“Going with the Flow”
Update on AAP guidelines for diagnosis and management of UTI

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Paying the Ferryman-Clinical Burden

- Urinary tract remains the most frequent site of occult and serious bacterial infections.
- Clinical presentation tends to be nonspecific in infants.
- Reliable urine specimens for culture involve invasive methods.
- Most experimental and clinical data support the concept that delays in the institution of appropriate treatment of pyelonephritis increase the risk of renal damage.

More to come...

- Updated AAP policy statement
- No studies of the efficacy of prophylaxis in High Grade Reflux.
- Results of the RIVUR study-

1999 Evidence Model Decision Tree

- Phase 1- Recognize at risk child
- Phase 2- Diagnostic strategies characterized by their cost, sensitivity, and specificity.
- Phase 3- Short-term treatment of UTI.
- Phase 4- Imaging evaluation of infants with the diagnosis of UTI to identify those with urinary tract abnormalities such as vesicoureteral reflux (VUR).

1999 guidelines

- Conceptual model evidence model depicts the relationships between the steps in the diagnosis and management of UTI.
2011 revised guideline

Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months

SUBCOMMITTEE ON URINARY TRACT INFECTION and STEERING COMMITTEE ON QUALITY IMPROVEMENT AND MANAGEMENT

Pediatric, originally published online August 28, 2011; DOI: 10.1542/peds.2011-1330

- no obvious neurologic or anatomic abnormalities known to be associated with recurrent UTI or renal damage.

Logical sequence of clinical questions

1. Which children should have urine tested?
2. How should sample be obtained?
3. How should UTI’s be treated?
4. What imaging is recommended after diagnosis of UTI?
5. How should children be followed after a UTI diagnosis?

Action statement 1

- Febrile infant with no apparent source for fever should be assessed for risk of UTI
- Urine specimen obtained for both culture and urinalysis before an antimicrobials administered
- Specimen obtained via catheterization or SPA

Define patients

- Define a priori probability of UTI

<table>
<thead>
<tr>
<th>Individual Risk Factors: Girls</th>
<th>Probability of UTI</th>
<th># Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>White race</td>
<td>≤ 1%</td>
<td>No more than 1</td>
</tr>
<tr>
<td>Age &lt;12 months</td>
<td>≤ 2 %</td>
<td>No more than 2</td>
</tr>
<tr>
<td>Fever ≥2 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No other source fever</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Individual Risk Factors: Boys</th>
<th>Probability of UTI</th>
<th>Uncircumcised</th>
<th>Circumcised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonblack race</td>
<td>≤ 1%</td>
<td>Risk &gt;1%</td>
<td>No more than 2</td>
</tr>
<tr>
<td>Temp ≥39°C</td>
<td>≤ 2 %</td>
<td>None</td>
<td>No more than 3</td>
</tr>
<tr>
<td>Fever ≥1 day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No other source of fever</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Action Statements 2a/2b

- Once identify at risk status of patient use stratification data to determine pathway
  - Sample methods
  - Treatment vs observation

Sample selection

- 1999 : SPA gold standard
- 2011 : Urethral Catheterization preferred
  - high success >80%
  - sensitive 95%
  - specific 99%
- SPA
  - success rate 20-70%
  - pain and invasiveness data suggest not optimal choice
- Bag: unacceptable
  - 85% all + bag cultures would be false positives
Febrile Infant – no source

Toxic?

YES
UA/Cx by cath/SPA prior to abx

NO
consider likelihood UTI

High
obtain urine specimen

Low
Clinical F/U - no testing

Option 1
cath/spa
Ucx/UA

Option 2
bag for UA

- UA
clinical F/U - no treat

+ UA(dip or micro)
cath/spa for Cx

Summary of action statements 1, 2a, 2b

How to use UA

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte Esterase</td>
<td>83%</td>
<td>78%</td>
</tr>
<tr>
<td>Nitrite</td>
<td>53%</td>
<td>98%</td>
</tr>
<tr>
<td>LE OR Nitrite</td>
<td>93%</td>
<td>72%</td>
</tr>
<tr>
<td>Micro WBC</td>
<td>73%</td>
<td>81%</td>
</tr>
<tr>
<td>Micro Bacteria</td>
<td>81%</td>
<td>83%</td>
</tr>
<tr>
<td>LE, Nitrite OR micro</td>
<td>99%</td>
<td>70%</td>
</tr>
</tbody>
</table>

New Data

<table>
<thead>
<tr>
<th>Study</th>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lockhart et al</td>
<td>LE or Nitrite &lt;6mo age</td>
<td>67%</td>
<td>79%</td>
</tr>
<tr>
<td>Hoberman et al</td>
<td>Any Bacteria, &gt;10 wbc</td>
<td>&lt;2yrs</td>
<td>96%</td>
</tr>
<tr>
<td>Shaw</td>
<td>Enhanced UA &lt;12mo, infants, &lt;2yr girls</td>
<td>94%</td>
<td>84%</td>
</tr>
<tr>
<td></td>
<td>Standard UA</td>
<td>83%</td>
<td>87%</td>
</tr>
<tr>
<td>Lin</td>
<td>hemocytometer &gt;10 cells</td>
<td>83%</td>
<td>89%</td>
</tr>
</tbody>
</table>

Action Statement 3

To establish the diagnosis of UTI:
both urinalysis results that suggest infection
(pyuria and/or bacteriuria)
and at least 50 000 CFUs/ mL
of a uropathogen cultured from an appropriate urine specimen.

Action Statement 4a and 4b

- Pyuria w/o infection not uncommon
  - Inflammatory conditions
- Infection w/o pyuria rare
  - Contaminated specimen
  - Asymptomatic bacteremia
    - 0.7% afebrile girls had 3 succesive cxs +

- Route based on practical consideration- parenteral vs oral
- Choice of agent should be based on local antimicrobial sensitivity patterns and adjusted according to sensitivity testing of the isolated uropathogen
- Duration of antimicrobial treatment for febrile UTI and or pyelonephritis should be 7 to 14 days
Goals of short term treatment

- Eliminate the acute infection
- Prevent complications of bacteremia & reduce the likelihood of renal damage
  - Delay >48 hours may confer 50% higher risk of acquiring renal scar.
  - Bacterial sepsis 10%
  - Bacteremia 2-36 months 3%, <2months 22%

Treatment / How

- Oral therapy is as effective as parenteral
  - No difference in duration of fever and or renal damage at 6-12 months
- <30 day infants-initial IV therapy recommended
  - may not be possible to distinguish complicated vs uncomplicated pyelonephritis on presentation
  - very little data on primary oral therapy

Treatment / How Long?

- 7-14 days range –no discernable difference
- Data on shorter courses demonstrate inferior results in febrile infants

Treatment -What

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>75 mg/kg, every 24 h</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>150 mg/kg per d, divided every 6-8 h</td>
</tr>
<tr>
<td>Gatifloxin</td>
<td>100-150 mg/kg per d, divided every 6-8 h</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>7.5 mg/kg per d, divided every 8-12 h</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>5 mg/kg per d, divided every 24 h</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>200 mg/kg per d, divided every 6-8 h</td>
</tr>
</tbody>
</table>

Abx Prophylaxis

Data from the most recent 6 studies do not support the use of antimicrobial prophylaxis to prevent febrile recurrent UTI in infants without vesicoureteral reflux (VUR) or with grade I to IV VUR

Pennesi, Garin, Conway...

Action Statement 5

- Febrile infants with UTIs should undergo renal and bladder ultrasonography
RBUS
- Identify obstructive lesions
- Evaluate nonresponse to therapy
- Evaluation of the renal parenchyma
- Assessment of renal size used to monitor renal growth
- Impact of Prenatal US
- For Detection of VUR
  - Poor sensitivity overall (30% to 62%)
    - As low as 14% in low grade VUR
    - As high as 98% in high grade VUR
  - Good specificity (85% to 100%)

Action Statement 6a/6b
- VCUG should not be performed routinely after the first febrile UTI
- VCUG is indicated if
  - RBUS reveals hydronephrosis, scarring, or suggests high-grade VUR / obstructive uropathy
  - atypical or complex clinical circumstances
- Further evaluation if there is a recurrence of febrile UTI

Outcomes
- Reported renal scarring rates
  - 1% - 40% in association with febrile UTI & VUR.
- Higher grades of VUR = higher risk of scar progression.
  - 4-6 times more likely than low-grade VUR
  - 8-10 times more likely than without VUR

The House of Cards
- VUR
- Progressive Renal Scarring
- ESRD
- HTN

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Action Statement 7

- After first UTI, instruct parents or guardians to seek prompt medical evaluation (ideally within 48 hours) for future febrile illnesses, to ensure that recurrent infections can be detected and treated promptly.

- Early treatment limits renal damage better than late treatment and the risk of renal scarring increases as the number of recurrences increase.

UTI recurrence

Adapted from Jodal.

The House of Cards

Adapted from The House of Cards.
Still ahead....

1. The relationship between UTIs in infants and young children and reduced renal function in adults
2. Alternatives to invasive sampling and culture
3. The role of VUR (and therefore of VCUG) is incompletely understood
4. Understanding the role for antimicrobial or antiseptic prophylaxis for the prevention of UTI
5. Better insight into risk factors that lead to increased scarring.
6. Data regarding rates among Hispanic individuals are limited and would be useful for prediction rules.
7. Optimal course of management in specific situations
8. Optimal duration of antimicrobial treatment

Revisit conclusions

- Strategies to correct VUR or to prevent UTI to decrease reflux nephropathy-no impact on ESRD
  - may be more important to identify and treat acute UTI early and accurately
  - Use of a modified imaging algorithm may be more sensitive to detect those at risk for renal damage with less costly and invasive intervention
- Risks of antibiotic overuse with little evident benefit
  - Excepting special populations

More to come...

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