

## MANAGEMENT OF FEVER IN INFANTS

### Introduction

“...since the advent of modern clinical thermometry by Wunderlich in 1871, the ritual of temperature taking has been surpassed only by Alexander Graham Bell’s invention in 1874 as the major curse of pediatrics” -- DS  
Smith from “Fever and the Pediatrician”

- Definition: rectal temperature greater than 37.9 degrees Celsius
  - Based on 2 standard deviations from 37.0 (normal infant body temperature)
  - Rectal temperature is the core body temp, and generally 1 degree higher than all other generally utilized sites
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- Incidence: serious bacterial infection (SBI) is found in 6-10% of all infants with fever
  - <1mo the incidence may be as high as 13%
  - <2mo, less than 1% with serious bacterial infection will have fever
- Etiology: UTI is the most common cause of SBI in a febrile infant
  - 1/3 of all bacterial disease in infants < 3mo
  - conjugated hyperbilirubinemia as sign
- Importance: younger infants often show no signs of clinical illness
  - Clinical scoring systems (see Yale AOIS) are unreliable in <2mo
  - Up to 2/3 of <2mo with serious bacterial illness (SBI) are assessed as well appearing by physicians

### Criteria for Admission

Multiple protocols have been established to determine the need for inpatient management. The Boston, Rochester and Philadelphia Criteria have all attempted to create screening criteria that were sensitive, specific and had high negative predictive values (NPV). Though they vary in protocol and recommendations, they all focused on stratifying febrile infants into high and low-risk categories. Low risk infants could be justifiably sent home with close follow-up. The key difficulty with all three criteria is that follow-up must be assured, which is difficult in a child in an urban ER who does not have a medical home.

Of Note:

- Rochester focused on a younger age group and did not use any Infant Observation Score
- Rochester did not routinely obtain CSF
- Boston was the only group to recommend empiric antibiotics, even as an outpatient.
- Even with antibiotics, Boston was determined to be more cost-effective since with a lower risk stratification, less children were admitted.

Recent data has demonstrated that Philadelphia and Boston criteria are not applicable to 0-1 month old infants and could result in 10% of neonates with SBI being categorized as low-risk. Therefore,

*ALL CHILDREN UNDER ONE MONTH MUST BE ADMITTED*

|   | Philadelphia Criteria  | Rochester Criteria  | Boston Criteria  |
|---|--|---|--|
| Age   | 29-60 d  | ≤60 d   | 28-89 d  |
| Temperature   | ≥38.2°C  | ≥38.0°C   | ≥38.0°C  |
| History   | Not specified  | <ul style="list-style-type: none"> <li>• Term infant</li> <li>• No perinatal antibiotics</li> <li>• No underlying disease</li> <li>• Not hospitalized longer than the mother</li> </ul>                                       | <ul style="list-style-type: none"> <li>• No immunizations within preceding 48 h</li> <li>• No antimicrobial within 48 h</li> <li>• Not dehydrated</li> </ul>   |
| Physical examination                                | <ul style="list-style-type: none"> <li>• Well-appearing</li> <li>• Unremarkable examination</li> </ul>   | <ul style="list-style-type: none"> <li>• Well-appearing</li> <li>• No ear, soft tissue, or bone infection</li> </ul>  | <ul style="list-style-type: none"> <li>• Well-appearing</li> <li>• No ear, soft tissue, or bone infection</li> </ul>   |
| Laboratory parameters (defines lower risk patients) | <ul style="list-style-type: none"> <li>• WBC &lt;15 000/mm<sup>3</sup></li> <li>• Band-neutrophil ratio &lt;0.2</li> <li>• UA &lt;10 WBC/hpf</li> <li>• Urine Gram stain negative</li> <li>• CSF &lt;8 WBC/mm<sup>3</sup></li> <li>• CSF Gram stain negative</li> <li>• Chest radiograph: no infiltrate<sup>a</sup></li> <li>• Stool: no blood, few or no WBCs on smear<sup>2</sup></li> </ul> | <ul style="list-style-type: none"> <li>• WBC &gt;5000 and &lt;15 000/mm<sup>3</sup></li> <li>• Absolute band count &lt;1500/mm<sup>3</sup></li> <li>• UA ≤10 WBC/hpf</li> <li>• ≤5 WBC/hpf stool smear<sup>2</sup></li> </ul> | <ul style="list-style-type: none"> <li>• CSF &lt;10/mm<sup>3</sup></li> <li>• UA &lt;10 WBC/hpf</li> <li>• Chest radiograph: no infiltrate<sup>a</sup></li> <li>• WBC &lt;20 000/mm<sup>3</sup></li> </ul> |
| Higher risk patients                                | Hospitalize + empiric antibiotics  | Hospitalize + empiric antibiotics   | Hospitalize + empiric antibiotics  |
| Lower risk patients                                 | <ul style="list-style-type: none"> <li>• Home</li> <li>• No antibiotics</li> <li>• Follow-up required</li> </ul>   | <ul style="list-style-type: none"> <li>• Home</li> <li>• No antibiotics</li> <li>• Follow-up required</li> </ul>  | <ul style="list-style-type: none"> <li>• Home</li> <li>• Empiric antibiotics</li> <li>• Follow-up required</li> </ul>  |
| Reported statistics                                 | Sensitivity 98% (92-100%)<br>Specificity 42% (38-46%)<br>Positive predictive value 14% (11-17%)<br>NPV 99.7% (98-100%)   | Sensitivity 92% (83-97%)<br>Specificity 50% (47-53%)<br>Positive predictive value 12.3% (10-16%)<br>NPV 98.9% (97-100%)   | Sensitivity—not available<br>Specificity 94.6%<br>Positive predictive value—<br>not available<br>NPV—not available   |

<sup>a</sup> If obtained.

### Interpreting Labs

Upon admission, by the above criteria, all patients will have CBC, Blood culture, UA, Urine culture, CSF counts, chemistries and cultures.

- Chest x-rays
  - Not required in most protocols unless presence of respiratory symptoms
  - In data from the Philadelphia study, 5/36 patients with positive chest x-rays did not have respiratory symptoms. However, they were not necessarily bacterial in origin.
- HSV PCR
  - Controversial: routine in some hospitals, not in others
  - Not recommended routinely in the well-appearing febrile infant

- Consider when symptoms of HSV present (see antibiotic discussion below)
- Lumbar Puncture
  - Bloody taps (traumatic vs. pathologic) will obscure picture (15-20% occurrence)
  - WBCs in traumatic taps can represent blood contaminant instead of infection
  - Bloody tap that does not clear in subsequent tubes is highly suggestive of HSV
  - Traumatic taps: controversial data on “correcting”. Ratios include
    - WBC:RBC ratio
    - Observed to Predicted Ratio (O:P)
  - Ratios are intended for discharge from the ER
- Urine culture
  - Suprapubic tap: any growth indicates a UTI
  - Catheterized: >10,000 organisms
  - Clean Catch: >100,000 organisms of one bacteria
- Culture Growth
  - Data in children 28-90 days and older
  - In one study, 100% of CSF positive at 24h, 93% of blood at 28h, 100% urine at 30h

## Antibiotics

Empiric antibiotic coverage is best determined by the age of the patient.

- Birth to 28d: Ampicillin *plus* Gentamicin or 3<sup>rd</sup> generation Cephalosporin  
(*plus or minus Acyclovir*)
- Covering for Listeria (Ampicillin), E. coli, GBS, other gram negatives
  - Ceftriaxone is not recommended before 2-4 weeks due to the incidence of biliary sludging
  - Gentamicin use necessitates following levels secondary to nephro-/ototoxicity
  - Acyclovir: currently not recommended as standard empiric therapy
    - Indicated with elevated suspicion for HSV (i.e. presents with seizures, abnormal EEG, cutaneous lesions, acutely ill)
    - Also indicated if patient not responsive to standard Abx at 48-72h

- 29-90 days: 3<sup>rd</sup> Generation Cephalosporin
- Congenital HSV no longer in differential
  - Listeria can present late (up to 3months), but would only add Ampicillin if patient presented with CSF pleocytosis
  - Otherwise covering for S. pneumo, E. coli

Viral source: There is varying literature on the work-up of fever in an infant with documented viral infection.

- Retrospective study in 0-56do: 2/174 RSV (+) had SBI (2 UTI)
- Prospective study in 0-60do: 17/244 RSV (+) had SBI (14UTI, 3 bacteremic)
- Prospective study in 0-90do: Rochester risk stratified high risk vs. low risk
  - LR/+: 3/167 with SBI

- LR/-: 9/289 with SBI
- HR/+: 18/323 with SBI (15 UTI, 3 bacteremic)
- HR/-: 100/599 with SBI (61 UTI, 18 bacteremic, 6 meningitis)

Adverse Effects:

- Ceftriaxone increases the risk of biliary sludging/pseudolithiasis
- Cases tend to spontaneously resolve after cessation of the drug

**Miscellaneous**

- Defervescence
  - There is no correlation between defervescence with antipyretics and incidence of SBI
- Antipyretics
  - Alternation of Tylenol and Motrin has not been proven to provide faster defervescence or has greater efficacy
  - Parental confusion and subsequent overdose can lead to toxicity
- Temperature taking
  - Counsel family to appropriate temperature taking technique
  - Provide guidelines for concerning temperatures

**References**

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