WELL-APPEARING INFANTS WITH FEVER

Division of Pediatric Emergency Medicine
NY-Presbyterian Morgan Stanley Children’s Hospital
Columbia University Medical Center

Supported by a grant from the R-Baby Foundation
I. Definition of Terms:

1. Sepsis: Fever or other evidence of infection in a toxic-appearing infant or child.

2. Bacteremia: Presence of bacteria in the bloodstream of a well-appearing infant or child.

3. Complications of Bacteremia:
   “Serious Bacterial Infections” (SBI):
   - Fulminant septicemia
   - DIC
   - Shock and multiple organ failure
   - Meningitis
   - Bacterial gastroenteritis
   - Serious focal infections
   - Death

CLINICAL CONCERN:
IDENTIFYING THOSE WELL-APPEARING INFANTS WITH FEVER WHO MAY BE BACTEREMIC AND PROGRESS TO DEVELOP A LIFE-THREATENING-serious bacterial infection (SBI)

4. “Partial Sepsis Workup”:
   (Infants ≥ 61 days old)
   1. CBC and differential
   2. Blood culture
      Only if indicated:
      - CXR
      - Stool culture
      - Urinalysis and urine culture

5. “Full Sepsis Workup”:
   (Infants ≤ 60 days old)
   1. CBC and differential
   2. Blood culture
   3. Straight-cath urine for urinalysis and culture
   4. Lumbar puncture
      Only if indicated:
      - CXR
      - Stool gram stain & culture

A full sepsis workup is essentially a Partial Sepsis workup (always including urine) plus an L.P.
II. **Normal Vital Signs in Infants**

<table>
<thead>
<tr>
<th>AGE</th>
<th>RR</th>
<th>HR</th>
<th>SYSTOLIC BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full-term newborn</td>
<td>40-60</td>
<td>60</td>
<td>60 (FT newborn)</td>
</tr>
<tr>
<td>(≤ 1 month)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-5 months</td>
<td>30-50</td>
<td>100-170</td>
<td></td>
</tr>
<tr>
<td>6-12 months</td>
<td>20-40</td>
<td>70</td>
<td>70 (12 months)</td>
</tr>
</tbody>
</table>

**NOTE:** Respiratory rates should always be counted for 30 seconds, because infants have irregular periodic breathing (due to immature respiratory centers). Counting for < 30 seconds will produce falsely high, normal, or low results.

III. **Heights of Fever You Should Know:**

- **100.4°**
  - Triggers workup in infant ≤ 90 days old.

- **102.2°**
  - Lowest fever ever shown to be associated with risk of bacteremia or SBI in well appearing infants ≥ 3 months old.
  - Triggers workup only if unreliable follow-up, or incompletely immunized, or < 6 months old, or prolonged for several days.

- **105.0°**
  - Higher fever than usually seen with most viral illnesses.
  - Triggers workup even in well appearing infants who are fully immunized and have good follow-up.

Children with history of documented fever who are afebrile in the emergency department should be considered to be febrile to the degree reported by history.

Temperature in the ED should be measured using a [rectal thermometer](https://en.wikipedia.org/wiki/Rectal_temperature), because axillary, oral and tympanic thermometers are unreliable in infants and young children.
IV. Evidence-Based Rationale for Risk Stratification of Infants According to Age and Height of Fever:

<table>
<thead>
<tr>
<th>Evidence-Based Rationale</th>
<th>Risk Stratification Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger infants (≤ 90 days old) have less well-developed immune systems and are more immunocompromised than older infants.</td>
<td>Lower fever (≥ 100.4) triggers workups in younger infants (≤ 90 days old). Changes consistent with illness (decreased suck/feeding or irritability/somnolence) triggers a workup in younger infants, even in absence of fever.</td>
</tr>
<tr>
<td>Higher risk of bacteremia at higher fevers.</td>
<td>Higher levels of fever trigger workups even in older more immunocompetent infants.</td>
</tr>
<tr>
<td>Very young infants (≤ 60 days old) do not clinically demonstrate signs of meningitis.</td>
<td>Lumbar puncture always performed as part of fever evaluation in infants ≤ 60 days old with or without any clinical signs of meningitis.</td>
</tr>
</tbody>
</table>

V. Risk Stratification of Infants According to Age and Height of Fever:

When evaluating a well-appearing infant with fever, the first step is to note patient’s age (calculate age in days, if infant ≤ 90 days old) and height of fever, and see which of the following risk groups the patient falls into:

<table>
<thead>
<tr>
<th>GROUP</th>
<th>AGE</th>
<th>HEIGHT OF FEVER TO TRIGGER WORKUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.</td>
<td>0-28 DAYS</td>
<td></td>
</tr>
<tr>
<td>II.</td>
<td>29-60 DAYS</td>
<td>100.4°</td>
</tr>
<tr>
<td>III.</td>
<td>61-90 DAYS</td>
<td></td>
</tr>
<tr>
<td>IV.</td>
<td>≥91 DAYS</td>
<td>UNIMMUNIZED OR &lt; 6 MO: 102.2°</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IMMUNIZED &amp; ≥6 MO: 105°.</td>
</tr>
</tbody>
</table>
VI. Overview of Management

An Overview of the Evaluation and Treatment of Well-appearing Febrile Infants

<table>
<thead>
<tr>
<th>Group</th>
<th>Age Cutoff</th>
<th>Fever Cutoff</th>
<th>Evaluation</th>
<th>Results</th>
<th>Treatment</th>
<th>Disposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0-28 Days</td>
<td>≥ 100.4°</td>
<td>Full Sepsis workup (Blood, urine &amp; LP)</td>
<td>All Patients</td>
<td>IV Antibiotics</td>
<td>Admit</td>
</tr>
<tr>
<td>II</td>
<td>29-60 Days</td>
<td>≥ 100.4°</td>
<td>Full Sepsis workup (Blood, urine &amp; LP)</td>
<td>Low risk criteria met*</td>
<td>IM or IV Antibiotics</td>
<td>Discharge</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Low risk criteria NOT met*</td>
<td>IV Antibiotics</td>
<td>Admit</td>
</tr>
<tr>
<td>III</td>
<td>61-90 Days</td>
<td>≥ 100.4°</td>
<td>Partial Sepsis Workup (blood &amp; urine only)</td>
<td>UTI Cellulitis Pneumonia (focal infiltrate)</td>
<td>IV Antibiotics</td>
<td>Admit</td>
</tr>
<tr>
<td>IV</td>
<td>3-6 Months</td>
<td>≥ 102.2°</td>
<td>Partial Sepsis Workup (blood &amp; urine only)</td>
<td>ALL PATIENTS</td>
<td>Antibiotics IF: WBC ≥ 15K (IM or IV) or positive urine (PO)</td>
<td>Discharge</td>
</tr>
<tr>
<td></td>
<td>Or ≥ 6 Months AND not immunized OR No reliable follow up</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 100.4° lasting ≥ 4 Days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>≥ 6 Months</td>
<td>≥ 105° or Fever ≥ 4 days with Tmax ≥ 102.2°</td>
<td>Partial Sepsis Workup (blood always, &amp; test urine if at high risk for UTI**)</td>
<td>ALL PATIENTS</td>
<td>Antibiotics IF: WBC ≥ 15K (IM or IV) or positive urine (PO)</td>
<td>Discharge</td>
</tr>
<tr>
<td></td>
<td>And immunized AND reliable follow up</td>
<td>ANY fever (≥ 100.4°) lasting ≥ 4 Days</td>
<td>Test Urine Only if at high risk for UTI: **</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SUMMARY**

1. Well-appearing febrile patients are stratified by age into 5 groups, corresponding to their risk of bacteremia and SBI.
2. Fever cutoff (to initiate a workup is 100.4° in groups I, II, III.
3. All babies 0-28 days old (Group I) get a full sepsis workup and get admitted.
4. All babies 29-60 days old (group II) get a full sepsis workup and get admitted, unless they meet ALL low risk criteria for discharge*.
5. All well-appearing patients ≥ 60 days old (Groups III, IV, and V) are discharged to outpatient management. (If no UTI, cellulites, or lobar pneumonia).
6. Febrile infants ≥ 91 days old (Group IV and V) represent the largest group of febrile children seen in the ED, with the most variation in diagnostic and management options.

*see below box on Low Risk Criteria
VII. Workups:

<table>
<thead>
<tr>
<th>FULL SEPSIS WORKUP FOR ALL 0-60 DAY OLDS:</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC and differential</td>
</tr>
<tr>
<td>Blood culture</td>
</tr>
<tr>
<td>Catheterized urine: Dipstick &amp; microscopic urinalysis, Gram stain and culture</td>
</tr>
<tr>
<td>Lumbar puncture: Cell count &amp; differential</td>
</tr>
<tr>
<td>Protein/glucose</td>
</tr>
<tr>
<td>Gram stain and culture</td>
</tr>
<tr>
<td>Stool gram stain and culture if clinically indicated</td>
</tr>
<tr>
<td>Chest X-ray</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PARTIAL SEPSIS WORKUP FOR OLDER INFANTS (≥ 61 DAYS OLD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC and Differential</td>
</tr>
<tr>
<td>Blood culture</td>
</tr>
<tr>
<td>Urinalysis and urine culture:</td>
</tr>
<tr>
<td>Girls &lt; 2 yo</td>
</tr>
<tr>
<td>Boys:</td>
</tr>
<tr>
<td>Circumcised &lt; 6 mo</td>
</tr>
<tr>
<td>Uncircumcised &lt; 1 y.o.</td>
</tr>
<tr>
<td>CXR only if indicated</td>
</tr>
<tr>
<td>Stool gram stain and culture only if indicated</td>
</tr>
</tbody>
</table>
VIII. GROUP #I: 0-28 DAYS OLD:

Why have these babies (0-28 days) been singled out as a group?

<table>
<thead>
<tr>
<th>REASONS WHY BABIES 0-28 DAYS OLD ARE HIGHEST-RISK GROUP FOR LIFE-THREATENING BACTERIAL DISEASE AND ALWAYS GET ADMITTED</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High prevalence of bacteremia and (SBI):</strong> 5% -17 %</td>
</tr>
<tr>
<td><strong>Pathogens not community-acquired, so prevalence not reduced in immunized populations</strong></td>
</tr>
<tr>
<td><strong>Immune system immature:</strong></td>
</tr>
<tr>
<td>More susceptible to invasive disease</td>
</tr>
<tr>
<td>Unable to localize infections well</td>
</tr>
<tr>
<td>Do not demonstrate symptoms early in illness observation</td>
</tr>
<tr>
<td>Appearance and exam unreliable</td>
</tr>
<tr>
<td><strong>Screening tests/labs not sensitive</strong></td>
</tr>
<tr>
<td>3-10% of bacterial disease miss by currently available screening criteria.</td>
</tr>
</tbody>
</table>

*THEREFORE, ANY FEVER (≥100.4°) IN THIS AGE GROUP MANDATES A FULL SEPSIS WORKUP FOLLOWED BY ADMISSION FOR IV ANTIBIOTICS: **

**IV Cefotaxime (50mg/kg) q6H + Ampicillin (50mg/kg) q6H.**

**Add IV Acyclovir if any of the following:**

- Ill-Appearance
- Maternal h/o HSV
- Presence of vesicular or pustular lesion(s)
- Associated seizure
IX. GROUP #2: 29-60 DAYS OLD

Low-Risk Criteria for Discharge from ED:

<table>
<thead>
<tr>
<th>LOW RISK CRITERIA FOR DISCHARGE OF INFANTS 29-60 DAYS OLD:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HISTORY:</strong></td>
</tr>
<tr>
<td>Previously healthy, full-term</td>
</tr>
<tr>
<td>Normal behavior and feeding</td>
</tr>
<tr>
<td>Reliable caretaker with phone access</td>
</tr>
<tr>
<td>Caretaker able to return to ED if recalled for positive culture</td>
</tr>
<tr>
<td><strong>EXAM:</strong></td>
</tr>
<tr>
<td>Well-appearing</td>
</tr>
<tr>
<td>Normal vital signs and exam</td>
</tr>
<tr>
<td><strong>LABS:</strong></td>
</tr>
<tr>
<td>Blood: WBC $\geq$ 5,000 and $&lt; 15,000$ and band to neutrophil ratio $&lt; .2$</td>
</tr>
<tr>
<td>Urine: Negative gram stain, negative dipstick urinalysis, and micro $&lt; 10$ WBC/HPF</td>
</tr>
<tr>
<td>CSF: $&lt; 8$ WBC/HPF, negative gram stain, and normal protein &amp; glucose</td>
</tr>
<tr>
<td>Stool: $&lt; 5$ WBC/HPF on gram stain (obtain only if diarrhea)</td>
</tr>
<tr>
<td>CXR: Normal (obtain only if respiratory symptoms)</td>
</tr>
</tbody>
</table>

- Any infant 29-60 days old who does not meet all of these low-risk criteria must be admitted for IV antibiotics and observation.
- For discharged patients, antibiotic coverage (ceftriaxone 50mg/kg IM) is optional.
- Discharged patients must be re-examined every 24 hours by PMD or ED physician for next 48 hours until cultures negative and then followed closely until fever resolves.
- Caretaker must be deemed reliable by examining physician, accessible by phone (in case cultures become positive and patient needs to be recalled for admission), and instructed to return immediately if any decreased feeding or change in baby’s appearance or behavior.
- If blood, urine, or CSF culture becomes positive (or change in feeding, appearance, or behavior) admit for IV antibiotics.
X. GROUP #3: 61-90 DAYS OLD:

61-90 DAYS

BABY IN TRANSITION FROM YOUNGER TO OLDER INFANT

FEVER CUTOFF 100.4º (LIKE YOUNGER INFANTS)

NO LP UNLESS CLINICALLY INDICATED (LIKE OLDER INFANTS)
XI. GROUP #4 and Group #5: OTHERWISE HEALTHY AND WELL-APPEARING INFANTS ≥3 MONTHS OLD (≥91 DAYS OLD):

1. What distinguishes these infants as distinct groups?
   These infants represent the largest group of febrile babies seen in the ED, with the most variation in diagnostic and management options. The purpose of this section is to demystify their evaluation and management.

2. A clarification about the following discussion:
   There are always 4 types of fever that can occur in otherwise well-appearing infants:
   1. A typical viral-like picture:
      Fever that is not too high (<105°) and not too long duration (<5 days) in an otherwise healthy infant (no significant PMH).
   2. Prolonged fever (≥5 days)
   3. Very high fever (≥105°)
      (Sickle cell, cancer, HIV, DM, indwelling central lines, etc.)

Therefore, you will always need to classify your patient with fever into one of these four categories, because the approach to each type of fever is different. However, the following discussion applies only to the first type of fever:
   The otherwise healthy infant (no co-morbidity) who appears well, with a typical fever (<105° and <5 days duration). This type of fever comprises the majority of ED visits by infants for fever.

3. What are the main issues to focus on when evaluating an infant with fever?

   4 major issues must be addressed in ALL patients with fever:
   1. Hydration status
   2. Is the patient septic?
   3. Is the patient bacteremic?
   4. Does the patient have a focal bacterial infection* that requires antibiotics?

   * Focal Bacterial Infections:
     Meningitis
     Otitis media
     Strep, pharyngitis
     Pneumonia
     UTI
     Petechiae > always fully undress patient
     Cellulitis > and examine skin
Therefore, your history and physical should always focus on these 4 issues. We will now discuss each of these 4 issues individually:

1. HYDRATION STATUS

HISTORY: 1) Quantify change, if any, in po intake:

   Is baby breast-feeder or bottle-feeder?

   If bottle-feeder: How many oz does baby normally (pre-illness) feed? How often?

   During present illness, how many oz per feed and how often is baby feeding?

   If Breast-feeder: Normally (pre-illness), how many minutes is baby feeding on each breast? How often?

   During present illness, how many minutes on each breast and how often?

2) Is the baby still sucking vigorously during feeds? Does the baby get SOB during feeds (have to stop feeding in middle of feed due to trouble breathing)? These can be early signs of more significant illness in a baby who otherwise appears well.

3) Is there any vomiting or diarrhea?
   If yes, quantify color (? bloody or bilious), number of episodes per day, and volume. This information will help you decide if patient is a candidate for p.o. hydration (i.e. decreasing frequency/volumes of vomiting/diarrhea), or needs IV hydration (large volumes, not holding po liquids, or increasing frequency of vomiting and/or diarrhea).

4) Quantify frequency of urine output (#of wet diapers per day) compared to normal.

5) Ask about any change in activity or playfulness (for babies < 90 days old, ask if baby is waking up for feeds and sucking well, and level of alertness and consolability).

Earliest signs of significant dehydration:
   1. Decreased urine output (less wet diapers/day)
   2. Decreased activity

A less vigorous suck, decreased feeding, or SOB while feeding can be early signs of more significant illness in an otherwise well-appearing infant.
2. ? SEPSIS

If vitals are stable (normal for age) and infant well-appearing, patient not septic.

Consider sepsis if:

- Ill-appearing
- Unstable vitals
- Persistent or marked tachycardia
- Wide pulse-pressure
- Mottled skin or delayed capillary refill

Even if patient appears otherwise well

* Differential diagnosis of tachycardia out-of-proportion to degree of fever:

- Hypoxemia – (check pulse ox)
- Dehydration – (give IV fluids and reassess)
- Sepsis - (if remains very tachycardic, even after antipyretics and IV fluids)
- Myocarditis – (if new heart murmur or EKG changes or cardiomegaly on CXR)
3. BACTEREMIA

Definition: Presence of bacteria in the blood of a well-appearing child.

Risk: 1) Unimmunized infant, < 6 months old, with rectal temperature ≥ 102.2°C.
2) Immunized infant, ≥ 6 months old, with rectal temperature of 105°F.

Rationale: ≥97% of bacteremia in children ≥ 3 months old caused by pneumococcus or H. flu. The H. flu (HIB) and pneumococcus (prevnar) vaccines are given at 2, 4, and 6 months of age. Risk of bacteremia in a “fully immunized” infants (s/p 3 vaccines) is about 0.68% (very low). Therefore, infants ≥ 6 mo old who are well appearing do not require a bacteremia workup.

Strategy: If infant is 3-6 months old (not completely immunized, since 3rd vaccine not given until 6 months old), get CBC and blood culture (and urine). If WBC < 15,000 low risk of bacteremia: no antibiotics, 48 hour follow-up. (make sure patient has access to follow-up).

If infant/child ≥ 6 months old, appears well, has at least 2 immunizations, and reliable follow up, no workup is needed (meaning no CBC & blood culture) unless baby has one of the indications listed in the table below:

<table>
<thead>
<tr>
<th>IMMUNIZED (HIB VACCINE, PREVNAR) PATIENTS ≥6 MONTHS OLD FOR WHOM BACTEREMIA WORKUP AND ANTIBIOTIC TREATMENT SHOULD BE CONSIDERED:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ill-appearance</td>
</tr>
<tr>
<td>2. Very high fever (≥105°F) OR prolonged fever (≥ 4 days, if T max ≥ 102.2)</td>
</tr>
<tr>
<td>3. Unreliable follow-up</td>
</tr>
<tr>
<td>4. Patients with co-morbidities:</td>
</tr>
<tr>
<td>Hemoglobinopathies</td>
</tr>
<tr>
<td>Congenital heart disease</td>
</tr>
<tr>
<td>Immunocompromised or debilitated: HIV</td>
</tr>
<tr>
<td>DM</td>
</tr>
<tr>
<td>CNS Disease</td>
</tr>
<tr>
<td>5. Incompletely immunized (&lt; 2 immunizations)</td>
</tr>
</tbody>
</table>
4. FOCAL BACTERIAL INFECTIONS (≥3 MONTHS OLD):

MENINGITIS –  
Consider LP if:  
- Lethargic  
- Irritable or difficult to console  
- Bulging fontanelle

OTITIS MEDIA –  
Dx by exam

STREP PHARYNGITIS –  
no testing needed if < 3 y.o.  
(since no significant risk of rheumatic fever in < 3 y.o, no need for strep testing before this age)

PNEUMONIA -  
consider CXR if:  
- Tachypnea (after defervescence)  
- Localized lung findings on auscultation  
- Retractions  
- Hypoxemia (pulse ox)  
- Significant cough  
- WBC ≥ 20,000

UTI -  
Consider straight-cath urinalysis and culture if fever ≥ 105°F for:  
- Circumcised boy < 6 mo  
- Uncircumcised boy < 1 y.o  
- Girl < 2 y.o  
- or h/o UTI in past

CELLULITIS -  
Consider admission if cellulitis is source of fever

PETECHIAE -  
Always undress and examine entire infant for presence of petechiae with fever. If any petechiae, draw blood culture, CBC with differential (to r/o both ITP and neutropenia), and give ceftriaxone (50mg/kg) IV or IM.

- If no progression of petechial rash while observed in ED, may be discharged to 24 – hour follow-up.

- If many petechiae present or petechial rash increases while observed in ED, admit for IV antibiotic and observation to r/o meningococcemia.


