Evidence-based Management of Fever in Infants and Young Children

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Objectives

• Understand an evidence-based approach for managing febrile infants and young children in the outpatient setting

• Review Children’s Healthcare of Atlanta fever guidelines
Fever in Infants and Young Children

• Very common childhood illness
• Vast majority are benign/self limited
• Some can be serious/life threatening (SBI)
  – Meningitis, bacteremia, UTI, pneumonia...
• Challenge is to distinguish the two
  – when to initiate antibiotics

Risk Stratification
Systematic approach to a febrile child

- **General Appearance:**
  - Well appearing patient

- **Past History:** previously healthy
  - Separate guidelines available for sickle cell, immuno-compromised, etc

- **Age**
  - 0-28 days
  - 29-60 days
  - 2-6 months
  - >6-24 months

- **Source of Fever**
Definition of fever

• Rectal temperature of >38 °C (100.4 °F)

• Highest *documented* temperature at home or in ED is the degree of fever

• Temp threshold for screening may be higher
  – Under 2 months: any fever requires attention
  – >2 months: screening cut-off is higher
1. Febrile neonate (0-28 days)

• High risk of serious bacterial infections (SBI)
  – reduced immunity
  – localize poorly
  – maternal pathogens (E coli, GBS), listeria, HSV

• Exhibit few early signs of infection

• General appearance alone can be deceptive

*Routine testing and routine treatment*

*Byington et al; Pantell et al, Pediatrics, July 2012*
Management: 0-28 days

• **Complete** sepsis evaluation for any fever (temp>38 °C)
  – CBC/diff and blood culture
  – UA and urine culture
  – LP (cell count, gram stain, gluc/prt, culture)

• Chest X-ray - if resp symptoms or signs
• Stool culture - if diarrhea

• HSV screening: based on risk factors
Management: 0-28 days

• Routine sepsis work-up (blood, urine, CSF)
• If risk factors for HSV: send HSV tests
• Anti-infectives:
  – Ampicillin 50-100 mg/kg IV
    AND
  • Cefotaxime 50 mg/kg IV
  – Acyclovir: 20 mg/kg/dose (if HSV screening done)
• Admit to hospital
Key Concepts: 0-28 days

- Temp threshold: Any fever (>38 °C)
- Routine testing (complete sepsis evaluation)
- Routine admission for empiric antibiotics
2. Febrile 29-60 day old

- Risk of SBI remains, but less
  - Lower risk of perinatal infections
  - Listeria much less likely
  - HSV much less likely
- No objective criteria to reliably identify infants at high risk
- Screening tests to identify infants at low risk *
- *Routine testing, selective treatment (if not at low risk)*

*1990s: Baker, Baskin, Jeskiewicz*
## Boston, Philadelphia, Rochester Criteria

<table>
<thead>
<tr>
<th></th>
<th>Boston</th>
<th>Philadelphia</th>
<th>Rochester</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>28-89 days</td>
<td>29-60 days</td>
<td>&lt;60 days</td>
</tr>
<tr>
<td><strong>Temp</strong></td>
<td>&gt;38</td>
<td>&gt;38.2</td>
<td>&gt;38</td>
</tr>
<tr>
<td><strong>History/Exam</strong></td>
<td>No immuniz/ abx/well appearing/no SSTI</td>
<td>Reassuring exam</td>
<td>Full term, no abx, well/ no focal infection</td>
</tr>
<tr>
<td><strong>WBC</strong></td>
<td>&lt;20,000</td>
<td>&lt;15,000</td>
<td>5-15 K (ABC&lt;1,500)</td>
</tr>
<tr>
<td><strong>UA</strong></td>
<td>&lt;10 WBC</td>
<td>&lt;10 WBC, GS-</td>
<td>&lt;10 WBC</td>
</tr>
<tr>
<td><strong>CSF</strong></td>
<td>&lt;10/HPF</td>
<td>&lt;8/HPF, GS-</td>
<td>-</td>
</tr>
<tr>
<td><strong>CXR</strong></td>
<td>Neg (if done)</td>
<td>Neg</td>
<td>-</td>
</tr>
<tr>
<td><strong>Antibiotics</strong></td>
<td>IM Ceftriaxone</td>
<td>No abx</td>
<td>No abx</td>
</tr>
</tbody>
</table>

*99% NPV for SBI*
Low Risk Criteria (29-60 days)*

- Well appearance
- Previously Healthy
- No focal bacterial infection
- Labs:
  - WBC: 5-15 K
  - ABC < 1,500
  - UA < 10 WBC/hpf, no nitrite
- CSF:
  - <10 WBC, neg gram stain
- Chest X-ray: no infiltrate

*CHOA fever guideline 29-60 days
Management (29-60 days)

• Partial sepsis evaluation (CBCD/bld cx and UA/UCx)
  – Consider LP

• If work-up negative and reliable follow-up - may d/c
  – Without antibiotics
  – With Ceftriaxone 50 mg/kg (LP must be done)

• If low risk criteria not met:
  – Perform LP if not already done
  – Admit for antibiotics (Cefotaxime 50 mg//kg)
What about a URI/OM/UTI?

• URI does not ‘rule in’ a viral etiology*
• Neither does it ‘rule out’ an SBI
  – Same management with or w/o URI
• What about OM?
  – With fever – same management
  – No fever – forego sepsis eval with caution
    • Mask SBI
    • Difficulty if fever occurs later
• What about UTI?
  – LP and admit for antibiotics**

**Paquette et al, PEC 2011
**Dore-Bergeron et al, Pediatrics, 2009

*Byington et al; Pediatrics 2004
What about bronchiolitis?

- Recognizable viral syndrome - lower risk of SBI
- <28 days: substantial risk of SBI
- > 28 days: SBI 1-7% with bronchiolitis VS 10-17% w/o
- UTI risk remains

- 0-28 days: full w/u, abx
- 29-60 days: Blood & urine screen (may hold LP if RSV+)
- If starting antibiotics – need to do LP

*Greenes, PIDJ 1999; Purcell, ADC 2002
Titus, Pediatrics 2003; Levine, Pediatrics 2004
Key Concepts: 29-60 days

- Temp threshold: Any fever (>38 °C)
- Routine testing, selective treatment
- Other viral source of infection - lower risk of SBI
- LP not mandatory
- Antibiotics not always necessary
- If starting antibiotics – perform LP
Common sources of fever

• Viral:
  – Non-specific viral illness eg URI, AGE, flu
  – Well defined viral illness eg bronchiolitis,
  – varicella, croup, stomatitis

• Bacterial:
  – Non-specific bacterial illness eg Otitis media
  – Well defined bacterial infection eg pneumonia, localized cellulitis, UTI
3. Febrile 2-6 month old

- Usually have benign source of fever
- At risk for occult bacteremia (Pneumococcus, HIB) and UTI
- Starting to develop immunity (innate and/or vaccinations)
- Exam more reliable but signs and symptoms not completely developed

**Selective testing & selective treatment**

*(based on source and height of fever)*
Management (2-6 mth age)

• Targeted history to determine exposures and symptoms that may suggest a source for the fever
• Thorough exam to determine findings suggesting an etiology for the fever

*Many children in this age group do not need testing (depending on source and temp)*
Management (2-6 mth age)

- CBC diff and blood culture
- UA, Urine Cx

*CHAOA Fever clinical practice guideline*
Key Concepts: 2-6 month old fever

- A source for the fever is important and helpful in limiting work-up
- Temp cut-off: >39 °C
- UTI is the most common SBI
- Selective testing, selective treatment
Should we worry about fever > 6 months of age?

- **Early 1990s** (H flu invasive organism, high risk of complications)
  - Conservative approach to febrile child
- **Late 1990s** (H flu gone, Pneumococcus main etiology of OB)
- **2000s**- Pneumococcal vaccine
  - PCV-7 in 2000, PCV-13 in 2010
  - Given at 2, 4, 6 months + booster
  - Highly immunogenic, 97% effective
Invasive Pneumo Disease <5 yr age after PVC 7

*Pilishvili et al, J Infect Dis, 2010
Pneumococcal 13 Vaccine*


**PIDJ, Mar 2013 Kaplan et al
4. Febrile >6-24 mth olds

• High immunization rates
  – Risk of bacteremia in FWLS: 0.25% *
• Pneumococcus usually self resolves
• Clinical exam is very helpful
  – Risk of bacterial meningitis: 3/10,000
• UTI is most common occult bacterial infection
• **Vast majority of children in this age group do not need blood testing**
  – “Benign neglect”……..”Watchful waiting”

  **Selective UTI screening**

*Wilkinson et al, Acad Emer Med, 2009*
Management of fever >6-24 mth old

In well-appearing, previously healthy, 6-24 month old with fever:

• Primary immunization status
  – If UTD - routine blood work not needed

• Source of fever
  – If source present - routine blood work not needed

• *Urine*

• If immuniz not UTD and no source of fever and temp>39 °C :
  – CBCD, bld cx
  – UTI screening (based on risk factors)
Fever >6-24 months*

- CBCD, blood cx
- UTI screening (based on risk factors)

*CHOA Fever clinical practice guideline
**UTI**

- Pyelonephritis: most common SBI in childhood
- UTI (<8 yr of age): 7-8% girls; 2% boys
  - Fever without source 2-24 mth: UTI prevalence 5%*
- Prevalence depends on:
  - Age: first year of life
  - Gender: F:M relative risk 2.27
  - Race: less in blacks
  - Circumcision: 3- to 4-fold decrease
  - Presence of other source**: reduces risk of UTI
  - Duration (>2 days), height of temp (>39)**

Diagnosis and Management of Initial UTI in febrile (>38 C) infants and children 2-24 mth

In a child with fever without source:

- Ill-appearing and abx planned: screen for UTI (UA and UC)
- Not ill appearing: assess probability of UTI
  - Low probability—f/u without testing
  - Not low probability—screen for UTI

*Selective urine testing based on probability of UTI*

*Pediatrics Sep 2011, Dec 2016*
Probability of UTI*

<table>
<thead>
<tr>
<th>Individual Risk Factors: Girls</th>
<th>Probability of UTI</th>
<th>No. of Factors Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>White race</td>
<td>≤1%</td>
<td>No more than 1</td>
</tr>
<tr>
<td>Age &lt; 12 mo</td>
<td>≤2%</td>
<td>No more than 2</td>
</tr>
<tr>
<td>Temperature ≥ 39°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever ≥ 2 d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence of another source of infection</td>
<td></td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Individual Risk Factors: Boys</th>
<th>Probability of UTI</th>
<th>No. of Factors Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonblack race</td>
<td>≤1%</td>
<td>a</td>
</tr>
<tr>
<td>Temperature ≥ 39°C</td>
<td>No more than 2</td>
<td></td>
</tr>
<tr>
<td>Fever &gt; 24 h</td>
<td>None</td>
<td>No more than 3</td>
</tr>
<tr>
<td>Absence of another source of infection</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a Probability of UTI exceeds 1% even with no risk factors.

*AAP UTI Clinical Practice Guideline, Pediatrics, 2011/2016
Who to Test for UTI*?

- Threshold to test should be < 3% probability of UTI
- <1% or <2%, depending on:
  - Contact during illness
  - Comfort with diagnostic uncertainty

*AAP UTI Clinical Practice Guideline, Pediatrics, 2011/2016
How to obtain sample?

• Option 1: catheter / suprapubic

• Option 2: bag specimen
  • if negative  monitor
  • if positive  catheter/suprapubic

UTI Treatment

• Route: Oral and parenteral equally efficacious*
• Most children can be treated orally, except:
  – Toxic
  – Unable to take orals
  – Noncompliance
• Choice of abx: based on local patterns
  – Cefprozil
• Duration: 7-14 days

*Hoberman Pediatrics 1999
Key Concepts: Fever >2 mth age

• Screening tests based on source of fever and height of temp
• After 6 months of age, if immunizations UTD – blood work usually not needed
• UTI screening based on probability of UTI (# of risk factors)
Summary

Initial management of fever in infant/young child:

• Appearance
• Past Medical history
• Age
• Immunization status
• Source of fever
• Current epidemiology
• Combination of clinical and lab criteria
• Balancing risk of disease and risk of testing/therapy
## Management of febrile infants/young children

<table>
<thead>
<tr>
<th>Age</th>
<th>Blood</th>
<th>Urine</th>
<th>CSF</th>
<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td>0-28 days</td>
<td>All</td>
<td>All</td>
<td>All</td>
<td>All</td>
</tr>
<tr>
<td>29-60 days</td>
<td>All</td>
<td>All</td>
<td>Many</td>
<td>Selective</td>
</tr>
<tr>
<td>2-6 months</td>
<td>Selective</td>
<td>Selective</td>
<td>Based on clinical indications</td>
<td>Based on clinical dx/results</td>
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<tr>
<td>&gt;6-24 mths</td>
<td>Few</td>
<td>Selective</td>
<td>Based on clinical indications</td>
<td>Based on clinical dx/results</td>
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<tr>
<td>&gt;2 years</td>
<td>Based on clinical indications</td>
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