A Tribute to Howard M. Snyder, III, M.D.

FROM THE GUEST EDITOR

Stephen A. Zderic, M.D.
Children’s Hospital of Philadelphia

On Saturday November 19, 2011, family, friends, colleagues, and former trainees gathered to pay tribute to Howard M. Snyder, III, MD at the third Quinquennial John W. Duckett Festschrift held at the Children’s Hospital of Philadelphia. At this joyful celebration we had the opportunity to reflect on the remarkable 31 year career in pediatric urology of this unique man. It is altogether fitting that Howard’s legacy at the Children’s Hospital of Philadelphia will live on forever in the form of the Howard M. Snyder III endowed chair in pediatric urology. The future holder of this endowed chair will have an interest in long term outcomes and in the challenges we face in transitioning complex patients with congenital anomalies from pediatric to adult care. When Howard came to CHOP over 30 years ago, the future was not always so bright for the neonate with complex urologic

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FROM THE EDITORS

Anthony A. Caldamone, M.D.

Howard is an educator, an advocate, a surgeon’s surgeon, and a family man. I had the privilege of being trained by Howard Snyder shortly after he joined John Duckett as a second pediatric urologist at Children’s Hospital of Philadelphia. Howard had already trained as a general surgeon, pediatric surgeon, urologist, and then finally pediatric urologist. What one learned from Howard foremost was a disciplined approach to disease. Whether it was in the office setting or in the operating room, he taught one to logically progress through a problem. In the operating room he would often say “Routine operations should be done in a routine fashion.” Indeed through repetition he taught the development of surgical techniques as well as the ability to anticipate in the operative setting. Whatever Howard did and

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Elizabeth B. Yerkes, MD

At the first Fall Congress in Pediatric Urology in September 2013, the Pediatric Urology Medal was bestowed upon Dr. Howard Snyder. This Edition is now a dual tribute to his impactful career. Although many of us never had the opportunity to stand across the table from Dr. Snyder, we can all imagine his influence through the words of these mentees and colleagues and through partaking in his microphone comments/ “dissertations” from the aisle at annual meetings. As the presentation of the Medal unfolded, many of those seated around me remarked how he had lived a life full of ‘once in a lifetime’ experiences before he even started his incredible contributions to Pediatric Urology.

Congratulations to you, Dr. Snyder, on your inspired career and support of children, young adults and pediatric urologists worldwide!
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anomalies. The need to transition these patients to adult care is a reflection of the tremendous advances made by Howard and his generation of pediatric urologists. For those of us who were fortunate enough to have trained under Howard’s watchful eye, we reflected on his skill and passion for intraoperative teaching. Howard is blessed with a remarkable gift for teaching operative steps in a logical and reproducible manner. His methodical approach to even the most complicated reconstructive problems made him a most sought-after visiting professor; the only continent he has missed (thus far) is Antarctica. Howard is a devoted family man, married for 37 years to Mimi; they have 3 children and 3 grandchildren. A surgeon’s busy life often leads to inopportune absences, but generations of patients and their parents and all his trainees and partners extend their thanks to the Snyder family for allowing us to be the beneficiaries of Howard’s expertise.

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Whatever Howard did and whatever challenge he took on, he did with an intense sense of commitment. Whether it was teaching a medical student, advocating on Capitol Hill for the Health Policy Council of the AUA, or fighting for surgeons’ rights as a regent of the American College of Surgeons, it was all done with the same compassion and energy.

Howard has left his mark by improving the care of children during his clinical tenure and for years to come through those that he has trained, and pediatric urology in particular has been the biggest beneficiary.

About Dr. Snyder

Dr. Howard M. Snyder was born August 25, 1943, in Carlisle, Pennsylvania. He graduated from Princeton University in 1965 with honors and from the Harvard Medical School class of 1969. He received further postgraduate medical training at the Peter Bent Brigham Hospital, Boston Children’s Hospital, the Massachusetts General Hospital, the New England Medical Center, the Great Ormond Street Hospital for Children (London) and the Alder Hey Children’s Hospital (Liverpool).

Dr. Snyder has worked in the Division of Urology at The Children’s Hospital of Philadelphia for more than three decades. He is currently the Director of Surgical Teaching in the Division of Urology at The Children’s Hospital of Philadelphia and also a Professor of Surgery in Urology at the Perelman School of Medicine at the University of Pennsylvania. He has been Board certified in Adult and Pediatric General Surgery; and Adult and Pediatric Urology.

Following in the strong family tradition of military service, Dr. Snyder served for over 20 years in the Active Reserves, U.S. Army Medical Corps and was deployed to Active Duty in 2003 for Operation Iraqi Freedom. He retired as Colonel in the Army Medical Corps Reserves in 2004. In addition to serving as editorial consultant for more than 20 peer-reviewed journals, Dr. Snyder is a Regent of the American College of Surgeons and serves on the Advisory Board for the Health Policy Research Institute. He is a former Trustee for the American Board of Urology, and is a longstanding member of the American Association of Genitourinary Surgeons.

In honor of his lifetime contributions to pediatric urology internationally, the British Urologic Association honored Dr. Snyder with the St. Paul’s Medal in 2002. Dr. Snyder’s interests include reconstructive pediatric urologic surgery, especially hypospadias. He worked with the late Dr. John Duckett to develop many of the one-stage approaches to hypospadias used worldwide today. He has demonstrated reconstructive pediatric urologic surgery in all parts of the world.

Dr. Snyder has written and contributed to hundreds of peer-reviewed publications and book chapters. He is revered for his teaching skills, and has served as a visiting professor countless times, on 6 continents.

Dr. Snyder resides in Haverford, Pennsylvania, with his wife of 37 years, Mimi. They share their home with two West Highland White Terriers. Mimi is an accomplished artist who serves on the Women’s Board of the Pennsylvania Academy of Fine Arts. Her sister is very involved with the Garden Club of America. They have three children: Emily is married and runs a Family Medicine private practice in Rochester, New York; Curtis is a doting newlywed and Manager of Corporate Financial Strategy at Cisco in San Jose, California; Jonathan is a successful online marketing entrepreneur and lives in downtown Philadelphia, Pennsylvania. Dr. Snyder and his wife are the proud grandparents of three grandsons: Rowen, Riley and Robert.
Hypospadias is the second most common urogenital anomaly in children. The etiology remains unknown with a general consensus that both genetic susceptibility and environmental exposure are at play as the cause of this anomaly.\(^1,2\)

While Alford Jost’s theory of external genitalia development focuses exclusively on the presence or absence of androgen action is undoubtedly correct, it neglects that possibility of other endocrine mechanisms such as estrogen action relegating female development as a default pathway.\(^3\) Recent murine work has emphasized that normal female sex differentiation of the external genitalia is a uniquely active process and not simply a default pathway associated with the absence of androgens.\(^4,5\) The presence of estrogen receptor alpha (ER1), estrogen receptor beta (ER2) and aromatase in the developing external genitalia in the mouse, as well as estrogen ligands in serum when sex differentiation is occurring, emphasizes the potential importance of estrogenic mechanisms during external genitalia development.\(^6\) In addition, signaling via androgen receptor (AR) and ER can be antagonistic at the cellular, tissue and systemic levels, and thus the balance between AR and ER signaling may be critical in normal male and female development of the external genitalia.

We have extended our knowledge of the role of estrogen in patients with hypospadias by first documenting the presence of the ER1 and ER2 receptor in the preputial tissue of patients with hypospadias and in the urethral, corporal cavernosa and surrounding tissue of normal human fetal tissue.\(^7\) For estrogen to be an important ligand during normal and abnormal penile development it certainly has to be expressed in the affected tissue, i.e. the penis and foreskin. Indeed we found a difference in ER1 and ER2 receptor expression and location in the foreskin of patients with hypospadias compared to controls. (Figure 1) These findings are consistent with
The Role of Estrogen in Hypospadias  (continued from previous page)

References

The Mitchell Repair at The Children’s Hospital of Philadelphia

Douglas A. Canning, M.D., Aileen Schast, Ph.D., Michael C. Carr, M.D., Ph.D.

In November 2011, At the Third John W. Duckett Quinquennial, we honored Dr. Howard M. Snyder and endowed a Chair in his name. The Howard M. Snyder Chair in transitional urology will support care for aging children of The Children’s Hospital of Philadelphia (CHOP) Pediatric Urology practice. No individual has made more difference in these children’’s lives than Howard M. Snyder. Further, those of us who have been fortunate enough to work with him over the years have gained immeasurably from Dr. Snyder’s technical excellence, his surgical judgment, and his ability to break complex operations into small steps and then to teach them. All of us have benefitted from Dr. Snyder’s selfless commitment to teaching, and to the Division of Urology that he helped to build over these past 40 years. The work we will describe would not have been possible without his never-ending dedication to his patients and his thoughtful guidance across his four-decade career.

The Mitchell Repair at CHOP

The reconstructive surgery to provide children born with classic bladder exstrophy the ability to void with continence without the use of a catheter is one of the most difficult tasks in Pediatric Urology. The staged classic bladder exstrophy repair, as described by Jeffs and Gearhart, evolved from, in Jeffs’ words, “a realization” that he made when attending the 1972 American Urological Association Annual meeting. During the discussion at a session on reconstructive surgery, Lattimer referred to his published exstrophy series.1 Culp had just presented his series of 28 complete epispiadias repairs. Lattimer’s continence rate in his exstrophy series was 17%, but Culp’s series of reconstructed epispiadias patients had a continence rate of 42% as defined by voiding without leakage, and the upper tracts were largely preserved.2

Jeffs began to believe that the solution to improve continence and minimize renal damage in children born with classic bladder exstrophy was to first convert bladder exstrophy to epispadias and then correct the epispiadias. By 1987, Jeffs had the largest published series of consecutive exstrophy closures in infants. At that time, 67% of the children who had either undergone osteotomy or were closed within 48 hours were voiding and dry with a greater than 3-hour continence interval. In those who were closed outside of 48 hours, without osteotomy, the voiding with continence rate was only 22%.3

Around that same time, Hollowell et al. reviewed a series of reconstructed bladder exstrophy patients from the Great Ormond Street and noted that those who maintained good bladder compliance demonstrated a urethral leak point pressure of between 1 and 10 cm of water pressure.4,5 This suggests that there is a “sweet spot” following the closure of the bladder neck where resistance to voiding is ideal, and if bladder function is good, some of these children void with continence.

At about the same time, we reviewed a similar series of patients at the Children’s Hospital of Philadelphia. Only 12% of our patients were continent as defined by voiding and dry for more than 3 hours without the aid of intermittent catheterization.6

Taking these data together led us to believe: 1) Continence with voiding in bladder exstrophy is difficult to achieve. 2) Osteotomy may help continence if the surgeon closes the bladder outside of the first 72 hours 3) The hallmarks of success are consistent surgical repair, high surgical volume, and tenacity. Jeffs and Gearhart spend considerable time making sure that the resistance to voiding for their patients is “just right.”

On the other hand, in 1996, Woodhouse and Redgrave, following a series of patients from the Great Ormond Street, noted that of 57 bladder exstrophy patients born between 1965 and 1974, there were 32 that were reconstructed compared with 25 that underwent early diversion. Of the 32 reconstructed patients 13 achieved continence. Of the 13 early successes, there were 8 subsequent reconstructions, 2 urethral sphincters that were placed, leaving only 3 of the original 57 (5.3%) voiding with continence.7

Not long after that, Mitchell shared video footage of a newborn boy with bladder exstrophy who had a complete disassembly of the corpora, bladder neck and proximal urethra. Mitchell believed that separating the corpora from each other and from the spongiosum allowed him to place the urethra deep in the confluence of the pelvic diaphragm. His initial results suggested that following his newly described “complete repair,” as many as 88% of the bladder exstrophy patients could potentially be dry without intermittent catheterization.8

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The Mitchell Repair at CHOP (continued from previous page)

These results were exciting enough that we used the Mitchell repair on our next patient referred with classic bladder exstrophy. Following the complete repair, this child voided in the postoperative period immediately, underwent reimplants at age 4 months, but with no other surgery has continued to be dry day and night with near complete bladder emptying. Following that experience, we shifted our approach to the complete repair for patients with classic bladder exstrophy.

Between 1997 and 2000, in order to avoid osteotomy, we “added on” our patients and often operated into the middle of the night at the end of a busy clinic or busy OR schedule. We frequently operated with residents and fellows who had never before seen the repair. To help prevent dehiscence, we placed the infant in a “mermaid dressing” designed to hold the legs together and stabilize the newly closed pubis. During this period, we had two dehiscences, both in boys that did not have an osteotomy. In addition, we had two glans injuries, one following a dehiscence, and one in a 6-month-old with complete epispadias who had the symphysis split as part of the original repair without an osteotomy. At this time, we recognized that the complete repair is a long and tedious procedure that requires prolonged intensive concentration, particularly in boys. If the procedure is done poorly or infrequently, the penis is placed at risk and the operation may even be dangerous.9

Our concerns about the safety of the complete repair led to our current approach, which we adopted in 2002. We now have a consistent team of four attendings: two urologists, one orthopedist and one anesthesiologist. Our nursing team and technical support is also the same for each case. This team operates together for all of our patients. We perform a complete repair for exstrophy or epispadias as early as possible. But we wait until we can convene the team. We have a team meeting a few days before the procedure to reorient and make sure that we all know our job. We run through a checklist based on our experiences during the last several procedures to see if there are ways that we can improve our process and to make sure that all of the appropriate equipment is available.

We run through a checklist based on our experiences during the last several procedures to see if there are ways that we can improve our process and to make sure that all of the appropriate equipment is available.

Since 1997, we have treated 29 consecutive patients with bladder exstrophy and/or epispadias using the complete repair. We performed surgery in 17 with classic bladder exstrophy and 12 with epispadias. Surgery occurred at age 24 hours to 123 days in the exstrophy group and from 24 hours to 299 days after birth in the epispadias group. Fifteen patients had osteotomies at the time of closure, 11 with bladder exstrophy, and 4 with epispadias. Three children had re-closures. Two required re-closure due to dehiscence, and one had re-mobilization of the bladder neck and re-closure with ostomies due to a vesicovaginal fistula. To date, no child has had a subsequent formal bladder neck reconstruction. Of 17 patients with classic bladder exstrophy, one is dry day and night, one is dry during the day but has nocturnal wetting, 4 have dry intervals and are damp, 3 are currently toilet training, and 4 are wet; there are 2 infants under 2 years of age. Two additional patients underwent bladder neck closure and augmentation cystoplasty and are dry with intermittent catheterization. Of 12 with epispadias, 7 are dry day and night, 2 are toilet training, and 3 patients were under 2. If we presume that all patients who are currently toilet training or under 2 years of age become dry, of the classic bladder exstrophy group, 11 of 17 or 64% have the potential of voiding with continence compared with 100% of those with epispadias. If each child who is toilet training and the infants under 2 years of age all fail to develop continence, then 35% in the classic exstrophy group will develop continence compared with 58% of those with complete epispadias. Either way, if these results are durable with longer term follow up, this represents an improvement over our earlier series. While we performed no further open surgery other than that described, 14 patients (9 exstrophy patients and 4 epispadias patients) had 28 Deflux® injections. Three exstrophy patients have had a series of 10 urethral dilations.

In conclusion, the complete repair without bladder neck reconstruction seems well suited for boys and girls with epispadias, but many patients with exstrophy will require a bladder neck reconstruction. We also believe that bilateral iliac osteotomy may be helpful, not only for bladder exstrophy, but for epispadias as well, and that immediate bladder closure may not be critical to achieve continence as long as osteotomy is deployed in all children.

References
Voiding Function and Development

Vignette: A Case of Mistaken Identity

We were at Howard’s house during the summer of 2001. Chris Austin and I were both due to graduate the next year. Chris had been smart enough to choose the 2 year path, I chose the 3 year route. Like most fellows, I was considering whether to stay on at CHOP. Chris’ wife, Ha, found my wife Ruth and said, “I’ve just heard from Howard what a great husband you have. Howard told me that he really enjoyed having him as a fellow, and that he was one of the best trainees to come along in a long time. He told me about the great academic environment here and how this would support a young surgeon-scientist. I thought he was talking about Chris until he said, ‘So, Ruth, I really hope that you and Yang will seriously consider staying here at the Children’s Hospital of Philadelphia.’” Ha was too polite to tell Howard that he had made the sales pitch to the wrong spouse.

Topic: Voiding Function and Development

Howard’s influence on my research career extends to my medical school days, when as a fourth year student in clinic, I learned from Howard how to educate patients on how their bladder and sphincter work (Howard’s term for the sphincter was “your hold-on muscle”). A few years before, Howard and John had invited Jan van Gool to set up the DOVE (Dysfunctional Outpatient Voiding Evaluation) clinic. I’ve spent a very satisfying 10 years since then, studying the bladder and external urethral sphincter (EUS) mainly so I can tell my patients something new, and something that Howard didn’t teach me. I have focused on the CNS switch and maturational changes of the bladder smooth muscle and EUS responsible for coordinated voiding.

The concept of how infants control their lower urinary tract has progressed from an involuntary spinal reflex to a more nuanced picture of the brain being in control of the bladder and EUS from the time of birth. The concept of how infants control their lower urinary tract has progressed from an involuntary spinal reflex to a more nuanced picture of the brain being in control of the bladder and EUS from the time of birth. Successful cortical control leads to continence, whereas dysfunctional voiding is due to persistent immaturity of the connections between the brain, bladder and EUS. The big question remains: what happens in the central nervous system that allows us to decide when to void? Chet de Groat was the first to explain the maturation of the perigenital-bladder reflex in neonatal rats, in which mother rats lick the genital area of their pups for the first 3 weeks of life in order to get them to void. If you take a pup away from its mother, it will die of urinary retention. After 3 weeks, the pups start to void on their own in response to bladder filling. This switch is a result of perigenital afferents initially driving the efferent neurons controlling the bladder, then having the reflex taken over by brainstem afferents which read bladder fullness. The wiring is all in place; it’s a matter of which input is stronger. My first project was to make the mature voiding reflex start at an earlier age. If we could do this, we might figure out which CNS mechanisms were responsible for this switch. I first used bladder distension caused by maternal separation. By taking the mother rat away from the pups for 6 hours daily for 2 weeks, their bladders became twice as large as they should have been. The separated rats still waited until 3 weeks to void on their own. However, the perigenital reflex, which normally goes away at 3 weeks, persisted for an additional 2 weeks in the maternally separated rats. This showed that the timing of when the brain assumes voluntary control is pre-programmed. However, the suppression of the immature reflex is dependent on bladder distension. Next, we tried C.K. Yeung’s bladder reduction model, by tying a 5-0 PDS across the midportion of the bladder in a 1 week old rat pup. The next day, we could see that the pups were voiding. Cystometry at 1 week of life confirmed that they were not in overflow incontinence, but voiding at elevated pressures. Surprisingly, by the time the pups were adults, they had double the bladder capacity of control rats, and were voiding at lower pressures. The bladder reduced animals suggested that improved EUS relaxation may account for the lower voiding pressures.

Chet de Groat’s summary of neonatal bladder function is classic: “The bladder changes from a conduit into a good storage organ.” The smooth muscle of the bladder progresses from having high amplitude, low frequency spontaneous contractions at 1 week to low amplitude, high frequency contractions at 3 weeks of life, which are more compatible with low pressure storage. We found that the mechanisms for this stabilization included decreased sensitivity to muscarinic agonists, and increased expression of ion channels such as the K_{Ca} (large conductance calcium-activated potassium) channels which minimize spontaneous contractions.

This neonatal bladder phenotype re-emerges after spinal cord injury, suggesting that the normal CNS tonically inhibits bladder overactivity. Determining which neurotransmitter is responsible for this inhibition may lead to the development of centrally active agents for the treatment of overactive bladder, although delivery to the spinal cord would be a hurdle.

The EUS remains the biggest challenge to control. There is a clear sex difference in EUS function between male and female rats during voiding. Male rats often have non-voiding contractions, where they generate high bladder pressures but do not relax their EUS, whereas female rats almost always have a smooth voiding pattern with EUS relaxation during voiding. Interestingly, intravenous serotoninergic agonists (5HT_{1A}) convert the irregular male pattern into a smoother female pattern. The reverse effect, changing a female pattern into a male pattern by giving a serotoninergic antagonist, does not occur, although males may be more likely to go into retention when a serotoninergic antagonist is given. These findings suggest that serotonin plays an important role in the maturation of EUS function.

Does this research give us something to offer our patients? On the CNS side, we need more targeted efferent therapy to reduce bladder overactivity, while improving EUS relaxation. For the bladder smooth muscle, we need medications with fewer side effects, so that our patients will be more likely to stay on them. For the EUS, we need a more effective combination of medications and behavioral therapies for patients who are refractory to alpha blockers and biofeedback. There are still many challenges in the treatment of pediatric overactive bladder and dysfunctional voiding. Thanks to Howard’s encouragement and support, we are getting a clearer picture of how the brain teaches the bladder and EUS to grow up.
Lessons Learned from the MOMS Trial (Management of Myelomeningocele Study)

Michael C. Carr M.D., Ph.D.

As surgeons, we recognize that identifying a problem as early as possible and then intervening may change and improve the outcome. This in essence was the premise for the MOMS Trial. Myelomeningocele represents a primary failure of the neural tube with both genetic and micro-nutrient causes. Folic acid supplementation has had a significant impact on the prevention of myelomeningoceles, but there are still 1 in 2000 live births of infants born with myelomeningocele, representing over 1,500 infants born each year in the United States, who are afflicted with this. We all recognize the lifelong quality of life issues, including hydrocephalus, hindbrain herniation, motor and cognitive impairments, bladder and bowel incontinence and the social, as well as emotional challenges that confront these children. Traditional therapy has included early surgical coverage of the defect and placement of ventriculoperitoneal shunts for hydrocephalus with posterior fossa decompression occurring. Future neurosurgical considerations include shunt malfunction and re-tethering of the spinal cord. In addition, there are both orthopedic and urologic issues that remain with these patients.

The rationale for in utero intervention of a myelomeningocele was dependent upon experimental work that suggested that a myelomeningocele was the result of failure of neurulation along with acquired secondary damage to the exposed spinal cord. Hence, early experimental studies that were conducted in the laboratory of Mike Harrison at UCSF demonstrated that in utero surgery could rescue the neurologic function at birth in sheep with spina bifida. This pioneering work led to several centers perfecting in utero closure of a myelomeningocele. This pioneering work was accomplished at UCSF, Vanderbilt, and The Children’s Hospital of Philadelphia. Based upon the experience gleaned from other in utero procedures, a number of patients underwent fetal repair with very encouraging results being noted. In particular, the incidence of ventriculoperitoneal shunting in those patients who had in utero repair was considerably less than what had been noted historically. A review in the Spina Bifida Clinic at The Children’s Hospital of Philadelphia between 1983 and 2000 noted that 88% of patients with lumbar myelomeningocele underwent shunting as opposed to only 41% who had undergone fetal repair. These exciting results were tempered by some of the obstetrical complications that were also noted. In the first 50 patients who had been treated at The Children’s Hospital of Philadelphia with in utero repair of their myelomeningocele, chorioamniotic separation was noted in 28%, preterm labor requiring magnesium sulfate in 6%, maternal transfusions in 4%, postoperative oligohydramnios in 6%, and delivery before an elective C-section which was planned at 36 weeks occurred in 44% of patients with a mean gestational age of 32 weeks and 2 days. No uterine dehiscence was noted at the time of delivery in any patient as well. In addition, neuro-developmental outcome after fetal myelomeningocele repair noted in 30 patients at 2-years of age that 67% were normal, 20% showed mild delay and 13% had significant delay. There was a lower incidence of significant cognitive deficits compared to historical controls.

Urologic testing of these patients consisted of early postnatal renal and bladder along with video urodynamic evaluation. Patients return at 1 year, 2½ years, and 5 years for comprehensive evaluation as well. This early cohort of patients showed a decreased need for ventriculoperitoneal shunting, which reduced the hydrocephalus and in the long run should improve shunt related morbidity. The reversal of hindbrain herniation may also reduce the Chiari-II related accumulative mortality and morbidity, and preliminary data suggested improvement in neurofunctional outcome along with ambulatory status and urologic function. The criticism, though, was that this cohort of patients was being compared to historical controls and thus there would be selection bias, a non-randomized group of patients, ascertainment bias, no match controls and a short follow up.

The NICHD recognized the importance of this work and sponsored the MOMS Trial. The goal of the Trial was to compare the safety and efficacy of in utero repair of open neural tube defects with that of standard postnatal repair. The first R01 application was submitted in January 1999 and over the course of several years the Trial went from a single center study to a multicenter study in which CHOP, UCSF and Vanderbilt would be the clinical sites, with George Washington University being the data and study coordinating center. Candidates would be fetuses identified with isolated myelomeningocele and a Chiari-II malformation, between the ages of 19-25 weeks gestation, with 100 patients being randomized to in utero intervention and 100 for postnatal surgery. The study was officially begun in March 2003. Strict inclusion and exclusion criteria were agreed upon, geographically randomization was agreed upon and potential candidates who were seen at various MFM sites were then referred for comprehensive 2-day evaluation for testing and discussions with maternal-fetal surgeons, perinatologists, neonatologists, social workers, ethicists, nurse coordinators, neurosurgeons, and anesthesiologists to fully understand the study. In utero surgery would occur within 1-3 days after randomization was performed with strict bed rest for two weeks following in utero repair and then weekly visits to the MOMS center. Delivery was planned by C-section at 37 weeks gestation. If a patient was randomized to postnatal surgery, they were allowed to return home with monthly ultrasounds by local physicians and then a return to the MOMS center at 37 weeks for fetal lung maturity testing, C-section if fetal lung maturity was documented, followed by neonatal repair by the MOMS neurosurgical team. For the purposes of the MOMS trial it was agreed that evaluation would occur during the neonatal period, at 1-year and then at

The goal of the Trial was to compare the safety and efficacy of in utero repair of open neural tube defects with that of standard postnatal repair. The first R01 application was submitted in January 1999 and over the course of several years the Trial went from a single center study to a multicenter study in which CHOP, UCSF and Vanderbilt would be the clinical sites, with George Washington University being the data and study coordinating center.

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Lessons Learned from the MOMS Trial (continued from previous page)

2½ years. Oversight was conducted by the MFMU network advisory board, Data and Safety Monitoring Committee, Steering Committee, local institutional review boards and local oversight committees. It was initially projected that recruitment for patients would be conducted for the first two years so that 30-month follow up evaluation would be completed by March 2008. As is true for many clinical studies, the recruitment took much longer than anticipated as well the expense of the trial.

At the December 7, 2010 Data Safety Monitoring Board Meeting, it was shown that the efficacy of prenatal surgery was demonstrated, and as result the trial was stopped with the New England Journal of Medicine reporting an online version of the outcome on February 9, 2011 followed by the print version on March 17, 2011. A total of 1,087 were screened for the trial, 530 met exclusion criteria, 258 decided not to participate, 299 were referred to the MOMS centers and a total of 183 patients were randomized. At the time the trial was stopped, there was 12-month follow up on 158 patients and 30-month follow up on 136 patients. The take home lesson from the MOMS trial is that shunts were placed in only 40% of the prenatal surgery group compared with 82% of the postnatal surgery group. In addition it was emphasized that prenatal repair is not a cure for myelomeningocele. There is improved motor outcome including the ability to walk at 30-months in those that underwent fetal repair. Prenatal repair is associated with significant maternal and neonatal risk including premature birth and uterine scar problems. What was critical of this trial was that there was cooperation of all sites and an agreement that fetal repair of myelomeningocele would only be conducted at these three sites and not at other institutions until the results of the MOMS trial were completed. The centralized intake of data was critical, but enrollment was much slower than what had been anticipated. What was critical was NICHD remained committed to additional funding until the study was complete. What’s equally critical going forward is to determine a complete set of data at 2½ years including urologic follow up and to see if based upon the data that there are prenatal predictors such as degree of ventriculomegaly, the level of the myelomeningocele, or the presence of talipes that may be helpful in predicting outcome. It will also be important to assess maternal morbidity, the effects on future pregnancies as well as psychological issues for these mothers. The overall cost of prenatal versus postnatal for the first five years of life will be critical to assess and that the MOMS II Trial will be able accumulate follow up data in those between the ages of 6-10 years. What also remains to be seen is how this data will become universally disseminated to other fetal centers and whether the outcomes from this study can be translated into a much broader group. Further refinement in the in utero repair will be important and ultimately can our healthcare dollars afford universal dissemination of this technique.

In my nearly 15 years of working with Howard Snyder, I drew the analogy of the famous movie and play, A Man For All Seasons. Howard is a consummate surgeon, an extraordinary teacher, an outstanding researcher and a urologic and surgical scholar. His influence in Pediatric Urology has been far reaching and his presence at meetings serves as a reminder of where Pediatric Urology has its origins and where we will be moving to in the future.

Oncofertility in the Male Adolescent

Cure rates for childhood cancer now approach 80%, with >270,000 childhood cancer survivors living in the USA. Currently, one of every 640 young adults is a survivor of cancer in childhood or adolescence. Gonadal damage is a common consequence of the treatments used to cure pediatric cancer. The extent of cytotoxic germ cell damage depends on the specific agents used and the cumulative doses received. Alkylating agents are the most common class of drugs known to affect gonadal function, and their impact has been studied extensively. Testes have a very low threshold for radiation exposure; even small doses are known to be gonadotoxic (as low as 600 cGy). There is no protection for the prepubertal testes.

Cancer therapy is more likely to affect a male’s ability to produce sperm but is less likely to affect ability to develop secondary sexual characteristics and less likely to affect sexual function. Sperm-producing cells are more sensitive to toxic effects of therapy than Leydig cells. For most survivors, sexual function and pubertal development are preserved, but fertility may be affected. Developments in the area of sperm banking and reproductive technologies have made it possible to offer fertility preservation to pubertal males undergoing cancer therapy. Pubertal males can produce a semen sample prior to starting gonadotoxic therapy and cryopreserve sperm for future use. Thus, viable sperm can be collected from adolescent boys who are newly diagnosed with cancer.

Parents and teens want information regarding sperm cryopreservation early. Providers should offer it as soon as possible to reduce treatment delays. Parents play an important role in the decision to sperm bank. Finances, ethics, religion do not seem to be important considerations for the families. Sperm banking should be offered to all eligible adolescents- regardless of the gonadotoxicity of the planned chemotherapy. Prepubertal males pose a particular challenge for fertility preservation. Prepubertal boys cannot produce semen for cryopreservation and they do not have mature spermatozoa. A recent and encouraging approach is the use of cryopreserved testicular tissue. The use of testicular tissue cryopreservation in humans currently remains experimental.

This topic touches upon two areas in which Howard has been particularly active during his long tenure at The Children’s Hospital of Philadelphia: andrology and oncology. Ever inquisitive, and never one to shy away from expressing an opinion, Howard takes pride in having been present and played a role as the treatment of these medical conditions evolved. Those of us fortunate enough to have spent time with him appreciate learning of this history first hand.

Sperm banking should be offered to all eligible adolescents- regardless of the gonadotoxicity of the planned chemotherapy. Prepubertal males pose a particular challenge for fertility preservation.
Application of Nanotechnology for a Catheter-Free Voiding Cystourethrogram

Andy Y. Chang, Emine Boz, Xinping Wu, Vincent Li, Anna Dawsey, and Travis J. Williams

During my fellowship interview at The Children’s Hospital of Philadelphia, I missed the opportunity to meet Dr. Howard M. Snyder, III. He was fulfilling his military obligations somewhere in the Midwest. I heard many great things about him; how he was a wonderful teacher, a superb surgeon, and a wealth of knowledge. I found out first-hand that all of these things were true, and then some, especially during Wednesday afternoon radiology rounds and Friday morning indications conferences. He was affectionately nicknamed Torquemada, the infamous Spanish inquisitor, by one of the other attendings (who shall remain nameless to protect the guilty). And yes, we fortunate house staff often bore the brunt of his questions until we begged for mercy. Through the haze of the unrelenting pimpling, it was easy to lose sight that Dr. Snyder was only trying to make us better. He has accumulated a wealth of knowledge and experience surpassed by few, in and outside of medicine. (Did you know he survived a plane crash in the Andes Mountains?) Dr. Snyder only wanted us to learn from his hard-fought lessons so that we can be better physicians to provide superb care for our patients. To this, his unwavering support, and friendship, I thank him. I am extremely fortunate to have walked in Dr. Snyder’s shadow.

In 2006, the NIDDK listed as a basic science priority the “development of noninvasive radiologic or biological methods for detecting and monitoring VUR.” We propose that the application of nanotechnology can result in a noninvasive radiologic detection of vesicoureteral reflux.

Nanotechnology is the study of particles 1 billionth of a meter small. To put this in perspective, 1 carbon atom has a diameter of 1/5th of a nanometer. When working with matter at this minuscule scale, we can exploit the atomic interactions to develop useful particles. We aim to exploit the molecular properties of gadolinium (Gd), a paramagnetic atom.

In a magnetic field, gadolinium enhances T1 contrast by decreasing the relaxation time of the surrounding spinning water molecules. If gadolinium is encapsulated in a protective water-proof shell, contrast enhancement will not occur. An “on/off” switch for contrast enhancement can be created if this shell can be selectively removed with ultrasound. The gadolinium nanoparticle can be intravenously injected and delivered to the bladder in an “off” state. Once in the bladder, the shell will be removed with ultrasound and thus “activate” the gadolinium. Any MRI contrast enhancement visualized in the upper collecting system would then be a result of vesicoureteral reflux. Thus, VUR can be imaged without catheterization.

Our first generation nanoparticle was designed with three layers; gold core, gadolinium inner particle, and outer shell (Figure 1). This construct allowed us to overcome a very important design hurdle: size. The kidney will not filter anything greater than 10 nanometers. The size of the complete nanoparticle was measured by dynamic light scattering (DLS). Our synthesized nanoparticle in various formats were placed into a 7 T MRI scanner, and image planes were acquired with a fast low-angle shot-based T1 contrast map sequence.

We synthesized a complete nanoparticle composed of gold core, gadolinium-containing inner particle, and fluorocarbon-polyethylene glycol shell that was 10 nanometers in diameter by DLS. MRI contrast intensity baseline was determined by the solution of gold particle only in water. The nanoparticle without shell had a 2-fold increase in signal intensity compared to gold particle only. When the shell was placed on the core nanoparticle, signal intensity decreased by 50%, or 1.5 times that of baseline. Exposure of the complete nanoparticle (core particle and shell) to ultrasound increased the contrast enhancement to 1.8 times of baseline (Figure 2).

We propose the application of nanotechnology for the diagnosis and surveillance of VUR. Using gadolinium encased in a protected shell, we should be able to deliver “switched off” gadolinium to the bladder via the blood stream. Initially, we envision an intravenous route of delivery, but formulation for an oral route may be feasible. Because our nanoparticle is less than 10 nm, it should be filtered through the kidneys. One study demonstrated close to 95% excretion of nanoparticles <8 nm into the bladder within 45 minutes of intravenous injection. Once in the bladder, the shells can be removed from exposing the gadolinium and turning it “on.” Once the nanoparticle has been “activated”, any MRI contrast enhancement seen in the upper tract will be a result of reflux.

In our first generation nanoparticle, we have shown the ability to mitigate gadolinium induced MRI enhancement by 25%, from 205 to 156. We partially restored gadolinium activity with ultrasound exposure. As we optimize our system and improve upon the nanoparticle, we expect to have better contrast enhancement.

Some may question the use of expensive MRI scanners, especially when sedation or general anesthesia is required for most children. Though this is not within the scope of our initial study, we have given much thought to this concern. MRI technology has advanced to the point where dynamic images of a beating heart can be captured in 20 milliseconds. This technique can be applied for our test. Additionally, we will not need to image the whole abdomen, just certain cross sections where the majority of the collecting system can be imaged. This will dramatically decrease the time needed for image acquisition and mitigate motion artifact that necessitates sedation. But more importantly, the goal of the exam is to determine if reflux exists and thus

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Application of Nanotechnology (continued from previous page)

image resolution is not vital for a useful test. Scanner time will be a fraction of any other MRI test and we are hopeful that this will make a future catheter-free MRI based VCUG affordable.

We have demonstrated an ability to synthesize a 10 nm nanoparticles composed of gold cores, covalently bound gadolinium-containing inner particles, and protective fluorocarbon shells. In a preliminary experiment, we demonstrated our ability to limit water exposure to gadolinium when the shell is attached. With exposure to ultrasound and removal of the shell, MRI contrast is enhanced. Refinement of these nanoparticles may pave the way to an MRI based catheter-free voiding cystourethrogram.

References

Figure 2

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Left: 7 T MRI image of Eppendorf tubes containing finished particles as well as control solutions. Right: The image intensities were computed using NIH ImageJ.
MCDK: Stick to the Facts!

CHOP was at the top of the list of centers I wished to visit when awarded a travelling scholarship in 1986. Cherished memories of my visit to Philadelphia include Howard and Mimi’s generous hospitality and Howard’s consummate surgical skills—both as an operating surgeon and an inspirational surgical teacher and trainer.

Shortly after my visit to CHOP my colleagues and I in Leeds published a paper documenting the natural history of a series of prenatally detected MCDKs, which included a population-based calculation of incidence of 1:4300.1 At that time, antenatal ultrasonography was used less routinely, and was less sensitive as a screening tool. For these reasons, this figure of 1:4300 probably understated the true incidence, and calculations of 1:2,400 - 1:3,600 published later from other centers are possibly closer to the true incidence. If we regard a birth incidence of 1:3,300 as a reasonably accurate figure, this translates into a total of more than 30,000 children born with MCDK in the United States since the advent of prenatal diagnosis in the 1980s. It is important that occasional case reports of malignancy and hypertension are viewed within this overall context.

Abdominal mass, unequivocal hypertension and diagnostic uncertainty are widely accepted as legitimate indications for nephrectomy. By contrast, controversy continues to surround the “prophylactic” surgical removal of clinically undetectable, prenatally detected MCDKs in healthy, asymptomatic children. The possible risks of malignancy and hypertension are the arguments usually advanced to justify this practice.

Malignancy

Until the mid to late 1990s publications on prenatally detected MCDK relied mainly on historical case reports of malignancy, in adults as well as children. In 1997, however, the distinguished paediatric pathologist Beckwith observed that the literature was “burdened with poorly documented or unconvincing cases” arguing that “the report should prove beyond reasonable doubt that the tumor is what it is purported to be and that the cysts truly represent multicystic dysplastic kidney disease.” Beckwith concluded “Most of the reported cases fail on one or both tests.”2

It is no longer necessary to resort to inaccurate historical case reports since there is now a substantial body of prospectively collected outcome data on conservatively managed MCDKs. For example, Narchi analyzed reported outcomes of 1041 children with conservatively managed MCDK in 26 published series – without a single reported malignancy.3 Cambio and associates4 reviewed 105 publications – to which they added some previously unpublished data from approximately 900 cases recorded on the MCDK registry. This extensive review identified only 3 malignancies in prenatally detected MCDKs, none of which occurred after 4 years of age or in involuted MCDKs. A systematic prospective study of 323 patients followed for a median of 10.1 years (0.3-15.4 years) by the Trent and Anglia MCDK Study Group encountered no malignancies.5 At the time of an earlier report in 2006 this group had observed that “the UK cancer study registry has no documented cases of Wilms tumour in MCDK kidneys.”6 There were no instances of malignancy in an (unpublished) prospective study of 350 children with prenatally detected MCDKs at The Great Ormond Street Hospital – 180 of whom were followed for more than 10 years [Dhillon H, Personal communication].

This question can be viewed differently by asking what proportion of children with proven hypertension is this due to MCDK? Hypertension is a relatively uncommon disorder in children and if MCDK was causing it on any appreciable scale this would be readily apparent from the published data. This is not the case. For example, Deal and associates published a series of 454 children with hypertension managed at the nephrology unit at Great Ormond Street Hospital over a 10-year period – without a single case of MCDK.8 In a later publication from the same institution, a series of 21 children undergoing nephrectomy for hypertension included only one case of MCDK.

Thus, the best available evidence indicates that the incidence of true hypertension in a genuine MCDK is very low – probably of the order 0.5% or less. Validated ultrasound diagnostic criteria for MCDK based on the published studies of Stuck and associates and other groups have been widely accepted since the 1980s. Amongst these diagnostic criteria is the absence of solid parenchymal renal tissue. As recently as 2011, however, a case report was published in which hypertension was attributed to a lesion purported to be a MCDK despite ultrasonography which clearly demonstrated that it was a predominantly solid dysplastic kidney with cystic elements confined to one pole.

Advocates of ‘prophylactic’ nephrectomy often justify their practice with the argument that ‘all bets are laying on a Wilms tumor arising in a prenatally detected MCDK’. Reviewing the North American Study Group data on a series of 7,500 Wilms tumors, Beckwith found that only 5 had arisen within MCDKs.9 In summary, whilst the literature (which now includes sizeable prospective series) does contain a small handful of credible reports of Wilms tumour arising in a prenatally detected MCDK, the best available evidence probably puts the absolute risk in the range 1:4000 - 1:7,500. Factoring survival rates into the calculation puts the risk of a child with a prenatally detected MCDK dying from Wilms tumour at around 1:50,000.

Hypertension

The Trent and Anglia MCDK Study Group did not encounter any cases of hypertension in 323 patients with MCDK who underwent systematic nephrological follow up for a median of 10.1 years (0.3-15.4 years).9 Similarly, MCDK Registry data on 441 MCDKs did not include a single case of hypertension. Narchi’s review of 1041 children in published series identified an incidence of hypertension of 0.5%.7 In the (unpublished) Great Ormond Street series of over 300 children, 1.8% underwent nephrectomy for a presumed diagnosis of hypertension. However, the existence of genuine hypertension in some of these patients was doubtful. (Dhillon H, Personal communication). Establishing a reliable diagnosis of genuine hypertension can be very problematic in this age group because of the difficulties inherent in obtaining accurate reproducible blood pressure readings in fractious infants.

But, with malignancy, this can be viewed from another angle by asking in what proportion of children with proven hypertension is this due to MCDK? Hypertension is a relatively uncommon disorder in children and if MCDK was causing it on any appreciable scale this would be readily apparent from the published data. This is not the case. For example, Deal and associates published a series of 454 children with hypertension managed at the nephrology unit at Great Ormond Street Hospital over a 10-year period – without a single case of MCDK.8 In a later publication from the same institution, a series of 21 children undergoing nephrectomy for hypertension included only one case of MCDK.

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Advocates of ‘prophylactic’ nephrectomy often justify their prac-
 tense by arguing that the decision is not theirs but the parents’ – “I counsel them and offer the choice.” This is a highly disingenuous argument since so much depends upon the manner in which the surgeon imparts information and treatment options to the parents. Asked to decide between “a simple operation” or “leaving the abnormal kidney in place and putting your child at risk of cancer” (I paraphrase), which parents would not opt for surgery? Remuneration may also influence clinicians’ thinking in some healthcare systems.

In summary, the overwhelming weight of evidence now indicates that routine ‘prophylactic’ nephrectomy for prenatally detected MCDK is an unnecessary operation. Since Pediatric Urologists can presumably all agree that it is never justifiable to submit healthy asymptomatic children to unnecessary surgery, logic dictates that we should now view prophylactic nephrectomy for MCDK as both an outdated and an unethical operation.

References

The Future of Deflux is the Future of Reflux

“Medicine, my friend, is a changing science.”

This quote by Howard M. Snyder III could not be more germane to the discussion regarding vesicoureteral reflux (VUR). When I was a fellow at CHOP (1996-98), the Cohen, Politano-Leadbetter, Paquin and Lich-Gregoir ureteral reimplantation procedures were the primary surgical methods to correct VUR. These highly successful operations remain wonderful teaching opportunities, exquisite surgery – perfect resident level experiences. Out of all of these procedures, the extravesical approach became very popular as a less invasive way to correct mostly unilateral VUR. After I departed my fellowship, endoscopic injection with Deflux was introduced in the USA – still the only FDA approved agent to treat VUR. Since our first case in 2001, our group at Children’s Healthcare of Atlanta has performed over 2,500 surgical cases for VUR, of which 85% were endoscopic surgeries. Since 2004, more than 200 urologists have participated in endoscopic training academies to learn the method. Today, endoscopic injection of Deflux has become the surgical procedure of choice for correcting VUR in over 50 countries worldwide.

“If you have a better way of doing an operation let me know”, Howard would often tell his fellows. I viewed these words a bit incredulously since I was sure Howard, with all of his experience, meant that he had already “been there, done that”. I was mistaken. Howard wanted to learn – even from his fellows – and I would soon understand the logic of his wisdom.

The future of Deflux is really a question of the future of reflux. Our ability to impact this area through surgical innovation and talented research protocols, such as the RIVUR trial, will hopefully change the landscape of VUR and UTI management. Over the past several years, however, articles in the pediatrics literature challenged our tenets regarding UTI and VUR. Despite the countless flaws these studies possess, the culmination of this work has lead to the AAP UTI guidelines which gave credence to the faulty reasoning that somehow diagnosing VUR is unwarranted unless it’s associated with two febrile UTIs or an abnormal renal sonogram. As a result, we have seen substantially fewer referrals to our specialty and an imposed limit in our capacity to manage UTIs and VUR.

The timing couldn’t be worse, since over the past 10 years, the success of endoscopic injection has gone from 70 to over 90% and has replaced open surgery throughout the world. Now that we are able to cure more children, the number of children referred has dropped substantially. Our experience with over 300 patients over a 4-year period using the Double HIT method has resulted in a cure of over 90% for up to grade 5 VUR. We have learned that the way one defines success requires long-term follow-up and may vary. If success is defined as a “negative VCUG,” then the success is 90%. If cure is defined as “no need for open surgery,” it’s 95%. For “no febrile UTIs after 1 treatment,” it’s 91%. Either way you view it, success is sufficiently high that we no longer feel it is necessary to routinely recommend VCUGs after treating primary VUR. Instead, we reserve the study for clinical failures, which we have seen in about 6% of patients. Finally, we have a safe injectable agent that is easy to use and highly successful in treating VUR.

Most pediatric urologists are appropriately concerned about the recent AAP UTI guidelines, as many more children will be put at risk for complications of UTI and VUR. On the other hand, many will avoid unnecessary and invasive testing. Determining who falls within these groups has yet to be determined. As a specialty group, we wonder if there will be more children admitted to the hospital with pyelonephritis or if the rate of renal scarring and its sequelae will increase. The VUR pendulum has swung from open surgery to non-diagnosis and it seems plausible that it will swing back. We must educate our colleagues on the paucity of supporting data that encompassed the AAP guidelines, the results of the Swedish Reflux Study (not included in the AAP UTI guidelines), and the much-anticipated RIVUR trial.

“When you stop learning it’s time to hang it up.” Howard told me at a recent meeting. Now I know the secret to being a great mentor: Be an excellent teacher but also an ardent learner. We can all benefit from the wisdom that teaching and learning go hand in hand. For mentors, friends, and role models like Howard Snyder, intellectual growth knows no bounds.
Pediatric Urology Workforce: Will Future Reimbursement Systems Support the Increasing Workforce?

Jean Hollowell, M.D., FACS

The prediction of needing more urologists is based on the analyses of the physician workforce, concluding that, “The principle drivers of health care utilization are not the ones commonly spoken of such as aging, technology or overall burden of disease. ….The magnitude of future workforce requirements, therefore, is a function of the aggregate ability of society to purchase services through private and governmental means.”

If the “burden of disease” in our field is perceived as the complex GU anomalies (such as neurogenic bladder, Prune Belly Syndrome and bladder exstrophy) truly requiring subspecialty expertise, then indeed the burden of disease has not been driving the utilization of our workforce. These types of cases have decreased, yet we have increased the number of pediatric urologists by about 40% over the last 15 years. This is largely due to increased “demand” (and “ability” to pay) for subspecialists for minor cases; we are now primarily doing minor pelvic and groin cases. Likewise outpatient visits are heavily weighted in cases such as monosymptomatic nocturnal enuresis, constipation, physiologic phimosis, penile adhesions, asymptomatic labial adhesions, excess skin after circumcision, etc. Most of these type “problems” (variants of normal in many cases) used to be taken care of by the PCPs.

A closer look at our astronomical increase in health care costs suggests the shift to specialist consultations is encouraged, or at least enabled, by our current system for paying for medical care. Copays are relatively small and many types of coverage require no copay. Primary care providers (PCPs) are reimbursed per patient visit, whether they write a referral slip to a specialist or they discuss that phimosis or penile adhesions are variants of normal in babies, etc. (Lack of TORT reform also further encourages PCPs to refer to specialists.) Subspecialists are also reimbursed fee for service, with “service” defined as the encounter with the patient, not by the level of expertise needed, nor by the health benefit the patient receives.

If our current reimbursement system for medical services does not change, this trend may continue and support the increasing number of pediatric urologists. However, if our current system does not change, our country will not be able to sustain the increasing costs of medical care. It is expected that the HC Reform Act of 2010 will move forward with a different reimbursement system, such as with Accountable Care Organizations (ACO), where there will effectively be no additional payment to the provider organization for subspecialist consultations.

In this type system we can expect many less referrals and I believe we will then have far too many pediatric urologists.

During my fellowship at The Children’s Hospital of Philadelphia, I learned an enormous amount from Howard and have appreciated his help over the years. One of many things I have valued is him drilling us on preparation for cases. One day before a bladder augmentation, Howard called me in his office and asked how I was going to do the case. He wanted me to tell him every minute step, including each type incision, excision, closure of incision, suture, instrument, tube, drain, etc. I cannot deny that it was intimidating that day. But it was the beginning of my writing up detailed notes that have been invaluable to me over the years. Thank you, Howard, for all you have taught me and for your support through the years.

References


Tribute to Howard Snyder, Friend, Scholar, Leader, Humanitarian

George F. Sheldon, M.D., FACS, FRCS Edin (Hon), FRCS Engl (Hon) and Erin Fraher, Ph.D.

I am honored to participate in an appropriate tribute to my friend. He is an acknowledged leader in health policy, urology and surgery in the 20th century. We became friends in 1970 when Howard was training in general surgery, pediatric surgery, and pediatric urology at the Harvard Service at the Peter Bent Brigham Hospital and at Boston Children’s Hospital with Dr. Robert Gross and Dr. Hardy Hendren. I was a research fellow in the laboratory of Francis D. Moore, MD, who was program director and chairman of the department of surgery in which Howard was trained. Our paths crossed frequently in subsequent years. We both worked with the Uniformed Services University of the Health Sciences (USUHS). We shared interests in health policy and also in medical history. From Harvard, Dr. Snyder was appointed to the faculty at The Children’s Hospital of Pennsylvania (CHOP).

Dr. Snyder and I shared an interest in an important historical figure, Philip Syng Physick, MD, the first professor of surgery in the oldest medical school in the United States. Howard chaired a committee with Philip Randolph, a direct descendent of Dr. Physick, to establish a small museum at the Physick home at 321 S. 4th Street in Philadelphia, Pennsylvania. The Physick House is one of the four homes on the historical tour of Philadelphia. I was scheduled to lecture on Dr. Physick at the Hunterian Society meeting—held for the only time outside of London—at the Physick house. An untimely death precluded my attending the Hunterian Society meeting, so Howard was kind enough (and learned enough) to make the presentation about Dr. Physick.

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In recent years, our association has been in the leadership of the American College of Surgeons (ACS). Howard is now approaching his third term as the Urology Regent, one of 21 surgeons representing all specialties that guide the fortunes of the ACS, the largest organization of surgeons in the world, with 77,000 members.

My tribute to Howard is focused on health policy. The American College of Surgeons’ Health Policy Research Institute, which has had the privilege of Dr. Snyder’s presence on its Advisory Board, convincingly demonstrated that the United States has a worsening shortage of surgeons. Currently the United States ranks 24th in the world in the ratio of practicing physicians per hundred thousand population; 21 specialty groups report shortages and 27 states report physician shortages.

Secretary of Health and Human Services Kathleen Sebelius has properly noted that “Health systems reform cannot happen without an adequate supply of well-trained, well distributed providers.”

John K Igelhart, commenting on the Affordable Care Act (ACA) in the New England Journal of Medicine, noted that “the law takes only modest steps [GME] to expand the workforce.” Moreover, to the degree that there is some focus on workforce, the focus is almost exclusively on primary care. The National Health Service Corps provides loan forgiveness in return for a time commitment into Health Profession Shortage Areas (HPSA). This is available only to primary care practitioners, dentists, nurses, midwives, and similar types of providers; this is not available to surgeons. The ACA adds 30 million people to Medicare which already has 10,000 people each day becoming 65 and eligible for Medicare. Moreover, the administration believes that monies can be saved through the legislation passed. Notable in the dialogue is the lack of recognition that physicians are necessary and that specialties are not interchangeable. A generalist obviously cannot provide definitive and needed therapy for a subdural hematoma, abdominal injury, most of oncology, and certainly the increasing number of urologic illnesses.

Dr. Snyder has labored mightily in educating lawmakers as to the need for sufficient workforce of all of the recognized 24 core specialties, essential for the balanced healthcare system expected by all Americans. The shortage will intensify reorganization of the health system. Regionalization of specialty services, already occurring, will address some of the problem. Small specialties such as pediatric urology will need a mechanism such as regionalization to make the unique skills of the specialty available to a citizenry that expects them.

Work from our Health Policy Research Institute has established that a diminishing supply of urologic surgeons relative to population is occurring. The urologic workforce is an aging and insufficient workforce, with notable shortages in rural areas. In recent years a slight increase in female urologic surgeons has occurred. Prior to 1981, the supply of urologic surgeons expanded faster than the population. That trend had reversed by 1991 and continues to decline.

Currently, the number of urologic surgeons is less than the ratio of 3.18 per 100,000 which existed in 1981. Likewise, general surgeons have not increased their numbers relative to population. In 1981, 1,074 general surgeons were certified by the American Board of Surgery; in 2008, 909 general surgeons were certified by the American Board of Surgery. It is not possible for primary care practitioners to fill the need. Expansion and creative deployment of the physician workforce is needed. We rely on accurate data to direct the best decisions. Opinions that are not supported by data are inadequate. Dedicated and articulate spokespersons of the nature of Dr. Howard Snyder are needed to accomplish that goal.

References
2. Igelhart JK. “Health Reform, Primary Care, and Graduate Medical Education”. NEJM. August 5, 2010; 363(6):584-590

| Table 1. U.S. Surgeons per 100,000 population, ordered by % change since 1981 |
|-------------|--------|--------|--------|--------|--------|--------|--------|--------|
| Thoracic    | 1.71   | 1.84   | 1.83   | 1.80   | 1.79   | 1.62   | 1.54   | -10.2%   |
| Urologic    | 3.23   | 3.36   | 3.49   | 3.43   | 3.39   | 3.29   | 3.18   | -1.3%    |
| Ophthalmologic | 5.41   | 5.69   | 5.05   | 6.09   | 6.21   | 5.95   | 5.86   | 8.2%     |
| Neurosurgery | 1.37   | 1.46   | 1.57   | 1.66   | 1.64   | 1.63   | 1.61   | 17.6%    |
| OB/GYN      | 11.03  | 11.76  | 12.68  | 13.05  | 13.55  | 13.23  | 13.21  | 19.8%    |
| Otolaryngology | 2.71   | 2.87   | 3.16   | 3.25   | 3.30   | 3.31   | 3.26   | 20.0%    |
| Orthopaedic | 5.74   | 6.32   | 7.30   | 7.51   | 7.27   | 7.35   | 7.26   | 26.4%    |
| Colorectal  | 0.34   | 0.35   | 0.35   | 0.38   | 0.41   | 0.45   | 0.46   | 34.9%    |
| Pediatric   | 0.18   | 0.21   | 0.23   | 0.23   | 0.25   | 0.25   | 0.26   | 43.2%    |
| Plastic     | 1.33   | 1.60   | 1.80   | 1.96   | 2.03   | 2.13   | 2.15   | 61.8%    |
| Vascular    | n/a*   | 0.33   | 0.52   | 0.64   | 0.74   | 0.83   | 0.85   | 157.2%   |