in many fields that range from the humble vasectomies to the complexities of transplantation and from the abundance of oncology, sexual dysfunction and andrology, to the rarity of congenital deformities and reconstructive surgery. From the simplicity of circumcisions to the challenges (to the robot?) of laparoscopic and robotic surgery. Ours is truly a splendid specialty brimming with opportunities and possibilities of discovery.

Why all these long reminiscences? Simply as background for the message to my younger colleagues.

The main purpose of our training is to establish a career as well informed and skillful urological surgeons, look after patients competently and to the best of our ability, prepare for retirement and then fade away as graciously as we can. But there are many detours from this seemingly straight road. The routine performance of our duties leads to boredom which, for some mysterious reasons, seems to coincide with middle age, decreasing levels of testosterone, endothelial dysfunction, glucose intolerance, hypertension (the metabolic syndrome) and the "middle age-crisis". This can be battled in different ways by different folks: sedentary or active hobbies such as breeding horses or dogs, bird watching, acquiring a sports car or more dynamic activities such as a passion for golf, sky diving or bungee jumping. Hopefully, nothing more risky and dangerous than that.

Let me mention the importance of advancing the goals of the specialty as an alternative without necessarily rejecting recreational endeavors. The dramatic progress in surgical techniques and pharmacological treatments experienced over my professional life is simply astonishing. If our deceased predecessors were to resurrect and observe that urolithiasis only rarely requires open surgery, that urinary incontinence is corrected with minimally invasive procedures, that radical prostatectomies are carried out through a few small abdominal openings (and, more recently, through natural orifices) or that BPH and "impotence" are treated with pills, I would suspect that they will collapse (it has not been established if resurrected bodies can suffer syncope) and die again. How has all this progress come about? There is no doubt that it is the results of inquiring minds, each contributing small bricks to this large edifice. Embarking on a journey of discovery is not just by colleagues working in an academic environment. The possibility of participating in clinical trials, accumulating and reporting useful clinical information, is truly open to all. The option to test, patent and publish innovative ideas is not the exclusive domain of the university centers.

We all have a responsibility to enhance the specialty from different angles but research is, probably, the most rewarding because of its lasting effects and because its benefits impact on so many. It may be in the fields as diverse as medical education, surgical techniques, pharmacotherapy, patient education and dissemination of information for the professional and lay publics. It does not matter. Testing ideas is, frequently, frustrating and disappointing but once in a while true progress can be achieved.

In these days when recent graduates, more often than not, expand their knowledge with additional training and fellowships, the opportunity for real contributions to the art and science of Urology is a welcome prospect. For

those who prefer a practice primarily rich in clinical activity and direct patient management, the opportunity to participate in investigative projects generated from other institutions or industry can be very rewarding. Medications, equipment and techniques need to be tested in this era of evidence-based medicine. If we pull together, the advancement in knowledge and improvement in techniques can be accelerated for the benefit of all.

A final word. If an application for support, at first does not succeed, do not blame yourself first you for poor "grantmanship" (it does not change the agency's opinion and does not improve the quality of the application). It might be that your submission needs further tuning … it might not. Occasionally, reviewers are narrow minded, legends in their own minds, lack imagination and farsightedness. Persist, ask honest friends for advice, improve what needs to be improved and re-apply. Research money is currently tighter than ever, most large granting agencies tend to support "centers of excellence". This may not be the best policy since it leaves the individual researcher isolated, discouraged and frustrated. Fortunately, smaller agencies still have the vision and the funds to kick start a career.

I hope these comments will be profitable to my young colleagues. Incidentally, I no longer review grant applications. It is too onerous. So when your application forms ask for "potential reviewers" put someone else, more current and better informed. To paraphrase Yogi Berra, when you come to a fork in your career… take it! One never knows what pleasant surprises might be waiting.

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References

1. Funk & Wagnallis Standard College Dictionary. 9th Edition, Toronto, 1973 p. 772.
2. Alan Alda "*Things I overheard while talking to myself*". Random House, New York, 2007.
3. Morales A, Eidinger D. Bruce A W. Intracavitary Bacillus Calmette-Guerin in the treatment of superficial bladder tumors. *J Urol* 1976;116:180.
4. Morales A. Treatment of carcinoma-in-situ of the bladder with BCG. *Cancer Imunol Immunother* 1980;9:69.
5. Jones JS, Campbell SC. Non-muscle invasive Bladdder Cancer (Ta,T1, ans CIS). Campbell-Walsh Urology. Wein A et al eds. Saunders/Elsevier. Philadelphia, 2007. pp. 2447-2467.