

# Updates in Pediatric Urology

*Highlights of the American Academy of Pediatrics Section on Urology Annual Meeting,  
October 8–10, 2005, Washington, DC*

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Deflux • Cryptorchidism • Nephrolithiasis

**T**he American Academy of Pediatrics Section on Urology's Annual Meeting was held in Washington, DC, October 8-10, 2005. More than 100 papers and posters were presented on a wide range of topics, including cryptorchidism, genitourinary tumors, varicocele, exstrophy, sexual differentiation, reflux, hypospadias, neurogenic bladder, hydronephrosis, valves, and voiding dysfunction. Dr. Dixon Walker received the Pediatric Urology Medal. He is known for his numerous contributions to pediatric urology, especially in the area of vesicoureteral reflux. He also served as the first pediatric section editor of the *Journal*

*of Urology*. The meeting was well attended by pediatric urologists from North America, South America, Europe, and Asia. Select clinical abstracts from the meeting are highlighted below.

### Bladder Reconstruction

The need for subsequent bladder surgery after bladder augmentation has not been defined in a large series with long-term follow-up. Metcalfe and colleagues<sup>1</sup> performed a retrospective review on the first 500 bladder augmentations performed at Riley Hospital for Children in Indianapolis, IN, from 1978 to 2003. The need for additional surgery due to the development of malignancy, bladder perforation, reaugmentation, bowel obstruction, or bladder calculi was examined, with a mean follow-up of 13.3 years. There were 258 male and

242 female patients, with a mean age of 11.8 years at the time of bladder augmentation. Patients with a neurogenic bladder accounted for 72%; 54% had myelomeningocele. Ileum was used in 61% of augmentations. Sigmoid (19% of augmentations) and cecum (9%) were used primarily early on in the series. Gastric augmentations were performed in 9% and ureter in 2%. Complications occurred in 169 patients (34%). The incidence was 0.04 operations per patient per year of augmentation. There were 3 patients with transitional cell carcinoma (0.6%), all of whom presented with metastatic disease and died. Bladder perforations occurred in 41 patients (8.2%), with a total of 53 events leading to 1 death. Of these, 37 were repaired surgically, and 6 were managed conservatively. An increased risk of perforation was seen

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when bladder neck surgery was performed at the time of augmentation, whereas a decrease occurred with a catheterizable channel. Sixteen patients (3.2%) required a laparotomy for a bowel obstruction, with a higher rate found in patients with a gastric augmentation. There were 47 patients (9.2%) who required a second augmentation, for either inadequate compliance or bladder volumes. Ileal augmentations were associated with

was 28.4 months, and the rate of channel-related complications was 23%. In 7 ACE procedures, stomal stenosis developed within the first year, whereas stomal stenosis occurred in 9 continent bladder channels within 2 years after surgery. False passages occurred in 5 ACE procedures within approximately 1 year of surgery, and a similar finding was reported in 4 CCCs. Half of the patients with stomal stenosis required

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the lowest risk of requiring a second augmentation. Bladder stones were treated in 75 patients (15%), who required a total of 125 surgeries. Of these, 27% (34 of 125) required an open cystolithotomy, and 73% (91 of 125) were treated endoscopically. A higher incidence of stone formation was seen with catheterizable channels. This review provides important data on a large cohort of patients undergoing bladder augmentation, highlights the subset of patients who require additional surgery, and underscores the need for lifelong follow-up of these patients.

The group from Vanderbilt Children's Hospital in Nashville, TN,<sup>2</sup> reviewed their experience with continent catheterizable channels (CCCs) and the timing of their complications. This retrospective review identified 78 patients (mean age, 3.9 years) with 117 stomas. The appendix was used in 92% of antegrade continent enema (ACE) procedures, ileal Monti tube in 6%, and the cecal tube in 2%. For CCC, the appendix was used in 44%, the Monti tube in 37%, and bladder tube in 19%. The investigators found that almost all (98%) of the patients were continent. The mean follow-up

surgical revision, whereas the others were dilated without further problems. Catheter drainage alone was used to treat false passages. The investigators concluded that CCC led to a high rate of bowel and bladder continence and that stomal-related complications usually occur within the first year after surgery.

### **Vesicoureteral Reflux**

Investigators from Children's Hospital of Boston<sup>3</sup> examined a 15-year prospective database of patients with prenatal hydronephrosis (HN). The grade of HN was 3 or less, according to the Society for Fetal Urology grading system. The group was divided into patients who did and did not undergo a voiding cystourethrogram (VCUG) to determine the rates of reflux and the development of infection. The investigators identified 1514 of 2076 patients (72%) with prenatal HN of grade 3 or less. Three quarters of the patients had an initial VCUG, and 28% were found to have reflux. In patients with no reflux who were not taking antibiotics, urinary tract infection developed in 1.3%. In the group with reflux taking preventive antibiotics, a urinary tract infection

developed in 1.5% at a median age of 4 months. The investigators estimated that in those who did not undergo an initial VCUG, 98 of 347 would have reflux, and 1 of 347 would develop a urinary tract infection. Sixteen patients in this group developed a urinary tract infection. When a VCUG was subsequently performed, 12 of 16 had reflux. Therefore, of the estimated 98 patients with reflux, 12.2% developed a febrile urinary tract infection at a median age of 5.5 months. The investigators conclude that the VCUG performed in patients with low-grade HN aids in the identification of those with reflux who require preventive antibiotics, which reduces the risk of infection in this group. In addition, of the 140 of 1514 patients who had an initial VCUG and dimercaptosuccinic acid (DMSA) scan, 38% had primary reflux: 14% grade 1 to 2, 46% grade 3, and 40% grade 4 to 5. Of the 53 patients with grade 3 or less, 57% had abnormal results on DMSA scans. In patients with no reflux, no abnormalities were found on DMSA scanning. Therefore, patients with even low grades of reflux can be found to have abnormalities on DMSA scan.

The investigators from Children's Hospital of Iowa<sup>4</sup> examined predictive factors of spontaneous reflux resolution. They reviewed 120 children with primary reflux, aged 0 to 7 years. Parameters included age, gender, height, weight, urinary tract infection, history, reflux grade/laterality and bladder volume at onset of reflux relative to predicted bladder capacity, and reflux during filling or voiding for the first, second, and most recent cystogram obtained before spontaneous resolution or surgery. The average age of the patients was 2.3 years, and the average follow-up was just over 4 years. Reflux resolved in 64%, was surgically corrected in 23%, and was followed without intervention in 13%. The average time to resolution

was 2.2 years, and the average time to surgery was 3.6 years. Reflux was bilateral in half the patients. Low-grade reflux resolved more rapidly than higher grades. If the initial bladder volume was greater than 75% of predicted bladder capacity at the onset of reflux, reflux was more likely to resolve. Improvement in reflux grade between the first and second cystogram was also associated with higher rates of resolution. Interestingly, bilaterality and age were not predictors of resolution. The investigators conclude that in addition to grade, bladder volume at the onset of reflux and improvement between the

coureteral reflux. Of 382 infants, 203 were male, 274 had bilateral reflux, and 108 had unilateral reflux. This represented 642 high-grade refluxing units, (grade 3: 232; grade 4: 339; grade 5: 71). Teflon or Deflux was used in 432 and 210 ureters, respectively. The median duration of follow-up was 7 years. Complete resolution of reflux occurred in 443 ureters (69%) (Deflux: 73%; Teflon: 65%). More than one injection was used to correct the reflux in 127 ureters (20%). In 60 ureters, reflux was downgraded to grade 1 or 2, and no further treatment was given. Open surgery was performed on 12 ureters.

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Investigators from the Mayo Clinic and Pediatric Surgical Associates of Minneapolis<sup>5</sup> reported their results for 220 consecutive patients undergoing dextranomer/hyaluronic acid copolymer injection (Deflux; Q-Med AB, Uppsala, Sweden) for correction of reflux. The mean age was 5.4 years. Reflux resolved in 138 (63%) and improved in 44 (20%). There were 19 patients with duplications, and their cure rate was significantly reduced (42%). Low-grade (grade 1 to 2) reflux resolved more frequently than high-grade (grade  $\geq$  3) reflux (71% vs 53%). A second injection cured 5 of 10 patients. The investigators concluded that Deflux is a safe first therapeutic alternative, even though the success rate is significantly less than that of open surgery.

Investigators from Dublin<sup>6</sup> performed a retrospective review of 382 infants with grade 3 to 5 vesi-

These investigators present important long-term data on high-grade reflux in infants with vesicoureteral reflux.

Lorenzo and colleagues<sup>7</sup> at the Hospital for Sick Children in Toronto used polydimethylsiloxane for endoscopic treatment of reflux in 232 children with 350 refluxing units. They examined 23 variables to determine predictors of reflux resolution after injection. They found that the overall success rate by patient and renal unit was 65% and 72%, respectively. The success rate in low-grade (grade 1 to 3) vesicoureteral reflux that had not been previously injected was 80%. Physician experience, preoperative vesicoureteral reflux grade, presence of renal scars, and the number of previous injections were statistically significant determinants of success. This study is important in providing information to better select and counsel patients who require a treatment for reflux.

Kitchens and colleagues<sup>8</sup> from Cincinnati Children's Hospital and the

Children's Hospital in Denver reported on the use of Deflux injection for correction of reflux after failed uretero-neocystostomy. Seven patients underwent a Cohen procedure, 2 of whom had ureteral tailoring. Eight patients underwent extravesical reimplantation, 3 of whom required tailoring. Deflux injection was performed with a standard subureteric technique for extravesical reimplants, and a percutaneous access was used in some cases of cross-trigonal reimplants. Of the 15 patients injected, 87% had a good result at 14 months' follow-up. Approximately 75% were documented to have resolution of their vesicoureteral reflux. All 3 patients with extravesical tailoring had resolution of reflux, whereas only 50% of those with a tailored Cohen procedure showed resolution, with 2 patients showing improvement. The investigators conclude that endoscopic treatment of persistent reflux after ureteral reimplantation is safe and efficacious in patients with and without tapered ureters.

### Cryptorchidism

The group from Karolinska Hospital in Stockholm<sup>9</sup> performed a prospective randomized study of 162 boys aged 0 to 3 weeks and 6 months. Testicular volumes were obtained by ultrasonography at 6 months of age. Seventy-two boys were randomized to surgical treatment at 9 months, and 81 boys were randomized to surgical treatment at 3 years of age. The boys were then examined at 12 and 24 months. The investigators found that once orchidopexy was performed at 9 months, the testis resumed growth and was significantly larger than the delayed surgical cohort at 2 years. The improved testicular growth after orchidopexy was demonstrated by an increased ratio between the previously retained intrascrotal testis of the individual boys at 2 years. The

investigators concluded that surgical treatment at 9 months resulted in catch-up growth by 2 years compared with a nontreated group.

The investigators from Children's Hospital of Philadelphia<sup>10</sup> examined the role of TPX-1 in cryptorchid patients. TPX-1 is a testis-specific gene that is involved in Sertoli cell adhesion during spermatogenesis and is a component of the sperm acrosome and tail. In fertile men with poor motility, there is decreased expression of TPX-1. The study group was composed of 10 normal control patients, 8 patients with unilateral cryptorchidism, and 4 patients with a history bilateral cryptorchidism. Mean semen volume did not differ between the control and cryptorchid patients, but sperm density differences were noted between the unilateral and bilateral groups: the unilateral group had a sperm density of  $87 \times 10^6/\text{mL}$ , compared with  $17 \times 10^6/\text{mL}$  in the bilateral group. Sperm motility and forward progression were also shown to be poor in the bilateral group. A significant difference was found in TPX-1 expression, with the bilateral

cryptorchid patients showing a 7.3-fold difference in the expression compared with the bilateral group. TPX-1 expression was highly correlated with semen quality. The investigators conclude that diminished expression of the TPX-1 gene is associated with lat-

ent differences in the urinary metabolic evaluations between normal and stone-forming children. Most importantly, the supersaturation levels of calcium oxalate and calcium-to-creatinine levels were significantly higher in stone-forming children.

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*Diminished expression of the TPX-1 gene is associated with laterality of undescended testis in subsequent sperm parameters.*

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### **Nephrolithiasis**

DeFoor and colleagues<sup>11</sup> from the Cincinnati Children's Hospital and the University of Chicago reported a prospective study to assess urinary metabolic profiles in children with no history or family history of urinary calculi. The investigators performed 24-hour urinary collections and compared the data with those from a historical cohort of stone-forming, age-matched patients. Sixty-two patients who submitted 240 samples were evaluated. The study showed signifi-

DeMarco and colleagues<sup>12</sup> from Vanderbilt University Medical Center in Nashville, TN, presented a chart review of 44 patients with upper tract calculi. The objective of the study was to examine the role of hypocitruria in pediatric stone disease. The stone composition was primarily calcium oxalate (86%), carbonate apatite (9%), and other (5%). Just over half (55%) of patients had hypocitruria, defined as urinary citrate excretion less than 320 mg per 24 hours. The average citrate excretion in the hypocitruria group was 173 mg per 24 hours, compared with 492 mg per 24 hours in patients without hypocitruria. There

### **Main Points**

- A retrospective review of the first 500 bladder augmentations performed at Riley Hospital for Children from 1978 to 2003 showed that complications occurred in 34% of patients, underscoring the need for lifelong follow-up of these patients.
- Investigators from Vanderbilt Children's Hospital reviewed their experience with continent catheterizable channels (CCC) and the timing of their complications; they concluded that CCC led to a high rate of bowel and bladder continence and that stomal-related complications usually occur within the first year after surgery.
- Examination of a 15-year prospective database of patients with prenatal hydronephrosis (HN) showed that a voiding cystourethrogram performed in patients with low-grade HN aids in the identification of those with reflux who require preventive antibiotics, which reduces the risk of infection in this group.
- Results from 220 consecutive patients undergoing dextranomer/hyaluronic acid copolymer (Deflux) injection (Q-Med, Uppsala, Sweden) for correction of reflux show that Deflux is a safe first therapeutic alternative, though the success rate is less than that with open surgery.
- A report on the use of Deflux injection for correction of reflux after failed ureteroneocystostomy showed that endoscopic treatment of persistent reflux after ureteral reimplantation is safe and efficacious in patients with and without tapered ureters.
- Investigators from Vanderbilt University Medical Center report that pediatric stone formers often have associated hypocitruria, and stone recurrence rates are high in all prior pediatric stone formers; despite medical therapy, patients with hypocitruria are at risk for recurrence of stone disease.

was a significant difference in stone recurrence rates between patients with hypocitruria, who had a stone recurrence rate of 38%, and those without hypocitruria, who formed stones at a rate of 44%. Further evaluation of the group showed a stone recurrence rate of 33% in patients with hypocitruria without hypercalcuria, hypocitruria with hypercalcuria, and hypercalcuria without hypocitruria. Interestingly, 8 of 24 patients with hypocitruria were taking potassium citrate therapy, and 6 of the 8 had stone recurrence. The investigators conclude that pediatric stone formers often have associated hypocitruria, and stone recurrence rates are high in all prior pediatric stone formers. Despite medical therapy, patients with hypocitruria are at risk for recurrence of stone disease. ■

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