Fever in Infants
29-60 Days of Age:
Emergency Department Management
Clinical Practice Guideline (CPG)

Clinical Practice Guideline
Protocol Approved by: Division of Pediatric Emergency Medicine, Division of General Academic Pediatrics and Infectious Diseases
Date of Approval: 2/17
Fever in Infants (age 29 to 60 days)

**INCLUSION CRITERIA**
- Infant 29-60 days of age
- Temp ≥38°C (100.4°F) by any route/parental report

**EXCLUSION CRITERIA**
- Identified focus of infection
- Bronchiolitis (with or without RSV)

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**Febrile Infant 29 to 60 days of age**

- **Ill appearing?**
  - Yes
  - No

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**Herpes Simplex Virus (HSV) Checklist**

**Part I**
- ☐ Vesicles on skin/scalp/oral mucosa
- ☐ Known maternal primary HSV outbreak at time of delivery

**Part II**
- ☐ History of seizures
- ☐ CSF pleocytosis (CSF WBC ≥9/HPF)

- **If any “Yes” proceed to HSV High Risk recommendations**

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**Perform lumbar puncture (LP)**
(See “Initial evaluation of high risk bacterial infection”)

- Administer antibiotics

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**Complete HSV Part II Checklist**
(See “Initial evaluation of Herpes Simplex Virus high risk”)

- Administer Acyclovir

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**Obtain:**
- UA and urine culture
- CBC with diff
- Blood culture
  (See “Initial evaluation for serious bacterial infection”)

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**Complete Bacterial Infection AND HSV Part I Checklist**

- **High risk?**
  - Low or High risk?
  - **Low Risk**

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**UTI present?**
(UA positive for nitrites, leukocyte esterase or WBC >5/HPF)

- **Proceed to UTI recommendations**
- **Yes**
  - Administer Ceftriaxone
  - Clinical decision to administer antibiotics?
    - **Yes**
    - Clinical decision to perform LP?
      - Yes
      - CSF
        - Abnormal
        - Normal
          (See “Initial evaluation of high risk bacterial infection”)
          - Can be discharged?
            - Yes
              - Discharge Home
            - No
              - Administer antibiotics
    - No
      - Consult Infectious Disease if LP gram+
      - Admit

- **No**
  - Admit
  - Consult Infectious Disease if LP gram+

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**Discharge Disposition Checklist**

- Parents are comfortable with monitoring the infant at home
- Parents have reliable means of communication from the hospital/ED
- Bacterial culture results can be followed daily by the hospital/ED
- The patient can follow-up with their PCP in 24 hrs (Consult PCP)

If any “No” proceed to admit
Use the Yale Observation Scale to assess whether the patient is ill or well appearing. A score greater than 10 will be considered ill appearing; a score of 10 or less will be considered well appearing.

Prolonged newborn nursery stay is defined as a hospital stay after birth longer that 48 hours for vaginal delivery or longer than 72 hours for cesarean delivery.

The category of High Risk should be awarded to infants with a “yes” response in either the Bacterial Infection Checklist OR Herpes Simplex Virus Part I Checklist.

Fever in Infant Definition
Fever is one of the most common reasons for emergency department (ED) evaluation of young infants. Because of an immature immune system, vaccine naïvety, and exposure to unique pathogens in the perinatal period, the febrile young infant is at high risk for serious bacterial infection (SBI), such as urinary tract infection (UTI), bacteremia, and bacterial meningitis. Signs of a serious bacterial infection include cyanosis, poor peripheral circulation, petechial rash, and inconsolability.

Up to 10% of infants 29 to 60 days of age who present with fever without an evident source of infection may have a bacterial infection. The prevalence of SBI among this age group is 10% for UTI, 2% for bacteremia and 1% for meningitis. Infants who present low risk factors have <5% risk for any bacterial infection and <0.5% for bacterial meningitis. For infants who are at low risk of Herpes Simplex Virus (HSV) infection, the estimated risk of HSV disease is <0.3%.

Fever in Infant 29-60 days Clinical Practice Guideline Application
This guideline was developed for the evaluation and management of infants from 29 to 60 days of age who present with fever on exam or by history and without focus of infection. This guideline can also be applied to premature infants who were born at less than 37 weeks gestation, infants with prior history of hospitalization, prolonged newborn nursery course, or co-morbid conditions predisposing to severe or recurrent bacterial illness, including genetic, congenital, neuromuscular or neurodevelopmental abnormalities. This guideline does not apply to infants with a known focus of infection, clinical diagnosis of bronchiolitis with or without respiratory syncytial virus (RSV) infection, or age ≤28 days or ≥61 days old.

Alternative Clinical Practice Guideline Considerations
Febrile Neonate/ Fever in Infants ≤28 Days of Age Clinical Practice Guideline: Infants who are ≤28 days who present with fever by exam or history without an associated focus of infection.
Bronchiolitis/ Wheezing in children <24 Months of Age Clinical Practice Guideline: Patients with signs and symptoms of viral lower respiratory tract infection, associated with rhinitis, cough, tachypnea, wheezing, rales, use of accessory muscles and/or nasal flaring; consistent with a clinical diagnosis of bronchiolitis.
Yale Observation Scale
An observational scale consisting of 6 observational items originally characterized and clubbed by McCarthy et al. (Pediatrics 1982), and validated in young febrile children to detect a serious illness. An infant with a score greater than 10 is considered ill appearing; while a score of 10 or less is considered well appearing.

<table>
<thead>
<tr>
<th>Observation item</th>
<th>Normal (Score=1)</th>
<th>Moderate Impairment (Score=3)</th>
<th>Severe Impairment (Score=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Quality of cry</td>
<td>Strong with normal tone OR Content and not crying</td>
<td>Whimpering OR Sobbing</td>
<td>Weak OR Moaning OR High pitched</td>
</tr>
<tr>
<td>2. Reaction to parent stimulation</td>
<td>Cries briefly then stops OR Content and not crying</td>
<td>Cries off and on</td>
<td>Continually cry OR Hardly responds</td>
</tr>
<tr>
<td>3. State variation</td>
<td>If awake-&gt; stays awake OR If asleep and stimulated -&gt; wakes up quickly</td>
<td>Eyes close briefly awakes up with prolonged stimulation</td>
<td>Awake OR Falls to sleep OR Does not wake up</td>
</tr>
<tr>
<td>4. Color</td>
<td>Pink</td>
<td>Pale extremities OR Acrocyanosis</td>
<td>Pale OR Cyanotic OR Mottled OR Ashen</td>
</tr>
<tr>
<td>5. Hydration</td>
<td>Skin normal, eyes normal AND Mucous membranes moist</td>
<td>Skin, eyes-normal AND Mouth slightly dry</td>
<td>Skin doughy/tented AND Dry mucous membranes AND/OR Sunken eyes</td>
</tr>
<tr>
<td>6. Response (talk, smile) to social overtures</td>
<td>Alerts</td>
<td>Alerts briefly</td>
<td>No alerting</td>
</tr>
</tbody>
</table>

The observation item for response to social overtures (#6) was modified to present only the characteristics corresponding to infants less than 2 months of age.

Initial evaluation of the febrile infant

<table>
<thead>
<tr>
<th>Serious bacterial Infection recommendations</th>
<th>UTI and bacteremia</th>
<th>a. CBC with differential, b. Blood culture, c. Urine analysis with microscopy, d. Urine culture (catheter/suprapubic specimen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>Order chest radiography only if any of the following are met: a. Presence of respiratory symptoms (nasal congestion with cough), OR b. Fever &gt;102.2°F (39°C), OR c. WBC ≥20,000 x 10⁹/L</td>
<td></td>
</tr>
<tr>
<td>High Risk Bacterial Infection Recommendations</td>
<td>Meningitis</td>
<td>Only for ill appearing infants (Yale score &gt;10), infants at high risk of bacterial infection (See Bacterial Infection Checklist) and infants with a clinical decision to perform a lumbar puncture prior to antibiotic administration: a. Lumbar puncture (Cerebrospinal fluid (CSF) studies) i. Bacterial culture ii. Gram Stain (GS) iii. Cell count and differential iv. Protein v. Glucose</td>
</tr>
</tbody>
</table>

(See Bacterial Infection Checklist)
Urinary Tract Infection (UTI) recommendations
The management of UTI in febrile infants 29-60 days is determined by the evaluating physician’s clinical criteria. Infants who are at low risk of SBI, and who have been diagnosed with UTI, have <0.3% risk of bacterial meningitis. A lumbar puncture (LP) is not required. If a clinical decision to administer antibiotics is reached, a lumbar puncture can be performed with CSF gram stain, cell count, differential, protein, glucose, and bacterial culture, prior to antibiotic administration. If the CSF results are abnormal, the infant should be managed in accordance to high risk bacterial infection or HSV recommendations, as appropriate. If the clinical decision to NOT perform a lumbar puncture is reached, the infant may receive an initial IV/IM Ceftriaxone dose and be safely discharged home with oral Cefdinir if they meet discharge criteria. The decision to hospitalize and observe vs discharge home with close follow up in 24 hours should be made in conjunction with the parent(s)/caregiver(s), given that the infant may require a second dose of IV/IM Ceftriaxone. The results of bacterial cultures should be followed daily by the hospital or Emergency Department (ED). If a culture is found to be positive for bacterial infection, the infant should be called back to the ED. If an LP was not previously done, it may be done at this time and started on IV antibiotics. CSF culture after antibiotic therapy may yield negative results, but CSF cell count, differential, protein, and glucose will remain suggestive of bacterial meningitis. Infectious disease service may be consulted for further management recommendations, particularly in the presence of gram+ stain. The prevalence of adverse events or delayed SBI diagnosis in infants at low risk with diagnosis of UTI is 0.1%.

Additional laboratory studies for consideration

<table>
<thead>
<tr>
<th>Type of infant</th>
<th>Study</th>
<th>Evaluation</th>
</tr>
</thead>
</table>
| *IF the infant presents fever and respiratory symptoms* | * Rapid RSV  
* Rapid Influenza  
* Respiratory viral panel* | * Presence of viral illness.  |

Treatment considerations

<table>
<thead>
<tr>
<th>Clinical setting</th>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTI first dose</td>
<td>Ceftriaxone</td>
<td>50 mg/kg IV/IM</td>
</tr>
<tr>
<td>Outpatient</td>
<td>Cefdinir (250mg/5mL)</td>
<td>14mg/kg PO daily for 10 days</td>
</tr>
</tbody>
</table>
SBI Inpatient

(High Risk Bacterial Infection Recommendations)

<table>
<thead>
<tr>
<th>Ampicillin AND EITHER Cefotaxime OR Ceftriaxone OR Gentamicin</th>
</tr>
</thead>
</table>
| 50-75 mg/kg IV/IM every 6 hours
50-75 mg/kg IV/IM every 6 hours
50 mg/kg IV/IM every 12 hours
5mg/kg IV every 24 hours |

Suspected meningitis
(Unless LP shows gram-organism)

<table>
<thead>
<tr>
<th>Vancomycin AND Ceftriaxone</th>
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</thead>
</table>
| 15mg/kg IV every 6-8 hours
50 mg/kg IV/IM every 12 hours |

HSV coverage
(HSV High risk recommendations)

| Acyclovir
Ganciclovir (First line alternative therapy) |
|-----------------------------------------------|
| 20 mg/kg IV every 8 hours
6 mg/kg IV every 12 hours |

Alternative regimen to IV acyclovir should be considered when there is national shortage or depleted hospital supplies. In this setting, IV acyclovir should be reserved for neonates (infants 0-28 days) with any positives on the HSV checklist and/or proven HSV disease.

**Indications for disposition**

<table>
<thead>
<tr>
<th>Disposition</th>
<th>Criteria</th>
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</thead>
<tbody>
<tr>
<td><strong>Discharge home</strong></td>
<td>a. Parents are comfortable with monitoring the infant at home</td>
</tr>
<tr>
<td></td>
<td>b. Parents have reliable means of communication from the hospital/ ED</td>
</tr>
<tr>
<td></td>
<td>c. Bacterial culture results can be followed daily by the hospital/ ED</td>
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<tr>
<td></td>
<td>d. The patient can follow-up with their primary care physician (PCP) in 24 hrs (Consult PCP prior to discharge)</td>
</tr>
<tr>
<td><strong>Hospitalization</strong></td>
<td>a. Toxic/ill appearance</td>
</tr>
<tr>
<td></td>
<td>b. Clinical signs of sepsis, like hypotension or poor capillary refill</td>
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<tr>
<td></td>
<td>c. Confirmed SBI: meningitis, bacteremia</td>
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<tr>
<td></td>
<td>d. Vomiting or inability to tolerate oral medication</td>
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<td></td>
<td>e. Lack of adequate outpatient follow-up (no telephone, parents live far from hospital, no PCP)</td>
</tr>
<tr>
<td></td>
<td>f. Failure to respond to outpatient therapy</td>
</tr>
<tr>
<td><strong>Inpatient observation/discharge recommendations</strong></td>
<td>a. Infants should be admitted to the hospital for 24-36 hours pending blood, CSF, and urine culture results, and viral testing (if done)</td>
</tr>
<tr>
<td></td>
<td>b. If respiratory virus or enterovirus testing is positive (if done), it is safe to discharge infants after 24 hours of negative CSF, blood, and urine cultures if discharge criteria are met</td>
</tr>
<tr>
<td></td>
<td>c. If viral testing is negative (if done), it is safe to discharge well appearing infants after 24-36 hours of negative CSF, blood, and urine cultures if discharge criteria are met</td>
</tr>
<tr>
<td></td>
<td>d. Note that children who undergo HSV testing may need to be observed longer than 26 hours</td>
</tr>
<tr>
<td></td>
<td>e. If HSV testing or any bacterial cultures grow a pathogen, treat appropriately</td>
</tr>
<tr>
<td></td>
<td>f. High risk infants who do not meet discharge criteria should remain hospitalized until safe and adequate follow up can be provided in the outpatient setting</td>
</tr>
</tbody>
</table>
Goal and Metrics

- Document the use of the Yale Observation Scale to identify well appearing infants.
- Reduce length of hospitalization for infants who are hospitalized to <30 hours for infants who are low risk.
- Increase the percent of hospitalized infants who are hospitalized appropriately.
- Increase the percent of infants who have a UA performed via any method of collection on the first day of encounter.
- Decrease the percent of infants who get a CXR within 24 hours of presentation without documented respiratory symptoms.
- Increase use of recommended empiric antibiotic regimens within 24 hours of presentation.
- Increase use of recommended empiric antibiotic regimen within 90 minutes for infants at high risk for SBI or HSV.

REFERENCES


Huebner RE,Mbelle N, Forrest B, Madore DV, Klugman KP. Immunogenicity after one, two or three doses and impact on the antibody response to coadministered antigens of a nonavalent pneumococcal conjugate vaccine in infants of Soweto, South Africa. Pediatr Infect Dis J. 2002;21(11):1004–1007


