Fever Without Source in Infants < 90 Days
Care Guideline

Inclusion Criteria: Previously healthy children 0-90 days of age who have:
• Fever 38.0°C or greater
• No apparent focus of infection
• Require hospitalization for concern for serious bacterial infection (SBI) or not meeting criteria for outpatient management

Exclusion Criteria: PICU status

Assessment
• Vital signs
• Hemodynamic stability
• Signs of sepsis
• Determination of risk for SBI
• Continuous pulse oximetry if respiratory distress, hypoxia present or pneumonia is suspected

Interventions - Option 1
• Blood & urine cultures
• Lumbar puncture
• CXR if signs of pneumonia*

Antibiotics
• Ceftriaxone 50 mg/kg IV q 12 hr

Interventions - Option 2
• Blood & urine cultures
• Lumbar puncture
• CXR if signs of pneumonia*

Antibiotics
• Ceftriaxone 50 mg/kg IV q 12 hr

Suspected bacterial meningitis requires significant additional management

Does Patient Meet Low Risk Criteria?
• Non-toxic appearing
• Previously healthy term infant with uncomplicated nursery stay
• No focal bacterial infection apparent on exam
• WBC 5-15,000/mm³
• < 1500 bands/mm³
• Urinalysis: < 5 WBC/hpf and negative leukocyte esterase and nitrite
• Stool with negative blood, negative mucus: < 5 WBC/hpf stool, if done
• CSF < 8 WBC/ul and negative Gram stain (if done)
• CXR negative (if done)

Interventions
• Blood & urine cultures
• Lumbar puncture
• CXR if signs of pneumonia*

Antibiotics
• Ampicillin AND Cefotaxime

Antibiotic Dosing Guidance
• Ampicillin
  50 mg/kg IV q 12 h
  < 7 days, < 2000g
  > 7 days, < 1200g
  OR
  50 mg/kg IV q 8 h
  <7 days, > 2000g
  > 7 days, 1200g-2000g
  > 7 days, > 2000g, non-meningitis
  OR
  100 mg/kg IV q 8 h
  <7 days any weight, GBS meningitis
  OR
  100 mg/kg IV q 6 h
  >7 days any weight, GBS meningitis

• Cefotaxime
  50 mg/kg IV q 12 h
  < 7 days, < 2000g
  > 7 days, < 1200g
  OR
  50 mg/kg IV q 8 h
  <7 days, > 2000g
  > 7 days, 1200-2000g
  OR
  50 mg/kg IV q 6 h
  > 7 days, > 2000g, non-meningitis
  OR
  75 mg/kg IV q 6 h
  >1 month; pneumococcal meningitis

* Signs of pneumonia
• Respiratory signs (i.e. abnormal breath sounds, tachypnea)
• Respiratory symptoms (i.e. cough)
• Respiratory distress
• SaO₂ < 95%

Reassess the appropriateness of Care Guidelines as condition changes and 24 hrs after admission. This guideline is a tool to aid clinical decision making. It is not a standard of care. The physician should deviate from the guideline when clinical judgment so indicates.

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**Recommendations/Considerations**
- If planning to treat with antibiotics, would obtain all cultures, including Lumbar Puncture, beforehand.
- Due to difficulty in evaluation of behavioral state, decreased immune function, potential pathogens, & higher frequency of SBI in infants < 90 days of age, a structured clinical approach is mandated.
- Serious bacterial infections include bacterial sepsis, pneumonia, meningitis, UTI/pyelonephritis, cellulitis, septic arthritis, osteomyelitis, & bacterial enteritis.
- Goal of management strategy is to identify those at low risk for SBI & thus reduce the need for either or both hospital admission & antibiotic exposure.
- Infants < 90 days with an apparent focus of bacterial infection should, in general, be considered as high risk, i.e., full septic evaluation, hospital admission, & appropriate antibiotics. These patients should not be included in this guideline.
- In general, febrile infants <28 days should be considered at high risk for SBI & thus undergo a full septic work-up, hospital admission, & empiric antibiotics.
- Always consider evaluation and treatment for possible herpes simplex infection (HSV PCR and intravenous acyclovir) in meningitis or sepsis syndrome especially in infants 0-6 wks (see Statement on Acyclovir Therapy in Neonates on next page).
- Consider viral studies (VRP, rapid viral screen, CSF/blood PCR, viral culture) in the febrile infant especially during the enteroviral season and respiratory viral season. Keep in mind that a positive viral test does not preclude the possibility of SBI.
- Criteria for outpatient management include age 28-90 days, non-toxic appearance, meeting low risk criteria, reliable parents, secure follow-up, & access to timely medical care.

**Continued Considerations**
- When meningitis can be excluded, adjust antibiotics to non-meningitic dosing
- Adjust antibiotics per culture results, LP results, and clinical status
- D/C antibiotics if cultures negative or VRP/viral study positive and no other high risk criteria met
- Re-evaluate if worsening signs & symptoms

**Discharge Criteria**
- Vital signs & clinical status are stable
- Bacterial cultures are negative
- Follow-up care is coordinated

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**28 – 90 days old**
May discharge at 36 hrs if:
- Cultures negative
- Afebrile
- Good follow-up available

**Parent Education**
- Fever in Infants 0-90 days old (located Patient in Family Education on PAWS)

**Significant Additional Management for Suspected Bacterial Meningitis**
- ICU monitoring
- Conservative fluid management
- Vancomycin
- Electrolyte monitoring
- Frequent neuro checks, serial head circumference
References
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http://pediatrics.aappublications.org/cgi/content/abstract/113/6/1662

http://cpj.sagepub.com/cgi/content/abstract/39/2/81

http://pediatrics.aappublications.org/cgi/content/abstract/113/6/1728
CHOC Children's Evidence Based Medicine Committee

Statement on Acyclovir Therapy in Neonates

Neonates < 4 weeks with fever:
Parenteral acyclovir (20 mg/kg IV q8hours) should be added empirically to antibiotics for neonates admitted with fever in the following situations;

1. Clinical signs of sepsis, toxic (including hypothermia, apneas, hypotension, other signs of shock)
2. Seizure
3. Maternal HSV
4. Physical exam findings consistent with Herpes simplex involvement (skin, eye, mucous membrane)
5. CSF pleocytosis with negative gram stain and consistent with aseptic meningitis.

Anytime acyclovir therapy is started on neonates one should perform a lumbar puncture and send the cerebrospinal fluid for HSV PCR.

In high risk situations where there is concern for disseminated HSV or SEM disease please send whole blood for HSV PCR, obtain swabs for HSV viral culture of at least 3 different mucous membrane (i.e. mouth, conjunctiva, nasopharynx, rectum), and any skin lesions and a panel 18. Obtain an Infectious Disease Consult.

Because of the risk of renal toxicity, patients on intravenous acyclovir should receive maintenance IV fluids and have urine dipped for heme q shift to evaluate for early evidence of nephrotoxicity.

In the absence of the above findings, in the neonates admitted with fever, the following scenarios demand specific attention.

1. Traumatic lumbar puncture: attempts to interpret traumatic CSF may lead to serious misdiagnoses. CSF with RBC > 2000 should be interpreted with caution and should be dealt with on an individual basis.
2. Unsuccessful lumbar puncture: same as above; increased LFTs and low platelets would be suggestive of disseminated HSV. These neonates are addressed above.
3. Strongly consider adding acyclovir in the presence of:
   a. Decreased platelets
   b. Increased liver function tests (LFTs), if done
   c. Pneumonia

In these scenarios when the infant appears more ill than would be expected, the physician's judgment should be used to determine acyclovir use on a case by case basis.

Obtain an Infectious Disease consult if Acyclovir is to be continued more than 48 hours or if index of suspicion for HSV is high.

Afebrile Neonates
Acyclovir should empirically be given to patients admitted with seizure and or physical exam findings consistent with Herpes simplex involvement (skin, eye, mucous membrane) and/or altered mental status.
References:


Updated and Approved by the CHOC Evidence-Based Medicine Committee 1-15-14; 5-17-17