

Fever in Infants ≤ 28 Days of Age:

Emergency Department Management
Clinical Practice Guideline (CPG)

Protocol approved by:
Division of Pediatric Emergency Medicine
and Infectious Diseases
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Fever in neonates (age 0 to 28 days)

INCLUSION CRITERIA

- Infant ≤ 28 days of life
- Temperature ≥ 38°C (100.4°F) by any route/parental report

EXCLUSION CRITERIA

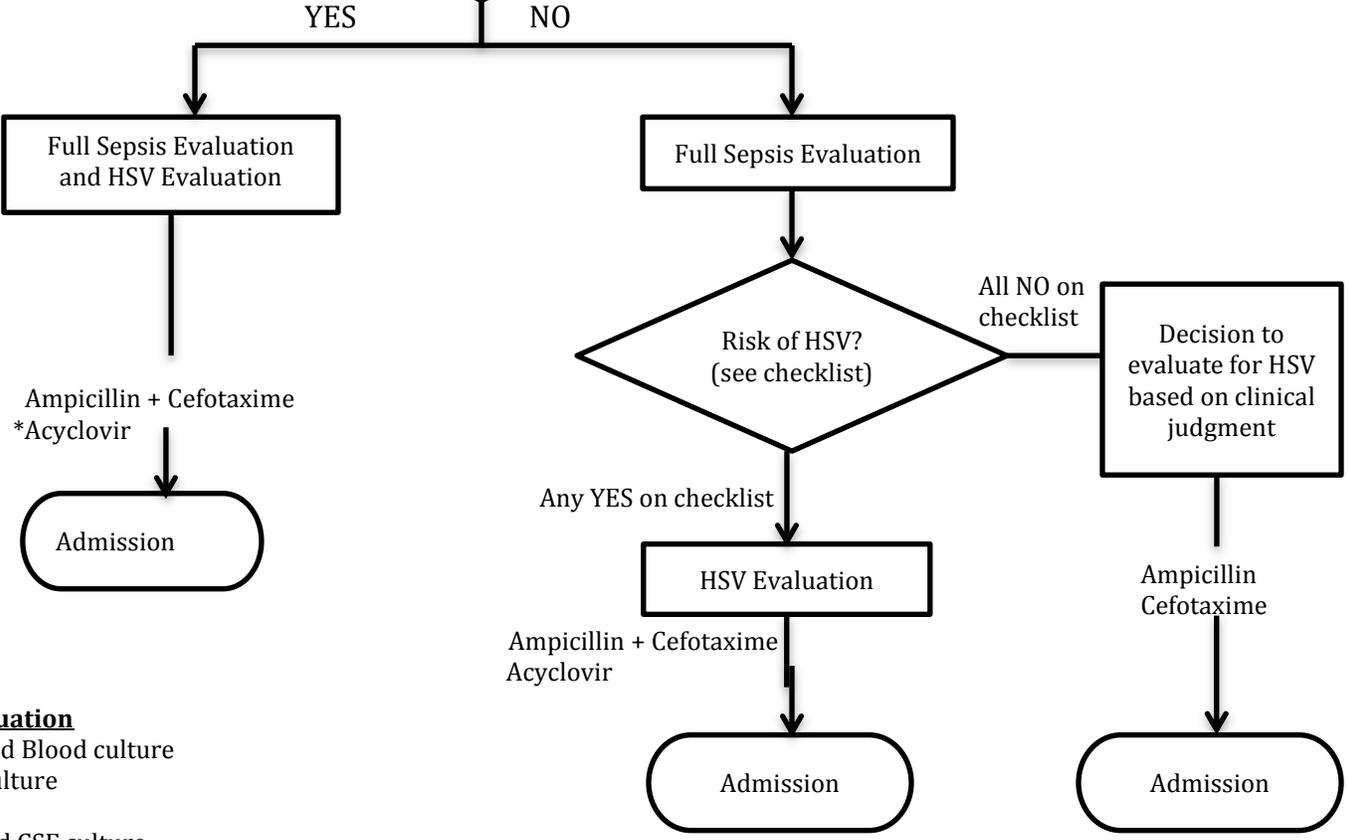
- Infants with RSV

Febrile Infant
≤ 28 days old

Ill appearing?

HSV Checklist

- | YES | NO |
|--------------------------|---|
| <input type="checkbox"/> | <input type="checkbox"/> History of seizures |
| <input type="checkbox"/> | <input type="checkbox"/> Vesicles on skin/scalp |
| <input type="checkbox"/> | <input type="checkbox"/> CSF pleocytosis (CSF wbc >20/μL) |
| <input type="checkbox"/> | <input type="checkbox"/> Elevated transaminases |
| <input type="checkbox"/> | <input type="checkbox"/> History of maternal HSV |
| <input type="checkbox"/> | <input type="checkbox"/> History of maternal fever at L&D |
| <input type="checkbox"/> | <input type="checkbox"/> Thrombocytopenia |
| <input type="checkbox"/> | <input type="checkbox"/> Active Herpes in household contact |



- Full Sepsis Evaluation**
- CBC with diff and Blood culture
 - UA and Urine culture
 - CMP
 - CSF Analysis and CSF culture

- Empiric Treatment**
- **Infants ≤7 days** : ampicillin 50mg/kg/dose every 8 hours, cefotaxime 50mg/kg/dose every 8 hours
 - **Infants >7 days**: ampicillin 50mg/kg/dose every 6 hours, cefotaxime 50mg/kg/dose every 6 hours

- HSV Evaluation and Empiric Treatment**
- CSF and Blood HSV PCR
 - Nasopharyngeal, eye, rectal viral culture swabs
 - Liver function tests (if CMP not done above)
 - Acyclovir 20mg/kg/dose every 8 hours (if one or more 'Yes' on HSV Checklist)
 - * Alternative therapy during Acyclovir shortage (and all 'No" on HSV Checklist): Ganciclovir 6mg/kg/dose every 12 hours

Objective: The purpose of the Febrile Neonate Clinical Practice Guideline is to standardize care around the management of the febrile neonate without a focus of infection and at risk for serious infection.

Target Population: Infants, 28 days of age or less, presenting with a fever of unknown origin.

Exclusions:

- Infants greater than 29 days of age,
- Infants without fever on exam or by history
- Infants with RSV bronchiolitis

Inclusion Criteria:

- Infants with temperature greater than or equal to 38.0°C by any route by healthcare worker or parental report
- Infants with gestational age less than 37 weeks, congenital medical and/or surgical co-morbidities, and those hospitalized at any time since birth are included in this guideline

Target Users: Clinicians, nurses at Cardinal Glennon Children's Medical Center Emergency Department(ED) and inpatient units; primary care providers, and clinicians caring for infants in other EDs and urgent care centers.

Introduction

An infant with fever is a very common presentation to pediatric emergency departments, urgent care centers and primary care offices. The source of fever is not always apparent and clinical exam alone cannot reliably predict serious illness in neonates and young infants. The most common cause of fever is usually a self-limited viral infection but the incidence of serious bacterial infections (SBI) may be higher in infants compared to older children, and neonates are even at a higher risk (Laupland et al. 2009).

As many as 12% to 18% of all febrile neonates presenting to the pediatric emergency department have serious bacterial illness (Baker 1999, Kadish 2000, Maniaci 2008). Neonates are infected typically by more virulent bacteria such as group B *Streptococcus*, *Escherichia coli*, and *Listeria monocytogenes*. The most common bacterial infections in this age group are UTIs and occult bacteremia (Baker 1999, Kadish 2000).

Neonatal herpes simplex virus (HSV) is an important consideration in neonates as they are more likely to experience serious sequelae from HSV meningitis. Risk factors include primary maternal infection, cutaneous vesicles, seizures, CSF pleocytosis, and contact with household contact with active herpes. Acyclovir is not recommended routinely for empiric treatment but should be considered in febrile

neonates with risk factors for neonatal HSV as early treatment may improve outcomes (Kimberlin 2005).

Assessment and Diagnosis

Clinical Assessment

1. It is recommended that a rectal temperature be measured to establish fever $\geq 38^{\circ}\text{C}$ (Claudius 2010).
 - a. Infants who had a reliable rectal temperature measured at home undergo the same evaluation as if the temperature was measured in the office or ED (Claudius 2010).
 - b. A response to antipyretic medication does not change the likelihood of an infant having a serious bacterial infection (American College of Emergency Physicians Clinical Policies Committee 2003).
2. A thorough history, including questions about symptoms, sick exposures, infant birth history, maternal prenatal and intrapartum history, and physical exam be obtained by the provider

Laboratory Studies

Recommendations for an initial full sepsis evaluation of all febrile neonates include:

- a. Complete blood count with differential
- b. Blood culture
- c. Urine analysis with microscopy
- d. Urine culture (catheter/suprapubic specimen)
- e. Cerebrospinal fluid (CSF) cell count with differential, protein and glucose
- f. CSF gram stain and culture

Radiology Studies

It is recommended that a chest x-ray be performed in febrile neonates with respiratory symptoms such as tachypnea (>60 breaths/min), crackles in the chest, retractions, nasal flaring, cyanosis, or oxygen saturation $\leq 95\%$ (National Collaborating Centre for Women's and Children's Health 2007).

Management

Because of the high rates of SBI, it is recommended that all febrile neonates should receive intravenous (IV) antibiotics and be admitted to the hospital (Ishimine 2007).

Medication: IV ampicillin **plus** a 3rd generation cephalosporin **or** gentamicin pending culture results.

Drug	Route	Dose
Ampicillin	IV, IM	Infants 0-7 days: 50mg/kg/dose every 8 hours Infants 8-28 days: 50mg/kg/dose every 6 hours
Cefotaxime	IV, IM	Infants 0-7 days: 50mg/kg/dose every 8 hours Infants 8-28 days: 50mg/kg/dose every 6 hours
Gentamicin	IV, IM	Infants 0-30days: 4 mg/kg/day every 12-24 hours* *adjust doses based upon measured serum peak and trough levels.

Treatment of the neonate with a positive blood, urine or CSF culture should be tailored to the bacteria identified and the infection site.

HSV Risk Factors, Evaluation and Management

Neonatal HSV has significant morbidity and mortality if untreated. The risk of neonatal HSV approaches that of bacterial meningitis in the second week of life. Clinicians should have a high index of suspicion, and HSV testing and empiric treatment is recommended for neonates with following risk factors (Caviness et al. 2008):

- a. Ill or septic appearing, hypothermia, severe respiratory distress
- b. Seizures (or history of seizure)
- c. Herpetic lesions/vesicles
- d. CSF pleocytosis for age (white blood cell count > 20/ μ L)
- e. Elevated AST and/or ALT on previous labs obtained

Additional factors that may increase the risk of HSV over the general population (Caviness et al. 2008):

- a. Known maternal HSV
- b. Thrombocytopenia
- c. Maternal fever at labor and delivery
- d. Close contact with a person with active herpetic lesions

Laboratory testing:

- a. Cerebrospinal fluid and blood HSV polymerase chain reaction (PCR)
- b. Nasopharyngeal, eye, and rectal viral cultures
- c. Liver function tests

Management

In addition to IV ampicillin and cefotaxime, empiric treatment of suspected HSV is required.

- Acyclovir IV 4 mg/kg/day every 12-24 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 with any positives on the HSV checklist and/or proven HSV disease.
- First line alternative therapy: Ganciclovir IV 6 mg/kg/dose every 12 hours

References:

Children's Mercy Hospitals and Clinics, Evidence Based Practice Guideline, Febrile Infant. http://www.childrensmercy.org/Health_Care_Professionals/Medical_Resources/Clinical_Practice_Guidelines/Febrile_Infant/Febrile_Infant/

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