Febrile UTIs in Practice
AAP Guidelines and New Evidence

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Emergency Medicine
Hospitalist Medicine
Emergency Medicine

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Future of Pediatrics Conference
No Disclosures
Learning Objectives

1) To review the 2011 AAP Guidelines
2) To review recent evidence in the management of febrile UTIs in children
3) To apply the guidelines and recent evidence
Case 1: 5 month old male
Case 2: 7 week old female
Case 3: 2 yo female with recurrent UTI
Case 1

- 5 mo Caucasian, circumcised, male
- T40 for 48 hours
- Well-appearing with defervescence and no localizing signs on exam
- Last immunizations 3 weeks ago

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Does it differ by age, gender, or race?

Do we test?

What is the risk of UTI in febrile children?
Risk Factors for UTI

AGE

GENDER

RACE

~7%* ~2%*

*Age 3-12 months

Circumcised ~1%

NOT Circumcised ~6%
### Infant GIRLS: Individual Factors

<table>
<thead>
<tr>
<th>Race: White</th>
<th>Age: &lt;12 months</th>
<th>Temperature: ≥39°C</th>
<th>Fever: ≥2 days</th>
<th>Absence of another source of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1%</td>
<td>No more than 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2%</td>
<td>No more than 2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Infant BOYS: Individual Factors

<table>
<thead>
<tr>
<th>Race: Nonblack</th>
<th>Temperature: ≥39°C</th>
<th>Fever: &gt;24 hours</th>
<th>Absence of another source of infection</th>
<th>Circumcised</th>
<th>Probability of UTI</th>
<th># of Factors Present</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>≤1%</td>
<td>No more than 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
<td>*</td>
<td>No more than 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>≤2%</td>
<td>None</td>
</tr>
</tbody>
</table>
### Infant GIRLS: Individual Factors

- Race: White
- Age: <12 months
- Temperature: ≥39°C
- Fever: ≥2 days
- Absence of another source of infection

### Probability of UTI

<table>
<thead>
<tr>
<th># of Factors Present</th>
</tr>
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<tbody>
<tr>
<td>≤1%</td>
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</table>

### Infant BOYS: Individual Factors

- Race: Nonblack
- Temperature: ≥39°C
- Fever: >24 hours
- Absence of another source of infection

### Probability of UTI

<table>
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</thead>
<tbody>
<tr>
<td>≤1%</td>
</tr>
<tr>
<td>≤2%</td>
</tr>
</tbody>
</table>

### Circumcised

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1%</td>
<td>*</td>
</tr>
</tbody>
</table>

| ≤2% | None | No more than 3 |

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How do we make the diagnosis?

- 10K?
- 50K?
- 100K?
- LE? Nitrites? WBC count?

How do we test?

- Urinalysis
- Urine Culture
- Bag vs Catheter
Diagnosis  = Positive Culture + Positive UA:

Positive culture: $\geq 50,000$ cfu/mL of uropathogen

AND

Positive urinalysis

✓ Evidence quality: C
✓ Recommendation
Where Did 100,000 Come From?


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TESTING

What is a positive UA?
### TABLE 1  Sensitivity and Specificity of Components of Urinalysis, Alone and in Combination

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (Range), %</th>
<th>Specificity (Range), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte esterase test</td>
<td>83 (67–94)</td>
<td>78 (64–92)</td>
</tr>
<tr>
<td>Nitrite test</td>
<td>53 (15–82)</td>
<td>98 (90–100)</td>
</tr>
<tr>
<td>Leukocyte esterase or nitrite test positive</td>
<td>93 (90–100)</td>
<td>72 (58–91)</td>
</tr>
<tr>
<td>Microscopy, WBCs</td>
<td>73 (32–100)</td>
<td>81 (45–98)</td>
</tr>
<tr>
<td>Microscopy, bacteria</td>
<td>81 (16–99)</td>
<td>83 (11–100)</td>
</tr>
<tr>
<td>Leukocyte esterase test, nitrite test, or microscopy positive</td>
<td>99.8 (99–100)</td>
<td>70 (60–92)</td>
</tr>
</tbody>
</table>
3-24mo Febrile Boy

Circumcised
LR = 0.33
Probability of UTI ~1%

≥2 UTI risk factors listed below or suprapubic tenderness?

<table>
<thead>
<tr>
<th>History of UTI</th>
<th>Temperature &gt;39°C</th>
<th>Fever without an apparent source</th>
<th>Ill appearance</th>
<th>Fever &gt;24 h</th>
<th>Nonblack race</th>
</tr>
</thead>
</table>

No

Yes

<table>
<thead>
<tr>
<th>Probability of UTI</th>
<th>2% to 4%</th>
<th>&lt;2%</th>
</tr>
</thead>
</table>

Obtain urinalysis and urine culture

Clinical follow-up in 24 h to reassess risk of UTI

Urine dipstick nitrite and leukocyte esterase negative
LR = 0.2
Probability of UTI <2%

Urine dipstick nitrite or leukocyte esterase positive
LR = 6
Probability of UTI ~15% to 34%

Urine dipstick nitrite and leukocyte esterase positive
LR = 28
Probability of UTI ~46% to 71%
<table>
<thead>
<tr>
<th>Organism</th>
<th>n</th>
<th>Urine Culture Growth, CFU/mL</th>
<th>UA Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;10K 10–25K 25–50K</td>
<td>Pyuria &gt;3 WBC/HPF</td>
</tr>
<tr>
<td>E coli</td>
<td>12</td>
<td>1 7 4</td>
<td>11/12</td>
</tr>
<tr>
<td>GBS</td>
<td>5</td>
<td>4 1 0</td>
<td>1/5</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>1</td>
<td>1 0 0</td>
<td>0</td>
</tr>
<tr>
<td>GAS</td>
<td>1</td>
<td>1 0 0</td>
<td>ND</td>
</tr>
</tbody>
</table>

GAS, Group A Streptococcus; ND, not done.

* Denominators reflect that not all infants had UA bacteria results.
TESTING

Is there only 1 way
Two-Step Process for ED UTI Screening in Febrile Young Children: Reducing Catheterization Rates

Jane M. Lavelle, Mercedes M. Blackstone, Mary Kate Funari, Christine Roper, Patricia Lopez, Aileen Schast, April M. Taylor, Catherine B. Voorhis, Mira Henien, Kathy N. Shaw
Bag UA appropriate to screen for UTI

- Single center, ED based QI study
- Two step process to screen for UTI
  - Bag UA
  - IF Udip + (mod/lg LE OR nitrites) → Ucath + Abx
- 6mo-24 mo with concern for UTI
- No difference in culture positivity rates
- No difference in return visits
- No difference in length of stay

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Lavelle et al. Pediatrics 2016
Diagnostic Practice 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

Culture >50K AND UA (+LE/nitrates OR WBC)

Two step method, using bag UA to screen is appropriate
Case 1: 5 month old male

Case 2: 7 week old female

Case 3: 2 yo female with recurrent UTI
Case 2

- 7 week old female
- T 38.5
- No other symptoms
- Well appearing
Case 2

- Partial sepsis work-up completed and UA is positive with WBC and mod LE
- Is an LP needed before starting treatment?
- Infant is well appearing and has no other medical history.
Risk of meningitis in a ‘low risk’ 29-60 day old infant with UTI is rare

• Schnadower et. al, Pediatrics 2010
• Retrospective, 20 centers, n=1895
• 29-60 day old with cx proven febrile UTI
Predicting Low Risk

• 4 Factors to Predict Low Risk
  – not clinically ill
  – no underlying disease
  – ANC > 1500
  – band count < 1250

→ consider discharge home after single dose of IV or IM Ceftriaxone with 24 hour follow-up OR short observation period

*If any concern for inability to follow-up consider admission*
Case 2 -- revised

• Now let’s assume our infant is 10 weeks old and has received her 2 mo vaccinations.
How do we treat?

Follow-up?

Do we admit?
Oral and IV Antibiotics equally efficacious (2-24 mo)

- Evidence quality: A
- Strong recommendation

Take into account:
- Ability to tolerate oral abx
- "toxicity"
- Any concern regarding adherence
Antibiotic choice based on local sensitivity

- Evidence quality: A
- Strong recommendation
Abx of Choice: 2\textsuperscript{nd} - 3\textsuperscript{rd} Gen Cephalosporin

- **Ecoli** (75-90%)
  - 60% of *Ecoli* isolates are susceptible to TMP/SMZ
  - 41% susceptible to ampicillin
  - 93% susceptible to second generation cephalosporins

- **Enterococcus**
  - 100% susceptible to ampicillin

- **Klebsiella, GBBS...**

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2015 CNMC Antimicrobial Susceptibility Data
Duration of Abx: 7-14 days

✓ Evidence quality: B
✓ Recommendation
Case 2 -- continued

• Infant is in your office for follow up at 48 hours.
• Doing well, fevers improving.
• Will you complete any imaging for first time UTI?
Renal/Bladder Ultrasound on all infants

✓ Evidence quality: C  
✓ Recommendation

WHY?
• Yield of abnormal findings: 12–16%  
• Permanent renal damage (1 year later)
  – Sensitivity: 41%  
  – Specificity: 81%

WHEN?
IF ill and not improving then within first 48 hours  
IF improving then, if done, better done > 48 hours
DIAGNOSIS

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

TESTING

Culture >50K AND UA (+LE/nitrates OR WBC)

TREATMENT

Oral = IV
Local resistance 7-14 days

FOLLOW-UP/IMAGING

Follow-up @ 48h RBUS
Case 1: 5 month old male
Case 2: 10 week old female
Case 3: 2 yo female with recurrent UTI
Case 3

- 2yo girl with previous febrile UTI in France
- Febrile illness since am
- Do we test?
- Do we image?
- If VUR → What do we do?

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No VCUG for first febrile UTI if RBUS is nml

VCUG is not recommended to be performed routinely after the first febrile UTI if RBUS is normal.

- Evidence quality: B
- Recommendation

Further evaluation should be conducted if there is a recurrence of febrile UTI.

- Evidence quality: X
- Recommendation
VUR: To Treat or To Not Treat

Evidence from the RIVUR Trial

Randomized Intervention for Children with VesicoUreteral Reflux
Antimicrobial Prophylaxis for Children with Vesicoureteral Reflux

The RIVUR Trial Investigators*
RIVUR Trial

• 2-year randomized, double blind, placebo controlled trial

607 Children
2 to 71 months
Grade I-IV VUR after 1 or 2 UTI

TMP/SMZ
Placebo
Patient Characteristics

- Median age: 12 months
- 92% girls
- 8% boys (63% uncirc)
- 80% had grades II or III reflux
- 56% BBD
Study Outcomes

Recurrent UTI

Renal Scarring

Abx Resistance
Decreased recurrences of UTI
<table>
<thead>
<tr>
<th></th>
<th>Difference Overall</th>
<th>Prophylaxis 11.9%, Placebo 10.2% (p=0.55)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Difference in Severe Renal Scarring</td>
<td>Prophylaxis 4.8%, Placebo 2.6% (p=0.37)</td>
</tr>
<tr>
<td></td>
<td>Difference in New Renal Scarring</td>
<td>Prophylaxis 8.2%, Placebo 8.4% (p=0.94)</td>
</tr>
</tbody>
</table>
Greater Antibiotic Resistance

• E.Coli from stool culture →
  – Resistance to TMP/SMZ was greater in treatment group, but not statistically significant

• 1\textsuperscript{st} recurrent UTI with E.Coli →
  – Resistance to TMP/SMZ was greater in treatment group (p<0.0001)
Debate continues

Prophylaxis Abx for VUR

No prophylaxis for VUR

Reduced UTI

No change in renal scarring

Family/patient stress

Avoid abx resistance

Avoid alterations in microbiome
DIAGNOSIS

Oral = IV
Local resistance
7-14 days
No prophylaxis

TESTING

Two step method, using bag UA to screen is appropriate

TREATMENT

Culture >50K AND UA (+LE/nitrates OR WBC)

FOLLOW-UP/IMAGING

Oral = IV
Local resistance
7-14 days
No prophylaxis

Follow-up @ 48h
Not better - RBUS
VCUG only if abnl
RBUS or second UTI
Future Directions

• Due for revision of AAP guidelines
• Novel POC testing; non-invasive testing
• Smart diapers
References

• AAP Clinical Practice Guideline: *Pediatrics*. 2011
  – http://pediatrics.aappublications.org/content/early/2011/08/24/peds.2011-1330

• AAP Webinar by Kenneth Roberts:
  – http://www2.aap.org/pcorss/webinars/pcos/AAP%20Webinar_UTI-Roberts-Final.ppt
SUMMARY: 2011 AAP GUIDELINE FOR DIAGNOSIS AND MANAGEMENT OF UTIS IN FEBRILE INFANTS
• **Inclusion**: Infant 2-24 mo with unexplained fever (≥ 38°C)
  – Rate of UTI: ~5%
  – Rate of scarring higher than older children

• **Exclusion**: neurologic or anatomic abnormality known to be associated with recurrent UTI or renal damage
### DIAGNOSIS: 2011 AAP Guidelines

<table>
<thead>
<tr>
<th>Specimen collection for urine culture must be catheterization or suprapubic aspiration</th>
<th>Strong</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk stratification based on bag urinalysis and if positive then catheterize or suprapubic tap for culture</td>
<td>Recommend</td>
</tr>
</tbody>
</table>
| Diagnosis established with both suggestive of infection:  
  1. Urinalysis suggestive of infection  
  2. Culture with >50K CFU | Recommend |
### MANAGEMENT: 2011 AAP Guidelines

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>YES</strong> – oral and parenteral abx equal efficacy</td>
<td>Strong</td>
</tr>
<tr>
<td><strong>YES</strong> – 7 to 14 days of antimicrobial therapy</td>
<td></td>
</tr>
<tr>
<td><strong>YES</strong> – RBUS: Febrile infants with UTIs should undergo renal and bladder sonography (RBUS)</td>
<td>Recommend</td>
</tr>
<tr>
<td>IF ill and not improving then within first 48 hours</td>
<td></td>
</tr>
<tr>
<td>IF improving then, if done, better done &gt; 48 hours</td>
<td></td>
</tr>
<tr>
<td><strong>NO</strong> – VCUG after first febrile UTI</td>
<td></td>
</tr>
<tr>
<td><strong>YES</strong> – VCUG after second UTI or if abnormal RBUS</td>
<td></td>
</tr>
<tr>
<td><strong>YES</strong> – Once documented febrile UTI, instruct parents to return within 48 hours for another febrile illness</td>
<td></td>
</tr>
</tbody>
</table>
Changes from previous UTI Guidelines

• Diagnosis:
  – Abnormal urinalysis + positive culture (need both)
  – Positive culture is >= 50K CFU/mL
  – Assessment of likelihood of UTI
• Treatment:
  – Oral as effective as parenteral
• Imaging:
  – VCUG not routinely recommended after first febrile UTI
• Follow-up:
  – Emphasis on urine testing with subsequent febrile illnesses

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ALGORITHMS
Figure 2. Diagnostic Algorithm for Febrile Male Infants Aged 3 to 24 Months Suspected of Having a UTI

Febrile male infant aged 3 to 24 mo with no known urinary tract abnormalities

Probability of UTI = 2%

Uncircumcised
LR = 2.8
Probability of UTI = 6%

≥1 UTI risk factors listed below?
History of UTI
Temperature >39°C
Fever without an apparent source
Ill appearance
Suprapubic tenderness
Fever >24 h
Nonblack race

Yes

Probability of UTI = 10% to 25%
Obtain urinalysis and urine culture

No

Clinical follow-up in 24 h to reassess risk of UTI

Urine dipstick nitrite and leukocyte esterase negative
LR = 0.2
Probability of UTI = 2% to 6%

Urine dipstick nitrite or leukocyte esterase positive
LR = 6
Probability of UTI = 40% to 68%

Circumcised
LR = 0.33
Probability of UTI = 1%

≥2 UTI risk factors listed below or suprapubic tenderness?
History of UTI
Temperature >39°C
Fever without an apparent source
Ill appearance
Fever >24 h
Nonblack race

Yes

Probability of UTI = 2% to 4%
Obtain urinalysis and urine culture

No

Probability of UTI = 2%
Clinical follow-up in 24 h to reassess risk of UTI

Urine dipstick nitrite or leukocyte esterase positive
LR = 28
Probability of UTI = 15% to 34%

Urine dipstick nitrite and leukocyte esterase negative
LR = 0.2
Probability of UTI = 2%

Urine dipstick nitrite or leukocyte esterase positive
LR = 6
Probability of UTI = 46% to 71%

UTI indicates urinary tract infection; LR, likelihood ratio.

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Figure 3. Diagnostic Algorithm for Febrile Female Infants Aged 3 to 24 Months Suspected of Having a UTI

Febrile female infant aged 3 to 24 mo with no known urinary tract abnormalities

- Age <12 mo
  - Probability of UTI ~7%
  - ≥1 UTI risk factors?
    - History of UTI
    - Temperature >39°C
    - Fever without an apparent source
    - Ill appearance
    - Suprapubic tenderness
    - Fever >24 h
    - Nonblack race

- Yes
  - Probability of UTI ~10% to 25%
  - Obtain urinalysis and urine culture

- No
  - Probability of UTI <2%
  - Clinical follow-up in 24 h to reassess risk of UTI

- Urine dipstick nitrite and leukocyte esterase negative
  - LR = 0.2
  - Probability of UTI 2% to 6%

- Urine dipstick nitrite or leukocyte esterase positive
  - LR = 6
  - Probability of UTI 24% to 66%

- Urine dipstick nitrite and leukocyte esterase positive
  - LR = 28
  - Probability of UTI 75% to 90%

- Urine dipstick nitrite and leukocyte esterase negative
  - LR = 0.2
  - Probability of UTI <2%

- Urine dipstick nitrite or leukocyte esterase positive
  - LR = 6
  - Probability of UTI 15% to 34%

- Urine dipstick nitrite and leukocyte esterase positive
  - LR = 28
  - Probability of UTI 46% to 71%

UTI indicates urinary tract infection; LR, likelihood ratio.
Figure 4. Diagnostic Algorithm for Verbal Children Older Than 24 Months With Urinary or Abdominal Symptoms

Verbal child with urinary or abdominal symptoms

Females and uncircumcised males
Probability of UTI ~8%

Dysuria or frequency? No

Yes

Energy density: 2.5
Probability of UTI ~18%

Obtain urinalysis and urine culture

Urine dipstick nitrite and leukocyte esterase negative
LR = 0.2
Probability of UTI 4% to 8%

Urine dipstick nitrite or leukocyte esterase positive
LR = 6
Probability of UTI 60% to 70%

Urine dipstick nitrite and leukocyte esterase positive
LR = 28
Probability of UTI 86% to 92%

Circumcised males
Probability of UTI <1%

Abdominal pain, back pain, or new-onset incontinence? No

Yes

UTI unlikely; consider other conditions in the differential diagnosis

Consider urinalysis and culture only if multiple signs or symptoms of UTI

UTI indicates urinary tract infection; LR, likelihood ratio.