Cortical renal scan in febrile UTI:
Established usefulness and future developments

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UTI is common in the pediatric population!

<table>
<thead>
<tr>
<th></th>
<th>Girls</th>
<th>Boys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verified UTI up to age 7 (%)</td>
<td>8.4</td>
<td>1.7</td>
</tr>
<tr>
<td>Febrile UTI (PN) up to age 7 (%)</td>
<td>2.7</td>
<td>1.0</td>
</tr>
</tbody>
</table>
Old (good?) times

• diagnosis of acute pyelonephritis is made by clinical and biochemical signs

• Treatment of acute pyelonephritis is established

• Indications for prophylaxis are clear

• VCUG is mandatory after the first febrile UTI
The radical approach


“…An ultrasonogram performed at the time of acute illness is of limited value.

A voiding cystourethrogram for the identification of reflux is useful only if antimicrobial prophylaxis is effective in reducing reinfections and renal scarring.

The routine performance of urinalysis, urine culture, or both during subsequent febrile illnesses in all children with a previous febrile urinary tract infection will probably obviate the need to obtain either early or late scans. …”
NICE guidelines 2007

« ...neither clinical nor laboratory tests performed well for prediction of UTI using DMSA as Gold standard, so clinical criteria with low threshold are recommended... »

Infants and children with bacteriuria and fever above 38°C should be considered to have pyelonephritis / upper tract infection

NICE workgroup, Ped Nephrol. 2008, 23:1596
What is your opinion about NICE guidelines?

1. It is mandatory to follow their suggestion
2. They are worthless
3. Their use must be weighted case by case
4. I do not know them
Cortical scan in febrile UTI

Why?
NICE guidelines, 2007

Imaging is unnecessary during or after the first febrile UTI

Late DMSA scan is recommended in case of recurrent UTI, i.e.:

- 2 or more episodes of APN
- 1 episode of APN + 1 or more lower UTI
- 3 or more episodes of lower UTI

“…there is always some uncertainty as to whether the first documented UTI is truly the first UTI…”

(Smith E.A., Pediatr Radiol 2008, 38 [suppl.1]:s76-82)
Nammalwar BR et al., Indian Pediatr 2005; 42(7): p270-1

"… The DMSA was abnormal in 26 children with clinical evidence of UTI but negative urine culture, of whom 65% had VUR…"

Kanellopoulos TA et al., Eur J Pediatr 2005; 164: p355

"… The DMSA was abnormal in 10 out of 33 children with less than $5 \times 10^4$ CFU in urine, 6/10 not E.Coli…"

Garin EH et al., Diagnostic significance of clinical and laboratory findings to localize site of UTI. Ped Nephrol. 2007 Jul 22 (7):1002-1006.

"… 33% of patients with cystitis were diagnosed as Pyelonephritis …"

"… 22% of those with pyelonephritis were considered to have cystitis …"
Permanent renal damage

Multivariate analysis shows the following significant factors

- reflux grade
- no of recurrences
- CRP
- duration of fever
Risk of developing hypertension

DMSA extent of defects

4.5 years old boy, born Feb ’04

Referred for the first time for febrile UTI.

US report:

Left kidney normal

Right kidney enlarged (probable infection)

No dilatations
What additional imaging do you suggest in this child

1. None

2. Late DMSA scan

3. VCUG

4. Acute DMSA scan, late cystogram if +
What additional imaging do you suggest in this child

1. None
2. Late DMSA scan
3. VCUG
4. Acute DMSA scan, late cystogram if +
8 years old girl, born August ‘99

Admitted in the Paediatric ward for febrile UTI

In the past previous episodes of high fever were thought to be due to upper airways infection.

Likely scar in the upper pole of the left kidney at ultrasound.
MAG3 scan + indirect radionuclide cystography

GFR
$^{51}\text{Cr}-\text{EDTA}$
70 ml/min/m$^2$BS
These children should have not been imaged according to NICE guidelines

Could we do better?

For a reference, see

*Coulthard MG, Arch Dis Child 2008 Mar; 93(3): 196-9*

*YES, WE CAN!*
“Pyelonephritis, like virtue, is easier to talk about than to define”


But we can define APN!
Acute pyelonephritis
What is the most accurate method for imaging acute pyelonephritis?

1. DMSA

2. MRI

3. CT

4. US + power doppler

5. US + contrast media
What is the most accurate method for imaging acute pyelonephritis?

1. DMSA
2. MRI
3. CT
4. US + power doppler
5. US + contrast media
## Acute pyelonephritis - diagnosis

<table>
<thead>
<tr>
<th>Method</th>
<th>Sens.</th>
<th>Spec.</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSA</td>
<td>92 %</td>
<td>94 %</td>
</tr>
<tr>
<td>helical TC</td>
<td>87 %</td>
<td>88 %</td>
</tr>
<tr>
<td>MRI</td>
<td>90 %</td>
<td>88 %</td>
</tr>
<tr>
<td>Power doppler</td>
<td>74 %</td>
<td>57 %</td>
</tr>
<tr>
<td>US + contrast</td>
<td>90 %</td>
<td>75 %</td>
</tr>
</tbody>
</table>

Farhat W. et al., J Urol 2002, 168(3): 1114-17
Scars - diagnosis

- DMSA reference
  Sens.

- US 22-31 %

Sinha MD. et al., Nephrol Dial Transplant. 2007, 22(8):2213-6

...if the detection of renal scars is the reason for imaging in children with UTIs, US alone is inappropriate at any age and DMSA ought to be the primary investigation.
Median agreement: 94%
What is your diagnosis?

1. Bilateral reflux, normal kidneys
2. Bilateral reflux and bilateral fixed defects
3. Bilateral reflux and left fixed defects
4. Bilateral reflux, bilateral fixed defects and left duplex kidney
What is your diagnosis?

1. Bilateral reflux, normal kidneys
2. Bilateral reflux and bilateral fixed defects
3. Bilateral reflux and left fixed defects
4. Bilateral reflux, bilateral fixed defects and left duplex kidney
## “Acute” DMSA vs VUR

<table>
<thead>
<tr>
<th>DMSA</th>
<th>No</th>
<th>grade I-II</th>
<th>grade III-V</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>120</td>
<td>20</td>
<td>7*</td>
</tr>
<tr>
<td>abnormal</td>
<td>103</td>
<td>24</td>
<td>29</td>
</tr>
</tbody>
</table>

- *All grade 3, no acquired renal damage
- children < 2 yrs

*Hansson S. et al., J Urol 2004, 172: 1071-74*
Girl, born 1994, known left VUR

MAG3 05/98                     DRC, 4/2000

Dubious febrile episodes after CAB prophylaxis withdrawal

MAG3 02/2003
What result do you expect from a following cystogram?

1. Left side VUR
2. Right side VUR
3. Bilateral VUR
4. No VUR
What result do you expect from a following cystogram?

1. Left side VUR
2. Right side VUR
3. Bilateral VUR
4. No VUR

DRC, 3/2003
## Dosimetry – ICRP rating

<table>
<thead>
<tr>
<th>Risk level</th>
<th>Category</th>
<th>Eff. Dose (mSv)</th>
<th>expected beneficial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negligible</td>
<td>I</td>
<td>&lt; 0.1</td>
<td>minimal</td>
</tr>
<tr>
<td>Minimal</td>
<td>IIa</td>
<td>0.1 – 1</td>
<td>low</td>
</tr>
<tr>
<td>Low</td>
<td>IIb</td>
<td>1 – 10</td>
<td>medium</td>
</tr>
<tr>
<td>Medium</td>
<td>III</td>
<td>&gt; 10</td>
<td>noteworthy</td>
</tr>
</tbody>
</table>
Dosimetry

<table>
<thead>
<tr>
<th>Effect.</th>
<th>Dose</th>
<th>risk/ICRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRC</td>
<td>0.05-0.1 mSv</td>
<td>negligible</td>
</tr>
<tr>
<td>DRS MAG3 +IRC</td>
<td>0.5 mSv</td>
<td>minimal</td>
</tr>
<tr>
<td>CRS DMSA</td>
<td>0.7 mSv</td>
<td>minimal</td>
</tr>
<tr>
<td>VCUUG</td>
<td>1.2 - 2 mSv</td>
<td>low</td>
</tr>
<tr>
<td>Spiral CT</td>
<td>5-20 mSv</td>
<td></td>
</tr>
<tr>
<td>Natural background</td>
<td>2 mSv / year</td>
<td></td>
</tr>
</tbody>
</table>
New doubts, New answers!

- differential diagnosis between acute pyelonephritis and other kind of febrile UTI is important?
- It allows early identification of children at risk

- VCUG is useful after the first febrile UTI?
- It is safe to perform VCUG only in children with DMSA-proven renal involvement

- which are the indications for prophylaxis?

- next presentation!
Biochemical Markers

C-reactive Protein (CRP)

Benador et al., Pediatrics 1998; 102:1422
  cutoff 10 mg/l  Sens = 100 %

Pecile et al., Pediatrics 2004; 114: 249
  cutoff 20 mg/l  Sens = 94.4 %

Tuerlinckx et al., Eur J Pediatr. 2005; 164: 651
  cutoff 34 mg/l,  Sens. = 94 %

Güven et al., Nucl Med Comm 2006; 27:715
  cutoff 20 mg/l,  Sens. = 95 %

Thayyil et al., Acta Pediatr 2005; 94: 155
  cutoff 50 mg/l,  Sens. = 75 %
Biochemical Markers

Procalcitonin (PCT)

Benador et al., Pediatrics, 1998; 102:1422
  cutoff 0.6 ng/ml   Spec = 82.6%

Pecile et al., Pediatrics 2004; 114: 249
  cutoff 0.8 ng/ml   Spec = 93.6%

Tuerlinckx et al., Eur J Pediatr. 2005; 164: 651
  cutoff 0.5, Spec. 23%   cutoff 1.7 Spec. 77%

Güven et al., Nucl Med Comm 2006; 27:715
  cutoff 0.5, Spec. 42%   cutoff 2 Spec. 100%

Thayyil et al., Acta Pediatr 2005; 94: 155
  cutoff 2 ng/ml,   Spec. 86 %
Varese, febrile UTIs 2001-2008

- 243 children, 157 females, 86 males

- Acute DMSA positive in 116 (47.5%) 77 f, 39 m

- serum CRP 121 ± 86 mg/l - DMSA positive

- serum CRP 75 ± 62 mg/l - DMSA negative

\[ p < 0.001 \]

- CRP ≤ 12 mg/l (8%) \( \Rightarrow \) 98.3% PPV for DMSA neg.

- VCUG performed in 192

- VUR + 33/106 DMSA positive

- VUR + 8/86 DMSA negative

- Fixed defect in 4/52 pts, all with an acute defect involving at least 30% of the kidney
Febrile UTI Flow Chart

US → abnormal → Imaging mandatory

↓ normal

↓

CRP → <12 mg/l → STOP

↓

>12 mg/l

↓

DMSA → normal → STOP

↓

abnormal → VCUG + Late DMSA (PCT? % of involved parenchyma?)
Customer satisfaction...
What do you think of the proposed follow-chart for febrile UTI?

1. Worthless
2. Useful
3. Interesting
4. Wonderful
Recent papers – Take home messages

Soccorso et al., J Pediatr Urol, 2009; 18
...We recommend US and DMSA in all febrile UTI...

Mantadakis et al., J Pediatr, 2009; 155(6): 875
...a serum PCT >0.5 ng/ml...may aid to identify children necessitating more intense evaluation

Lee et al, Pediatr Nephrol 2009; 24(10)
...Among 220 children with first febrile UTI, VUR was detected in 30%....

Coulthard et al., Pediatr Nephrol 2009; 24(10): 2059
...prompt treatment appears to prevent scarring...

Montini & Hewitt, Pediatr Nephrol 2009; 24(9): 1605
...for higher grade VUR there is no definite conclusion about the usefulness of prophylaxis