

Current Concepts and Controversies in the Imaging Evaluation of Children with UTI



Eglal Shalaby-Rana, M.D.
Children's National Medical Center
The George Washington University
Washington, D.C.

Work-up of UTI in Children: A Challenging Task

- Different imaging algorithms are used to evaluate children with UTI
- Numerous studies in pediatric, urologic, radiologic and nuclear medicine literature in past 20 years—often with conflicting data and conclusions

Different Diagnostic Protocols for Investigation of a First Febrile UTI in a Young Child

	US	VCUG	DMSA
AAP 1999	+	+	-
Kass 2000	+	+	+
Hoberman 2003	-	+	-
Hansson 2004	+	-	+
Royal Childr Hosp Melbourne	+	<6 mos	-
Cincinnati Childr	+	+	+/-
Westwood 2005	-	-	-
NICE 2007	+/-	-	+/-

From Montini et al. Pediatrics 2009

Guidelines for Imaging Work-up of UTI in Children

AAP Subcommittee on UTI

Recommends VCUG and US

States that the role of DMSA is unclear

Pediatrics 1999 (In process of revision)

NICE Guidelines (National Institute for Health and Clinical Excellence)

Complex—multiple guidelines for various combinations of US, DMSA and VCUG depending on patient age, patient response to therapy and if offending bacteria is typical (E coli) or atypical.

August 2007

**WARNING!! You may leave this session
more confused than you
were when you entered this session!!!!**



Imaging Modalities

Commonly used:

Renal sonography

Cystography (radiographic or nuclear)

DMSA renal scan

Less commonly used:

MRI

CT

Is US an important study in the work-up of UTI?

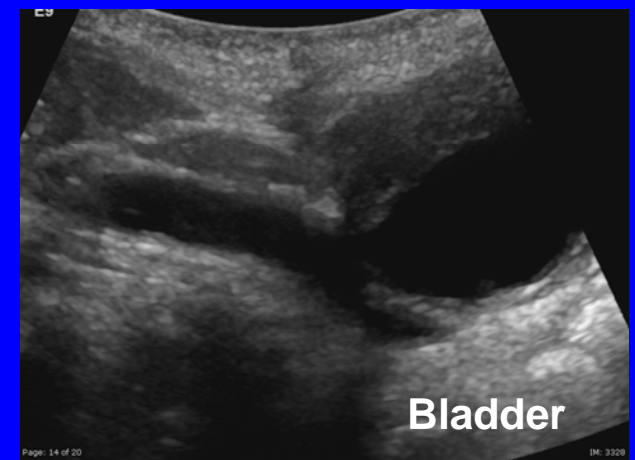
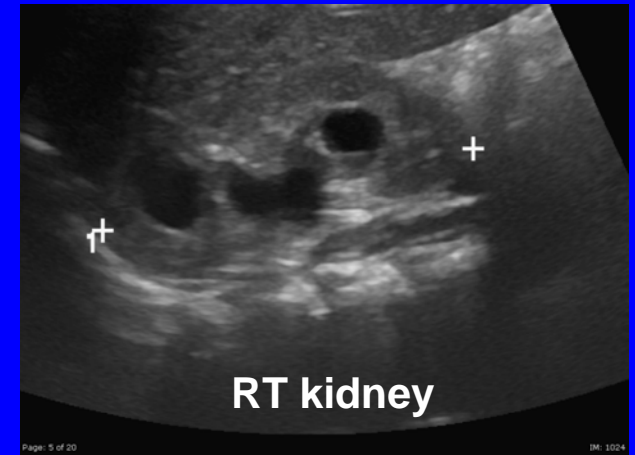
Best study for hydronephrosis/hydroureter (H/H):

- UPJ obstruction
- UVJ obstruction
- Posterior urethral valve
- Complicated duplications
- High grade VUR

H/H typically detected on prenatal sonography—
No need for US if prenatal study is normal
(Hoberman. N Engl J Med 2003)

US is indicated in UTI evaluation—H/H, duplex
collecting system *(Huang. Urology 2008)*

US in the diagnosis of acute pyelonephritis—low
sensitivity (74%) and specificity (57%)
(Majd. Radiology 2001)



DMSA Cortical Scintigraphy in the Diagnosis of Acute Pyelonephritis— Piglet Models

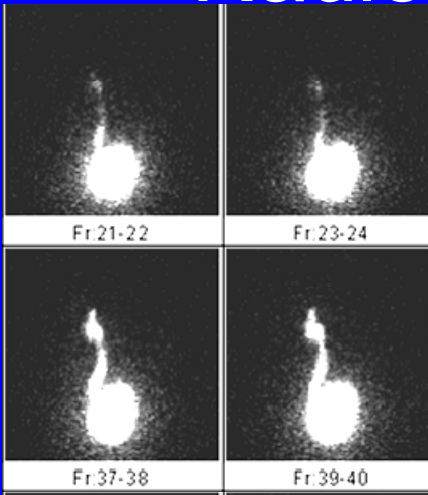
87% sensitivity and 100% specificity

Rushton et al. J Urol 1988

92% sensitivity and 94% specificity-- equivalent
to CECT and gad MRI

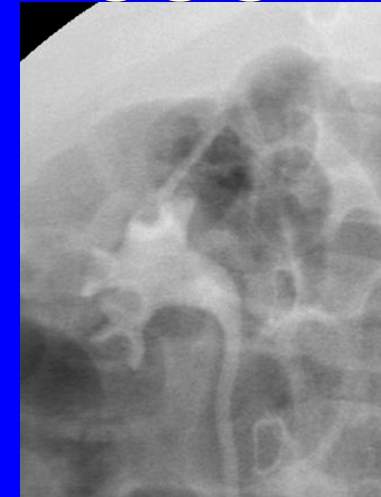
Majd et al. Radiology 2001

Radionuclide Cystography and VCUG in Reflux Imaging



RNC

- Extremely **sensitive** for diagnosing VUR-continuous imaging
- Much less radiation
- Less resolution
 - Inability to evaluate urethra
 - Less accurate grading of VUR



VCUG

- Sensitive for diagnosing VUR-intermittent imaging
- Higher radiation
- Excellent **resolution**
 - Able to evaluate urethra
 - Very accurate grading of VUR

Imaging in UTI

General Agreement:

Main goal is to identify those kidneys at risk for acute pyelonephritis and scarring

Major Disagreements:

What studies? When? How?

Risk Factors for Acute Pyelonephritis and Scarring

Host factors:

Vesicoureteral reflux (VUR)

Obstruction

Bacterial virulence factors

What we know about VUR

- Most common abnormality seen in patients with UTI
- Prevalence ranges from 25% to 40% in various studies
- Most lower grades will spontaneously resolve over time

Traditional Beliefs about VUR in UTI

It is important to know if VUR exists because its presence is directly related to acute pyelonephritis, renal scarring and its sequelae, as well as recurrent UTI.

Once VUR is identified:

- Antibiotic prophylaxis to prevent recurrent UTI
- F/U cystogram 12 – 18 mos
- If no spontaneous resolution--Deflux or ureteral reimplantation.

Traditional Evaluation: Focus on VUR— "Bottom Up" Approach

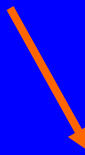
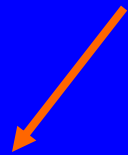
Child with UTI

US

CYSTOGRAM

VUR

no VUR



DMSA

No DMSA

Prophylaxis

**No
prophylaxis**

**F/U cystogram
12-18 mos**



Majd et al. J Pediatr 1991

94 children with febrile UTI

66% with acute pyelonephritis on DMSA
37% with VUR

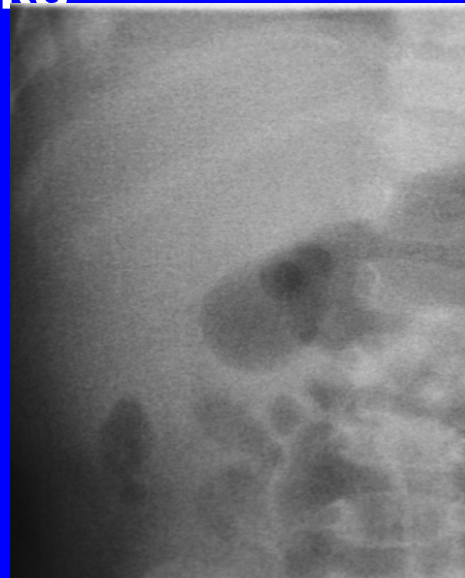
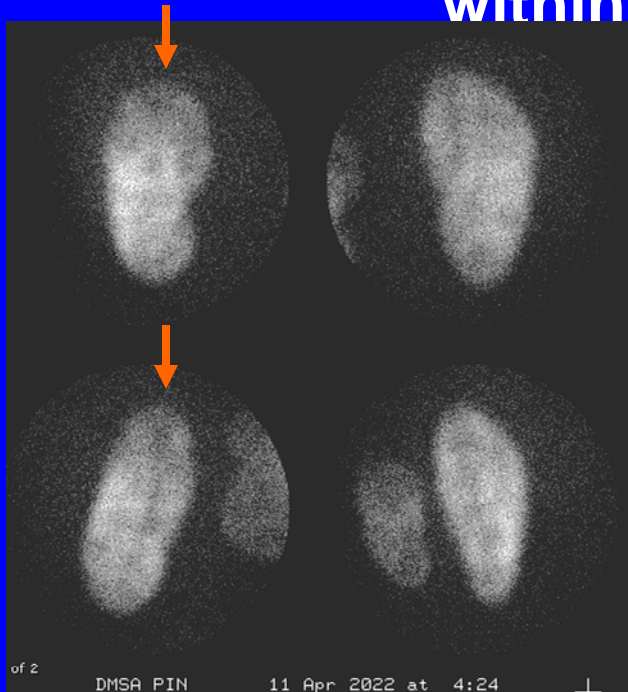
63% ***without*** demonstrable VUR

Acute Pyelonephritis occurring in the Absence of VUR

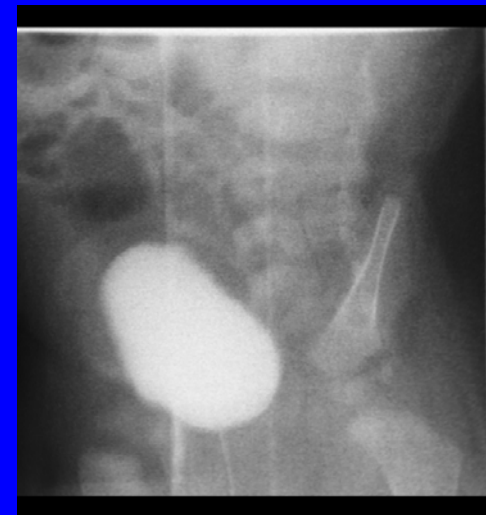
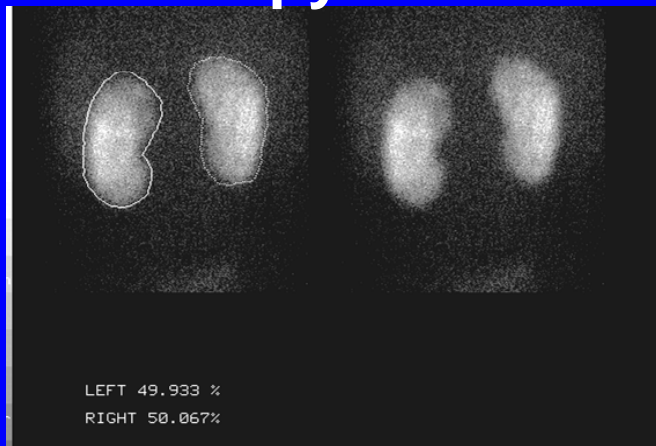
STUDY	% Pts with APN and NO VUR
Majd 1991	63
Ditchfield 1994	61
Hansson 2004	66
Moorthy 2005	50
Preda 2007	70
Tseng 2007	63

So if focus only on the patients with VUR, will miss the majority of patients with APN

6 month old girl with febrile UTI; DMSA and VCUG done within 5 wks



Acute pyelo LUP



No VUR

Is VUR predictive of APN?

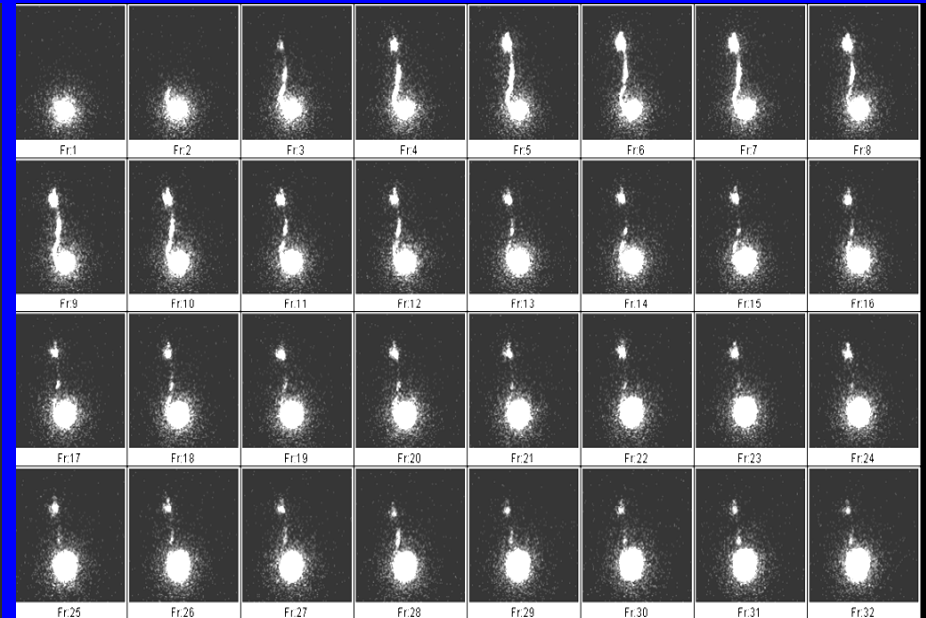
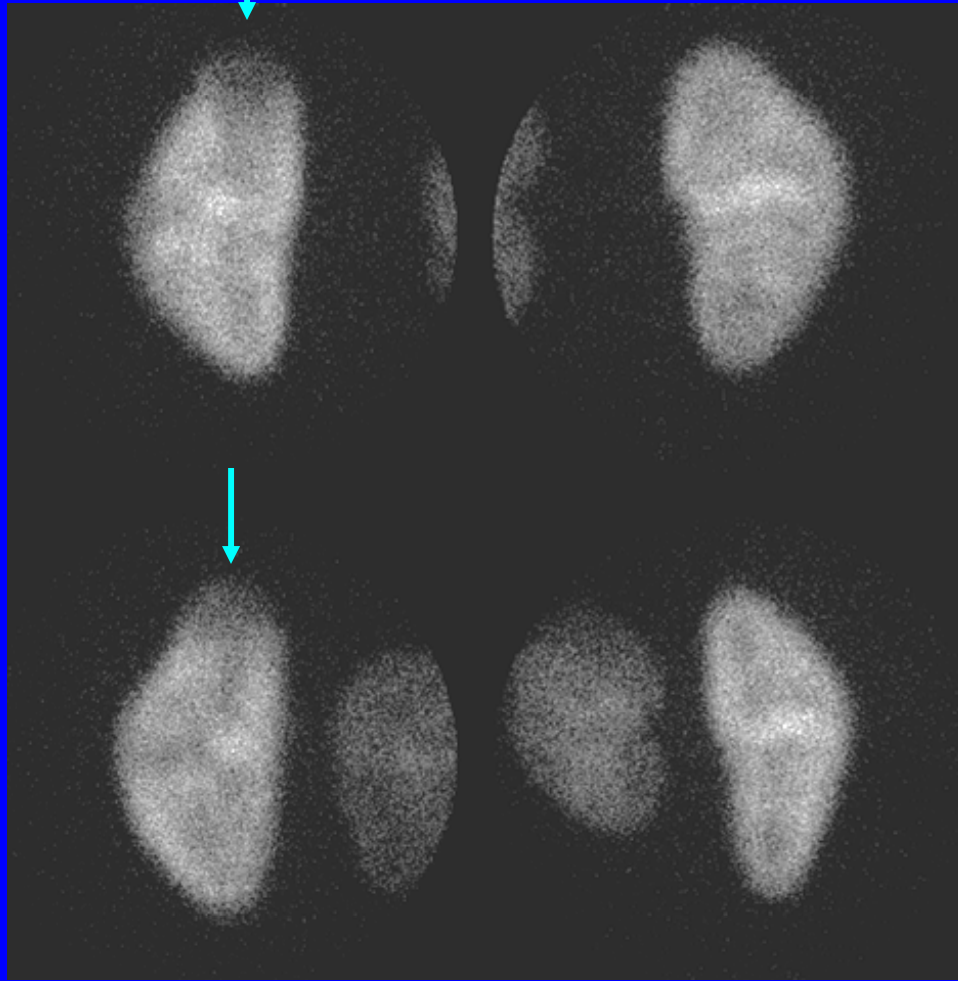
% Patients w/ VUR and APN

Majd 1991	37
Rosenberg 1992	40
Jacobsson 1994	34
Stokland 1996	47
Benador 1997	38
Hansson 2004	34
Ataei 2005	13
Tseng 2007	30
Preda 2007	30
AVERAGE	34

Slide courtesy of L. Binkovitz

Slides are not to be reproduced without permission of author

14 mos old girl with febrile UTI; DMSA and nuclear cystogram done within 3 weeks



Moderate LT VUR

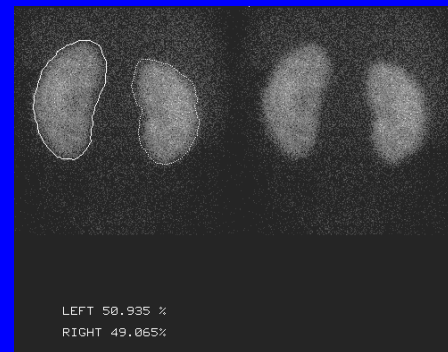
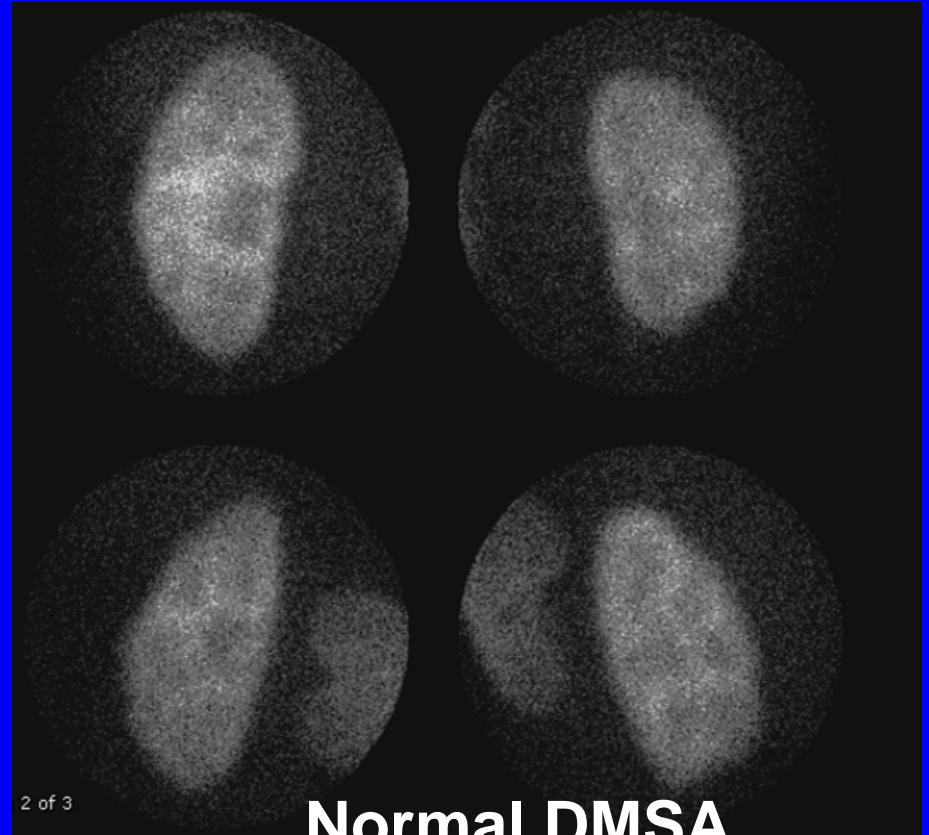
Acute pyelo LUP

Slides are not to be reproduced without permission of author

2 yr girl with febrile UTI: DMSA and VCUG done within 4 wks



Bilateral grade III VUR



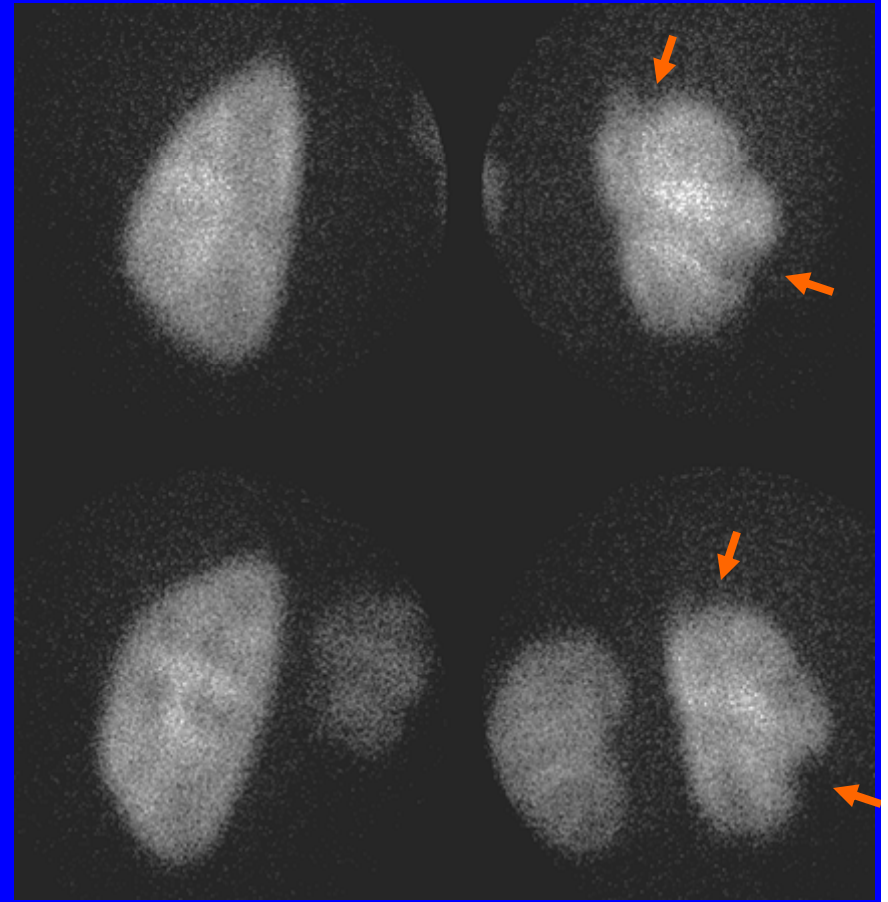
Acute Pyelonephritis and VUR in Renal Scar Formation

Rushton and Majd. J Urol 1992:
Initial and follow-up DMSA scans
on 33 pts with APN

Prevalence of scarring: 42%
40% with VUR
43% without VUR

All new scars formed at the exact site
of the acute pyelonephritic lesions

**Conclusion: Acute pyelonephritis--
the prerequisite for renal scar
formation**



Acute Pyelonephritis and VUR in Renal Scar Formation

STUDY

Scar Rate (%) in pts without VUR

Rushton 1992	43	(4-42 mos f/u)
Jakobsson 1994	62	(2 yr f/u)
Stokland 1996	53	(1 yr f/u)
Moorthy 2005	50	(3-6 mos f/u)
Garin 2006	46	(1 yr f/u)
Montini 2009	51	(1 yr f/u)
Siomou 2009	60	(6 mos f/u)

Shift in Focus

Most patients with acute pyelonephritis do not have demonstrable VUR

Acute pyelonephritis appears to be a more important risk factor than VUR for scar formation

Focus is changing from the presence of VUR to the status of the kidney—acute pyelonephritis or scar

Evolving Evaluation: Focus on Kidney Status—“Top Down” Approach

Child with Febrile UTI

DMSA

APN/scar



Cystogram

NL



No
Cystogram

Central
photopenia



US





VCUG!!

DMSA!!

US!

MR!

Does the Presence of VUR Matter at all?

High grades of VUR are associated with higher rates of renal scarring

Jakobsson . Arch Dis Child 1994

Stokland. J Pediatrics 1996

Can DMSA identify most patients with higher grades of VUR?

No consensus on “High grade VUR”:

≥grade III by some authors and

≥grade IV by other authors

Identification of Dilating VUR with DMSA

Pts with Abnormal DMSA who have
Dilating VUR

	#	%
Majd 1991	21/21	100
Rosenberg 1992	10/11	91
Jakobsson 1994	14/15	93
Stokland 1996	19/25	76
Hansson 2004	29/36	81
Ataei 2005	3/3	100
Moorthy 2005	1/1	100
Tseng 2007	21/21	100
Preda 2007	26/27	96
TOTAL	144/160	90%

Slide courtesy of L. Binkovitz--modified

Slides are not to be reproduced without permission of author

Hansson et al. J Urol 2004

303 patients, retrospective study

27/80 with VUR had normal DMSA

20/27 were grades I & 2

7 /27 were grades III-V: none of these 7 pts had scar on f/u DMSA

Conclusion: DMSA can replace VCUG for identification of kidneys at risk for APN and scar

Preda et al. J Pediatr 2007

290 children, prospective study

8/52 with VUR had normal DMSA

7/8 with grade I-II

1/8 with grade III-V—repeat DMSA at 2 yrs was normal

Conclusion: using DMSA as the first study, a significant number of VCUG exams can be avoided

Top-Down Approach

Therefore, using DMSA as the first study in evaluation of a child with UTI, most of the cases of high grades of VUR, considered to be a risk factor in scarring, will be detected.

Also this approach will decrease the number of cystograms performed.

How does the “Top-Down” Approach affect Management?

Traditionally, only those patients with VUR were placed on prophylaxis

With a decrease in the number of cystograms performed, fewer patients will be placed on prophylaxis

Antimicrobial Prophylaxis for VUR

Prophylaxis maintains the urine infection-free and gives time for the VUR to spontaneously resolve.

Questions:

- Does prophylaxis truly decrease the rate of recurrent UTI?
- Does prophylaxis result in a decrease in the rate of renal scarring?

Does prophylaxis decrease rate of recurrent UTI?

Garin et al. Pediatrics 2006

218 patients with UTI (3 mos to 18 yrs) randomized to prophylaxis vs placebo for 1 yr—with or without VUR (only grades I-III VUR were included)

Rate of recurrent UTI (cystitis and AP):

	Prophylaxis	No Prophylaxis
w/VUR	23.6%	22.4%
w/o VUR	8.8%	23.3%
	(p=0.06)	(p=0.99)

Does prophylaxis decrease rate of renal scarring?

Garin et al. Pediatrics 2006

13/218 (5.9%) developed scars

Rate of renal scars

	Prophylaxis	No Prophylaxis
w/ VUR	9%	3.4%
w/o VUR	4.5%	6.6%
	(p=0.99)	(p=0.99)

Conclusions:

Lower grades of VUR (I-III) did not increase the incidence of UTI and did not result in increase in renal scarring.

Prophylaxis did not decrease the rate of recurrent UTI nor did it decrease the rate of renal scarring

Does prophylaxis decrease rate of recurrent UTI?

Craig et al. N Engl J Med 2009

- 4 centers

- 576 children (age 0-18 yrs) with UTI with or w/o VUR
(all grades)

- Randomly assigned to prophylaxis or placebo for 12 months

Conclusions:

Prophylaxis decreased rate of recurrent UTI as compared to placebo, regardless of presence of VUR.

Typically recurrent UTI in the prophylaxis group were due to resistant bacteria.

The Randomized Intervention for Children With Vesicoureteral Reflux (RIVUR) Study

Keren et al. *Pediatrics* 2008

- Double-blind, randomized, placebo-controlled trial.
- 600 children with VUR to be enrolled, age 2 mos to 6 yrs
- Initial DMSA, US and VCUG on all patients.
- Randomized to receive placebo or trimethoprim/sulfamethoxazole for 2 years
- F/U DMSA at 1 and 2 years post infection
- F/U VCUG at 2 years post infection

The Randomized Intervention for Children With Vesicoureteral Reflux (RIVUR) Study

Keren et al. *Pediatrics* 2008

Primary outcome: recurrence of UTI

Secondary outcomes

1. time to recurrent UTI
2. renal scarring (assessed by DMSA scan)
3. treatment failure
4. development of antimicrobial resistance in stool flora

So...Who should receive prophylaxis?

Patients with VUR and a normal DMSA

Or

Patients with positive DMSA and no VUR

Pending results of the RIVUR Study

In the words of the True Pediatric GU Guru Massoud Majd, 18 years ago:

“Currently, the indication for low-dose antibiotic prophylaxis in infants and children with UTI is usually based solely on the presence of VUR regardless of its severity.

Perhaps direct scintigraphic evidence of parenchymal involvement at the time of acute symptomatic UTI is a more important determinant of the need for prophylaxis.

A child with a positive DMSA scan, regardless of the status of reflux, may be a more reasonable candidate than a child with low-grade reflux and a normal DMSA scan.”

Renal Cortical Scintigraphy in the Diagnosis of Acute Pyelonephritis. M. Majd. Semin in Nuclear Medicine, 1992.

In Summary

Evolving changes are occurring in the diagnostic work-up of children with UTI

Focus is shifting from emphasis on VUR to emphasis on the status of the kidney—acute pyelonephritis and scar on DMSA—“Top Down Approach”

Role of prophylaxis and role of VUR in renal scarring yet to be determined (RIVUR Study)

