Guidelines: UTI in Children

National Institute for Health and Clinical Excellence (NICE)—UK; American Academy of Pediatrics

Saul P. Greenfield, MD
Clinical Professor of Urology
State University at New York at Buffalo School of Medicine & Biomedical Sciences
Women & Children’s Hospital of Buffalo

Recent Buffalo Patient

3 month old girl admitted with a first time febrile UTI
Renal USG: normal
Family told that VCUG was not needed
Pediatrician objected
VCUG obtained
UTI in Children

*National Institute for Health and Clinical Excellence (NICE)*

**NICE: Who are they?**
- Established in UK by NHS, 1999
- Citizen’s Council—members of the public
- Provides guidance, sets quality standards, manages national database
- *Not* meant to “override the individual responsibility of healthcare professionals”
- “Comparative Effectiveness Institute” in US—new legislation

**NICE: Major Aim**
- “Maximise health gain from limited resources...of the NHS”
  *NICE, 2004*
- “…a failure to consider some costs...for example, those borne by patients...and the increasing value of future health…”
  *Gravelle, Health Econ 16:307, 2007*

**NICE: UTI in Children**
- Published in August 2007
- Current management places a heavy burden on NHS...resources
- *It is costly...and is unpleasant for children and distressing for their parents*
- Aim is to achieve consistent clinical practice

**NICE: UTI Diagnosis**
- Clean catch urine recommended
- Urine collection pads can be used
- Catheter or SP aspirate, only if other methods are not possible
- Microscopy and culture needed
- *u/a: UTI can be diagnosed if no pyuria, but if bacteriuria seen*

**NICE: U/A Dipstick Criteria**
- Leukocyte esterase positive, nitrite positive
  - start antibiotic treatment
- Leukocyte esterase negative, nitrite positive
  - start antibiotic treatment
- Leukocyte esterase positive, nitrite negative
  - treat only if clinically warranted
- Leukocyte esterase negative, nitrite negative
  - do not treat for UTI
### NICE: UTI Treatment

Infant < 3 months: IV antibiotics  
Infant > 3 months with fUTI, pyelonephritis:  
oral antibiotics 7-10 days, or IV antibiotics for 2-4 days followed by oral for a total of 10 days  
Infant > 3 months with cystitis, lower urinary tract infection: oral antibiotics for 3 days and reassess

### NICE: UTI Imaging Guidelines

3 categories of UTI

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I: Typical</td>
<td>Responds well to treatment by 48 hrs</td>
</tr>
<tr>
<td>II: Atypical</td>
<td></td>
</tr>
<tr>
<td>III: Recurrent</td>
<td></td>
</tr>
</tbody>
</table>

### Imaging for Infants < 6 Months

(I: Typical—Responds by 48 hrs, II: Atypical, III: Recurrent)

<table>
<thead>
<tr>
<th>Type</th>
<th>Imaging Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical</td>
<td>Renal USG alone, VCUG if USG is abnormal</td>
</tr>
<tr>
<td>Atypical</td>
<td>Renal USG, DMSA scan, VCUG</td>
</tr>
<tr>
<td>Recurrent</td>
<td>Renal USG, DMSA scan, VCUG</td>
</tr>
</tbody>
</table>

### Imaging for Ages 6 mos to 3 yrs

(I: Typical—Responds by 48 hrs, II: Atypical, III: Recurrent)

<table>
<thead>
<tr>
<th>Type</th>
<th>Imaging Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical</td>
<td>None</td>
</tr>
</tbody>
</table>
| Atypical   | USG during infection  
VCUG only if non-e coli UTI, Fam. Hx of VUR, abnormal USG, poor urine flow  
DMSA scan |
| Recurrent  | Same as Atypical, but USG can be delayed |

### Imaging for Children > 3 yrs

(I: Typical—Responds by 48 hrs, II: Atypical, III: Recurrent)

<table>
<thead>
<tr>
<th>Type</th>
<th>Imaging Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical</td>
<td>None</td>
</tr>
<tr>
<td>Atypical</td>
<td>USG during infection</td>
</tr>
<tr>
<td>Recurrent</td>
<td>USG at any time, DMSA scan</td>
</tr>
</tbody>
</table>

VCUG *never initially recommended in this age group*
Surgical Intervention

“Surgical management of VUR is not routinely recommended.”

-recommendation made by “consensus...based on limited evidence available.”

-well designed...trials are required to determine effectiveness of prophylaxis or various surgical procedures”

NICE Guidelines

“Nasty processes produce nasty guidelines” BMJ 2007; 335: 463

NICE members signed “secrecy” agreements
Brit. Assoc. of Pediatr. Nephrol not consulted
Outside peer reviews that were critical were ignored
Inadequate review of the literature
Misuse of statistics
Declared DMSA renal scan “too invasive”
Conclusions reflect opinion rather than fact
Decrease cost will “delight” the NHS

—M. Coulthard, consultant pediatric nephrologist

NICE Guidelines

< 6 months: All—VCUG, USG, DMSA scans

Atypical (36 infants)
more infants with abnormal VCUG, USG and DMSA scan

Typical: fever resolves by 48 hrs (98 infants)
NICE guidelines—USG alone:
Missed Pathology:
22 scarred kidneys
25 refluxing ureters (1-IV, 6-III,13-II,5—I)

Tse et al, Pediatr Nephol, 2009

Conclusions

NICE guidelines were arrived at by committee consensus
NICE acknowledges, however, that the published data is poor
NICE factors cost into their guidelines
Future health care costs may not have been factored in accurately

AAP Guidelines: Diagnosis and Management of Initial Febrile UTI in Children ages 2 to 24 months

Issued August 2011

AAP UTI Guidelines

 Subcommittee on Urinary Tract Infection,
Steering Committee on Quality Improvement
and Management
Update of 1999 AAP Guidelines
Participants: general pediatrics, epidemiology,
pediatric infectious disease,
pediatric nephrology, pediatric radiology,
pediatric urology
Subcommittee Members

Kenneth Roberts, Chair (gen. peds.)
Stephen Downs (epidem., gen. peds.)
S. Maria Fennel (epidem., gen. peds.)
Stanley Hellerstein (ped. nephrology)
Linda Shortliffe (ped. Urology)
Ellen Wald (ped. Infect. disease)
J. Michael Zerin (ped. radiology)

AAP UTI Guidelines

Reviewed by 17 groups within the AAP and 5 organizations outside the AAP
Review of the last 10 years of literature
Authors of 6 recent studies on the effectiveness of prophylaxis in preventing pyelonephritis in children with VUR submitted raw data on infants 2 to 24 months of age
Planned revision in 5 years, barring new evidence

AAP UTI Guidelines

7 recommendations (Action Statements)
Not intended as a sole source of management
Not intended to replace clinical judgment or establish exclusive protocol for the care of all children

Action Statement 1

If clinician suspects UTI as a source of fever and feels antibiotics are needed soon:
1. Urine specimen must be obtained before antibiotics are given for U/A, C&S
2. Urine must be obtained by catheter or SP aspiration. Bag specimens are not reliable
Evidence Quality: A; Strong Recommendation

Action Statement 1

SP aspiration may be only reliable method in boys with tight phimosis or girls with labial adhesions
Catheterized specimens: 95% specificity, 99% sensitivity
Bag specimens: unacceptably high false positive rate (88-99%)
Action Statement 2a
If clinician does not suspect a UTI as source of fever, clinical follow up without further testing is sufficient
Prediction for high likelihood of UTI:
girls: white race, < 12 mo., > 39 deg C, > 2 days duration, absence of another source
boys: uncircumcised, white race, > 39 deg C, > 2 days duration, absence of another source

Action Statement 2b
If clinician determines that child not a low risk, but antibiotics can be delayed:
Choice 1: obtain a cath or SP culture, u/a
Choice 2: obtain urine by any convenient means, and if u/a is negative for nitrites and leukocyte esterase—follow clinical course, **BUT—**
a negative u/a does not rule out UTI
Evidence Quality: A; Strong Recommendation (for both 2a, 2b)

Action Statement 3
To establish the diagnosis of UTI there are 2 requirements:
1. u/a shows pyuria and/or bacteriuria
2. > 50,000 colonies/ml from specimen obtained by either cath or SP aspiration
Evidence Quality: C; Recommendation

Action Statement 3 Urinalysis
Nitrite Test:
Positive nitrite is helpful, but a negative nitrite is not and does not rule out UTI
Leukocyte Esterase Test:
False positives are common
Absence of pyuria in infants with febrile UTI is rare
Most reliable u/a: gram stain of un-spun urine

Action Statement 3 Urine Culture
Must have > 50,000 cfu/ml
Can accept range: 10,000 to 100,000 cfu/ml,
u/a is confirmatory
Office dip slides should be used in collaboration with a certified laboratory

Action Statement 4a
Oral or parenteral antibiotic treatment may be equally efficacious
Choice of agent should be based on local sensitivity patterns and lab sensitivity data
Can be switched from parenteral to oral after 24-48 hrs, if improved clinically
Nitrofurantoin should not be used
Evidence Quality: A; Strong Recommendation
**Action Statement 4b**

7 to 14 days of therapy can be chosen  
Minimum: 7 days  
Head to head data comparing 7, 10 or 14 days not found  
Evidence Quality: B; Recommendation

**Action Statement 5**

Febrile infants should undergo renal and bladder sonography  
Sonography should be performed within the first 2 days of treatment, unless clinical improvement is rapid  
Normal pre-natal sonography does not exclude an abnormality  
Acute DMSA renal scanning is not recommended  
Evidence Quality: C; Recommendation

**Action Statement 6**

VCUG should not be performed after 1st febrile UTI, unless:  
- sonogram shows hydronephrosis or scarring  
Evidence Quality: B; Recommendation  
VCUG should be obtained if febrile UTI recurs  
Evidence Quality: X; Recommendation

**Action Statement 7**

After confirmation of a febrile UTI, parents should be advised to have a medical evaluation after any future febrile illnesses  
A properly collected urine specimen should be obtained after any future febrile illness  
Evidence Quality: C; Recommendation

**Six Papers: Raw Data Compared prophylaxis to no-prophylaxis**

1. Pennesi et al, Pediatrics 2008  
2. Garin et al, Pediatrics 2006  
5. Craig et al, NEJM 2009  
Summary of Data Weakness

Sex & Circumcision Status:
* Pennesi-50% male, all uncircumcised
  Garin-not disclosed
* Montini-31% male, not disclosed
* Roussey-Kessler-31% male, not disclosed
* Craig-36% male, 4% circumcised
* Brandstrom-37% male, not disclosed

*Circumcision not widely practiced

Summary of Data Weakness

Bagged Urine Specimens:
Pennesi, Montini, Roussey-Kessler, Craig, Brandstrom

Catheterized Urine Specimens:
Garin

Major problem, especially in uncircumcised males

Summary of Data Weakness

DMSA scans not uniformly performed:
Pennesi, Roussey-Kessler, Craig

VCUG’s & Renal USG’s not performed in everyone:
Craig

Compliance with antibiotic regimen not assessed:
Pennesi, Garin, Roussey-Kessler

Summary of Data Weakness

Blinded or placebo controlled:
– Craig

– None of the other studies were conducted with placebo or were blinded.

Contradictory Conclusions

Pennesi: no benefit to prophylaxis
Garin: no benefit to prophylaxis
Montini: prophylaxis may benefit grade III
Roussey-Kessler: prophylaxis may benefit boys with grade III
Craig: fUTI double in those not on prophylaxis
Brandstrom: prophylaxis provides clear benefit—no new scarring on prophylaxis

Urology Section-AAP
Official Response: March 2011

Given less than 7 calendar days to respond
Request additional time to relay comments to Board Reviewer
Would like to assist in final guidelines preparation
There are significant problems with the data
Garin paper has few patients under age 2
Separating groups by grade statistically inappropriate and underpowered
New “fugitive data” must undergo peer review
Urology Section-AAP
Official Response: March 2011

Urine sampling with bagged specimens is inaccurate and contradicts earlier recommendations in the AAP draft—most studies allowed bagged specimens.
Renal ultrasound cannot detect scarring and DMSA renal scanning was often not used.
Most studies are not blinded or placebo controlled.
Compliance with prophylaxis not always assessed.
While many with VUR have a benign course, some do not and it is imprudent to abandon looking for VUR in a child with a first febrile UTI. This places a large pool of infants and children at risk.

Risk factors for renal scar formation in infants with first episode of acute pyelonephritis: a prospective clinical study.
Lee et al, J Urol, March 2012

213 infants with febrile UTI
DMSA scans performed acutely & 6 months later
Risk of scar formation: 39% with VUR, 7.5% without VUR
Rate of scar formation related to grade: I-20%, II-22%, III-40%, IV-70%, V-56%