Evidence-based Management of Fever in Infants and Young Children

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Sep 10, 2016
Objectives

• Discuss an evidence-based approach for managing febrile infants and young children (0-24 months) in the outpatient setting

• Review Children’s Healthcare of Atlanta fever guidelines
Why Guidelines?

• Keep up with changing evidence
  ▪ rapid changes in epidemiology
• Standardize practice – reduce variation
• Optimize testing and treatment (antibiotic stewardship/cost)

80-20 rule!
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 $\geq 38 \, ^\circ\text{C} \ (100.4 \, ^\circ\text{F})$

- 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
- 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 age

Complete sepsis evaluation for any fever \((\text{temp} \geq 38 \, ^\circ \text{C})\)

- 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
**Neonatal Herpes**

- Rare: 8-60 /100 000 live births*
- Febrile neonates: 0.3-0.5%**,***
  - bacterial meningitis rates (1.3-1.6%)****

- Risk Factors
  - Recent maternal h/o herpes
  - Vesicular rash
  - Ill-appearing neonate (including hypothermia)
  - CSF pleocytosis
  - Neonatal seizures

- No risk factors:
  - 0-14 days: transaminase (ALT) >50 is risk factor

*Corey et al, NEJM 2009
**Caviness et al, J Pediatr 2008
***McGuire et al, PEC, 2012
****Long et al, PIDJ 2011
Neonatal herpes work-up

• If HSV risk factors (clinical or ALT):
  – CSF HSV PCR
  – Blood HSV PCR
  – “Surface” cultures for HSV
    • Any suspicious skin lesions
    • Eyes, nose, rectum
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
  - Cefotaxime 50 mg/kg IV
  - Acyclovir: 20 mg/kg/dose (if HSV screening done)
- Admit to hospital

*Jain, S et al. Pediatrics, Feb 2014
Key Concepts: 0-28 days

- Temp cut-off: *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 (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 les
- CSF:
  - <10 WBC, neg gram stain
- Chest X-ray: no infiltrate
**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)
Case 1

• 6 week old felt warm to parents this morning
• Temp of 100.8 F at home
• Feeds and sleeps well
• Birth hx: NSVD, no complications
• No ill contacts
• Alert, active, good eye contact
• Rectal Temp 37.6 C, HR 150, RR 44
• Exam negative
Case 1
Evaluation

Labs?
• WBC 14.1, diff N 60%, bands 7%, L 28%
• UA normal

Does the child need an LP?
• May be omitted cautiously

Treatment?
• May discharge without antibiotics, OR
• D/c after Ceftriaxone 50 mg/kg (ensure LP done)

Disposition?
• May discharge home
• Primary care follow up in 24 hours
What about a cold/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**

*Byington et al; Pediatrics 2004
**Dore-Bergeron et al, Pediatrics, 2009
**Paquette et al, PEC 2011
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 cut-off: *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
Systematic approach to a febrile child

• General Appearance-well appearing
• PMH-previously healthy
• Age:
  • 0-28 days
  • 29-60 days
  • 2-6 mths
  • > 6-24 mths
• Source of fever
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 months)

If no source or non-specific source and temp ≥ 39°C
• CBC diff and blood culture
• UA, Urine Cx

*CHOA Fever clinical practice guideline
Management (2-6 mth age)

- If definite/well defined source: treat etiology
- If no/non-specific source and temp < 39 °C: no blood; *urine*
- If no source or non-specific source (eg GE, URI, flu) and temp ≥ 39°C*,
  - CBC diff and blood culture
  - UA, Urine Cx
  - If WBC ≥ 20K or ANC ≥ 10K∞ -> Ceftriaxone
  - LP, additional tests (CXR, stool studies): based on clinical assessment and test results

* Browne, 1996; Lee, 1998; Kupperman, 2000* cf under 2 mth age group.
### Assessment of UTI Risk*

**Individual Risk Factors: Girls**
- White race
- Age < 12 mo
- Temperature ≥ 39°C
- Fever ≥ 2 d
- Absence of another source of infection

<table>
<thead>
<tr>
<th>Probability of UTI</th>
<th>No. of Factors Present</th>
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<tbody>
<tr>
<td>≤ 1%</td>
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**Individual Risk Factors: Boys**
- Nonblack race
- Temperature ≥ 39°C
- Fever > 24 h
- Absence of another source of infection

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<td>Uncircumcised: a, Circumcised: No more than 2</td>
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<tr>
<td>≤ 2%</td>
<td>Uncircumcised: None, Circumcised: No more than 3</td>
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*AAP UTI Clinical Practice Guideline, Pediatrics, 2011

*Probability of UTI exceeds 1% even with no risk factors.*
4. Fever in >6-24 mth old

In well-appearing, previously healthy, 6-24 month old, management depends on:

• Immunization status
  – If immuniz UTD – routine blood work not needed

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

If immuniz not UTD and no source of fever and temp >39 C:
CBCD, blood cx, UTI screening as indicated
Changing approach to Fever
(>6-24 mth old)

- **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

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

• 13-valent Pneumococcal vaccine
• Licensed in Feb 2010
• PCV-7 covered ~80% of pneumo disease
• PCV 13 covers ~ 64% of remaining disease (including 19A)
• Kaplan, S et al (2013):
  – In 2011, invasive pneumo infections decreased
    • Overall: ↓ 42% compared to 2007-09
    • Age<24 mth: ↓ 53%
Invasive Pneumococcal infections*

In 8 children’s hospitals

*PIDJ, Mar 2013 Kaplan et al
Management (>6-24 mth age)

- Clinical exam is very helpful
- Risk of bacterial meningitis: 3/10,000
- Risk of bacteremia in FWLS: 0.25% *
- Pneumococcus usually self resolves
- 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*
**Fever >6-24 months**

If immunizations not UTD and no source of fever and temp > 39 C: CBC, blood cx, UTI screening as indicated

*CHOA Fever clinical practice guideline*
Management (>6-24 mth age)

- If immuniz not UTD and no source of fever and temp > 39°C:
  - CBCD, blood culture
  - Ceftriaxone if WBC ≥ 20K or ANC ≥ 10K

- Other testing and treatment as clinically indicated

- UTI screening
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

Challenges with UTI in young infants

- Difficult diagnosis (symptoms not well developed)
- Many febrile UTIs in young children associated with pyelonephritis (34-70%)
- Recurrent untreated UTIs contribute to permanent renal scarring (risk for HTN, renal failure)
- Obtaining good specimen is not easy
- Can coexist with non-specific viral infections *

*1998, Shaw, Pediatrics
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*
## Probability of UTI*

### Individual Risk Factors: Girls

- White race
- Age < 12 mo
- Temperature ≥ 39°C
- Fever ≥ 2 d
- Absence of another source of infection

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### Probability of UTI and No. of Factors Present

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### Probability of UTI and No. of Factors Present (Uncircumcised vs. Circumcised)

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

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

- No fixed threshold over which to test
- 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
How to obtain sample?

- Option 1: catheter / suprapubic

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

Management of a well-appearing, previously healthy febrile child in ED based on:

- Age
- Immunization status
- Source of fever
- Current epidemiology
- Combination of clinical and lab criteria
- Balancing risk of disease and risk of testing/therapy
  - UTI: Risk Tolerance (MD, parent)
# Management of febrile young infants

<table>
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<th>Blood</th>
<th>Urine</th>
<th>CSF</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>0-28 days</td>
<td>All</td>
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<tr>
<td>29-60 days</td>
<td>All</td>
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<td>Many</td>
<td>Selective</td>
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<td>Based on clinical indications</td>
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