

MANY PEDIATRIC UROLOGISTS DON'T AGREE WITH REVISED AAP GUIDELINES

IN THIS ISSUE

CONFERENCE COVERAGE

Many pediatric urologists don't agree with revised AAP guidelines

Similar short- and long-term results seen with endoscopic and surgical treatment of reflux

Referral habits of pediatricians for children with reflux indicate improved dialogue is needed

Increased risk of reflux-related morbidity demonstrated among relatives of index patients with VUR

Survey provides insight into changing pediatric urology practice patterns

Downgrading of high-grade reflux with endoscopic correction may be an acceptable outcome

Independent risk factors identified for reflux-associated renal damage in young children

Safety and effectiveness of dextranomer/hyaluronic acid injection confirmed in over 1550 children

Low inter-rater reliability seen with the International VUR Grading System

Discrepancies seen in assignment of intermediate-grade VUR in the RIVUR Pilot Study

Concomitant anti-reflux surgery recommended for neurogenic bladder with associated high-grade reflux

Endoscopic treatment of secondary reflux in neurogenic bladder dysfunction considered suboptimal

Endoscopic treatment effective for urinary incontinence in neurogenic bladder

RECAP OF CME SYMPOSIUM TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

Fever without a source: How likely is it a UTI?

Antibiotic prophylaxis: Is it necessary?

Imaging strategy for infants and children with a first UTI

Dilemmas in treating febrile UTI: When in doubt, refer them out

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NEXT

The recent publication of the revised AAP guidelines for the diagnosis and management of febrile urinary tract infections (UTIs) in infants and children has generated a lively debate, with many pediatricians and pediatric urologists in disagreement over the recommendations. A glimpse into this controversy was provided during a point/counter-point panel discussion between **Kenneth Roberts, MD**, pediatrician and Chair of the AAP Subcommittee on Urinary Tract Infection that developed the guidelines, and pediatric urologist **Craig Peters, MD**.

In September, the AAP published its revised Clinical Practice Guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. The guidelines consist of seven Action Statements or recommendations based on a review of the recent literature.

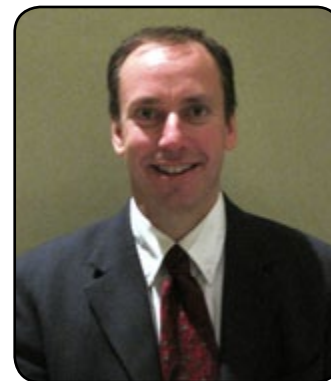
According to **Christopher S. Cooper, MD**, moderator of the panel, "A lot of pediatric urologists are angry over the new AAP guidelines, saying 'What are they thinking?'"

The most controversial recommendation is Action Statement 6, which was not endorsed by the Urology Section of the AAP during guideline development. According to this statement, voiding cystourethrography (VCUG) is not recommended routinely after the first UTI and is only indicated if renal and bladder ultrasonography reveals findings suggestive of high-grade vesicoureteral reflux (VUR), obstructive uropathy, or atypical/complex clinical circumstances.

Neither does Action Statement 6 endorse antibiotic prophylaxis as a means to prevent recurrent febrile UTI. A formal meta-analysis of 1091 infants aged 2 to 24 months found that there was no statistically significant benefit between children who received antimicrobial prophylaxis and those who didn't in preventing recurrence of febrile UTI/pyelonephritis. This was the case for infants without reflux and for those with Grades I, II, III, or IV VUR.

In developing this recommendation, data were adapted from six recent randomized studies. An analysis of the data suggests that of a hypothetical cohort of 100 infants with a first febrile UTI, only 10 will have a recurrence; therefore, the new guidelines will spare 90 children the trauma and discomfort of VCUG. Although the potential harm to an infant who is not found to have high-grade VUR until a second UTI is imprecise, the guidelines state that the data do not sufficiently justify routine VCUG.

Among many pediatric urologists, the common thread is the belief that there were methodological flaws in these studies and the revised guidelines are based on inappropriate analysis of the data. For example, some of the studies were insufficiently powered and most were not blinded or placebo-controlled, many included uncircumcised boys,



Christopher S. Cooper, MD

DMSA scans were often not performed, and compliance with antibiotic prophylaxis was not assessed.

In addition, Dr Peters feels that the guidelines do not consider the "real world" and do not provide an adequate safety net for patients with VUR, a complex condition that can result in significant renal injury with life-long implications. "Those who forget history are doomed to repeat the past," he warned, citing the fact that new scars were substantially reduced with treatment compared with surveillance in the Swedish Reflux Trial.

Dr Peters also feels that ignoring the first febrile UTI sends the wrong message to parents, whereas knowing about reflux changes behavior. In addition, he stated that good continuity of care is not always a given; one can't rely on proper follow-up after a second febrile UTI when patients move and don't always see the same doctor.

Dr Roberts agreed that the data are not perfect, but noted they are the best data available. In support of the guidelines he cited results of a just-published literature search on the association between childhood UTIs and chronic kidney disease (CKD), which suggest that a child with normal kidneys is not at significant risk of developing CKD because of UTIs. The authors of the Finnish study (Salo et al, Pediatrics) found only a 0.3% risk of CKD in infants with a febrile UTI. He posed a challenge to pediatric urologists as a group: In the next 4 to 5 years, could they create an algorithm, not by looking at the risk, but by looking at the outcome to determine how many children benefit from treatment?

Dr Peters also commented on what many feel is the lack of guidance in the revised guidelines. With these revised guidelines, he feels that the AAP is obligated to vigorously educate pediatricians. He said that one can't assume that pediatricians will just keep doing VCUGs as before, as they will think that they no longer have to do them to protect the child. "I suspect we'll see far fewer VCUGs," he noted. "We don't want to over-treat, but we truly don't want to under-treat."



SIMILAR SHORT- AND LONG-TERM RESULTS SEEN WITH ENDOSCOPIC AND SURGICAL TREATMENT OF REFLUX

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LUIS GARCIA-APARICIO, MD

Results of a recent randomized trial demonstrate that endoscopic treatment is an effective first-line treatment in children with Grade II to IV vesicoureteral reflux (VUR) that provides short- and long-term results similar to surgical repair.

"Endoscopic treatment has become the treatment of choice in VUR," noted **Luis Garcia-Aparicio, MD**, pediatric surgeon at the Hospital Sant Joan de Deu in Barcelona. "However, there has been a lack of randomized trials comparing the efficacy of endoscopic treatment and anti-reflux surgery."

In order to investigate the long-term outcome of endoscopic repair, clinicians at the Hospital Sant Joan de Deu and University of Barcelona conducted a study of children older than 1 year of age with primary VUR of Grades II, III, and IV that needed surgical repair. Between April 2002 and June 2004, they randomized children to endoscopic treatment with dextranomer/hyaluronic acid copolymer (Dx/HA, Deflux®) or surgical repair using Cohen's vesicoureteric reimplantation procedure. The same surgeon treated all children in the study.

Forty-one children comprising 67 refluxing ureters were included in the study. The median age was just under 5 years. Twenty-two children (35 refluxing ureters) were treated with Dx/HA and 19 children (32 refluxing ureters) were treated using Cohen's procedure.

There were no statistical differences between both treatment arms with respect to patient characteristics (ie, age, sex, time of VUR diagnosis), indication for surgery, and laterality) and renal unit characteristics (ie, VUR grade, renal side, renal

size, presence of renal scarring, and isotopic renal function).

Voiding cystourethrography (VCUG) was performed at 3 months, 9 months, and 60 months post-treatment in the endoscopic treatment group. If VUR was detected on follow-up, an additional endoscopic treatment was performed. In the surgical repair group, VCUG was performed at 6 months and 60 months. An absence of reflux on VCUG was considered successful treatment.

At 12 months, reflux was corrected in 32/35 (91%) refluxing ureters in the endoscopic treatment arm and 32/32 (100%) refluxing ureters in the surgery arm ($P=0.23$).

Twenty-eight percent of patients in the endoscopic arm required second injections of Dx/HA; 8 ureters required a second injection at 3 months, and an additional 4 ureters required a second injection at 12 months. Overall, the second injection successfully corrected reflux in 9 of the 12 ureters treated.

At 60 months, reflux was corrected in 30/35 (86%) refluxing ureters overall in the endoscopic treatment arm and 32/32 (100%) in the surgery arm. In the endoscopic arm, of the 32 ureters without reflux at 12 months, the majority (30 or 94%) remained free of reflux at 60 months.

Endoscopic repair resulted in significantly shorter procedure times and length of hospitalization compared with surgical repair, while offering similar complication rates and incidence of febrile urinary tract infections (UTIs) post-procedure.

Dr Garcia-Aparicio concluded that, "Endoscopic injection is as effective as surgical repair in both the short- and long-term."

Source:

12867 RANDOMIZED CLINICAL TRIAL BETWEEN ENDOSCOPIC TREATMENT WITH DX/HA AND COHEN'S URETERAL REIMPLANTATION FOR VESICoureTERAL REFLUX: LONG-TERM RESULTS

Luis Garcia-Aparicio¹, Jorge Rovira², Joan Rodo¹, Lucas Krauel¹, Bernardo Garcia-Nuñez¹, Pedro Palazon¹ and Luis Morales², (1)Pediatric Urology Unit, Pediatric Surgery Dept., Hospital Sant Joan de Deu, Barcelona, Spain, (2)Pediatrics and Pediatric Surgery Dept, University of Barcelona



REFERRAL HABITS OF PEDIATRICIANS FOR CHILDREN WITH REFLUX INDICATE IMPROVED DIALOGUE IS NEEDED

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The first study to date to assess primary care provider practice patterns for children with vesicoureteral reflux (VUR) showed that many pediatricians retain their reflux patients longer before referring to a specialist, which may lead to worsened outcomes for some patients.

VUR is common in children who present with a febrile urinary tract infection (UTI). However, according to **Michael Hsieh, MD**, of Stanford University School of Medicine in California, the management of children with VUR by pediatricians is not well characterized. For this reason, he and his colleague **Judith Hagedorn, MD**, also at Stanford, assessed practice patterns and referral habits of pediatricians who see children with VUR in their practices. An independent market research group administered a 34-question survey to pediatricians attending the AAP National Conference in October 2010.

One hundred and one pediatricians completed the survey. In general, respondents had been in practice for an average of 16 years and had varied practice locations.

On average, the respondents saw 6 patients per month with febrile UTIs. Of these, 22% returned with another UTI within 6 months. Of patients with febrile UTIs, 40% were confirmed as having VUR, and most had experienced just under two UTIs prior to their diagnosis.

The data suggest that pediatricians are closely following the American Academy of Pediatrics (AAP) 1999 guidelines for the work-up of a febrile UTI as far as the use of ultrasound and voiding cystourethrography (VCUG) are concerned. Most respondents (88%) use both imaging studies to work up a febrile UTI.

On average, the physicians treat a majority (73%) of VUR patients with prophylactic antibiotics. Forty-percent of survey respondents treat all of their VUR patients with prophylactic antibiotics, while 31% use antibiotics only for acute febrile UTIs. Thus, it appears that a significant number of pediatricians still follow the earlier 1997 American Urological Association (AUA) guidelines and treat all their VUR patients with prophylactic antibiotics regardless of age and reflux grade, rather than the more recent 2010 AUA guidelines that suggest limiting the use of antibiotics to certain patient subsets. This finding points to a need for better dissemination of the new guidelines to primary care providers, said Dr Hsieh.

Fifty-two percent of the responding pediatricians refer their VUR patients to a pediatric urologist immediately after the diagnosis is made, and 9%

refer after initial treatment failure. The remaining 39% treat their VUR patients themselves, even after initial treatment fails. More pediatricians who have been in practice for longer than 15 years indicated that they keep their VUR patients under their care than did those who have been in practice for less than 15 years (46% vs. 33%).

As one might expect, patients with higher grades of reflux were referred more frequently. Only 15% of patients with Grade I reflux were referred to a specialist, while virtually all patients with Grade IV and V reflux were referred out.

However, according to Dr. Hsieh, "The troubling part of the survey was the fact that 42% of those surveyed reported referring fewer of their complex reflux patients to a specialist in the past year." When asked about the primary rationale for delayed referral of patients, some of the most common reasons were "observation" and that "the urologist is very aggressive."

As a result, more children are suffering multiple episodes of febrile UTI prior to referral to a specialist, with more than 70% experiencing two or more febrile UTIs prior to referral.

Based on these findings, it is apparent that pediatricians are retaining their patients with VUR longer before referring them to a specialist. "This is worrisome because UTIs can lead to renal scarring, particularly in patients with reflux," commented Dr Hsieh. The results of the survey point to the need for clear referral guidelines. Improved dialog between urologists and pediatricians may help establish evidence-based referral guidelines for patients with VUR.

"The study had limitations in terms of convenience sampling and recall bias," noted Dr Hsieh. "But if even a fraction of these data are accurate, it is very troubling." ■

Source:

14402 PEDIATRICIANS' PRACTICE PATTERNS FOR CHILDREN WITH VESICoureTERAL REFLUX

Judith Hagedorn, and Michael Hsieh, Urology, Stanford University School of Medicine, Stanford, CA



INCREASED RISK OF REFLUX-RELATED MORBIDITY DEMONSTRATED AMONG RELATIVES OF INDEX PATIENTS WITH VUR

IN THIS ISSUE

CONFERENCE COVERAGE

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Results of a large, first-of-its kind, familial cohort study demonstrate that risk of reflux-related morbidity is increased beyond first-degree relatives of patients with vesicoureteral reflux (VUR).

"The familial nature of VUR is well known, with a prevalence of reflux of 27% to 51% in siblings of children with VUR, and transmission of reflux from parent to child in 31% to 66% of cases," according to **Manuela Hunziker, MD**, of the National Children's Research Centre in Dublin, Ireland. "However, there is little information about the prevalence of VUR and reflux-related morbidity in relatives of index patients with VUR."

Clinicians at the Research Centre, located at Our Lady's Children's Hospital, initiated a study to determine the prevalence of VUR and reflux-related morbidity in first-, second-, and third-degree relatives of index patients with high-grade reflux.

Between 1998 and 2010, the parents of 259 index patients with Grade III to V reflux were asked permission to screen siblings under the age of 6 years for VUR using renal ultrasound and voiding cystourethrography (VCUG). Families with two or more siblings with any grade of VUR were included in the analysis. Parents of index patients with affected siblings were contacted to obtain detailed information regarding history of VUR, recurrent urinary tract infections (UTIs), chronic renal failure, hypertension, and nephrectomy among first-, second-, and third-degree relatives.

Three hundred siblings of the 259 index patients were found to have VUR on VCUG. Besides siblings, the clinicians found that 127 additional relatives of the index patients also had radiologically proven VUR, including 18 parents, 36 second-degree relatives,

and 73 third-degree relatives. In 73% of these relatives, VUR was seen on the mother's side.

"The most striking finding of our study was the reflux-related morbidity observed in relatives of the index patients," noted Dr Hunziker. Evidence of renal scarring was confirmed in 49 (23%) of the 212 siblings who had dimercaptosuccinic acid (DMSA) scintigraphy performed. In addition, 21 non-sibling relatives had chronic renal failure, with 14 requiring renal transplantation and 7 requiring dialysis. Twelve non-sibling relatives underwent nephrectomies for reflux-related nephropathy and 4 suffered from reflux-associated hypertension. In addition, 59 non-sibling relatives continued to have recurrent UTIs for several years.

This was a large cohort of families from a single center worldwide with first-, second-, and third degree relatives affected with VUR. This study provides for the first time important information regarding presence of VUR and reflux-related morbidity in first-, second- and third degree relatives of index patients with high-grade VUR. "Our data clearly shows that there is increased risk of reflux-related morbidity among the relatives of index patients with VUR," noted Dr Hunziker. "This has implications for counseling."

Source:

14651 FAMILIAL VESICoureTERAL REFLUX AND REFLUX RELATED MORBIDITY IN RELATIVES OF INDEX PATIENTS WITH HIGH GRADE VESICoureTERAL REFLUX

Manuela Hunziker and Prem Puri, Our Lady's Children's Hospital, National Children's Research Centre, Dublin, Ireland

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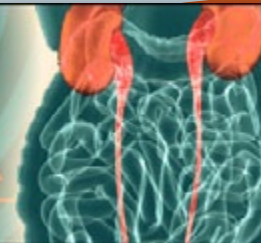
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Antibiotic prophylaxis: Is it necessary?

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SURVEY PROVIDES INSIGHT INTO CHANGING PEDIATRIC UROLOGY PRACTICE PATTERNS

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The increasing use of dextranomer/hyaluronic acid copolymer (Dx/HA, Deflux®) appears to be changing pediatric urology practice patterns. Lower long-term success rates recently reported in the literature have not appeared to impact clinician's use of Dx/HA, but suggest that follow-up with repeat imaging may be required.

Since its approval in 2001, Dx/HA has been widely used to treat vesicoureteral reflux (VUR). A large pediatric health information system database study published in the *Journal of Urology* in 2006 (Lendvay et al) described a 288% increase in the use of Dx/HA between 2002 and 2004. Although ureteral reimplantation rates remained steady over the study period, 60% of hospitals shifted toward Dx/HA use, suggesting that more clinicians were using it as first-line therapy or as earlier treatment.

"However, recent literature has questioned the long-term efficacy of Deflux," noted **Gina Cambareri, MD**, of the UMDNJ New Jersey Medical School. She cited a recent study of children treated with Dx/HA (Lee et al, *J Urology*, 2009) that reported complete resolution of reflux after 1 year in only 46% of patients, which is lower than previously reported studies.

Dr Cambareri and her colleagues at the New Jersey Medical School, Children's Hospital of New Jersey, and New York Weill Cornell Medical Center recently conducted a survey to determine if pediatric urology practice patterns have changed in this relatively new era of Dx/HA.

A 12-question survey was sent to 476 members of the Society for Pediatric Urology. The survey consisted of a series of questions regarding the use of Dx/HA, including its use as first-line therapy, factors that influence its use (ie, presence of renal scarring), success rates reported to parents, influence of recent reports of low efficacy on usage, imaging used during follow-up, use of repeated injections for initial failures, and if reimbursement affects decision making.

A total of 133 pediatric urologists answered the survey.

Of the respondents, 24% indicated that they use Dx/HA as first-line therapy for Grade III reflux or higher, while 20% indicated they perform open surgery and 24% indicated neither procedure. Thirty-two percent indicated that their choice of procedure depends on factors such as parental preference, which was the most commonly cited factor, grade of reflux, and presence of scarring. However, 55% indicated that they would continue to use Dx/HA in the presence of renal scarring.

The majority of respondents (82%) said they try a trial of observation with or without prophylactic antibiotics before using Dx/HA in a child who presents with reflux, and 80% continue observation in a child with or without antibiotic prophylaxis before moving to Dx/HA at an age considered appropriate

for surgery.

Only 23% of respondents indicated that the long-term success rate cited in the recent literature decreased their use of Dx/HA.

The success rates with Dx/HA that the respondents provided to parents varies according to the grade of reflux. The majority of pediatric urologists cited success rates of greater than 70% and greater than 80% for Grades II to III reflux, which is similar to what has been reported in the literature. For Grades IV to V reflux, respondents most frequently cited greater than 50%.

When questioned which imaging modality pediatric urologists routinely use for follow-up after endoscopic treatment of reflux, 87% indicated they use ultrasound. This finding is in line with the 2010 American Urological Association VUR guidelines, which delineates ultrasound as a standard in imaging modality for follow-up after Dx/HA injection. The majority of respondents perform ultrasound 1 to 2 months following the procedure.

Sixty-five percent of respondents routinely use voiding cystourethrography (VCUG), most often 3 months following Dx/HA injection. Interestingly, only 5% of clinicians perform a VCUG at 1 year. According to Dr Cambareri, "What is interesting about the Lee paper is they found failures at 1 year based on getting that VCUG at 1 year as opposed to 3 months after the initial procedure." This may indicate that follow-up with repeat imaging may be required in the long-term.

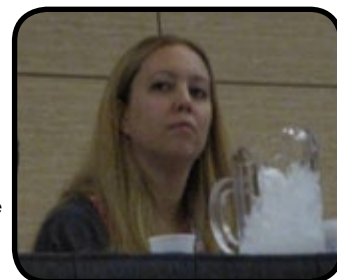
After an initial failed injection of Dx/HA with unchanged unilateral reflux, 60% of respondents indicated they would perform a second injection of Dx/HA as opposed to another treatment option (ie, surgical reimplantation or observation with or without antibiotics). This is supported by the high success rates reported in the literature with subsequent injections of Dx/HA.

The vast majority of respondents (94%) indicated that reimbursement for Dx/HA does not influence their decision to perform endoscopic repair versus surgical reimplantation. ■

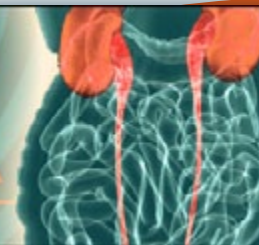
Source:

13564 PRACTICE PATTERNS IN THE USE OF DEFLUX® TO TREAT VESICoureTERAL REFLUX

Gina Cambareri, Urology, UMDNJ-New Jersey Medical School, Newark, NJ; Jeffrey A. Stock, Pediatric Urology, Children's Hospital of New Jersey, West Orange, NJ and Moneer K. Hanna, Pediatric Urology, New York Weill Cornell Medical Center, New York, NY



GINA CAMBARERI, MD



DOWNGRADING OF HIGH-GRADE REFLUX WITH ENDOSCOPIC CORRECTION MAY BE AN ACCEPTABLE OUTCOME

IN THIS ISSUE

CONFERENCE COVERAGE

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Investigators at the Shaare Zedek Medical Center in Israel found that downgrading vesicoureteral reflux (VUR) with endoscopic correction may be an acceptable outcome in patients with high-grade reflux who suffer from breakthrough infections while on antibiotic prophylaxis.

Boris Chertin, MD, and his colleagues investigated the incidence of UTI and the natural history of downgraded VUR in children with high-grade VUR following endoscopic correction. Their hypothesis was that downgrading of VUR following endoscopic correction may reduce the incidence of febrile UTI and additional renal parenchymal damage.

The association between high-grade VUR, febrile UTIs, and renal damage is well known. Endoscopic correction of VUR has become a first-line option in the treatment of VUR, but the outcome in high-grade VUR is inferior to that obtained with open surgery.

Between 1988 and 2010, over 1000 children underwent endoscopic correction of VUR at the center. Of these, 54 children (13 males and 41 females) with Grade IV to V reflux had experienced breakthrough infections while on antibiotic prophylaxis. Their mean age was 1.8 years (range, 8 – 34 months), and the majority (74%) had Grade IV reflux. The group comprised 95 renal refluxing units (RRU).

Preoperative dimercaptosuccinic acid (DMSA) scintigraphy documented renal scarring in 51 of 73 (70%) RRUs in patients with Grade IV VUR and in 15 of 22 (68%) RRUs in patients with Grade V VUR.

Endoscopic correction was performed utilizing polytetrafluoroethylene (Teflon[®], n=43), dextranomer/hyaluronic acid (Dx/HA) copolymer (n=50), or polyacrylate polyalcohol bulking copolymer (Vantris[®], n=2). All patients underwent ultrasound at 1 month and voiding cystourethrography (VCUG) between 3 and 6 months post-injection. VUR was considered to be downgraded if the VCUG indicated Grade II reflux, or if a patient with Grade V reflux improved to Grade III. All patients who demonstrated downgraded VUR were taken off antibiotic prophylaxis and observed.

Following endoscopic injection, reflux was corrected in 72 of the 95 (76%) RRUs and downgraded in 23 (24%) RRUs (18 patients). Of the downgraded RRUs, 21 were Grade II VUR and 2 were Grade III VUR.

The 18 patients with downgraded VUR received an annual ultrasound and DMSA scans were performed at the beginning of adolescence, after puberty, and if there were any signs of deterioration of the kidney on ultrasound. VCUG was repeated if requested by the primary care physician or upon enlisting in the army. Patients were followed for periods ranging from 2 to 22 years, with a median follow-up period of 14 years.



BORIS CHERTIN, MD

Following antibiotic discontinuation, 3 female patients (17%) with downgraded VUR experienced afebrile UTI, while no patients with downgraded VUR developed febrile UTI. Although preoperative renal scarring was present in 21 of the 23 RRUs with downgraded VUR, only one RRU developed a new renal scar or experienced renal function deterioration during follow-up.

Eight of the 18 patients underwent follow-up VCUG, 2 as a result of recurrent afebrile UTIs. Spontaneous resolution or downgrading to Grade I VUR was documented in 7 (88%) of these patients.

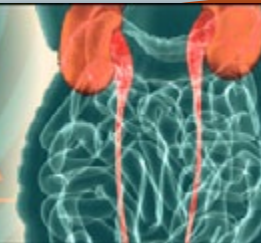
Limitations of the study included its retrospective nature, the relatively small number of patients with downgraded VUR, the possibility of undocumented afebrile UTIs, and potential missed VUR recurrences due to lack of consistent VCUG follow-up. In addition, the success rate seen is higher than previously reported in high-grade reflux.

"Our data show that downgrading of VUR is a reasonable option in patients with high-grade reflux suffering from breakthrough infections while on antibiotic prophylaxis," concluded Dr Chertin. "It leads to the cessation of febrile UTIs, further spontaneous resolution of VUR, and may potentially avoid renal damage." ■

Source:

12665 DOWNGRADING OF HIGH GRADE VUR IS A RELIABLE OPTION IN THE TREATMENT OF CHILDREN WITH GRADE IV-V VUR AND BREAKTHROUGH INFECTIONS

Boris Chertin, and Stanislav Kocherov, Pediatric Urology, Shaare Zedek Medical Center, Jerusalem, Israel



INDEPENDENT RISK FACTORS IDENTIFIED FOR REFLUX-ASSOCIATED RENAL DAMAGE IN YOUNG CHILDREN

IN THIS ISSUE

CONFERENCE COVERAGE

Many pediatric urologists don't agree with revised AAP guidelines

Similar short- and long-term results seen with endoscopic and surgical treatment of reflux

Referral habits of pediatricians for children with reflux indicate improved dialogue is needed

Increased risk of reflux-related morbidity demonstrated among relatives of index patients with VUR

Survey provides insight into changing pediatric urology practice patterns

Downgrading of high-grade reflux with endoscopic correction may be an acceptable outcome

Independent risk factors identified for reflux-associated renal damage in young children

Safety and effectiveness of dextranomer/hyaluronic acid injection confirmed in over 1550 children

Low inter-rater reliability seen with the International VUR Grading System

Discrepancies seen in assignment of intermediate-grade VUR in the RIVUR Pilot Study

Concomitant anti-reflux surgery recommended for neurogenic bladder with associated high-grade reflux

Endoscopic treatment of secondary reflux in neurogenic bladder dysfunction considered suboptimal

Endoscopic treatment effective for urinary incontinence in neurogenic bladder

RECAP OF CME SYMPOSIUM TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

Fever without a source: How likely is it a UTI?

Antibiotic prophylaxis: Is it necessary?

Imaging strategy for infants and children with a first UTI

Dilemmas in treating febrile UTI: When in doubt, refer them out

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Grade IV to V reflux, male gender, history of urinary tract infection (UTI), and not being screened for sibling reflux were identified as significant independent risk factors for reflux-associated renal damage in children under the age of 3 years in a recent retrospective chart review undertaken at the National Children's Research Centre in Dublin, Ireland.

The association of vesicoureteral reflux (VUR) and renal parenchymal damage is well known, with renal injury occurring early, before the age of 3 years in most patients. In order to determine risk factors associated with renal damage in patients with primary high-grade VUR during this critical timeframe, **Manuela Hunziker, MD**, and her colleagues retrospectively reviewed the medical records of children with Grade III to V VUR treated at their institution between 1998 and 2010.

VUR was diagnosed using voiding cystourethrography (VCUG), and dimercaptosuccinic acid (DMSA) scintigraphy was performed to evaluate the presence of renal scarring. Children were divided into those younger than 3 years of age and those 3 to 13 years of age at diagnosis. For multivariate and univariate analysis, risk factors such as gender, history of UTI, reflux grade, and not being screened for sibling VUR were analyzed in a logistic regression model.

A total of 1765 consecutive children (544 males and 1221 females) with primary high-grade VUR were treated during this time period and included 1154 patients younger than 3 years and 611 patients older than 3 years.

Renal scarring was documented in 384 (25%) of the 1529 patients who had a DMSA scan performed. The prevalence of renal scarring was significantly lower in children diagnosed with VUR prior to 3 years of age than in those diagnosed after the age of 3 years (18% vs. 38%, $P < 0.001$).

Univariate analysis revealed that Grade IV and V reflux ($P < 0.001$, OR=6.0 [95% CI, 3.2-15.4]), male gender ($P = 0.024$, OR=2.3 [95% CI, 1.3-3.9]), a history of UTI ($P = 0.042$, OR=1.6 [95% CI, 0.9-3.7]), and not being screened for sibling VUR ($P = 0.041$, OR=0.4 [95% CI, 0.2-1.0]) were significant independent risk factors for renal parenchymal damage in children younger than 3 years of age. In children older than 3 years of age, reflux grade ($P < 0.001$, OR = 6.8 [95% CI, 3.6-16/1]) was the only significant independent risk factor for renal parenchymal damage.

Multivariate analysis identified Grade IV and V reflux and not being screened for sibling VUR as significant risk factors for renal parenchymal damage in children less than 3 years of age, and Grade IV and V reflux as a significant risk factor for children older than 3 years.



MANUELA HUNZIKER, MD

"A history of UTI, male gender, Grade IV and V reflux, and not being screened for sibling VUR were the most significant risk factors for the development of reflux-associated renal damage in children under the age of 3 years," noted Dr Hunziker. "Early detection and treatment may prevent renal damage due to ongoing VUR or progression of renal damage."

Source:

14715 RISK FACTORS FOR THE DEVELOPMENT OF RENAL PARENCHYMAL DAMAGE IN PRIMARY HIGH GRADE VESICoureteral REFLUX DURING THE FIRST 3 YEARS OF LIFE

Manuela Hunziker¹, Balazs Kutasy¹, Federica D'Asta² and Prem Puri¹, (1)Our Lady's Children's Hospital, National Children's Research Centre, Dublin, Ireland, (2)Pediatric Surgery, National Children's Hospital, Dublin 24, Ireland



SAFETY AND EFFECTIVENESS OF DEXTRANOMER/HYALURONIC ACID INJECTION CONFIRMED IN OVER 1550 CHILDREN

IN THIS ISSUE

CONFERENCE COVERAGE

Many pediatric urologists don't agree with revised AAP guidelines

Similar short- and long-term results seen with endoscopic and surgical treatment of reflux

Referral habits of pediatricians for children with reflux indicate improved dialogue is needed

Increased risk of reflux-related morbidity demonstrated among relatives of index patients with VUR

Survey provides insight into changing pediatric urology practice patterns

Downgrading of high-grade reflux with endoscopic correction may be an acceptable outcome

Independent risk factors identified for reflux-associated renal damage in young children

Safety and effectiveness of dextranomer/hyaluronic acid injection confirmed in over 1550 children

Low inter-rater reliability seen with the International VUR Grading System

Discrepancies seen in assignment of intermediate-grade VUR in the RIVUR Pilot Study

Concomitant anti-reflux surgery recommended for neurogenic bladder with associated high-grade reflux

Endoscopic treatment of secondary reflux in neurogenic bladder dysfunction considered suboptimal

Endoscopic treatment effective for urinary incontinence in neurogenic bladder

RECAP OF CME SYMPOSIUM TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

Fever without a source: How likely is it a UTI?

Antibiotic prophylaxis: Is it necessary?

Imaging strategy for infants and children with a first UTI

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Results of a retrospective review of outcomes in over 1550 children from a single center confirm the safety and efficacy of dextranomer/hyaluronic acid copolymer (Dx/HA, Deflux®) in the treatment of intermediate- and high-grade reflux.

Endoscopic subureteral injection of Dx/HA has become an established alternative to long-term antibiotic prophylaxis and surgical management of vesicoureteral reflux (VUR).

Prem Puri, MD, and his colleagues at the National Children's Research Centre and National Children's Hospital in Dublin, Ireland, have been using Dx/HA as first-line treatment for Grades III to V reflux since its approval in 2001. "[I]n the past 10 years, I have not had to do an open operation for VUR," noted Dr Puri.

Dr Puri and colleagues conducted a retrospective study to evaluate the safety and effectiveness of their first-line use of endoscopic Dx/HA in the management of intermediate- and high-grade VUR.

Between 2001 and 2010, a total of 1551 consecutive children (496 male, 1055 female, median age 1.6 years) with Grade II to V VUR underwent endoscopic correction using Dx/HA soon after a diagnosis of VUR was made based on an initial voiding cystourethrogram (VCUG). Children with Grade II VUR were only treated endoscopically if they had a higher grade of reflux on the contralateral side, had evidence of renal scarring, or experienced breakthrough febrile urinary tract infections (UTIs).

VUR was unilateral in 761 children and bilateral in 790, for a total of 2341 refluxing ureters (RUs). Ninety-six percent of patients had Grade III to V reflux, with the majority being Grades III (57%) and IV (35%). Renal scarring was detected in 414 children (27%) at the time of endoscopic treatment.

Follow-up VCUG was performed 3 months after the outpatient procedure and renal ultrasound was performed at 3 months, 1 year, and then every 2 years. Patients were followed up from 6 months to 10 years (mean, 6.2 years) post-injection.

Reflux resolved after one injection in 87% of ureters, after two injections in 11% of ureters, and after three injections in the remaining 2% of ureters. Injections typically ranged from 0.5 mL to 1.5 mL in volume.



PREM PURI, MD

During the follow-up period, neocontralateral reflux developed in 75 patients (10%) with unilateral VUR. Sixty-nine patients (4%) developed a febrile UTI after successful correction of VUR.

No adverse side events were reported from use of Dx/HA as an injectable material. During follow-up, ultrasound revealed no evidence of delayed vesicoureteral junction obstruction or significant changes in sonographic appearance.

"Our results confirm the safety and efficacy of endoscopic injection of Deflux® in the eradication of high-grade VUR," concluded Dr Puri. "We recommend this 15-minute outpatient procedure as the first line of treatment in the management of high-grade VUR." ■

Source:

14194 SINGLE CENTRE EXPERIENCE WITH ENDOSCOPIC SUBURETERAL DEXTRANOMER/ HYALURONIC ACID INJECTION AS FIRST LINE TREATMENT IN 1551 CHILDREN WITH HIGH GRADE VESICoureteral REFLUX

Prem Puri¹, Manuela Hunziker¹, Balazs Kutasy¹, Nochiparambil Mohanan², Maria Menezes² and Eric Colhoun³, (1)Our Lady's Children's Hospital, National Children's Research Centre, Dublin, Ireland, (2)Pediatric Surgery, National Children's Hospital, Dublin, Ireland, (3) Department of Radiology, National Children's Hospital, Dublin, Ireland



LOW INTER-RATER RELIABILITY SEEN WITH THE INTERNATIONAL VUR GRADING SYSTEM

IN THIS ISSUE

CONFERENCE COVERAGE

Many pediatric urologists don't agree with revised AAP guidelines

Similar short- and long-term results seen with endoscopic and surgical treatment of reflux

Referral habits of pediatricians for children with reflux indicate improved dialogue is needed

Increased risk of reflux-related morbidity demonstrated among relatives of index patients with VUR

Survey provides insight into changing pediatric urology practice patterns

Downgrading of high-grade reflux with endoscopic correction may be an acceptable outcome

Independent risk factors identified for reflux-associated renal damage in young children

Safety and effectiveness of dextranomer/hyaluronic acid injection confirmed in over 1550 children

Low inter-rater reliability seen with the International VUR Grading System

Discrepancies seen in assignment of intermediate-grade VUR in the RIVUR Pilot Study

Concomitant anti-reflux surgery recommended for neurogenic bladder with associated high-grade reflux

Endoscopic treatment of secondary reflux in neurogenic bladder dysfunction considered suboptimal

Endoscopic treatment effective for urinary incontinence in neurogenic bladder

RECAP OF CME SYMPOSIUM TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

Fever without a source: How likely is it a UTI?

Antibiotic prophylaxis: Is it necessary?

Imaging strategy for infants and children with a first UTI

Dilemmas in treating febrile UTI: When in doubt, refer them out

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KOUROSH AFSHAR, MD

The International Reflux Grading System possesses a low degree of agreement among raters, especially for moderate degrees of VUR, according to the results of a recent study evaluating the system's reliability. Since this grading system is used to make important decisions regarding treatment of VUR, this finding has important implications for not only patient care, but also reliability of clinical data.

The International Reflux Grading System is based on subjective morphologic appearance of the collecting system during a voiding cystourethrogram (VCUG), and it has been used extensively in everyday practice and research studies mainly on the basis of face validity.

Nevertheless, according to **Kourosh Afshar, MD**, of the University of British Columbia in Vancouver, the clinometric features of this instrument, including validity and reliability, have not been studied. Therefore, Dr Afshar and his colleagues at the University conducted a study to estimate the inter- and intra-rater reliability of VUR grading using this system.

The investigators selected a series of 28 VCUG studies and assembled the images in an electronic file presentation in a random fashion. Four pediatric radiologists, five pediatric urologists, and four senior urology residents graded the studies. The images were then shuffled randomly and were re-rated 7 to 10 days later, for a total of 728 observations. Cohen-

weighted kappa statistics were used to determine inter- and intra-rater reliability. Subgroup analysis was then performed comparing the variability among the three groups of raters and among different VUR grades.

The average inter-rater reliability (ie, degree of agreement among raters) was fair at 0.51 (+/- 0.01), and reliability among urologists (0.61) was marginally better than among radiologists (0.56) and residents (0.52).

The lowest inter-rater agreement was seen in Grade III VUR (0.36, which is considered poor), and the highest agreement was seen in Grade I VUR (0.95). Agreement could be improved by combined grades; agreement was 0.79 when Grades II and III were combined and 0.63 when Grades III and IV were combined.

The average intra-rater reliability (ie, degree of agreement among multiple repetitions of the same test performed by a single rater) was high at 0.86 (+/- 4.5).

"The International VUR Grading System shows low inter-rater reliability, especially for moderate degrees of VUR, but it has high intra-rater reliability," concluded Dr Afshar. "Modifications of this system may improve its reliability, but the effects on this instrument's validity are not known."

Source:

14163 A RELIABILITY ASSESSMENT OF THE INTERNATIONAL VESICoureTERIC REFLUX GRADING SYSTEM

Charles B. Metcalfe, Andrew E. MacNeily and Kourosh Afshar, Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada



DISCREPANCIES SEEN IN ASSIGNMENT OF INTERMEDIATE-GRADE VUR IN THE RIVUR PILOT STUDY

IN THIS ISSUE

CONFERENCE COVERAGE

Many pediatric urologists don't agree with revised AAP guidelines

Similar short- and long-term results seen with endoscopic and surgical treatment of reflux

Referral habits of pediatricians for children with reflux indicate improved dialogue is needed

Increased risk of reflux-related morbidity demonstrated among relatives of index patients with VUR

Survey provides insight into changing pediatric urology practice patterns

Downgrading of high-grade reflux with endoscopic correction may be an acceptable outcome

Independent risk factors identified for reflux-associated renal damage in young children

Safety and effectiveness of dextranomer/hyaluronic acid injection confirmed in over 1550 children

Low inter-rater reliability seen with the International VUR Grading System

Discrepancies seen in assignment of intermediate-grade VUR in the RIVUR Pilot Study

Concomitant anti-reflux surgery recommended for neurogenic bladder with associated high-grade reflux

Endoscopic treatment of secondary reflux in neurogenic bladder dysfunction considered suboptimal

Endoscopic treatment effective for urinary incontinence in neurogenic bladder

RECAP OF CME SYMPOSIUM TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

Fever without a source: How likely is it a UTI?

Antibiotic prophylaxis: Is it necessary?

Imaging strategy for infants and children with a first UTI

Dilemmas in treating febrile UTI: When in doubt, refer them out

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SAUL GREENFIELD, MD

The RIVUR Pilot Study had a high level of inter-rater reliability in reflux imaging. Nevertheless, discrepancies in the assignment of intermediate-grade reflux were noteworthy, and an adjudication process most often resulted in a final determination of a higher grade. Thus, in practice, there may be some doubt regarding the distinction between Grades II and III reflux.

The Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) study is evaluating whether antimicrobial prophylaxis prevents recurrent urinary tract infections (UTIs) and renal scarring in children diagnosed with VUR after a first or second UTI.

Prior to enrolling patients in the study, completion of a pilot study to test the method of voiding cystourethrogram (VCUG) image transmission, evaluate the quality of imaging, and assess inter-observer variability was required of each of the participating centers. **Saul Greenfield, MD**, of the State University of New York at Buffalo School of Medicine, and his colleagues at several centers analyzed the radiologic reading concordance seen in this pilot study.

The analysis reviewed 75 VCUG studies from 19 sites. Two reference pediatric radiologists independently reviewed the digital images. Their responses were compared and discrepancies adjudicated by teleconference for a final assessment.

All 75 images were judged to be of adequate quality by both radiologists. Adjudication was required for one or more fields on 65 VCUGs (87%).

Overall, inter-rater reliability was high, ranging from 84% to 100% agreement.

However, there were several areas of disagreement. The most common was the presence of paraureteral diverticula, which was discordant in 20% of images. Noteworthy discrepancies in VUR grade level were noted on the left and right side in 11 patients (15%) and 12 patients (16%), respectively. Other areas of disagreement were the normality of the urethra (15%), whether the child voided (8%), presence of ureteral duplication (12%), and presence of bladder trabeculation (5%).

In the 68 ureters where reflux was seen, there was disagreement in 21 ureters (28%), particularly around Grade III reflux. On the left side, there was disagreement between Grades II and III in 5 of 38 studies, and 3 studies (60%) were adjudicated to the higher grade. On the right side, there were differences in opinion regarding Grades II and III and Grades III and IV in 8 of 30 studies (27%), and 7 (87%) were adjudicated to the higher grade.

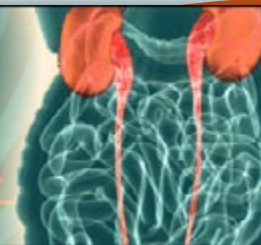
"In practice, therefore, there may be some doubt regarding the distinction between Grades II and III reflux," noted Dr Greenfield. "This becomes more important if one is not going to consider Grade II VUR to be clinically relevant, that is, not requiring treatment or follow-up imaging."

The data suggest that studies that rely upon a single radiologic reading are suspect. In particular, recent clinical recommendations for patients with Grade II or III reflux emanating from studies that categorize only Grade III or higher as significant, are based on questionable data and may not be valid.

Source:

12802 THE RIVUR VOIDING CYSTOURETHROGRAM PILOT STUDY: EXPERIENCE WITH RADIOLOGIC READING CONCORDANCE

Saul Greenfield, Urology, State University of New York at Buffalo School of Medicine, Buffalo, NY; Myra Carpenter, Department of Biostatistics, University of North Carolina at Chapel Hill, Chapel Hill, NC; Russell W. Chesney, Pediatrics, Le Bonheur Children's Medical Center, Memphis, TN; J. Michael Zerlin, Radiology, Children's Hospital of Michigan, Detroit, MI and Jeanne Chow, Radiology, Childrens Hospital Boston, Boston, MA



CONCOMITANT ANTI-REFLUX SURGERY RECOMMENDED FOR NEUROGENIC BLADDER WITH ASSOCIATED HIGH-GRADE REFLUX

IN THIS ISSUE

CONFERENCE COVERAGE

Many pediatric urologists don't agree with revised AAP guidelines

Similar short- and long-term results seen with endoscopic and surgical treatment of reflux

Referral habits of pediatricians for children with reflux indicate improved dialogue is needed

Increased risk of reflux-related morbidity demonstrated among relatives of index patients with VUR

Survey provides insight into changing pediatric urology practice patterns

Downgrading of high-grade reflux with endoscopic correction may be an acceptable outcome

Independent risk factors identified for reflux-associated renal damage in young children

Safety and effectiveness of dextranomer/hyaluronic acid injection confirmed in over 1550 children

Low inter-rater reliability seen with the International VUR Grading System

Discrepancies seen in assignment of intermediate-grade VUR in the RIVUR Pilot Study

Concomitant anti-reflux surgery recommended for neurogenic bladder with associated high-grade reflux

Endoscopic treatment of secondary reflux in neurogenic bladder dysfunction considered suboptimal

Endoscopic treatment effective for urinary incontinence in neurogenic bladder

RECAP OF CME SYMPOSIUM TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

Fever without a source: How likely is it a UTI?

Antibiotic prophylaxis: Is it necessary?

Imaging strategy for infants and children with a first UTI

Dilemmas in treating febrile UTI: When in doubt, refer them out

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A recent review of children undergoing augmentation ileocystoplasty for noncompliant neurogenic bladder with associated reflux found that high-grade reflux persists in nearly half of patients, and half of those develop pyelonephritis during follow-up. Thus, concomitant anti-reflux surgery is recommended when reflux is high-grade.

According to **Tamer Helmy, MD**, of the Urology & Nephrology Center at Mansoura University in Mansoura, Egypt, it has been routine practice not to perform anti-reflux surgery at the time of ileocystoplasty for a noncompliant neurogenic bladder at their center. As there are limited data regarding vesicoureteral reflux (VUR) resolution in these patients, Dr Helmy and his colleagues conducted a review of procedures performed at their center.

Between July 2002 and July 2009, 52 patients (mean age, 8.7 years; range 4-17 years) with noncompliant neurogenic bladder and associated reflux underwent ileocystoplasty. VUR was unilateral in 40% of the patients and bilateral in 60%. VUR was low-grade (Grade I-III) in 39% of the patients and high-grade (Grade IV-V) in 61% of patients. After a mean follow-up of 27 months (range, 12-80 months), reflux had resolved in 90% of the patients with low-grade VUR following bladder augmentation, but only 53% of the patients with high-grade reflux ($P=0.006$).

Although all patients received prophylactic antibiotics, 25% of patients who had high-grade reflux at the time of surgery developed pyelonephritis compared with no patients who had low-grade reflux. In addition, pyelonephritis developed in 6% of patients whose high-grade reflux resolved compared with 47% of patients with persistent high-grade reflux ($P=0.008$).

Based on the persistence of high-grade reflux and increased risk of developing pyelonephritis during follow-up, Dr Helmy concluded that concomitant anti-reflux surgery be performed at time of bladder augmentation for patients with noncompliant neurogenic bladder and associated high-grade reflux. ■

Source:

13251 THE NEUROPATHIC BLADDER WITH ASSOCIATED VESICoureTERAL REFLUX: IS ANTIREFLUX SURGERY REQUIRED WITH ILEOCYSTOPLASTY?

Tamer Helmy and Ashraf T. Hafez, Urology, Urology & Nephrology Center, Mansoura University, Mansoura, Egypt



TAMER HELMY, MD



ENDOSCOPIC TREATMENT OF SECONDARY REFLUX IN NEUROGENIC BLADDER DYSFUNCTION CONSIDERED SUBOPTIMAL

IN THIS ISSUE

CONFERENCE COVERAGE

Many pediatric urologists don't agree with revised AAP guidelines

Similar short- and long-term results seen with endoscopic and surgical treatment of reflux

Referral habits of pediatricians for children with reflux indicate improved dialogue is needed

Increased risk of reflux-related morbidity demonstrated among relatives of index patients with VUR

Survey provides insight into changing pediatric urology practice patterns

Downgrading of high-grade reflux with endoscopic correction may be an acceptable outcome

Independent risk factors identified for reflux-associated renal damage in young children

Safety and effectiveness of dextranomer/hyaluronic acid injection confirmed in over 1550 children

Low inter-rater reliability seen with the International VUR Grading System

Discrepancies seen in assignment of intermediate-grade VUR in the RIVUR Pilot Study

Concomitant anti-reflux surgery recommended for neurogenic bladder with associated high-grade reflux

Endoscopic treatment of secondary reflux in neurogenic bladder dysfunction considered suboptimal

Endoscopic treatment effective for urinary incontinence in neurogenic bladder

RECAP OF CME SYMPOSIUM TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

Fever without a source: How likely is it a UTI?

Antibiotic prophylaxis: Is it necessary?

Imaging strategy for infants and children with a first UTI

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Endoscopic treatment of secondary reflux in patients with neurogenic bladder dysfunction was shown to result in poor long-term success and significant recurrence, according to a recent retrospective chart review.

The off-label use of subureteral injection of dextranomer/hyaluronic acid copolymer (Dx/HA, Deflux®) in the treatment of secondary vesicoureteral reflux (VUR) in patients with neurogenic bladder dysfunction has been less thoroughly investigated, although some studies report high success rates with short-term follow-up.

A. Scott Polackwich, MD, reported on the Oregon Health and Science University (OHSU) Surgery/Oncology department's long-term experience with Dx/HA in the treatment of secondary VUR in patients with neurogenic bladders or severe voiding dysfunction (Hinman's syndrome).

A retrospective chart review of all subureteral injections of Dx/HA performed at OHSU between 2001 and 2010 (N=242) identified 10 patients with neurogenic bladder dysfunction and 2 patients with Hinman's syndrome (total, 17 ureters). The median age of these patients was 5.5 years (range, 2-18 years), and the median VUR grade was Grade III (range, I-IV). Fifty-eight percent of patients had a documented history of febrile UTIs.

After a median follow-up of 4.5 years (range, 1-9 years), it was found that although subureteral injection was initially successful in 50% of the patients (41% of the ureters), only 33% (29% of ureters) were cured over the long term. Forty-one percent of patients needed additional procedures at a median of 4 years after the procedure (range, 1.5-5 years), including bladder augmentation with ureteral reimplantation (n=3), nephrectomy (n=1), and bladder augmentation (n=1). However, subureteral injection of Dx/HA was successful in one patient who underwent bladder augmentation, thus eliminating the need for ureteral reimplantation.

Dr Polackwich concluded that, because treatment of secondary reflux with subureteral injection of Dx/HA in patients with neurogenic bladder dysfunction has a high long-term failure rate, it should not be considered optimal treatment in these patients. ■

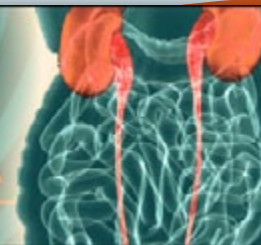
Source:

13712 LONG TERM FOLLOW UP AFTER ENDOSCOPIC TREATMENT OF VESICoureTERAL REFLUX WITH DEXTRANOMER/HYALURONIC ACID COPOLYMER IN PATIENTS WITH NEUROGENIC BLADDER

A. Scott Polackwich¹, Steven J. Skoog², and J. Christopher Austin¹, (1)Surgery/ Urology, Oregon Health and Science University, Portland, OR, (2)Surgery/ Urology, Oregon Health and Science University, Portland, OR



A. SCOTT POLACKWICH, MD



ENDOSCOPIC TREATMENT EFFECTIVE FOR URINARY INCONTINENCE IN NEUROGENIC BLADDER

IN THIS ISSUE

CONFERENCE COVERAGE

Many pediatric urologists don't agree with revised AAP guidelines

Similar short- and long-term results seen with endoscopic and surgical treatment of reflux

Referral habits of pediatricians for children with reflux indicate improved dialogue is needed

Increased risk of reflux-related morbidity demonstrated among relatives of index patients with VUR

Survey provides insight into changing pediatric urology practice patterns

Downgrading of high-grade reflux with endoscopic correction may be an acceptable outcome

Independent risk factors identified for reflux-associated renal damage in young children

Safety and effectiveness of dextranomer/hyaluronic acid injection confirmed in over 1550 children

Low inter-rater reliability seen with the International VUR Grading System

Discrepancies seen in assignment of intermediate-grade VUR in the RIVUR Pilot Study

Concomitant anti-reflux surgery recommended for neurogenic bladder with associated high-grade reflux

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Endoscopic treatment effective for urinary incontinence in neurogenic bladder

Results of a prospective study demonstrate that endoscopic treatment of congenital neurogenic urinary sphincter insufficiency with dextranomer-based implants is effective as a primary bladder neck procedure in a significant number of patients.

According to **Ilona Alova, MD**, pediatric surgeon at the Necker-Enfants Malades Hospital in Paris, treatment of urinary incontinence in children with neurogenic bladders is challenging. The use of bulking agents is an attractive alternative to continence surgery, but little is known about the efficacy of dextranomer-based implants (dextranomer/hyaluronic acid copolymer, Dx/HA, Deflux®) in this patient population.

Dr Alova and her colleagues at Necker-Enfants Malades Hospital and the Nancy Children University Hospital conducted a prospective study to evaluate the efficacy of dextranomer-based implants for the endoscopic treatment of urinary incontinence in patients with neurogenic bladders.

Since October 1997, 48 children and adolescents (3-18 years) with congenital neurogenic bladder and severe sphincteric incompetence have been enrolled in the study. None had had a previous bladder neck continence procedure. Patients were evaluated preoperatively using urine culture, ultrasound, and videourodynamic studies. This evaluation was repeated at 1 month, 6 months, and 1 year post-treatment, and then on a yearly basis except for videourodynamics, which was performed only when necessary for further management.

At each evaluation, patients were classified as cured (dry for 4 hours), significantly improved (minimal incontinence requiring no more than one pad per day and no further treatment), or treatment failure (no significant improvement observed).

Of the 48 patients, 63% received one dextranomer-based treatment session, 27% received two sessions, and 10% received three sessions. The mean injected volume was 4.6 mL per session.

Patients have been followed-up for a minimum of 2 years (mean, 7 years; range, 1-13 years). Fifty-two percent of patients were considered treatment successes (cured or significantly improved) and 48% were considered treatment failures. The success rate decreased with the number of treatment sessions (58% with one session, 50% with two sessions, and 38% with three sessions). However, previous surgery at the bladder neck or previous bladder augmentation had no significant effect on the success rate.

The investigators observed no serious adverse events or complications during follow-up. One female who had been dry for 4 years became incontinent again after starting sexual activity. The main reason for recurrence of incontinence more than 6 months after treatment was bladder deterioration, which developed in 7 dry patients; continence was restored following bladder augmentation. Two



ILONA ALOVA, MD

patients (both treatment failures) were lost to follow-up.

Dr Alova noted that the success rate in this study is similar to the 47% success rate previously reported with use of polydimethylsiloxane as a bulking agent for treatment of incontinence in neurogenic bladders (Guys et al, J Urology, 2006). In addition, her group has previously reported that endoscopic injections with Dx/HA do not adversely affect the outcome of further surgical procedures.

"Endoscopic treatment of neurogenic incontinence with dextranomer-based implants provides social continence to at least 50% of patients over the long term," Dr Alova concluded.

Source:

14688 LONG-TERM EFFECTS OF DEXTRANOMER ENDOSCOPIC INJECTIONS FOR THE TREATMENT OF URINARY INCONTINENCE IN PATIENTS WITH NEUROPATHIC BLADDER

Ilona Alova, Paediatric Surgery, Necker Enfants Malades Hospital, Paris, France; Marc Margaryan, Paediatric Surgery, Nancy Children University Hospital, Nancy, France and Henri Lottmann, Urologie Pédiatrique, Hôpital Necker Enfants Malades, Paris, France

RECAP OF CME SYMPOSIUM TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

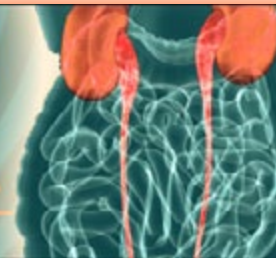
Fever without a source: How likely is it a UTI?

Antibiotic prophylaxis: Is it necessary?

Imaging strategy for infants and children with a first UTI

Dilemmas in treating febrile UTI: When in doubt, refer them out

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RECAP OF CME SYMPOSIUM: TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

IN THIS ISSUE

CONFERENCE COVERAGE

Many pediatric urologists don't agree with revised AAP guidelines

Similar short- and long-term results seen with endoscopic and surgical treatment of reflux

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Increased risk of reflux-related morbidity demonstrated among relatives of index patients with VUR

Survey provides insight into changing pediatric urology practice patterns

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Independent risk factors identified for reflux-associated renal damage in young children

Safety and effectiveness of dextranomer/hyaluronic acid injection confirmed in over 1550 children

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Much uncertainty exists amongst primary care providers and subspecialists about when to refer a child who has had a first febrile urinary tract infection (UTI) to a specialist. Divergence of opinion also exists about how and when to treat them.

A CME symposium, held on October 17, begins to answer these questions for pediatricians and provide the evidence-based advice of experts as they handle these issues in their practice. Summaries of the presentations appear below.

FEVER WITHOUT A SOURCE: HOW LIKELY IS IT A UTI? DONALD L. SHIFRIN, MD, UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE, SEATTLE

Fever is the most common reason for children to be taken to the doctor and accounts for 5.4 million visits to the emergency department each year. In 6% to 14% of cases, there will be no apparent clinical source (fever without a source, FWS). However, for well-appearing infants and children, there is no single reliable clinical and/or laboratory predictor of a serious bacterial infection. In addition, as vaccines have now eliminated the cause of many febrile illnesses, UTI is now a common febrile infection of infancy and early childhood with serious consequences if missed.

Three questions define the crux of an FWS workup looking for a UTI, explained **Donald L. Shifrin, MD**, of the University of Washington School of Medicine in Seattle, Washington.

1. What is the prevalence of infection, and can we identify specific factors that could enhance diagnosis?

The overall prevalence of UTI in febrile infants with FWS is approximately 5%; however, prevalence rates vary widely, by age, gender, and circumcision status. For example, the probability of a UTI in a febrile circumcised boy over the age of 1 year is less than 1%, whereas the probability in a febrile white girl under 2 years of age is 16%.

In recent meta-analyses, a number of clinical and demographic factors have been identified that increase the probability of a UTI diagnosis and therefore can be used to assess the likelihood of UTI and determine if further testing is warranted. For example, in a recent review (Shaikh et al, JAMA, 2007), UTI risk factors identified for boys who present with fever include no apparent fever source, temperature above 39°C for more than 24 hours, and nonblack race. In a 2000 cohort study (Gorelick and Shaw, Arch Pediatr Adolescent Med), risk factors identified in girls include no apparent fever source, age less than 12 months, temperature above 39°C for more than 48 hours, and white race.

2. Can we use targeted urine testing to reduce the risk of missing an infection?

Once it is determined that the febrile infant is at high risk of UTI, the next step is to obtain a urine specimen for urinalysis. Several rapid screening tests can be used to make a presumptive diagnosis. According to Dr Shifrin, assuming you have a good specimen



DONALD L. SHIFRIN, MD

to begin with, sensitivity and specificity are high if both the leukocyte esterase and nitrate tests are positive, and can help determine whether a culture is required. Catheterization or suprapubic aspiration are the preferred methods for urine collection for culture rather than use of a urine collection bag, as 85% of all positive bag cultures would be false positives.

3. How do we manage the non-toxic-appearing acutely febrile child using a 21st century approach?

There are a number of published algorithms outlining a diagnostic approach in infants and children suspected of having a UTI (eg, the AAP Clinical Practice Guidelines and those outlined by Sahsi et al, Ann Emerg Med, 2009). However, in the office setting, practitioners often don't use algorithmic guidelines consistently and have been shown to order tests selectively. "When you're in your office, you have to use your intuition," advised Dr Shifrin, "but you can also use things that will increase the likelihood [of making a diagnosis]."

"While we all want decision rules and algorithms that can increase our sensitivity and specificity for a diagnosis, we're not going to get hard and fast rules," reminded Dr Shifrin. He noted that the risk of missing a UTI cannot be reduced to zero even using these algorithms. "It's still your call; you have to use your gestalt view." ■



RECAP OF CME SYMPOSIUM: TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

IN THIS ISSUE

CONFERENCE COVERAGE

- Many pediatric urologists don't agree with revised AAP guidelines
- Similar short- and long-term results seen with endoscopic and surgical treatment of reflux
- Referral habits of pediatricians for children with reflux indicate improved dialogue is needed
- Increased risk of reflux-related morbidity demonstrated among relatives of index patients with VUR
- Survey provides insight into changing pediatric urology practice patterns
- Downgrading of high-grade reflux with endoscopic correction may be an acceptable outcome
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- Concomitant anti-reflux surgery recommended for neurogenic bladder with associated high-grade reflux
- Endoscopic treatment of secondary reflux in neurogenic bladder dysfunction considered suboptimal
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ANTIBIOTIC PROPHYLAXIS: IS IT NECESSARY? MARTIN A. KOYLE, MD, UNIVERSITY OF TORONTO AND THE HOSPITAL FOR SICK CHILDREN, TORONTO

Over the past quarter century, it has become evident that many scarred kidneys previously attributed secondarily to vesicoureteral reflux (VUR) and febrile UTI were actually primarily developmental in origin. This finding, in addition to recent data questioning the benefit of continuous antibiotic prophylaxis (CAP) in the management of VUR, has led to controversies regarding the optimal approach to the child with VUR.

According to **Martin A. Koyle, MD**, of the University of Toronto and The Hospital for Sick Children in Toronto, Ontario, CAP has over a 50-year track record in the management of VUR. Early studies comparing CAP to observation were inconclusive with regard to the true benefit of CAP in relation to surveillance. Later, a number of randomized controlled trials attributed no benefit or only a slight benefit to CAP in terms of preventing recurrent febrile UTI or renal damage, but all included mainly patients with low-grade reflux. The only randomized trial that included higher grades of reflux was the Swedish Reflux Trial, which demonstrated that in higher-risk patients (ie, girls less than 1 year of age), both CAP and endoscopic injection were superior to surveillance in preventing recurrent febrile UTIs.

However, if observation is offered rather than CAP, what are the consequences? Few studies address the chronic issues that can result from febrile UTIs and scarring, and most have been poorly controlled or have short follow-up. However, long-term consequences, including chronic kidney disease and increased blood pressure, have been reported, so the potential consequences must be considered.

There are now a number of guidelines for the management of UTIs and VUR and each differs with regard to their recommendations for use of CAP. For example, the recently revised American Urological Association guideline on management of primary VUR in children recommends CAP for virtually all children less than 1 year of age. CAP is also advocated in older children and when bowel/bladder dysfunction or renal cortical nephropathy is present.



MARTIN A. KOYLE, MD

However, Dr Koyle feels that such guidelines should not serve as rigid rules requiring emphatic adherence, as individualizing care is very important in the patient with reflux and UTI. "Algorithms lack tailoring options to an individual patient," noted Dr Koyle. "There really is no black and white when it comes to the right thing to do."

Dr Koyle stressed that observation (surveillance) does not mean non-treatment. "When you are looking at active surveillance versus an active treatment protocol, you are really pitting the patient and his degree of risk aversion to that disease entity versus treatment-associated morbidity," he noted.

Our understanding of VUR and febrile UTI and how we evaluate and manage it is still evolving. Therefore, a cooperative, open approach between the pediatric urologist/nephrologist, primary care provider, and the patient/parents is needed to tailor the appropriate therapeutic option to the patient. ■



RECAP OF CME SYMPOSIUM: TO REFER OR NOT TO REFER: MANAGING FEBRILE UTI IN CHILDREN

IMAGING STRATEGY FOR INFANTS AND CHILDREN WITH A FIRST UTI ANDREW J. KIRSCH, MD, EMORY UNIVERSITY SCHOOL OF MEDICINE; GEORGIA UROLOGY, PA; AND CHILDREN'S HEALTHCARE OF ATLANTA

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ANDREW J. KIRSCH, MD

The concept of universal radiologic evaluation for VUR of all children with febrile UTI has appropriately been challenged in recent years, as many children may be subjected to unnecessary imaging with low diagnostic yield. However, a significant number of children will serve to benefit from accurate diagnosis and

appropriate treatment of VUR since the majority of children with febrile UTI will have renal involvement.

According to **Andrew J. Kirsch, MD**, of the Emory University School of Medicine and Children's Healthcare of Atlanta, Georgia, imaging studies should be utilized to provide information to best evaluate and manage children with a febrile UTI. Dr Kirsch utilizes a risk-based approach to determine treatment strategy in these patients (see figure). With this approach, imaging is required to diagnose major risk factors prior to treatment. It is important to remember that, although reflux is found in the majority of infants with febrile UTI, it is not the only treatable anomaly.

Renal and bladder ultrasonography can evaluate factors such as renal architecture, size discrepancies, and hydronephrosis, and can suggest scarring. However, it does not reliably detect reflux, pyelonephritis, or scarring.

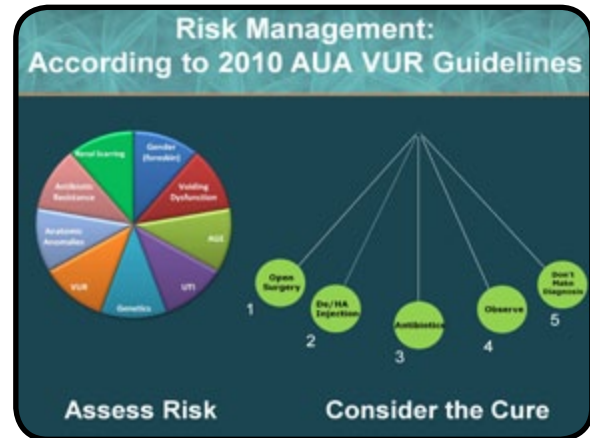
Voiding cystourethrography (VCUG) is not only best used to document the timing and presence of VUR in cases of febrile UTIs, but can evaluate the bladder and urethra and identify duplication anomalies and bladder diverticula.

Dimercaptosuccinic acid (DMSA) scintigraphy can evaluate for renal function and scarring, and is used mostly in cases of high-grade reflux or in cases of renal atrophy. In the acute phase, it confirms a clinical diagnosis of pyelonephritis, while scarring can be detected after 6 months. DMSA scans are an essential component of the "top-down" approach to identify clinically significant VUR, substituting for ultrasound with or without VCUG. Although this approach limits the number of VCUGs performed, acute studies may miss moderate to severe reflux.

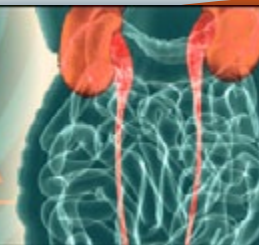
Three sets of UTI guidelines have been proposed to determine optimal approaches to assess and manage children after an initial febrile UTI. The NICE UTI guidelines limit VCUG and ultrasound, which Dr Kirsch feels would most likely lead to under-diagnosis

of VUR. The 2010 AUA VUR guidelines provide general recommendations based on a large study of the literature that stratifies patients for risk of recurrent infection, with a wide range of treatment options for VUR.

Dr Kirsch and many pediatric urologists feel that the new AAP UTI guidelines provide a very good rationale for obtaining appropriate urine specimens for culture, but the indications for VCUG are controversial. "It is evidence-based, but we believe that the evidence is flawed," he noted. These flaws include the fact that it is pooled data that is primarily looking at Grades I to II reflux, there are no data regarding antibiotic compliance, and there was no assessment of bladder/bowel dysfunction and other factors that would increase risk. "It insinuates that reflux is a benign anomaly," he stated.



Dr Kirsch concluded that screening imaging studies are appropriate in children following a first febrile UTI and must be interpreted for presence, grade, and timing of reflux, as well as associated abnormalities. Most importantly, management must be individualized to the patient. ■



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CONFERENCE COVERAGE

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DILEMMAS IN TREATING FEBRILE UTI: WHEN IN DOUBT, REFER THEM OUT CHRISTOPHER S. COOPER, MD, UNIVERSITY OF IOWA HOSPITALS AND CLINICS, IOWA CITY

Despite current controversies in the evaluation of a child with febrile UTI and management of VUR, it is likely that children at risk for recurrent UTIs or renal damage would benefit from further evaluation by a pediatric urologist, according to **Christopher S. Cooper, MD**, of the University of Iowa Hospitals and Clinics in Iowa City, Iowa.

Recurrent UTIs occur in up to 30% of children. Identifying and addressing factors that predispose a child to UTI are key in preventing recurrence. These factors include bacterial load, which can be affected by constipation, bladder instability, and a wet perineum; stasis, which can be affected by anatomic or physiologic obstruction, or high-grade reflux; status of host defenses, which can be compromised due to high pressure; and cellular receptivity for bacterial adherence.

The risk of renal scarring increases with the number of UTIs. About 60% of febrile UTIs have acute pyelonephritis and approximately 50% of cases of acute pyelonephritis lead to scarring. It is estimated that 8% to 15% of all children with a first UTI will develop a renal scar. However it is important to remember that about 60% of positive DMSA scans are not associated with VUR.

The literature is not clear on the impact of age on risk of renal scarring, but it is clear that a scar can develop after pyelonephritis at any age. Individual risk factors for pyelonephritis include bowel and bladder dysfunction; VUR, particularly higher grades; recurrent UTIs; female gender when under a year of age; and social situation (eg, delayed treatment). "Social situation is probably the greatest risk factor for how a child is actually going to do," noted Dr Cooper.

When reflux is identified, Dr Cooper explains to patients and parents that two problems need to be addressed: whatever led to the UTI, and the reflux itself. As the presence of reflux adds to the complexity and risk, he recommends that primary care physicians consider urology referral of their high-risk patients, including those with recurrent UTIs, febrile UTIs, bladder and/or bowel dysfunction, and those with abnormal kidneys.

The role and benefits of CAP remain unclear. It does not appear to benefit those patients with less than Grade II reflux, but appears to be beneficial in girls with Grade III or higher reflux. Of patients receiving CAP, 15% will have recurrent UTIs within several years and 15% of these will scar. An important concern is the increased antibiotic resistance seen with antibiotic exposure.

The International Reflux Study demonstrated a decreased incidence of pyelonephritis with



CHRISTOPHER S. COOPER, MD

surgical reimplantation compared with CAP, and the Swedish Reflux trial demonstrated efficacy of both Dx/HA and CAP in preventing recurrence compared with surveillance. However, the decision of when and in whom to correct reflux is complex and multifactorial, and requires individualized assessment.

A number of factors can impact VUR resolution. Dr Cooper encouraged participants to utilize his group's neural network (www.urocomp.net), which can predict VUR resolution with an accuracy of up to 86% without renal scan data and up to 94% when these data are included.

Dr Cooper concluded by summarizing his recommendations for individualizing patient care:

- During the evaluation for UTIs, consider not only patient history, but also family history and social situation.
- Get as much information as possible from each test.
- Identify potential risk factors.
- Consider referral for complex or high-risk patients.
- Individualize management and follow-up. ■