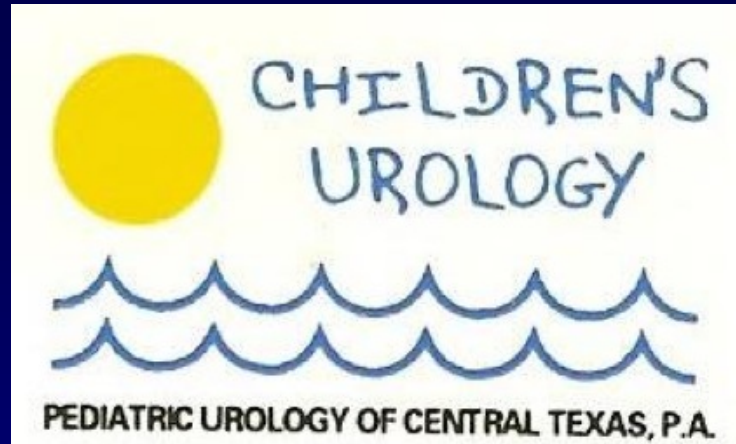


Vesicoureteral Reflux and Prenatal Hydronephrosis

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Pediatric Conference
Dell Children's Medical Center
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Vesicoureteral Reflux (VUR)

Learning Objectives for VUR

- Standard definition and etiology of reflux
- Sequele of reflux and the significance of pyelonephritis
- Management and treatment of reflux
- VUR controversies

Demographics

- Vesicoureteral reflux (VUR)
 - Retrograde flow of bladder urine into the upper urinary tracts
 - Combination of reflux and infection can cause renal scarring
- Occurs in 0.4 to 1.8% of normal children
- Diagnosis of VUR
 - Investigation of febrile UTI
 - Incidence of VUR 30-50%
 - Prenatal diagnosed hydronephrosis

Demographics

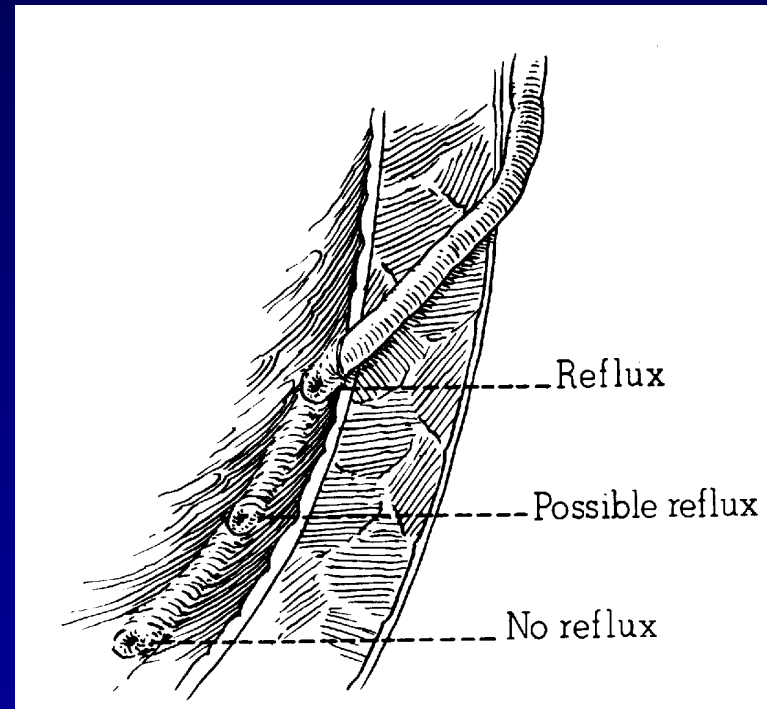
- Children presenting with febrile UTI
 - Female predominance
 - Caucasians > Asians and Africans
 - Ratio 3.4 : 1
 - Heritable disorder
 - Sibling VUR rate 30-35%
 - High incidence of parent to child transmission
 - 60%

Demographics

- Prenatal hydronephrosis
 - VUR 25% of infants with postnatal evaluation
 - Regardless of grade resolution in 50% by 18 months
 - Male predominance
 - Increased incidence of high grade VUR
 - Tend to spontaneously resolve

Etiology of Reflux

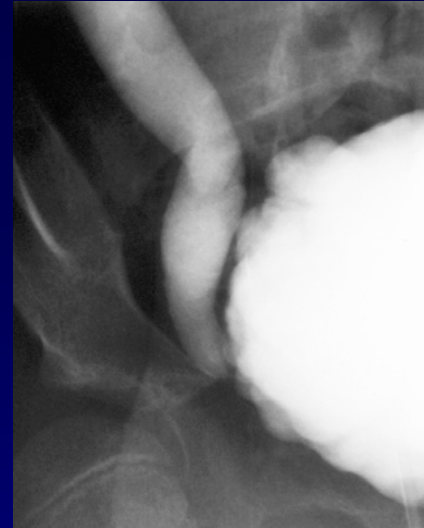
- Primary reflux
 - A congenital defect in the structure and function of the UVJ
 - Short intramural ureter and lateral ectopia of UO
 - Inadequate valve mechanism
 - Ratio of submucosal tunnel length to ureteral diameter is crucial
 - Ratio 5:1 (no VUR)



Bad Anatomy

Etiology of Reflux

- Secondary VUR
 - High intravesical pressure
 - Neurogenic, non-neurogenic voiding dysfunction



High Pressure

Etiology of Reflux

- Primary reflux often resolves spontaneously
 - Likelihood of resolution inversely related to radiological grade of reflux
- Secondary reflux will often resolve if underlying voiding dysfunction is treated
 - Anticholinergics, timed voiding, intermittent catheterization, biofeedback

Diagnosis and Evaluation

- Diagnosis and Evaluation
 - Assess for history of fever
 - Non-febrile UTI rarely need VCUG
 - Send U/A and urine culture
 - Radiographic imaging
 - Renal U/S
 - VCUG

Diagnosis and Evaluation

- Imaging studies
 - Renal U/S
 - Renal size
 - Hydronephrosis
 - Evidence of gross renal scarring or dysplasia
 - Duplication anomalies

Diagnosis and Evaluation

- VCUG (Contrast)
- Gold Standard for grading
 - Good anatomic details
 - Posterior urethral valves
 - Constipation, bladder wall changes
 - Higher radiation
 - Requires catheterizations
- Nuclear Renal Scans (DMSA)
 - Best study to identify pyelonephritis or renal scarring and overall renal function

Diagnosis and Evaluation

- Sibling Screening
 - ***CONTRAVERSIAL***
 - No consensus amongst pediatric urologists
- Old screening recommendations
 - Under age 5: VCUG and Renal U/S
 - Over age 5, no history of UTI: Renal U/S
 - Over age 5, history of UTI: VCUG and Renal U/S
- New screening recommendations
 - Greatest benefit in siblings under age 3
 - Parents should be aware of familial aspect of VUR
 - Prompt diagnosis and treatment of UTI in siblings

Diagnosis and Evaluation

- Sibling Screening
 - Journal of Urology, 2002-Review of literature
 - Reflux is found in 35 % of sibling proband
 - 2/3 had low grade reflux (Grade 1-2)
 - Only 2% had reflux > grade 3
 - Increased probability of spontaneous resolution when compared to index cases
 - Sibling screening does not prove that detecting reflux before the first UTI in siblings decreases renal scarring

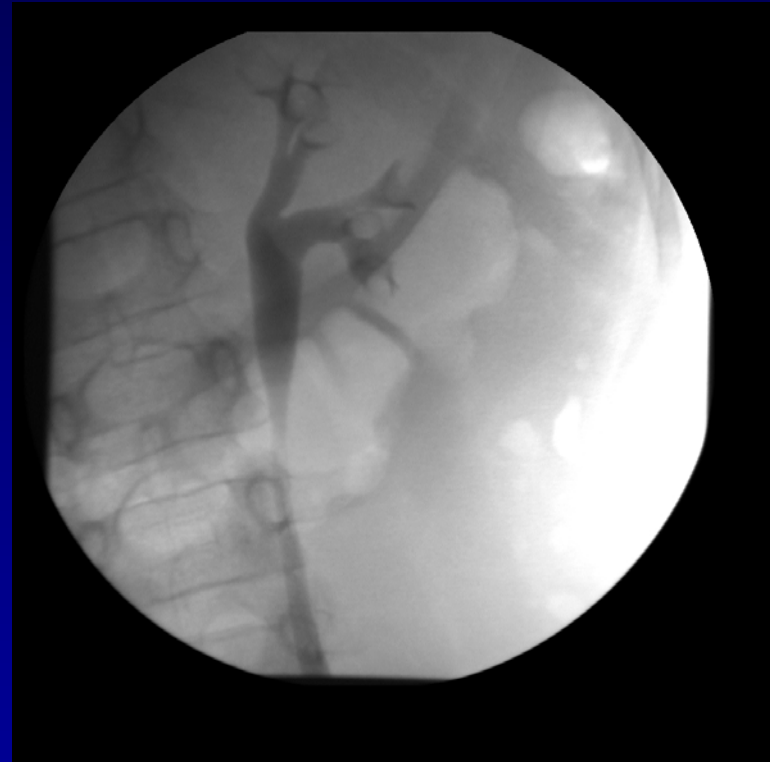
Diagnosis and Evaluation

- Radiologic monitoring
 - Annual VCUG
 - For reflux resolution
 - Can be stretched out to 18 months
- Serial renal ultrasound
 - Interval growth of the kidney
 - Anatomic anomalies

Grading of VUR



Grade I



Grade II

Grading of VUR

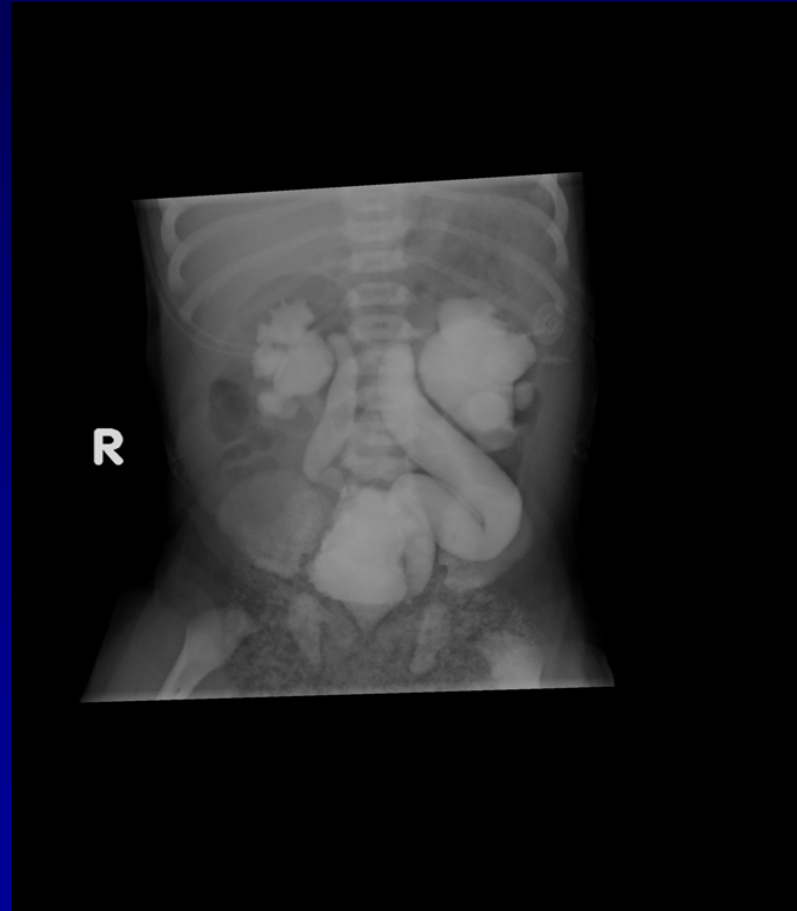


Grade III



Grade IV

Grading of VUR



Grade V

Grading of VUR



DMSA Scan with multiple cortical defects

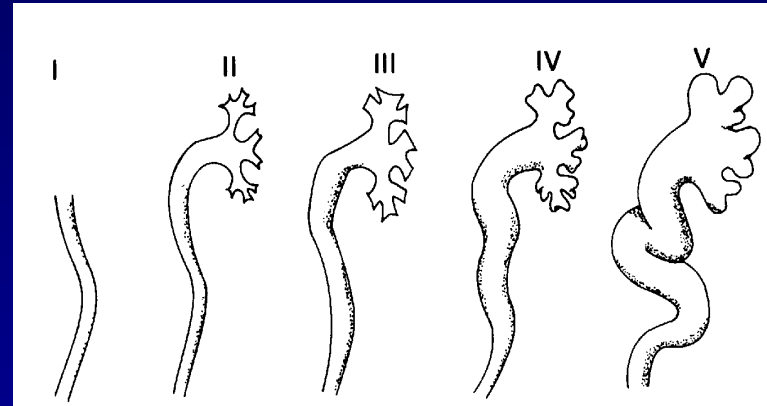
Natural History of VUR

- Younger children more likely to resolve
- Primary reflux often resolves spontaneously
 - Likelihood of resolution inversely related to radiological grade of reflux
 - Most grade 1-2 resolve spontaneously
 - Fewer grades 3-5 resolve spontaneously
- Secondary reflux will often resolve if underlying cause is treated

Natural History of VUR

Rates of primary reflux resolution over 3 years

- Grade I 87%
- Grade II 63%
- Grade III 53%
- Grade IV 33%



Bellinger and Duckett, Contrib Nephrol, 1984

Natural History of VUR

- Nomograms for predicting annual resolution
 - All males regardless of laterality and females with unilateral VUR
 - Had similar times to resolution
 - Less than 1 year at presentation, lower grade of VUR, prenatal hydronephrosis or sibling reflux and VUR in a single ureter
 - Significantly faster times to VUR resolution
 - Reflux in siblings and reflux discovered during postnatal diagnosis for prenatal hydronephrosis
 - More indolent course than index cases

Sequela of VUR

- Reflux nephropathy
 - Renal Scarring
 - Impaired renal growth and decrease renal function
- Hypertension
 - VUR nephropathy most common cause of severe HTN in children
 - 10-20% of children with VURN
 - Renin mediated
- Renal failure
 - Incidence of reflux nephropathy as primary cause of end-stage renal disease has fallen
 - < 2% currently
 - 30 years ago - 25%



Management

- *****Controversial*****
- Undergoing paradigm shift
- New AUA guidelines forthcoming
- No current consensus

Medical Management

- Issues with current UTI-VUR model
 - Percentage of patients with UTI and VUR who develop renal scarring is low
 - Many children with high grade VUR do not develop renal scars
 - Patients without VUR, but recurrent UTI can develop scars
 - Overtreated VUR in the past
 - Most studies or trials are underpowered
 - No consensus on prophylaxis

Management

AUA Guidelines - 1997

- All patients receive prophylactic antibiotics
 - Once daily low dose
- Long term treatment
 - Prophylaxis until resolved
 - Treat voiding dysfunction
 - Surgical repair if no resolution
 - Open or endoscopic

Medical Management

- Antibiotic Prophylaxis
 - Low dose abx given daily (bedtime)
 - Amoxicillin 10-15 mg/kg/day
 - < 8 weeks old
 - TMP-SMX 2 mg/kg/day
 - > 8 weeks old
 - Nitrofurantoin 5 mg/kg/day

Medical Management

- Conflicting Studies
 - Antimicrobial prophylaxis was not associated with decreased risk of recurrent UTI (JAMA, 2007)
 - Low dose continuous oral antibiotic therapy prevents UTI in predisposed children (NEJM, 2009)

Medical Management RIVUR Study

- Need for better designed studies
 - Resolve conflicting data related to the use of antimicrobial prophylaxis in a placebo controlled trial
 - Definitive study to determine the value of antimicrobial prophylaxis with regard to the recurrence of UTI and the incidence of renal scarring

Medical Management RIVUR Study

- Inclusion criteria (N=600)
 - Children with resolved first febrile or symptomatic UTI with diagnosis of grades 1-4 VUR
 - Randomly assigned placebo or prophylaxis
 - Primary end point recurrent UTI and secondary end point of renal scarring
 - Each child followed for 2 years

Medical Management

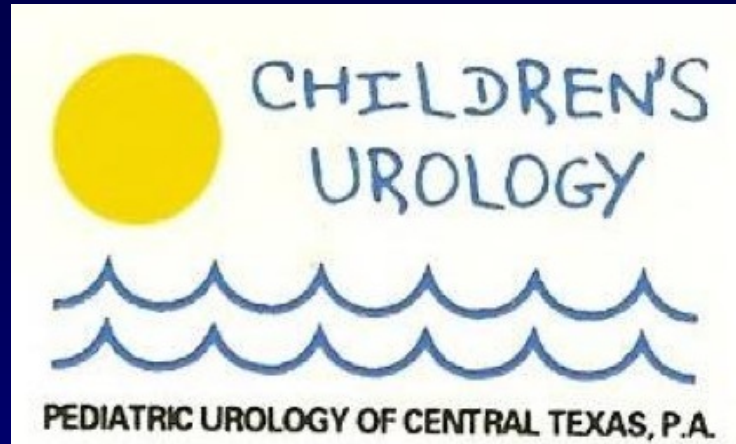
- What to do?
 - Manage low grade VUR off prophylaxis
 - Grades 1-3
 - Older children
 - Children without risk factors
 - Reliable families
 - Parental preference

Surgical Management

- Indications
 - Breakthrough UTI on prophylaxis
 - Lack of compliance
 - Failure to resolve with time
 - High grade reflux less likely to resolve
 - Impending puberty in girls
 - High grade reflux with decreasing renal function
 - New renal scarring while on medical management
 - Parental preference

Open vs. Endoscopic

- Open ureteral reimplantation
 - Requires hospital stay
 - Morbidity
 - Longer recovery
 - Gold standard
 - 95 % success
 - No VCUG follow-up
- Endoscopic injection of ureter
 - Short outpatient procedure
 - Few complications
 - Dysuria
 - Hematuria
 - Resume normal activity
 - Success
 - 40-90%
 - F/U VCUG
 - May need repeat procedure



Prenatal Hydronephrosis

Learning Objectives for Hydronephrosis

- Review the diagnostic algorithms for prenatal hydronephrosis
 - US appearance of major diagnoses
 - Management of hydronephrosis
 - Prenatal and postnatal scenarios

Fetal Diagnosis of Hydronephrosis

- 3-4 million US performed per year
- 1-2% Incidence of congenital abnormalities
- *Hydronephrosis 50-75% of all anomalies detected by US*



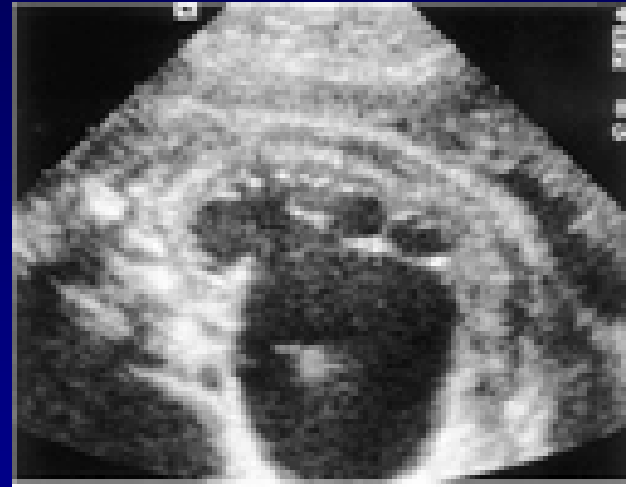
Prenatal US GU Findings

- Normal Fetal Kidney



- Echolucent pyramids

- Hydronephrosis



- Increased AP diameter of pelvis

Prenatal Hydronephrosis

- Definition: > 4 mm AP diameter of renal pelvis
- 0.5 – 1.4% of all pregnancies
 - Mild: 4 – 15 mm
 - Moderate: 15 – 25 mm
 - Severe: > 25 mm

Differential Diagnosis for Hydronephrosis

- Unilateral
 - UPJO (39-64%)
 - VUR (33%)
 - UVJO (9-14%)
 - MCDK (4-25%)
 - Ureterocele/ectopic ureter
 - Duplicated system
 - PCKD
- Bilateral
 - PUV (2-9%)
 - VUR
 - Urethral aplasia
 - Prune Belly syndrome
 - Megacystis-megaureter
 - PCKD
- Physiologic

Natural History of Prenatal Hydronephrosis

Ultrasound Obstet Gynecol 2001; 17: 191–196

Natural history of fetal hydronephrosis diagnosed on mid-trimester ultrasound

S. SAIRAM, A. AL-HABIB, S. SASSON and B. THILAGANATHAN

Feto-Maternal Medicine Unit, Homerton Hospital, Academic Unit of Obstetrics and Gynaecology, St Bartholomew's and The Royal London School of Medicine and Dentistry, London, UK

- Prospective study on OB patients undergoing 2nd trimester fetal US
- One of the largest published

Natural History of Prenatal Hydronephrosis

11,465 US at 18-23 weeks

Natural History of Prenatal Hydronephrosis

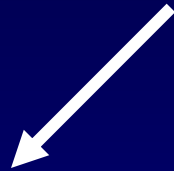
11,465 US at 18-23 weeks

Hydro in 268 (2.3%)

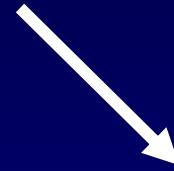
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81%: Mild Hydro (4-7mm)



19%: Mod Hydro (>7mm)

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80% Resolved antenatally
20% Persisted at birth

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82% Resolved @ 1 month
18% Persisted @ 1 month

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0% Resolved antenatally
100% Persisted at birth

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19%: Mod Hydro (>7mm)



0% Resolved antenatally
100% Persisted at birth



44% Resolved @ 1 month
31% Required surgery

14% On proph abx
11% Died or terminated

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- Only 5% (15/268) of all infants with a diagnosis of hydro required surgery
 - > 7mm AP diameter

Management of Prenatal Hydronephrosis

- Mild antenatal hydro associated with an *excellent prognosis*
- Moderate to severe fetal hydro associated with *poorer outcomes*, especially when there is caliceal dilation
 - Closer antenatal and postnatal follow-up is required

Management of Hydronephrosis

- Amoxicillin 10 -15 mg / kg daily after birth
 - If mild, some do not recommend
- Repeat ultrasound after birth
 - ~48-72 hours post delivery
- VCUG during first month of life

Management of Hydronephrosis

- No vesicoureteral reflux present
 - If mild follow with serial renal ultrasound
 - If grade 3 or above, evaluate for ureteropelvic junction obstruction
 - Lasix renal scan to determine function and drainage
 - » After 8 weeks of age

Prenatal Hydronephrosis

- Identify abnormal findings from normal
- Most cases of mild prenatal hydronephrosis will resolve after birth and will not cause morbidity
- Significant prenatal hydronephrosis will correlate with postnatal hydronephrosis, usually necessitating further evaluation
- US, VCUG, and renal scan findings at appropriate time points will lead you to a diagnosis and proper management

Thank You