A Tribute: William J. Cromie, M.D.

FROM THE GUEST EDITOR

Barry A. Kogan, M.D.
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Bill Cromie has been a visionary in the field of Pediatric Urology. Though I knew of Bill’s contributions before, since becoming the Chief of Urology at Albany Medical College, I have become increasingly aware of Bill’s many influences. As you will see from the contributions in this edition of the Dialogues, Bill has been an important contributor in virtually every aspect of our field.

In April 2011, a symposium was held in Bill’s honor. The following contributions were among those presented at that meeting.

Bill Cromie’s Vision and Changes in Pediatric Urology

Bill Cromie was among the first to recognize and document the sea change that occurred in Pediatric Urology as a result of the development of medical ultrasound technology. This new imaging modality allowed for the visualization of urinary tract abnormalities in a very non-invasive way. The extension of this technique to the fetus allowed for a completely new era of

FROM THE EDITOR

Anthony A. Caldamone, M.D.

What Would Pediatric Urology Be Like Without Bill Cromie?

I had the privilege of meeting Bill Cromie for the first time when I was a resident in Rochester, New York and considering going into pediatric urology having worked closely with Ron Rabinowitz. I had no idea what a career long influence Bill Cromie would be for me at every step of the way. What is apparent, however, is that my situation is not at all unique. He has had a significant influence on the careers of many, not just in pediatric urology, not just in urology, in fact not just in medicine. What I thought I would do is outline what my perception is of Bill’s critical contributions to the development of our specialty in pediatric urology.

I will take you back to the early to mid-1990s at a time when the pediatric urology community in the United States was looking for an identity. There was a suggestion that in its struggle to achieve subspecialty recognition, pediatric urology would disassociate itself from the American Urological Association and align itself with the American Academy of Pediatrics where it may have more independence in deciding its future. The Society for Pediatric Urology at that time, therefore, was struggling for an identity and a purpose as well, and its relationship with
FROM THE GUEST EDITOR (continued from page one)

fetal diagnosis and treatment. For better or worse, Dr. Cromie documented that many of the most challenging diseases cared for by pediatric urologists (e.g. spina bifida, Prune Belly Syndrome, bladder and cloacal exstrophy) were markedly reduced in number, presumably due to fetal diagnosis and termination.1

The implications of these changes for the practice of pediatric urology are significant. Prior to the advent of prenatal ultrasound, a large number of these children could be successfully treated, resulting in many productive and successful lives. These patients presented significant medical and surgical challenges and stimulated research in pediatric urology as well as new techniques. In addition, knowledge gained in caring for these patients and their families was able to be translated into many other aspects of pediatric urology. Indeed, many young people, including myself, were stimulated to pursue a career in pediatric urology because of the fascination with helping patients and families with these conditions. Prenatal diagnosis and the associated terminations have led to a marked reduction in these cases, thereby greatly altering the practice of pediatric urology.

We have limited data on the actual surgical practice of the “average” pediatric urologist in the pre-ultrasound era, but we surmise it was radically different than today’s pediatric urologist. Fortunately, thanks to the American Board of Urology being willing to offer a certificate of added qualification in Pediatric Urology, we have much more information today. As part of the requirement for this certificate, all candidates were mandated to submit complete billing logs that documented the surgical practice of pediatric urology. As part of the process, 230 candidates submitted logs that reflected their practice activities in 2006 and 2007. Though not a 100% sample of pediatric urologists (many older pediatric urologists did not go through the process), these data are very likely to represent the work of the “average” pediatric urologist during those years.2

Review of these data show that the average pediatric urologist does about 500 cases per year. Although this would seem to be about 10 per week, it is important to recognize that many of the patients had multiple codes billed for each operation. For example, a bilateral orchiopexy would probably be billed as 4 different codes (orchiopexy x2 and hernia repair x2). Consequently, the actual numbers of patients operated on would be much less than 500. The character of the cases is also quite interesting. Almost half of the cases (228/505) were very minor penile and endoscopic cases, e.g. circumcision, lysis of penile adhesions or meatostrum. Of the more major cases, the bulk of them were scrotal and penile (124 and 73/505 respectively), including about 40 orchiopexies and 12 distal hypospadias repairs per year. On average, only 17 open reflux operations were done per year and 12 kidney cases. Interestingly, more than half of pediatric urologists did no enterocystoplasties, exstrophy closures, epispidias repairs, clitoroplasties or vaginoplasties! Only 14% of pediatric urologists did more than 2 enterocystoplasties and only 2% did more than 2 exstrophy repairs, epispidias repairs or clitoroplasties.

The implications of these findings are considerable. First, they point to the importance of regionalization of the rare procedures. Many studies have shown a positive relationship between volume and outcome in surgery. One can safely say that these rare and complex cases should be managed by teams with the highest volume of these cases. Apparently this has been happening de facto. In my opinion this process should be encouraged.

How has the lack of complex cases in the “average” pediatric urologists surgical practice affected the desire of young people to go into this field? Though many of us relished caring for these unusual and challenging cases, they are much more limited today and are clearly being regionalized. The pediatric urologist today does much more office practice and more relatively minor cases. On the other hand, many medical students and urology residents today are more focused on life style and this type of practice may be more suited to the lifestyle that young urologists envision. In point of practice, there still seems to be a large interest in the field. A recent paper has shed more light on the effects of these changes, as well as financial issues on the pediatric urology workforce.3

What will be the next major sea change in our field? I suggest we ask Bill Cromie. Bill has been a real visionary and my guess is that he’ll recognize what is happening to our field before the rest of us.

REFERENCES
FROM THE EDITOR (continued from page one)

the AUA was becoming significantly ambivalent. Working with Michael Mitchell and Howard Snyder, Bill helped develop a special membership category of the SPU entitled “Fellow Member”. This would be reserved for those doing nearly 100% of pediatric urology and was thought to hopefully provide a stepping stone to sub-certification. The certificate came into existence when Bill was Secretary of the Society for Pediatric Urology (Figure 1).

The next key step in the process was the development of the Pediatric Urology Advisory Council. This group of leaders in pediatric urology representing the SPU, AAP, SFU and AAPU would have the opportunity to meet with the American Board of Urology at least once a year at the American Urological Association annual meeting. This was a critical step in developing an open line of communication with the American Board of Urology as the atmosphere and playing field changed regarding sub-certification in urology.

When I succeeded Bill as Secretary of the Society for Pediatric Urology, I knew I had big shoes to fill. I had no idea that I had a big hat to fill as well (Figure 2). Bill continued to be extremely influential in defining the direction not only of the Society but also of pediatric urology in the United States. Two of his critical initiatives took a while to come to fruition, but again were key in the establishment of pediatric urology as an acceptable subspecialty. In 2000 the Dialogues in Pediatric Urology edited by Rick Ehrlich and published by Bill Miller ceased publication after 25 successful years. Bill Cromie had the idea that this should be resurrected under the guidance of the Society for Pediatric Urology. Indeed after negotiations with both Bill Miller and Rick Ehrlich, the reigns where handed over to the SPU and the Dialogues restarted publication in April 2004 and have continued uninterrupted since then.

The second major thought that Bill had in 2003 was the development of a World Congress of Pediatric Urology. He felt that there was enough momentum internationally for our subspecialty to be able to bring everyone together under one meeting. As all of you know in May 2010 the first World Congress of Pediatric Urology under the leadership of Marc Cendron came to fruition. Nearly 1000 pediatric urologists from around the world were brought together in San Francisco. This most successful academic meeting served as a statement as to the arrival of the subspecialty of pediatric urology internationally.

An additional thought that Bill had was that the SPU needed to break out of its “mom and pop” infrastructure, basically run by the Secretary of the SPU and his office secretary. He felt that we should have an administrative organization to handle the day to day details. However, our operating budget was balanced within pennies each year with no overage. Bill’s concept was to hire a professional fundraiser for the SPU and that the money raised would be able to offset the cost of an administrative infrastructure. He had his eye on someone right from the start, Jean Stasik from Chicago, whose efficiency not only allowed for financing an administrator for the organization but also a tremendous increase in programmatic development within the organization. This included the development of research funding on a yearly basis.

As most of you know pediatric urology was never challenging enough for Bill as he headed off for business training. However, we were fortunate that he was able to apply this new expertise to urology and be instrumental in the development of a manpower survey. He was also one of the first to forecast to us the changes on the horizon for healthcare as noted in his John Duckett lecture at the AUA in 2004 entitled “Who will pay: An insider’s view of physician directed health plan” (Figure 3).

I was fortunate that my association with Bill did not end with our professional lives, but carried over to some extracurricular activities. The most outstanding of these have been two trips taken with Bill, Marc Cendron and Jack Elder to the heights of Mt. Rainer as well as three peaks in Ecuador. (Figure 4) Here again his systematic approach to even “play” resulted in a tremendous learning experience for me. Bill has been a role model, guidance councillor, and an inspiration. On a personal note his encouragement and sage advice has always pushed me a little beyond my perceived comfort zone. So in answer to the question “What would pediatric urology be like without Bill Cromie?”, not as much fun at all.
Bill Cromie, Man of the People

Bill recently sent me this quote, which, I think, exemplifies his attitude towards life; “No act of kindness, however small, is ever wasted” (Aesop). The one event that stands out in my memory of attending, for the first time, the prestigious meeting of the Section of Urology at the Academy of Pediatric in San Francisco many years ago, was meeting Dr. Cromie. As a young urology resident, the whole event was intimidating and overwhelming. To my surprise, Dr. Cromie sat beside me during one of the interminable bus rides to the gala dinner and engaged me in a most caring and considerate manner. He queried gently, listened and offered sage advice. In doing so, as I am sure he has done countless time throughout his life, he was reaching out and doing an act of kindness which may have been small to him but huge in my mind. His unbridled enthusiasm and his boundless energy showed at another time we spent together climbing Mount Rainier and mountains in Ecuador. Despite the fact that he was the senior member of the group by at least five years, he never faltered and kept our spirits up with anecdotes and colorful stories.

Bill’s multifaceted carrier as a surgeon, pediatric urologist, CEO, singer, white water rafter etc. has always allowed him to seek out people, bring them together and push whatever project, idea or organization forward. His involvement with the Society for Pediatric Urology is a perfect example. He took a small organization with virtually no budget and minimal recognition and helped make it what it is today, a major driving force behind pediatric urology, having established its own certificate of added qualification and the first world congress of pediatric urology. His ability to see the big picture and implement important changes was the key to success.

Bill’s travels through life have not always been easy, but he has maintained his smiling attitude and his caring for his fellow men. I was struck by the fact that he was more interested in talking about the great people he met during his cancer therapy than about his illness. These people and what he saw in them clearly sustained him.

In April of 2011, over 400 of his friends, colleagues and family members came together to celebrate the establishment of the William J. Cromie Pediatric Urology Foundation in Albany, NY. These people came from all walks of life to recognize Bill’s contributions on so many levels. The outpouring of goodwill seemed to measure up perfectly and it was a joy to see Bill take it all, spending the time to speak, hug and touch each of the participants of this splendid event.

What Bill Cromie has achieved over the years in Pediatric Urology and in the health field would take many pages, but what remains is the fact that Bill reached out to so many and found ways to bring out the best in them. Those acts of kindness can never be forgotten.

The Split Appendix Technique for Appendicovesicostomy and Appendicococostomy: The Indiana Extension of the Cromie Cecal Extension Mitrofanoff

Mark P. Cain, M.D., FAAP, Pediatric Urology, Riley Children’s Hospital, Indiana University School of Medicine, Indianapolis, Indiana

It is not often that we get to publicly reflect on the importance of our mentors’ impact on our careers in pediatric urology. It represents a true pleasure to have participated in both the First Annual Bill Cromie Pediatric Urology Research Symposium this past April, and also this Dialogues in Pediatric Urology commemorating a career well spent for the first time, the prestigious meeting of the Section of Urology at the Academy of Pediatric in San Francisco many years ago, was meeting Dr. Cromie. As a young urology resident, the whole event was intimidating and overwhelming. To my surprise, Dr. Cromie sat beside me during one of the interminable bus rides to the gala dinner and engaged me in a most caring and considerate manner. He queried gently, listened and offered sage advice. In doing so, as I am sure he has done countless time throughout his life, he was reaching out and doing an act of kindness which may have been small to him but huge in my mind. His unbridled enthusiasm and his boundless energy showed at another time we spent together climbing Mount Rainier and mountains in Ecuador. Despite the fact that he was the senior member of the group by at least five years, he never faltered and kept our spirits up with anecdotes and colorful stories.

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The appendix as a Mitrofanoff channel has at this point withstood the test of time and durability. It has clear advantages in that it is readily available in most patients, already tubularized, has predictable blood supply, and removal for the Mitrofanoff channel has no affect on bowel function or require a bowel anastomosis. It also is the perfect option for the hallmark characteristics of a Mitrofanoff channel, being short, straight and supple tube that can be implanted easily in a submucosal tunnel into the bladder. The initial difficulties with the Mitrofanoff appendicovesicostomy were related to its lack of availability or in the few patients with a non-suitable appendix. This led to multiple different options being described, including fallopian tube, vas deferens, stomach tube, continent bladder tubes, tapered ileum and even prepuce as a substitute channel. It was not until the Yang Monti tube was described in the early 1990’s that a reasonable suitable replacement for the appendix was described. The greatest competition,

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The Split Appendix Technique for .... (continued from previous page)

however, for using the appendix as a catheterizable channel was Malone’s description of a MACE catheterizable channel using the appendicovesicostomy technique. In patients desiring complete fecal and stool continence, it clearly became more reasonable to use the appendix for the cecal channel in an in-situ fashion.

The natural question that would then arise is what is the optimal channel for the Mitrofanoff procedure? We reviewed our Indiana University data of approximately 300 appendicovesicostomy and Monti channels for the bladder, and found that each of them carried a similar surgical complication rate with approximately 25% of patients requiring some type of revision or endoscopic therapy. The majority of these patients required simple skin revisions; however, there was a tendency to require more extensive bladder revision in the patients that underwent a Monti channel. Both provided almost equal outcomes with respect to overall channel continence at approximately 96%. Since the Monti channels in this series had been a newer alternative and had much shorter follow-up, I reviewed my personal experience between 1995 and 2009, including a total of 192 channels. In this review, there were 105 Mitrofanoff procedures, including 65 patients with a Monti channel, 31 with an appendicovesicostomy and 9 with a continent vesicostomy. The results with the longer follow-up for the Monti ileovesicostomy channel indicated a much lower open surgical revision rate for the appendicovesicostomy at only 6% compared to 18% of the Monti channels requiring revision and 33% of the continent vesicostomies (all for stomal stenosis). Again, the Monti channels required much more significant revision surgery, mostly due to a hinging effect at the detrusor hiatus, most frequently from either diverticular outpouching, angulation or perforation at this site.

The superior results for the appendix as a catheterizable bladder channel were quite similar to outcomes that we described for the MACE channels with an institutional experience of over 235 MACE procedures. This was reported by Bani Hani in 2008, indicating a 14% complication rate for the in situ appendix compared to 18% revision rate for a Monti/MACE channel and 20% for a colon flap MACE.

The simple answer to how to best use the appendix when facing a complex reconstruction requiring both a MACE and Mitrofanoff channel is to split the appendix and use it for both channels. Unfortunately, this usually requires an appendiceal length of 8 to 10 cm and an appendiceal mesentery that can be divided leaving adequate blood supply for both channels. The answer to this dilemma came from a paper that Bill Cromie published in Urology in 1991 titled Cecal Tubularization: Lengthening Technique for Creation of Catheterizable Conduit. In essence, the paper described a technique to lengthen a short appendix that was otherwise non-suitable for a Mitrofanoff procedure by using a bowel stapler to extend the appendiceal length into the cecum. This became the basic principle behind several techniques described to lengthen the appendix for the MACE procedure described by Sheldon et al in the Journal of Urology and also by Hernndor several years later.

Cromie’s cecal extension concept then became the basis for extending the potential of dividing the appendix, using the longer segment for the Mitrofanoff channel and then creating a cecal extension into the base of the cecum to allow for an adequate continence mechanism for the MACE channel.

We recently published our experience with the split appendix technique in 43 total patients. Although this represents a small fraction of the over 500 Mitrofanoff channels performed at our institution to date, it has allowed avoidance of a bowel anastomosis required to create a Monti-MACE or Monti-Mitrofanoff channel in each of these children. The overall success reported by Vanderbrink et al was very consistent with our prior experience with 100% continence for MACE channels and 95% continence for appendicovesicostomy channels. The overall revision rate of 19% for all channels with mean follow-up of over two years also is identical to our prior published series. The beauty of this technique is the ability to avoid a bowel anastomosis in a child undergoing continent reconstruction without bladder augmentation, still using the appendix for both channels. This concept has truly been enhanced by Cromie’s cecal extension idea, which is an idea that has both endured and returned to benefit children undergoing reconstructive procedures.

I think the one of the greatest tributes that trainees in surgery give to their faculty is to pursue careers that follow in their path. Bill Cromie has certainly inspired many people across the breadth of Pediatric Urology, but I think this was most clearly represented in the Albany Medical Center graduating class of 1992 residency program. At that time, there were 10 residents in the urology training program, five of these trainees became fellowship trained in Pediatric Urology and four pursued careers in Academic Pediatric Urology. Each of us were inspired by this unique individual who would show up in the operating theater having just rowed crew on the Hudson River in the middle of winter, spent his weekends obtaining an MBA, his evenings singing in a men’s choir, raising five wonderful children, and coming to work every day with energy, enthusiasm and a smile on his face. On the wall in my office hangs a small porcelain statue from Luca della Robbia, a graduation gift from Dr. Cromie. Residents will sometimes ask me what this is and my answer is always the same, “That is the logo for The Society for Pediatric Urology, but more importantly it’s a gift from a friend, colleague, mentor, and my inspiration for being a Pediatric Urologist”. Thank you, Bill Cromie, for setting us all in the right direction in Pediatric Urology and for teaching us all more than just the skills to operate on children.

Suggested Readings:
It is a special pleasure to present this manuscript in honor of Dr. William Cromie. During our residency training, Dr. Cromie taught us not only Urology, but also how we were to conduct ourselves as young physician surgeons. He taught us not only science, but the art of medicine. He instructed us in pediatric urology, and also in complex reconstructive urology techniques (Figure 1) which I continue to utilize in my daily practice as a urologic oncologist. Dr. Cromie reached our minds and touched our hearts. To be with Bill is to be inspired. Thank you Bill.

Dr. Cromie spoke to us during residency about the concept of “Financial Credentialing”. He cautioned us that in the coming future it may not simply be enough to provide a medical service without attention to both outcome and resource utilization. He spoke to us about effectiveness (achieving a favorable surgical outcome) and efficiency (minimal resource utilization to achieve that outcome).

INTRODUCTION

In surgical care, the components of resource utilization include case selection, operative time utilization, disposable instrument use, length of inpatient hospital stay, complications and readmissions. The present study examines the impact of a defined post-operative management pathway on the inpatient hospital length of stay following a single operative procedure. The concept of using a defined peri-operative patient care pathway “Fast Track” for patients undergoing open partial nephrectomy is reported on. At the time that this pathway was introduced in our institution, similar programs had been reported for other abdominal procedures, including colon resection1,2, radical prostatectomy3, open aortic surgery4,5,6, open transperitoneal nephrectomy7 and laparoscopic nephrectomy.8 We sought to determine whether a defined fast track management protocol was feasible and safe for the management of patients undergoing open partial nephrectomy. At the time of our study, partial nephrectomy had become our preferred management approach to the patient with T1 renal mass.9-16

MATERIALS AND METHODS

The present study was initiated in July of 2006. All patients undergoing open partial nephrectomy were prospectively managed on a defined fast track pathway (Table 1). Patients undergoing laparoscopic and robotic partial nephrectomy were excluded. In the event that the decision was made intraoperatively to perform complete nephrectomy, patients were included on an intention to treat basis. Demographic data, tumor size, estimated blood loss, transfusion rate, final pathology, margin status, length of hospital stay and complications were captured prospectively. The control group was comprised of a cohort managed immediately preceding the introduction of the fast track pathway at our institution by the same surgical team. The study cohort is reported in Table 2.

Figure 2 shows the axial and coronal contrast enhanced CT images of a 3.8 cm left sided renal mass detected incidentally in a 63 yo male during the evaluation of right renal colic secondary to a 3 mm ureteral calculus. The patient’s medical history included poorly controlled hypertension. Following stone management, the patient’s serum creatinine was 1.4 mg/dl, with an estimated GFR of 59. Following review of the patient’s management options, the patient opted for partial nephrectomy.

TECHNIQUE OF PARTIAL NEPHRECTOMY

The kidney is explored. Vessel loops are used to tag the ureter, renal artery and renal vein. A double loop is passed around the vein for subsequent occlusion if necessary. Patients receive mannitol 12.5 gm (gram) IV (intravenous) bolus prior to manipulation of the kidney, followed by a 5 gm/hour continuous infusion. The renal artery is clamped in all cases, and the kidney cooled. In a bloodless field, the lesion is (continued on next page)
Fast-Track Open Partial Nephrectomy (continued from previous page)

scored (Figure 3) using the cautery on a coagulation setting of 60. Deep resection into the sinus fat (Figure 4) is carried out. Frozen section analysis assesses margin status. The collecting system is closed in running fashion with 3-0 monocryl on SH needle. Vessels are oversewn in figure of 8 fashion using 3-0 monocryl on SH needle. Tisseel is applied to the resection bed. Prior to removal of the renal artery clamp, the kidney is reconstructed utilizing 0-Chromic suture on CT needle in horizontal mattress fashion essentially obliterating the resection defect. (Figure 5).

RESULTS

At the time of our outcome analysis, 33 patients had been managed by fast track and compared to 25 patients that comprised the control arm (Table 3). Tumor size, pathology, estimated blood loss, transfusion rate and complication rate were similar between groups. There was a slight difference in the percentage of patients having malignant lesions on final pathology. More patients had renal cell carcinoma in the fast track group compared to control, 85% versus 76%. This may reflect improved patient selection and increased use of percutaneous needle biopsy (data not shown). There was, however, a significant difference in the post-operative length of hospital stay between the fast track and control groups (Table 4). Of the 25 control patients, 4 (16%) were discharged to home by the third post operative day, compared to 22 (67%) of the 33 fast track patients. Overall, the fast track patients had a shorter hospital stay compared to the control group (median, 3 days versus 4 days; p = .012).

Table 3. Outcome measures of fast track management

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Control Group</th>
<th>Fast Track Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating Room Time (min)</td>
<td>146-210</td>
<td>110-195</td>
</tr>
<tr>
<td>Range</td>
<td>179</td>
<td>152</td>
</tr>
<tr>
<td>Median</td>
<td>60-600</td>
<td>50-500</td>
</tr>
<tr>
<td>Estimated Blood Loss (ml)</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Median</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Transfusions</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Conversion to complete nephrectomy</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Post operative bleed</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Urine leak</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Positive margin</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Transfusions refers to number of patients receiving blood transfusion.

Figure 2. Axial and coronal imaging of a 63 yo male with an incidentally left sided 3.8 cm renal mass.

Figure 3. The lesion is scored using the cautery on a coagulation setting of 60.

Figure 4. Resection is carried out into the sinus fat in a bloodless operative field.

Figure 5. The vascular clamp on the renal artery is released following renal reconstruction.

Table 4. Post-operative length of hospital stay

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Control Group</th>
<th>Fast Track Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay (days)</td>
<td>3 - 10</td>
<td>2 - 6</td>
</tr>
<tr>
<td>Range</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Average</td>
<td>4.4</td>
<td>3.3</td>
</tr>
<tr>
<td>Discharge ≤ 3 days</td>
<td>4 (16%)</td>
<td>22 (67%)</td>
</tr>
</tbody>
</table>

Length of stay = the postoperative inpatient hospital stay following surgery.
Fast-Track Open Partial Nephrectomy

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The complication rate overall was similar between groups. In the control cohort, 1 patient had respiratory distress requiring ICU admission, 3 patients received blood transfusion, and there were 2 conversions to complete nephrectomy. In the fast track cohort, 1 patient required ICU admission for respiratory distress, 2 patients received blood transfusion and there was 1 conversion to complete nephrectomy. In addition, though not statistically significant, there was one case each of delayed post-operative bleed (gross hematuria) requiring selective arterial embolization and 1 urine leak requiring percutaneous drainage and ureteral stent placement. An updated analysis of our extended experience with fast track management of 112 consecutive patients undergoing open partial nephrectomy reveals delayed bleed in 3 (2.6%) patients and urine leak in 1 (1.0%) patient.

DISCUSSION

Since 1950, there has been a 126% increase in the incidence of renal cancer. It is likely that this increase is not only due to advancements in imaging technology, but also due to changes in lifestyle and the increasing incidence of obesity. Since 1950, there has been an increase in the number of patients undergoing open partial nephrectomy, with a 10% increase observed in the last decade.

Earlier investigators have reported on the effective use of a fast track management pathway for patients undergoing major abdominal surgical procedure with favorable results. Favorable results were seen in elderly patients, high risk patients and in children. In the present study, the introduction of a fast track program for open partial nephrectomy resulted in a hospital stay of 3 days, compared to 4 days before implementation of the program. Sixty-six percent of patients achieved a target discharge by the third post operative day. We suspect that the main contributing factor responsible for the decrease in hospital stay was a clear protocol of expectations at each stage of the recovery period. This was accompanied by intensive preoperative instruction and preparation, effective postoperative pain relief, management of stress and anxiety through reassurance and anxiolytics as necessary, early mobilization and early enteral nutrition. It is, however, impossible to discern which components of our protocol are the “key factors” or “most essential”. In addition, we have no proof from the present investigation that the fast track protocol was advantageous to the patient. The purpose of the present study was to assess the feasibility of such an approach. It is generally agreed, however, that shortened hospital stay is not only advantageous financially but may result in a decrease in hospital acquired infection and related adverse events. The delayed postoperative bleed and postoperative urinary leak in the fast track cohort is unlikely to be a result of the management pathway, and likely represents technical factors associated with an increasing complexity of resections performed. An updated review of our entire cohort of open partial nephrectomy patients (n=112) managed on fast track protocol reveals a delayed bleed in 3 patients (2.6%) and urine leak in 2 patients (1.7%).

CONCLUSIONS

The investigated fast track clinical pathway after open partial nephrectomy reduced the postoperative length of hospital stay from a median of 4 days to a median of 3 days compared to the control group. Discharge by the third post operative day was achieved by 67% of the patients on fast track pathway versus 16% in controls. The fast track pathway did not appear to increase the postoperative complications rate, though this requires confirmation by additional investigators.

REFERENCES

Various Testicular Issues: Large and Small

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Children’s Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, New York

Bill Cromie has been a very good friend of mine for a very long time. I don’t remember when and how we first met. We have shared many meetings together, hiked and rafted together, published together and shared many life experiences together. I was privileged to take care of many of Bill’s patients when he moved to Chicago. They all spoke so highly of Bill’s care. When Bill returned and became CEO of CDCHP it was great to be a participating provider in his organization. He ran a first class organization, always reachable, always the problem solver, always a man of reason; always comforting to know he was the man in charge.

When I heard about Bill’s illness I was devastated. We all know that “bad things can happen to good people”. Bill was always in my thoughts and prayers during this time. It is so good to be able to be a part of this program honoring Bill and to see him as he is presently: the vibrant, energetic, in-control personality that we know and love.

When I thought about a presentation for this meeting I thought “what is it that Bill might not know about in pediatric urology?!?” In “Googling” his CV I found that 37% of his publications dealt with TESTES, a subject dear to my professional heart. Testicles have been my professional hobby, so it seemed like a good fit. So I’ve picked out three subjects dealing with testicular disorders in childhood which Bill might not know about.

WHY DO TESTES GROW TOO BIG OR TOO SMALL?

Initially, fetal testis organogenesis consists of primordial germ cell migration then tubule formation under influence of various growth factors (TGF-beta, neurotropins, fibroblast growth factor, platelet derived growth factor). Germ cell proliferation and Sertoli and Leydig cell growth and development result from interaction of various cytokines. Postnatally, testis size remains constant during pre-puberty (2-4 ml). Little growth is present until puberty occurs, resulting in an accelerated growth, associated with activation of the hypothalamic-pituitary axis. In particular, gonadotropin secretion stimulates interstitium/Leydig cells to secrete testosterone, which induces up-regulation and increases growth factors, increasing tubular size. Since the tubules constitute the majority of testis volume, testicular growth occurs.

Testes are smaller than normal because of a variety of situations:

- Location (i.e., cryptorchidism)
- Temperature
- Congenital/genetic
- Hormonal (hypogonadotropic hypogonadism)
- Various drugs (opiates, alcohol, AAS, antihypertensives, diuretics, antidepressants, chemotherapy)
- Illness (trauma, infection)
- Nutrition
- Specific (UDT, varicocele, post-herniotomy, pre-and post-natal torsion, Klinefelters

Aging

For example, cryptorchidism is widely recognized as being associated with smaller than normal testes. Untreated congenitally cryptorchid testes are smaller than normal. The longer a testis remains cryptorchid, the greater the risk of atrophy. In a study of 106 boys ages 5-14 years with cryptorchid testes, 19% of those in P-2 puberty, 29% in P-3,4, and 38% in P-5 had smaller than normal cryptorchid testes. Iatrogenic cryptorchidism results in a smaller-than-normal testis both in experimental animals and humans and timely replacement of testis in scrotum results in improved testis volume.

Varicoceles present another interesting clinical situation exhibiting abnormal testis growth. Forty to seventy percent of boys have smaller than normal testes ipsilateral to the varicocele at presentation. Catch up growth occurs in some while under observation with progressing pubertal stage. Fifty to seventy-five percent will also demonstrate catch up growth after varicocelectomy (even occurring sometimes after unsuccessful repair!). So this is a unique situation:...growth arrest and then catch-up growth! The cause of this growth arrest appears to be related to the abnormal increased temperature associated with the varicocele, causing impaired Leydig cell structure and function. There are little data accurately explaining the accelerated growth seen subsequent to repair so far and theories are speculative.

The aging testicle undergoes progressive atrophy. Between 40-60 years, approximately 10% of men have testes less than 15 ml in volume; by the age of 60-80 years, this number triples.

Various medications, most notably anabolic steroids, also may cause testicular atrophy. As an example we can ask the question:

What does Barry Bonds have to do with all this?

Answer: in testifying about his steroid use, his ex-girlfriend Kimberly Bell stated:.... The shape, size of his testicles were smaller, unusual, differently shaped.....

New York Times March 11, 2011

Testes may enlarge abnormally as well.

This may occur in genetic abnormalities (macro-orchidism with fragile-X monorchidism, after varicocelectomy with abnormal accelerated growth, precocious puberty, and in “idiopathic” circumstances (i.e., peri-pubertal).

In boys with macroorchidism associated with fragile-X syndrome, a clear relation to the extent of the genetic abnormality exists. Only 13% of pre-pubertal boys who have a mosaic gene expression will have macroorchidism, but 30% when the gene is 50% methylated, and (continued on next page)
39% when the gene is fully methylated. In boys developing abnormally enlarged testes ("compensatory hypertrophy") associated with monorchidism, a clear relation to hypersecretion of FSH is observed.

So why do testes grow too big or too small?

Existent evidences suggest that endogenous/exogenous hormones, medications, nutrition, aging, genetics, testis location and surrounding temperature all cause a net effect on intra-testicular steroids and numerous growth factors. Ample evidence exists.

SEQUENTIAL TESTICULAR LESIONS POTENTIALLY AFFECTING FERTILITY

Cryptorchidism, varicocele, congenital testis absence, testis torsion and later testis loss or injury from inflammation, ductal injury or cancer all occur in pediatric urologic practice, each having a potential individual effect on fertility, but little attention has been paid to their effects when two or more of these lesions occur sequentially in the same patient. I have studied the clinical material in 49 patients having sequential lesions:

<table>
<thead>
<tr>
<th>Initial</th>
<th>Subsequent</th>
<th>#</th>
</tr>
</thead>
<tbody>
<tr>
<td>R UDT</td>
<td>L varicocele</td>
<td>12</td>
</tr>
<tr>
<td>UDT</td>
<td>contralateral delayed ascent</td>
<td>10</td>
</tr>
<tr>
<td>bil UDT</td>
<td>delayed contralateral correction</td>
<td>3</td>
</tr>
<tr>
<td>absent T</td>
<td>contralateral delayed ascent</td>
<td>9</td>
</tr>
<tr>
<td>absent R</td>
<td>L varicocele</td>
<td>7</td>
</tr>
<tr>
<td>R torsion</td>
<td>L varicocele</td>
<td>4</td>
</tr>
<tr>
<td>unil torsion</td>
<td>contralateral torsion</td>
<td>4</td>
</tr>
</tbody>
</table>

...and found that 45% had reductions in germ cells, either the initially or subsequently treated testis and 39% had abnormal numbers of germ cells in both testes, some with severe reductions.

An example is:

### Results of Semen Analysis Before and After Left Varicocelectomy

<table>
<thead>
<tr>
<th>Time</th>
<th>Volume</th>
<th>Concentration</th>
<th>Motility</th>
<th>Morphology (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>1.3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6 mo</td>
<td>2.2</td>
<td>$&gt; 2 \times 10^6$</td>
<td>&gt;50%</td>
<td>&gt;30</td>
</tr>
<tr>
<td>6 mo</td>
<td>2.6</td>
<td>$1 \times 10^6$</td>
<td>43%</td>
<td>22</td>
</tr>
<tr>
<td>12 mo</td>
<td>1.5</td>
<td>$0.4 \times 10^6$</td>
<td>40%</td>
<td>30</td>
</tr>
</tbody>
</table>

These observations raise many previously unanticipated questions. It appears that sequential lesions may occur more commonly than normally recognized. When sequential lesions of this nature are present, many will have an additive detrimental effect. Testis biopsy and semen analysis are helpful for prognosticating and altering treatment in some cases. Follow up is important and a more aggressive approach may be more advisable in some.

FERTILITY PRESERVATION IN CANCER PATIENTS

A third area that Bill might not know about regarding testicles is the impetus and work that is being done regarding fertility preservation in pre-pubertal children undergoing gonadotoxic chemotherapy for blood dyscrasias or cancer. About 1:650 children will be diagnosed with cancer by age 16 and 80% will now be cured. Similarly, bone marrow transplantation is now used much more commonly for treating blood dyscrasias (sickle cell, thalassemia, etc.) The aftermath of these treatments is that about 15-30% may be rendered sterile in these efforts to cure. Combination therapy, i.e. alkylating agents, RT + CT treatments create a higher risk and likelihood of sterility.

Semen cryopreservation in post-pubertal males is well recognized as a means of fertility preservation and ovarian tissue preservation in women has been successfully utilized with some having actual resumption of menstrual function or even pregnancy. But is there an application in pre-pubertal children? Ample animal experimentation documents ability to cryo-preserve ovarian and testis tissue, and to retransplant with preservation of tissue and resumption of function. Presently a number of children’s hospitals have undertaken implementation of these programs. We initially undertook tissue harvesting in 8 boys and 26 girls diagnosed with malignancy or blood dyscrasias and bone marrow transplantation undergoing gonadotoxic chemotherapy. Partial orchiectomy or laparscopic donor oophorectomy were done for tissue preservation. Previous work has indicated that tissue handling techniques and the method of cryopreservation are critical in optimizing success. This area currently is a hotbed of interest and a very rapidly changing field, having the potential to change the prospects for fertility presently from 0 to ??????

Bill, I certainly hope that this presentation has updated you and added to your knowledge, an area I know that you have been interested in. It has been my pleasure to be a part of this Symposium honoring you and to see you well at this time.

15 y.o. boy with R orchidopexy at age 5 (O germ cells in initial R biopsy)
L varicocele (grade II) at age 15
LEFT testis biopsy at varicocelectomy: severe germ cell depletion
It is hard to believe that nearly 20 years have gone by since I was a resident at the Albany Medical Center Hospital. Bill Cromie was my inspiration to become a pediatric urologist and we residents not only had excellent surgical training but also received a firm foundation on the state of knowledge as it existed at the time. Indeed I still do open ureteral reimplantations the way I was taught by Dr. Cromie!

I really thought I understood reflux when I finished my residency. We all thought that reflux caused urinary tract infections. We learned that all children with infections needed to undergo a voiding cystourethrogram to look for reflux. Children needed to have a yearly cystogram to assess the degree of reflux and to look for resolution. The standard of care was to continue prophylactic antibiotics until the reflux resolved, either spontaneously or by surgical correction. We knew that if reflux did not resolve in 5 years, it was not going to do so and that surgery was indicated. We also learned that girls should not be allowed to go through puberty with persistent reflux due to concerns about infection-related complications of pregnancy.

It is amazing how much change has occurred in our understanding of reflux over the past 20 years. It is now apparent that reflux is like prostate cancer! It is diagnosed in a large number of patients and it does not matter for most. It is a horrible problem for a few and we over treat patients because we cannot tell at diagnosis for whom it may matter.

We used to think that a VCUG was required in all children, especially males, who have urinary tract infections. Well performed prospective studies on DMSA-proven pyelonephritis have shown that the majority of children with febrile urinary tract infections do not have vesicoureteral reflux. Furthermore, it is apparent that the majority of infections, in general, are associated with disorders of bladder and bowel function and have little to do with perceived abnormalities of the vesicoureteral junction or the length of the submucosal tunnel. Even in males, especially with a normal renal ultrasound, the likelihood of finding “significant” reflux is quite low suggesting that routine cystography is not needed after a first infection. Prospective studies have shown that an initial DMSA scan may assist in determining which children might benefit from undergoing a VCUG in the first place. Acknowledging that there are significant issues with regard to access to primary care, uncertainty about whether a first infection was truly the first infection and the difficulties in diagnosing and treating disorders of bowel and bladder function, it is now clear that we can no longer make the blanket statement that a child with a urinary tract infection needs to have a VCUG performed to look for reflux. Indeed, upper tract imaging in conjunction with a careful history may be sufficient in guiding further management.

Several recent studies have called into question the role of prophylactic antibiotics in the management of reflux. These studies have shown no difference in infection rate or the development of new scars, whether or not the child has been on antibiotics. A problem with these studies is that a significant number of children had lower grades of reflux and older children were included, children for whom the risk of renal injury is relatively low. It may be difficult to translate the outcome of these studies to the real world since the children had an idealized management plan, with routine follow-up and prompt access to medical care should symptoms of an infection develop. In contrast, the Swedish reflux study, looking specifically at younger infants with higher grades of reflux, did show a significant advantage to prophylactic antibiotics with fewer infections and new scars compared to surveillance. What these studies may actually be telling us is that first, prophylactic antibiotics may be useful but only in younger children with high grade reflux, and second, that the key to preventing renal injury is not so much urological care but good primary care, whereby patients have rapid diagnosis and treatment of infections should they develop.

The logical extension of the thought that prophylactic antibiotics may not matter is the concept that reflux does not necessarily have to resolve. There are a few studies in the literature looking at outcomes of discontinuing antibiotics after a period of observation. Interestingly, all have similar findings, namely that only 10 – 15% of children will have infections during follow-up and that this usually occurs 18 – 30 months after antibiotics have been discontinued. These studies are retrospective and certainly there will have been tremendous selection bias. However, these studies do demonstrate that reflux does not “absolutely” have to resolve and that observation may be appropriate. Observation, however, does not mean doing nothing. These families do need aggressive education about infections in general and treatment with regard to disorders of bladder and bowel function. What is needed are good prospective studies looking at multiple parameters, including age, sex, degree of reflux, presence of renal injury and most importantly objective parameters of bladder/bowel dysfunction in order to better determine who would be an appropriate candidate for discontinuation or even not starting antibiotics in a child with vesicoureteral reflux.

The concept of ignoring reflux or discontinuing antibiotics is totally counter to the idea that reflux must be corrected prior to a girl reaching child-bearing age. There is rather substantial data suggesting that significant renal scarring, hypertension and/or renal insufficiency do markedly lead to an increased risk of pregnancy-related complications so it may be prudent to correct reflux in these situations. However, there are no data suggesting that girls without evidence of renal scarring will have an increased risk of complications, especially with lower grades of reflux. Since the risk of developing renal injury is low in older girls, there is little reason to consider surgical correction if reflux, especially low grade, persists past puberty. Long term prospective studies into adulthood of children who have had antibiotics discontinued.
Vesicoureteral Reflux... The More I Know, The Less I Know (continued from previous page)

continued will be needed to adequately tell us if persistent reflux really matters during child-bearing years.

The discussion above may make it sound as if reflux is a completely benign entity. Nothing is farther from the truth since we all see children with recurrent febrile infections despite aggressive medical management. Many children will have evidence of significant renal injury at diagnosis, either due to congenital dysplasia or undetected infections in infancy. Ureteral reimplantation is still a commonly performed operation though perhaps not as common as in the past. The reasons for failure of medical treatment are unclear. It might be related to noncompliance with medical management. Diagnosis and treatment of bladder and bowel dysfunction is an inexact science at best and I am amazed how some families do not bathe their children daily or do not use soap! Perhaps the biggest factor is that we still do not understand why some children are biologically predisposed to having infections and others are not.

The purpose of this essay is to inform new graduates and fellows-in-training that pediatric urology is an evolving science and what one may take to be the gospel truth may be shown to be inaccurate over the course of time.

I am personally indebted to Dr. Cromie for showing me how joyful and humbling it is to take care of children. I still have a hard time understanding how a parent can entrust the life of their child to a complete stranger and I have strived hard to emulate his personality and mannerisms in an attempt at garnering the trust of families with children with severe medical problems. His infectious enthusiasm and exuberant personality gave families significant comfort as they navigated difficult times. Bill Cromie has touched and enhanced the lives of innumerable children over the years, just as he has mine.

Pediatric Urology Workforce: Too Few or Too Many?

Jean Hollowell MD FACS
Division of Urology, Albany Medical Center, Albany NY

In 2001 Dr. Cromie published a paper, “Implications of prenatal ultrasound in the incidence of major genitourinary malformations”. He predicted that decreased births with major genitourinary anomalies, “… may influence our training programs, manpower needs, medical facility requirements and character of our practices”. Dr. Cromie’s predictions have indeed held true. While prenatal diagnosis has led to termination of pregnancies, thereby decreasing births of children with major GU malformations, we have increased the number of pediatric urologists. Today pediatric urologists have a practice “primarily of penile cases with few major cases” (based on case logs submitted in 2008 by applicants taking the first subspecialty certification exams in pediatric urology) and we are rapidly shifting away from academic medicine toward private practice.

Are we producing too many pediatric urologists? In the 2006 pediatric urology workforce survey, 23 planned retirement over the next 5 years, by 2011. Currently we have 26 fellowships, potentially producing one new pediatric urologist per year, or 130 over five years. In 1995 there were 165 pediatric urologists. In 2008-2010, the first three years pediatric subspecialty examination (PSCE) were offered, 274 took the exam, indicating approximately 60% increase in pediatric urologists over the last 15 years. In fact the number taking the PSCE probably underestimates the number currently practicing because not all pediatric urologists chose to take the subspecialty certification exams.

Are we diluting the surgical experience of major pediatric urology cases? Review of the 230 twelve month billing logs submitted by applicants to take the PSCE in 2008 and 2009 revealed that less than 5% of pediatric urologists did more than 2 vaginoplasties per year or more than 2 bladder extrophy closures per year. On average the applicant for subspecialty certification in pediatric urology is performing 2 proximal hypospadias repairs per year and 4 hemi-nephrectomy/nephrectomy per year. Even pyeloplasties, the “bread and butter” of pediatric urology, are relatively low in number: only 8 per pediatric urologist per year. These numbers signify a lack of surgical expertise that comes with experience and lack of experience managing the sequelae of major GU anomalies. This affects those who work with us also. If you do two or less extrophy closures per year, how experienced is the orthopedist who works with you on ostotomies? Or the NICU/PICU team who takes care of them after surgery? The dilution trickles down – adversely affecting the expertise of pediatric anesthesiologists, radiologists, orthopedists, our nurse specialists, etc.

Is there a shift in case distribution relative to training programs? Not only are the major cases diluted per pediatric urologist, but half of the pediatric urologists are no longer doing their cases at teaching institutions. In 1981, 90% of pediatric urologists were in academic practice. In 2008 the academic to private practice ratio was 50:50. Will this do to training the next generation?

These are challenges for the future. If we were to use the number of births of major GU abnormalities per year and number of major GU cases being performed annually to determine the number of pediatric urologists we need, we would likely decrease the number of fellowships. Regionalization for care of the major GU abnormalities may also be needed to correct the diluted experience we currently have and shift care of these major anomalies back to major academic medical cen-

(continued on next page)
Pediatric Urology Workforce.... (continued from previous page)

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It gives me great pleasure to discuss the elimination habits of Dr. William Cromie throughout his illustrious career in medicine, for as archeologists have said, a great deal can be gleaned about a civilization (in this case a person) by the detritus that is left behind.

I first met Bill in the mid 1970’s when he was an attending Pediatric Urologist at Children’s Hospital of Philadelphia with Dr. John Duckett. In 1979 he moved to Albany, near his boyhood home where he had been affectionately known during his formative years as ‘Billie Joe,’ to become Chief of Pediatric Urology. He remained as chief in Albany until 1994 when he moved to the University of Chicago to be chief of Pediatric Urology, remaining in that position until 2001. Then, he returned to the Albany area to serve as President and CEO of the Capital District Physicians Health Plan (or CDPHP) until 2008, when he officially retired from this position.

The questions I posed are what can we learn about ‘Billie Joe’ from the flow meter that was surreptitiously installed in his office and transported whenever he moved? And, is it possible to recreate the innermost thoughts of such a complex individual? This is not an easy feat to accomplish. It is almost like being an undercover agent trying to gain as much circumstantial evidence as possible in order to have ‘probable cause’ for someone’s actions.

During his years as an attending pediatric urologist, his elimination habits were generally normal, voiding 4 times a day, about every 4 hours, except when he had an extrophy closure to perform. He had bowel movements daily that were type IV on the Bristol Stool Form Scale (BSF scale). From this record it was assumed he had normal bladder function, with appropriate storage capabilities, complete emptying with a bell shaped curve and little or no residual urine to speak of. He seemed happy with himself and his life.

When he assumed the role of ‘Chief of Pediatric Urology’ in Albany and again in Chicago, his elimination habits changed, but not for the better. Now, he was voiding much more frequently, at least 8 times a day, coupled with several episodes of urgency but no incontinence; his bowel movements increased in frequency as well, and were now often type VI (BSF scale). It is assumed he tried to rule with a tight sphincter but this was in response to an irritable bowel.

On assuming the position of President and CEO of CDPHP, his elimination habits changed drastically once again. Now he hardly voided at all during the day and had multiple episodes of urgency and incontinence. His bowel movements, Type I and II on the BSF scale, occurred on average twice a week. His bladder enlarged dramatically as he ignored the signals coming from it to void. When he did void he had a very intermittent and staccato type flow curve despite taking Flowmax. He was unable to achieve complete bladder emptying; his ability to initiate a flow, good or bad, was predicated more on trying to relax his sphincter muscle than the volume of urine in his bladder at the time. His bowel movements were now just pebbles - Type I on the BSF scale. The secret ultrasound transducer installed near the seat of the flow meter demonstrated an increasingly thick-walled bladder with an ever-increasing amount of residual urine and massive amounts of stool compressing against the bladder. A simultaneous flow/EMG, using some of the new infra-red technology, made it possible to understand that his staccato type flow was due to a non-relaxing sphincter, that could eventually lead to high voiding and storage pressures, reflux and progressive renal deterioration. Oftentimes, people he met at work would see him cross his legs and lean forward as if curtseying, or even grabbing his crotch when he thought no one was looking, in order to prevent himself from urinating in public. As time progressed, this behavior became so pervasive; I suspect that was why he retired. It seems his elimination habits controlled his personality because he was not comfortable with the decisions he made as head of the health plan. Being the consummate physician that he is who cares more about people than the policies he had to enforce as an administrator of a health plan, where the bottom line was all that mattered, changed his elimination habits that ultimately altered his demeanor.

Billie Joe went into medicine because he enjoys people; his infectious smile, his melodious voice, his propensity for laughter, his ‘old boy’ slap on the back greetings and his pure joy for life are the elixir that makes him such a icon for positive thinking and good health. Bill, your elimination habits speak very highly of a man of your convictions. By analyzing them in the way we did over all these many years without your knowledge, I think we have developed a full understanding of where you have come from and where you are going.

William J. Cromie and the Flow Meter

Stuart Bauer, M.D., Department of Urology
Boston Children’s Hospital, Harvard Medical School, Boston, Massachusetts

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