FROM THE EDITOR

Elizabeth B. Yerkes, MD

Thank you to Bryan Sack and Jason Van Batavia for bringing us this Edition of Dialogues. They have drawn upon the wisdom of decades of Pediatric Urology practice. Pioneering, perseverance, philosophy, proactivity, partnership, protected time and practical professional advice are found within this Edition. I am certain that the perspectives of the authors will resonate with you and inspire contributions, both large and small, as the realm of Pediatric Urology continues to evolve!

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FROM THE GUEST EDITORS

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A study of history is a fruitful endeavor because of not only what it tells us about the present, but also because of what it imparts on the future. Philosopher George Santayana said it best when he stated, “Those who cannot remember the past are condemned to repeat it.” While we often think of this in the setting of world history, warfare, and politics, it is also just as important to consider this phrase as it relates to medicine and, yes, even pediatric urology. In fact, clinical and, in particular, surgical training are at their root the ultimate examples of learning from the past – with mentors imparting “knowledge” and techniques based on their prior experience and complications. Wise mentors are often heard both in and out of the operating room saying, “Let me tell you my mistakes, so that you do not have to make them yourself,” or even “We used to do it that way 20 years ago, but now we know you can do it this way.” In the same way, learning about history is important in both helping us understand where we have come from and helping us continue to move forward, make progress, and avoid repeating the mistakes of the past.

The current generation of fellowship trained pediatric urologists are entering a field and health care environment that is drastically different from what our predecessors experienced. We often take for granted that pediatric urology is its own subspecialty and do not necessarily appreciate the effort and work that went into creating and defining our field. The noticeable cringe on the faces of our mentors and senior faculty at the blank stares from trainees when asked about the founders or giants of our field says it all. We, as a discipline, must do better at remembering our history but also at passing this down to each wave of pediatric urologists. Perhaps, Hinman’s classic written history of “American Pediatric Urology” should be required reading during the research year of fellowship or perhaps there should be a Urology History...
course in much the same way as there is a basic science course for residents. Either way, we need to continue to record, document, and pass down this history and the stories of where our specialty came from and how it evolved to what it is today.

It is for these reasons that we decided to focus this edition of the Dialogues in Pediatric Urology on both a review of our field from a historical prospective as well as a guide for future clinical and basic science progress. We asked several of the current thought-leaders in our field, to answer one of several questions on pediatric urology. Some were asked to focus on where pediatric urology came from and others on where it is going and advice for starting a research career. Each piece, offers unique insight and common themes which we enjoyed reading and hope you will to. While meant for the entire pediatric urology community, we believe these commentaries are especially valuable to the current fellows and recent graduates as a starting point for developing a roadmap to launching a successful career.

Figure 1. As you will read in all of the contributions below – strong mentorship is critical to both academic and clinical success. While we wish we could include pictures of everyone who has mentored us along the way (and there are many others!), here are two pictures of us with some of our most influential mentors. A. Jason with Dr. Douglas Canning (left), Dr. Kenneth Glassberg (2nd from left), and Dr. Stephen Zderic (right) at the AUA national conference in Boston, MA in 2017. B. Bryan with Dr. Rosalyn Adam (left) and Dr. Joseph Borer (right) at Boston Children’s Hospital in September, 2017.
Where Are We Now and How Did We Get Here?

CLINICAL PERSPECTIVES

Alan B. Retik, MD, Emeritus Urologist-in-Chief, Senior Associate in Urology, Professor of Surgery (Urology), Harvard Medical School

Pediatric Urology is a relatively new field. Interest in it evolved during the 60s. There was a lack of urology resident participation in that the pediatric surgical departments were doing virtually all of the evaluation and treatment. The first training programs originated in the late 1970s and began primarily as Divisions in Departments of Surgery. There was very significant overlap between pediatric surgery and urology and in the case of hypospadias, plastic surgery. The field evolved by evolution, not revolution. Programs were of one year duration.

In 1990, pediatric urology chairs decided to become more “academic” and increase the length of the fellowship to two years with the first year being basic science. In addition, the match was instituted. During the ensuing years, several programs achieved more independence by becoming departments in their institutions.

In the early 2000s, to accommodate increased interest in careers in academic medicine, several programs increased the duration of fellowship to 3 years with options to do 2 years of either basic science or clinical research with the possibility of obtaining a Masters Degree in Public Health. In 2011, one of the programs increased the number of fellows to 2 per year with the overall goal of enhancing the academic and non-surgical experiences of the fellows.

The stature of Urology as a specialty in children’s hospitals has been further enhanced by the appointment of several chiefs of urology as Surgeon-in-Chiefs in their respective hospitals. Therefore over a 35 plus year period, pediatric urology has developed as a strong specialty and a highly desired one for fellowship training.

The stature of Urology as a specialty in children’s hospitals has been further enhanced by the appointment of several chiefs of urology as Surgeon-in-Chiefs in their respective hospitals. Therefore over a 35 plus year period, pediatric urology has developed as a strong specialty and a highly desired one for fellowship training.

During this era, there was an evolution of major reconstructive surgery e.g. surgery for exstrophy – epispadias, hypospadias, megaureter repairs, incontinence operations, cloacal reconstructions, etc.

Ileal conduits, the preferred method of diversion in the pediatric age group was eventually replaced by non refluxing conduits such as the ileocecal conduit and sigmoid conduit. Ultimately there was the realization that many children who had been diverted could be undiverted. Thus there was a major change in philosophy and practice. Then it was learned that there were storage problems due to an inadequate urinary reservoir which consisted of problems with capacity, compliance, contractility and continence. Thus it became an era of reconstruction of the inadequate reservoir with various segments of bowel and stomach. During this period, Paul Mitrofanoff introduced the principle bearing his name using appendix. Ultimately other organs were used as conduits such as ureter and bowel.

During the past decade, there has been further expansion of pediatric urology with more active participation in oncology and renal transplantation.

Many aspects of pediatric urologic surgery have been transformed from major open reconstructive surgery to robotic assisted laparoscopic surgery where the earliest age for minimally invasive surgery gradually lowered and in some institutions is well under one year of age. In addition, instruments continue to be smaller. Many of our operative procedures years ago were done as inpatient and now many are done on an ambulatory basis.

In the future, urinary biomarkers should be able to help us identify patients requiring surgery for uretero-pelvic obstruction and vesico-ureteral reflux rather than some of the more non-specific indicators that we currently use.

I believe in the future we will see earlier fetal diagnoses and treatment of the fetus in utero with genes, drugs and surgery.

Regenerative medicine should also play a major role in reconstructive surgery. Several investigators have experimentally been very active and there are a number of organs undergoing current clinical trials.

Our basic and clinical research programs are strong, many of which have external funding. Many of the conditions we treat require major reconstructive surgery. I believe the future to be very bright for our specialty which continues to evolve.

Figure 2. This picture submitted by Dr. Alan Retik includes many of our most prominent mentors at a Society of Pediatric Urologic Surgeons meeting in 2000. Top Row (Left to Right): Dr. Roger De Filippo, Dr. Jonathan Roth, Dr. Martin Kaefer, Dr. David Diamond, Dr. Mark Adams, Dr. David McDermott, Dr. Richard Rink, Dr. Anthony Casale, Dr. Bartley Cilento, Dr. Craig Peters. Bottom Row (Left to Right): Dr. Samuel Kim, Dr. Joseph Borer, Dr. Michael Mitchell, Dr. Alan Retik, Dr. Hardy Hendren, Dr. Barry O’Donnell, Dr. Terry Hensle, Dr. Stuart Bauer, and Dr. Patricia Donahoe
As with almost everything in the universe, we in pediatric urology, find ourselves in a state of constant change. This is probably good because if this were not the case we’d be destined to become extinct as a discipline. Our real challenge is that we do not know what we don’t know so any correct predictions on my part would certainly be gratuitous. However, reflection on the origins and evolution of our specialty may actually provide some basis to projections of future strategy for survival.

Where we have been is worthy of reflection, where we are going is just conjecture but both seem to relate to two basic issues: 1. The politics of our professional discipline, Pediatric Urology, and 2. The science and execution of our discipline. In my view, each was shaped and abided by and will in the future be shaped and abide by the same basic evolutionary principle, that of appropriately adapting to the current scientific and political environment. Just as in nature where constant change is the rule of survival, in a changing environment, pediatric urology must continuously change and adapt to a world in transition. Politically we have evolved from urology and pediatric surgery and carry the genes of both parents, AUA/ABU/ACS/APS/AAP. This was totally appropriate because of the age and pathologies of the patients we were treating. Now, this would seem very logical, but was quite the controversial issue from the early 1960s through 1990s. Ultimately, with subspecialty certification we have evolved and pathologically we have also imagined three decades ago and should permit us to more completely define who needs what treatment and when.

We must always be able to accept change and do what is best for the patient, and always improve modalities of care.

The tools we have at our disposal offer possibilities we could not have imagined three decades ago and should permit us to more completely define who needs what treatment and when.

The future directions of pediatric urology can be readily seen by looking back at the last 3 decades of evolution in our field. There has been a clear movement towards reducing invasiveness in evaluation, therapy and surgery. We are less challenged today by the technical aspects of intervention than by determining who is best served by inter-}

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**The future directions of pediatric urology can be readily seen by looking back at the last 3 decades of evolution in our field. There has been a clear movement towards reducing invasiveness in evaluation, therapy and surgery. We are less challenged today by the technical aspects of intervention than by determining who is best served by intervention. True progress will be made with an effective integration of clinical and basic science and the robust integration of information into our clinical practice. To support this evolution, we all need to maintain an open mind to new ideas and scrupulous integrity in the process.

My own career has been enormously facilitated by working with individuals who have served as role models for this process. These have included basic scientists such as Don Coffey and Judah Folkman, who fully recognized the critical need to have a strong commitment to rigorous scientific inquiry with a view to direct application to our patients. While it has become ever more challenging for the surgeon to be involved in basic research, retreatring from that engagement would dissolve the relevance to our patients. Clinical innovators who challenged the prevailing dogma pushed us to question the need for clinical evaluation and treatments and changed the landscape of our field. We had become better at diagnosis and treatment, but sometimes without a full understanding of who needed to be treated. These innovators including Philip Ransley, Steve Koff and Barry Belman, prompted us to think outside of our comfortable boxes. Innovative surgeons such as Bob Jeffs, Patrick Walsh, Hardy Hendren, and Alan Retik defined standards of approaching clinical and surgical challenges while constantly asking how we could do this better. Only by rigorous and honest reporting and discussion was real progress made.

The tools we have at our disposal offer possibilities we could not have imagined three decades ago and should permit us to more completely define who needs what treatment and when. To continue this evolution, we must remember the examples of our predecessors as well as recognizing that novel ideas can just as readily become fixed dogma as those that they overturned. No one has a monopoly on truth. As Daniel Boorstin wrote, “...the greatest enemy of knowledge is not ignorance, it is the illusion of knowledge.” And while the tools such as modern genetic analysis, robotic surgical technologies, and big data analysis will clearly advance our abilities, we must always recognize that we treat individuals and that must remain our absolute priority.
Research has always been at the heart of our specialty. The first meeting of the Society for Pediatric Urology took place on June 22, 1952 in Atlantic City when a group of 14 urologists gathered to discuss approaches and outcomes for difficult cases. As captured by Dr Frank Hinman in his treatise “American Pediatric Urology” the organizers had no set membership requirements save for the request that participants treat no less than 5 or 6 pediatric patients per year. But even before the official birth of this organization, urologists with an interest in congenital anomalies described the anatomy and outcomes, and there was a steady increase in the number of papers published in the Journal of Urology dedicated to pediatric topics. The early research in our specialty was clinical and descriptive performed by clinicians blessed with curiosity and astute powers of observation. The seminal observations of F. Douglas Stephens are a great example of this. (He is surely beaming in the heavens knowing that his image of ureteric bud induction of renal parenchyma was reproduced 25 years later by Brigid Hogan in a paper showing the impact of FOXc1 and FOXc2 deletions on the development of the lower urinary tract in mice). This was because few urologists at that time could truly devote their entire practice to the care of children, and the modern world of molecular biology was also in its infancy. It is easy to forget that the structure of the double helix was not published by Watson and Crick until 1953.

In time the specialty grew, and a small number of urologists in academic centers were able to dedicate their full time clinical efforts to the care of children. In this era pediatric urologic problems were often managed by pediatric surgeons. It is also important to remember that until the mid 1970s, there were no formal fellowship training programs in North America. Interested urologists traveled to England for a year of training, observation, and clinical research with Sir David Innes Williams at the Great Ormond Street Hospital in London, or with Herbie Johnston at the Alder Hey Hospital in Liverpool. In time the number of full time pediatric urologists grew to a point that fellowship training programs could be established in North America, and these were essentially one year clinical apprenticeships. However, in the 1980s the leadership of American Pediatric Urology began to consider how to refine the training of pediatric urologists and began the move towards two year training programs that would include a full year fully dedicated to a research experience.

The diagnosis and management of vesicoureteral reflux began to emerge as a leading problem in this early era, and as summarized by Innes Williams in 1986, formed the center of a new specialty. To quote: “reflux made pediatric urology what it is, and sharpened its critical faculty.” The first International Reflux Study in Children was a randomized trial initiated in the early 1980s comparing surgical and medical management cohorts. This trial resulted in a large number of clinical papers that began to appear in the early 1990s and set up new thinking about the management of reflux which ultimately led to the RIVUR trial. In the late 1980s the size of pediatric urology faculty grew to a point where it was possible to have the protected time and resources to begin sustained basic scientific investigation.

Early work in pediatric urology basic research was centered around the creation of animal models to allow for the study of fetal physiology, or to study the response of the bladder and kidney to obstruction. Early investigators also developed medical and surgical models of cryptorchidism. Work in cell culture systems and tissue engineering followed. The work of this era is best characterized as descriptive meaning we would create the condition and then study the physiologic and histologic outcomes. In that time, gene expression could only be assessed by a Northern blot using a radioactive DNA probe and Western Blots would work only if the protein expressed was at a high level. Investigators were left to pursue one molecule at a time. Although first described in 1983 by Mullis, by the late 1990s PCR had begun to work its way into most labs allowing for a more sensitive assay of gene expression.

By the late 1990s high throughput analysis began as the RNA expression microarray was developed and the cost of using this approach dropped allowing more investigators to harness its power. Transgenic and knockout mice were developed and as the number of strains grew, pediatric urologists were ready to explore the impact of gene overexpression or deletion on a variety of urologic phenotypes. It is a credit to our founders and subsequent generations of leadership that as these modern tools of molecular biology evolved, enthusiastic young pediatric urologists were ready to embrace these new approaches.

So today 65 years after the first meeting of the SPU in Atlantic City, the program looks very different as a new generation of pediatric urologists will be talking about old clinical questions that can be answered with new scientific approaches.  

1) High quality outcomes research made possible by the EMR and a cadre of pediatric urologists with advanced epidemiology and statistical training  
2) Sophisticated murine models using conditional switching of targeted genes  
3) Surgical and Behavioral models and the use of optogenetics to explore the brain bladder connection  
4) The use of proteomics and genomics applied to both murine tissues but also to human samples – these multidisciplinary approaches stress the power of the well curated phenotype which is the great value an experienced clinician can bring to an investigation.

(continued on next page)
The founders of our specialty would be pleased to see that despite our small numbers, pediatric urologists have amassed an impressive record of funding from the NIH which serves as a barometer for high quality work. SPU members have also been consistently represented on study sections and advisory councils at NIH. But what the founders would appreciate most is that their innate curiosity and their desire to meet and exchange ideas to better the specialty and overturn the status quo has not changed. Although we will face some challenges ahead in terms of funding science, and allocating time for this work as academic medical centers become larger corporate entities, I feel that for pediatric urology research, the best years are ahead of us.

**References**

3) Kame, T, Deng, K, Hogan, B.: Murine forkhead/winged helix genes Foxc1 (Mf1) and Foxc2 (Mfh1) are required for the early organogenesis of the kidney and urinary tract. Development 127(7): 1387-1395, 2000

**Darius J. Bagli, MDCM, Professor of Surgery & Physiology, Senior Attending Urologist**

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Most clinical pediatric urology pathologies are driven by a relatively acquired stimulus: infection (± accelerated by reflux) → pyelonephritis, valves; spinal disease, or behavior → fibroproliferative bladder hypertrophy; and possibly even environment → hypospadias. Unlike cancer, they are far too common to be fundamentally driven by inherent genetic mutations alone. This is why I came to a conclusion that epigenetic biology, a powerful and systematic modifier of the otherwise normal genes regulating the genitourinary tissue phenotype, may be particularly relevant to the pediatric urological conditions we manage.

In the absence of congenital high-grade reflux kidney dysmorphism, UTI is most often the elephant in the reflux room. Why recurrent UTIs occur in some children and not others is not as simple as reexposure to bacteria. **How a patient responds to infection likely involves host epigenetic mechanisms triggered by micro-uroepithelial interactions that modify underlying genetic infection response cascades that form the basis of our clinically familiar concepts of “susceptibility and risk.”** The recent discovery of a ‘not-so-sterile-urine’ microbiome may hold further keys to UTI as a driver of pediatric urinary tract pathology.

**Hypospadias**, originally the purview of the plastic surgeon, is today a mainstay of pediatric urology management. Not surprisingly, an earlier review of the literature to 2008 showed the vast majority of nearly 4000 publications concerned themselves with the skin and vascular tissue: where to get it, cut it, move it, suture it; and the urethral plate: whether or not to incise it; and management of corporal curvature with grafts, plication, small cuts, big cuts, or fairy cuts. The only question missing is how many angels can dance on the head of a penis? Even the pharmacological consideration of sex steroids in genital surgery are focusing on their modulation of pre-op growth and post-op healing, rather than any systematic biomolecular understanding of their effect on genital vs. non-genital cells and tissues. While surgically relevant, these kinds of efforts alone do not bring us closer to the most impactful questions. Staring us in the face are increasing reports from all quarters on a rise in hypospadias incidence. Coupled with the growing concern for the prenatal and possibly generational effects of environmental endocrine disruptors on genital development or placental function, it would seem that a prime study target would be the epigenetic basis by which such environmental pressures modulate normal genital and related developmental programs and overall fetal development.

Another aspect of genital surgery in pediatric urology (of which hypospadias forms the bulk) is the ethical creep in the timing of surgery to preserve patient autonomy until decisional capacity is reached. This is in direct opposition to the ‘fresco intonaco’ of minimal scarring in pediatric wound healing. In fresco painting, intonaco is the final thin layer of wet plaster; it remains wet for a golden period of only 2-4 hours during which the plaster absorbs the paint pigments. Wait too long: the paint won’t adhere*, and the risk of post-surgical scarring (i.e., strictures, scars, fistulae) after infancy increases significantly. Efforts to realize the biomolecular therapeutic ability to reproduce the near perfection of fetal wound healing in later life, will obviate our current and understandable practice bias toward such timing decisions. Nevertheless, the psycho-developmental imperative for genital surgery in infancy remains, but it too needs deeper understanding by the pediatric urology community. Indeed, if perfect wound healing also virtually eliminated post-surgical pain, harmless painless surgery would make us rethink the current indications for “minimally invasive” surgical approaches.

While we battle against the many forms of bladder hypertrophy, fibrosis, and dysfunction brought on by various forms of ‘obstruction’, the sad fact is that the bladder often does not normalize despite treating obstruction. We had spent little time asking what might the fibrosis be doing biologically? This led us to the seminal finding that aberrant

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*The future of the pediatric urology specialty over the next 50-100 years will not be sustained by asking how to do the surgery better. It will be sustained by asking why we must do it at all.*
extracellular matrix (ECM) collagen is a powerful growth stimulus to bladder smooth muscle: a vicious cycle if there ever was one! More recently we confirmed that the ECM functionally activates epigenetic machinery that reduces smooth muscle cell differentiation. We are now engaged in understanding these mechanisms to reveal potential targets that could one day prevent or reverse this condition despite relieving obstruction itself.

One of my graduate students was recently asked, ‘what is a scientific fact?’ If you think about it for a moment, it is not an easy question to answer. It is easier to answer what is not a scientific fact. An observation is not a scientific fact just because it reaches statistical significance. It is not a scientific fact just because it is reproducible. And it is not a scientific fact because others say they have seen or heard the same thing over and over. If so, the earth may still be flat. Rather, when multiple approaches, in the widest variety begin to converge on the same observation, that observation moves closer to becoming a scientific fact. It is not unlike the three miracles required to become a saint.

Notwithstanding my own love for the surgical “Swiss-watchmaking” of pediatric urology, I would argue that the biggest impact and advances to be made by research in our and any surgical field must be driven by a motivation to render the “surgery” as we know it, obsolete. The future of the pediatric urology specialty over the next 50-100 years will not be sustained by asking how to do the surgery better. It will be sustained by asking why we must do it at all.

* Da Vinci ‘The Last Supper’; Milan. Because Leonardo sought greater detail, luminosity, and time to paint than could be achieved with the rush to paint in traditional fresco, he developed his own technique of painting on a layer of dried plaster he custom-treated himself to ensure the paint would adhere. It did not.

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**Where Do We Go From Here and How Do We Get There? Advice to Current and Future Pediatric Urologists**

**CLINICAL PERSPECTIVES**

I have been fortunate at almost every stage of my career to have excellent mentorship. It is hard to overstate how important this is in academic medicine, and it has been widely recognized and discussed. When I sought to launch a career in clinical and health services research in pediatric urology, it was challenging to be in a field where there were few role models or senior mentors with a background in both pediatric urology and health services research. I would advise young academic urologists to look for a job with a Chair who is committed to academics and has a track record of demonstrated support. Words are cheap, and it is easy to verbally commit to supporting academic faculty, especially junior staff. However, supporting academics takes money and the Department has to have both the will and ability to provide the resources. This is true at all levels – even R01 grants often do not provide sufficient funds to cover the salary of a surgeon-scientist, so senior leadership has to be committed to research as a core mission. When possible, look for urology Department that is independent. Divisions that are under the control of a Department of Surgery tend to have less control over their own fate (and less control of their revenues, spending priorities, hiring, etc). Department resources are key to research success; support for the needed infrastructure, including personnel, biostatistical support, and logistics, is essential for successful clinical research.

Choose a single area to make your own, if possible. Focusing on a well-defined subject allows you to develop a progression of ideas and projects that tell a story, and makes it easier to construct grant proposals that will convince readers that you are moving in a linear direction toward a defined goal, with a high likelihood of achieving meaningful results. It also helps your personal academic “brand” to be associated with a single idea or topic. Personally, I have not been very good at heeding this advice. My research has been all over the map, without a specific focus or subject, and this makes it hard to develop a “brand”. It does, however, keep things interesting.

Where are we going? I think the future of clinical research in our specialty will be driven by collaborative projects among groups of committed investigators with training in study design. Many of the more pressing questions in pediatric urology center around relatively uncommon conditions, and answering these questions will require multicenter cooperation to assemble the cohort sizes necessary. Luckily, there are already several groups of (mostly) younger urologists who are putting together such collaboratives, and this is very encouraging. These investigators will have to be patient and committed, willing to work around the extensive bureaucratic and institutional barriers that have been erected (usually in a misguided quest to mitigate any conceivable risk to human subjects or, more commonly, protection against regulatory penalties). Such barriers tend to slow multicenter projects to a crawl, but with tenacity and the support of senior leadership, they can be overcome.
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There are myriad paths to success as a clinical researcher in pediatric urology. While there is no one perfect mechanism to success that will work for every researcher or every situation, here are a few general principles that have thus far been useful for me:

1. **Consider a graduate degree.** Personally, my decision to pursue a Master’s degree was arguably the most important single building block that has facilitated my career in clinical research. Obtaining a graduate degree necessarily implies exposure to (and hopefully mastery of) several key aspects of clinical epidemiology and biostatistics. Familiarity with those core concepts helps to facilitate collaborations with the necessary members of the team; speaking the same language as your biostatistician (and regulatory coordinator, and clinical collaborators) is incredibly helpful. Likewise, having a research-focused graduate degree can come in handy when trying to convince stakeholders that you can successfully complete a research project.

2. **Collaborate with your colleagues.** The importance of multicenter research efforts is difficult to overstate. Multicenter mega-trials are becoming the standard of care in common conditions (heart disease or prostate cancer, for example). In pediatric urology, many of the conditions that we treat are sufficiently rare as to be un-study-able at any single center. Even relatively common conditions such as vesicoureteral reflux (RIVUR) or spina bifida (NSPBR) are primarily being studied using large, multi-center cohorts.

3. **Link your clinical and research strengths.** Surgeon-scientists have a crucial advantage over many other researchers: our clinical expertise. It is important to leverage that expertise and the conditions that we know best by making those conditions the subjects of our research efforts. When selecting what research questions you should prioritize or pursue, it helps to start by thinking about what clinical questions vex you most or have the greatest impact on your treating patients. Then think about what questions you have the ability and opportunity to address in your practice. That simple thought exercise should go a long way towards identifying a research topic that is clinically relevant and practically do-able.

4. **Funding helps.** Lastly, I would argue that the single most important pathway to research success is obtaining external funding. Doing high-quality clinical research requires adequate time and resources. Biostatisticians are crucial partners who can elevate the quality and methodological rigor of a study; study coordinators and regulatory personnel likewise are necessary additions who can facilitate studies and allow investigators to focus on the science of the study. However, these necessary components come at a price. External funding allows researchers to hire the talent we need to do the best possible work; it is well worth the time and effort to apply for grants to pay for those necessary components. Furthermore, external funding is often useful in and of itself as a marker of scientific quality and validity; landing a federal or foundation grant is a great way to convince your dean, chair, or division chief that you are a serious researcher (and that you really do deserve protected research time).

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The most fulfilling and exhilarating part of my career is the synergy that exists between clinical practice and clinical research. As a pediatric urologist who focuses on kidney stone disease, I am constantly confronted in the clinic with the boundaries of our knowledge. As a clinical epidemiologist and trialist, I am constantly striving to expand those boundaries. The desire to determine the best treatment for my patient in the operating room as well as the hundreds of thousands of children with nephrolithiasis whom I have never met has been my primary motivation and the central focus of my early career.

My research career began because of serendipity and developed because of mentorship, divisional support, and focusing on the big questions that, if answered, would improve the lives of the patients we see every day. My interest in nephrolithiasis developed because of the new “epidemic” of pediatric nephrolithiasis that emerged during my fellowship. Without the dramatic shift in the epidemiology of the disease, I may have very well focused on a different area in Urology.

While serendipity was important, a systematic approach to building a research career was equally so. As I finished fellowship, I established a mentoring team, both in and out of Urology, to understand “how to establish a research career,” something not often taught in residency or fellowship. Ron Keren MD, MPH, my mentor during my masters of science in clinical epidemiology (MSCE) degree advised me to focus on a problem that was “big or bad, or preferably both”. This advice has turned out to be the single most important factor in my early research career. In my first year in practice, I was fortunate to receive a K23 career development award from the NIDDK, which is mentored by Susan Furth MD, PhD, Chief of Nephrology at CHOP and an international expert in pediatric chronic kidney disease. While the “big and bad” nature of pediatric nephrolithiasis and a strong, established mentoring team were essential elements to obtaining my career development award, so too was time. At the beginning of your career, time is the most valuable resource you have (it took 6 months to write the K23 and 4 months to write my first UO1). I knew I needed 50% of my time protected for research to develop, build, and lead an active research program in kidney stone disease. The advancements we’ve made in understanding the epidemiology of nephrolithiasis would not have been possible without Dr. Douglas Canning’s strong and unwavering commitment to protecting my time and effort. Finally, as a surgeon with 50% protected time, I also knew that I could not master all pediatric urologic operations. I chose to focus my clinical effort on children with kidney stone disease so I could provide the best possible care to these patients. This approach has been immensely satisfying because my passion is improving the lives of children with nephrolithiasis and focusing my effort creates a tremendous synergy with my research program. In summary, the elements that have defined my early career in pediatric urology are: 1) opening yourself to new opportunities; 2) thinking big; 3) establishing a strong mentoring team; 4) protected time; and 5) building a focused clinical effort that is synergistic with your research program. I only hope the next 30 years are as exciting as the first 3.
When I think of where Pediatric Urology is going with scientific research, I have mixed feelings. On one hand, I see less pediatric urologists going into basic science research and I believe that this is primarily an economic issue with less research funding available and more pressures on departments to maintain their clinical revenue with shrinking reimbursements in parallel with increased time constraints and bureaucratic documentation. On the other hand, I am enthusiastic about the climate of pediatric basic research and have seen a recent resurgence of fellows and colleagues presenting excellent research at meetings using more sophisticated molecular biology techniques. In the past we have focused on observational changes looking at histopathology or variations of genetic or protein expression. I foresee that the basic science will become more mechanistic using genetically manipulated \textit{in vivo} and \textit{in vitro} models. I also foresee pediatric urology migrating toward precision oriented medicine using genomic and proteomic analyses and gene sequencing to provide better molecular insight of congenital disorders and how populations with congenital urologic abnormalities will fare in the future.

Lastly, I always recommend to any early investigator to expose themselves to as many scientific influences as possible. I remind them that they may think they know what they are interested in now, but they may find themselves doing research on things that they would have never thought they would be investigating. I cannot emphasize enough of the need to always keep an open mind and remain curious. Go to seminars and research presentations at your institution and learn what people are doing around you. There are always research activities at your institution that you may not realize and these may provide windows of opportunity for research collaboration. Always keep an open mind to maximize the strength within your institution that you can potentially apply towards pediatric urology!

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\includegraphics[width=\textwidth]{image3.png}
\caption{Dr. Paul Austin was honored with the John W. Duckett Pediatric Research Excellence Award from the American Urology Association’s Urology Care Foundation at the annual meeting of the AUA in San Diego, CA in 2016. Here he is pictured shortly after accepting his award with two of his mentors Dr. Stuart Bauer (left) and Dr. Yves Homsy (right).}
\end{figure}
I became involved in research because a year in the lab was required as part of my residency at Northwestern. Major early influences on my career were my chair, John Grayhack (Figure) and his basic science colleague, Chung Lee. Their collaboration was highly productive and collegial, and allowed Dr. Grayhack to maintain a productive lab as well as an active clinical practice. During my research year, I found myself truly fascinated with embryology as I studied chick embryos with the support of Max Maizels, and had the incredible opportunity to learn directly from Douglas Stephens when he was at Northwestern. I then had wonderful mentoring support by Julianne Imperato-McGinley and Darracott Vaughan at Cornell, through a Research Scholar award from the Urology Care Foundation (then known as the American Foundation of Urologic Disease) for research that cemented my interest in testicular descent and cryptorchidism. I think that the opportunity for uninterrupted research during my residency and research fellowship was critical for me. I learned everything I could and became truly passionate about this focused area of pediatric urology, and I realized that I wanted to continue to pursue research as part of my career. I have been able to continue to do both basic and clinical research because my pediatric urology chiefs at every institution – John Redman, Ricardo Gonzalez, and Sonny Figueroa – enthusiastically supported and followed through with my need for protected time. Ricardo’s support to attend a 2-week, hands-on molecular biology was critically important.

For anyone interested in a physician scientist career, I think it is important that you, your family, and your colleagues realistically understand and support the level of commitment required. To be successful, I think it helps to focus on and work towards becoming an expert in a particular area. Undoubtedly, it helps if you consider the time you spend on research after regular working hours as not really “work”. Even though NIH funding is now unbelievably competitive, I believe that physicians are key to moving clinical and translational research forward, because they have a special understanding of the knowledge gaps in their field. Although NIH funding is not essential for physician researchers, it can open doors for you, provide opportunities to widen your horizons, and facilitate ongoing success.

I think the things that are most important to remember are these:

1. It takes a long time to do good research;
2. It is important to foster as many collaborations with basic and translational researchers as you can;
3. Consider carefully, as you look for jobs, what institution is most likely to provide the type of academic environment that will help you learn and grow;
4. To be effective, you should read widely not just about your area of interest, but related fields;
5. It is important to consider pursuing further specialized training, or spending some time working with an expert in a related scientific field;
6. You will need support from your clinical colleagues for truly protected time, and you may need to limit your clinical practice in some way; and finally,
7. Never give up - most of us need to write many grants to get just one.
Conclusion

Jason Van Batavia & Bryan Sack

Reflecting on the wise words laid out so beautifully by the contributors, the newer and younger generation of budding pediatric urologists has much to be thankful for. We are fortunate to not have to deal with interdepartmental strife with our general surgeon and adult urologic colleagues. Our strong and well defined role within the greater surgical field, and within most of our hospitals, has allowed us to the ability to focus on patient care and research endeavors. We are forever thankful to our forefathers who shed blood, sweat, and tears to ensure that our field is respected, fellowship trained, and subspecialty certified.

The sage advice provided in these pieces hones in on a few consistent themes. As a small surgical subspecialty, we need to remember to reach out to each other for mentorship and collaboration. The emphasis on mentorship cannot be overstated. Look in your department, outside your department, or to a mentor from residency or fellowship. The opportunity to further ones career through simple, regular conversation with a mentor can have invaluable benefit personally and for the field. Similarly, collaborative research projects can be performed in the same manner. Reach out to your colleagues with similar clinical and/or research interests. From a clinical research perspective, the widespread use and improved access to EMRs for data acquisition and database creation, along with the advanced degrees obtained by our clinicians should make collaboration and study design easier to optimize. From a translational and basic science research perspective, sharing biodatasets (ie, genomics, proteomics, and metabolomics) or patient specimens to increase the statistical powering of our projects will help us gain essential knowledge for some of the rarer diseases for which we still lack a basic pathophysiologic understanding. You may feel that you do not have the time or the funding to embark on a project on your own, but you cannot let that be a deterrent. Align yourself with a PhD or another surgeon scientist or a clinical colleague who shares mutual interests. Go to seminars or conferences or lab meetings. Read journals from different fields or areas of expertise to learn about new techniques or clinically relevant innovations that you can apply to pediatric urology. Start to think outside of the box and remember that any contribution to the field is better than no contribution at all. The future is bright for the field of pediatric urology and we are excited to be a part of the next generation.