# Neonatal Fever/Suspected Sepsis Clinical Pathway

Updated: March 2022

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|---|---|
| **Outcomes/Goals** | 1. Identification and treatment of infants ≤ 28 days with temperature ≥38 C<br>2. Create a team-oriented approach to efficient and timely evaluation and work-up<br>3. Antibiotic administration within 60 minutes for acutely ill/toxic appearing infants |
| **Inclusion** | Aged 0-28 days with either rectal or axillary temperature ≥ 38.0 C at home, other healthcare facility, or in ED OR afebrile in the ED but home rectal/axillary temperature measured ≥38.0 C |
| **Exclusions** | History of prematurity < 37 weeks, pre-existing medical conditions, indwelling devices, focal bacterial infections (except otitis media), clinical bronchiolitis |
| **NURSE** documentation | Chief complaint. Onset of fever. Documented route of measuring temperature. Associated symptoms. Birth and medical history, medications, allergies, vital signs including naked weight. |
| **INTERVENTIONS** Initiate on arrival | ESI Triage level II<br>Full set of vitals including rectal temperature and naked weight<br>Evaluate for use of infant warming table<br>Continuous pulse oximetry and oxygen to maintain SaO2 > 93%<br>IV with bedside CBG<br>LMX to LP site & LP setup at bedside |
| **DIAGNOSTICS** | CMP, POC electrolytes or CBG *as needed*<br>Catheter specimen urinalysis, microscopy, and culture<br>CBC with differential, procalcitonin, CRP (if PCT not available), coagulopathy panel, blood culture<br>CSF per provider (gram stain, cell count, protein, glucose, culture, HSV panel, enterovirus PCR)<br>Chest x-ray if indicated (e.g. tachypnea, hypoxia, cough)<br>If suspected HSV infection: 3 separate viral swabs for HSV Culture: 1. Conjunctivae, 2. Oropharynx, 3. Rectum; Blood for HSV PCR; CSF for HSV PCR |
| **PHYSICIAN (LIP)** | |
| Fluids (if indicated) | Normal Saline bolus 10 ml/kg |
| Medication<br>Hypoglycemia | D10W bolus of 5ml/kg for CBG <50 |
| Antipyretics | Acetaminophen 12.5 mg/kg PO **or** Acetaminophen 15mg/kg PR |
| Antibiotics **(Administer within 60 minutes of arrival)** | **0-21 days:**<br>No concern for meningitis or HSV: Ampicillin 50 mg/kg IV and Gentamicin 5 mg/kg IV<br>CSF pleocytosis or concern for HSV: Acyclovir 20 mg/kg IV, ampicillin 75mg/kg IV, and either ceftazidime 50mg/kg IV (0-14 days, hyperbilirubinemia) OR ceftriaxone 50mg/kg IV (>14 days, no hyperbilirubinemia)<br>**22-28 days:**<br>No concern for meningitis or HSV: Ceftriaxone 50mg/kg IV<br>CSF pleocytosis or concern for HSV: Acyclovir 20 mg/kg IV, ampicillin 75mg/kg IV, and either ceftazidime 50mg/kg IV (0-14 days, hyperbilirubinemia) OR ceftriaxone 50mg/kg IV (>14 days, no hyperbilirubinemia)<br>*Do not delay antibiotics in cases of no IV access. Antibiotics may be given IM* |
| **ADMISSION** | Call primary care physician<br>Call peds ward/DNCC attending<br>Prepare family/infant for admission to DNCC, PICU or ward as appropriate |
| *HSV Risk Factors | ◦ Vesicular lesions<br>◦ Ill appearance<br>◦ Maternal HSV infection<br>◦ Exposure to HSV-infected person<br>◦ Hypothermia<br>◦ Seizures or abnormal neurological status<br>◦ Thrombocytopenia<br>◦ Hepatitis<br>◦ CSF pleocytosis with negative gram stain |

# Clinical Pathway & Decision-Making Process

## Neonatal Fever/Suspected Sepsis

Temp ≥38.0 R in infants' ≤28 days*

(*Rectal/axillary temp ≥38.0 at home, clinic, or ED)

March 2022

**Meets exclusion criteria?**

- History of prematurity < 37 weeks
- Pre-existing medical conditions
- Indwelling foley, vascular catheter
- Focal bacterial infections (except AOM)
- Clinical bronchiolitis
- Immunizations in last 48 hours

OFF PATHWAY

**Toxic/Ill appearance?**

YES

Fluid resuscitate, 10ml/kg PRN
CBC, CMP, coags, VBG/lactate, blood culture, HSV PCR/swabs
UA, urine micro, urine culture, CSF studies (including HSV PCR)
IV acyclovir, ceftazidime, ampicillin
Admit, consider NICU/PICU

NO

**Home temperature > 38C measured other than rectally or axillary AND afebrile in ED?**

YES

Consider period of observation in ED, serial temp checks, PO trial. Do not give antibiotics if full ROS not performed.

NO

0-21 days

22-28 days

**Immediate Action:**

1. CBG
2. Pulse oximetry/cardiac monitor
3. Catheter UA, microscopy, culture
4. IV/IO, CBC, procalcitonin[1], coags, blood culture
5. CSF GS/culture, cell count, protein, glucose

[1]If **procalcitonin** is not available, 'negative inflammatory markers' requires ALL of the following: ANC < 4000, CRP < 20, temp < 38.5.

**Immediate Action:**

1. CBG
2. Pulse oximetry/cardiac monitor
3. Catheter UA, microscopy, culture
4. IV/IO, CBC, procalcitonin[1], coags, blood culture

**HSV Risk Factors[1], CSF pleocytosis, or traumatic tap[2]?**

NO

Start ampicillin and gentamicin
Admit for observation

YES

ANC > 4000 or Procalcitonin[1] > 0.5 ng/mL?

YES

Perform LP

NO

MAY perform LP

**CSF pleocytosis**

**CSF not obtained or traumatic tap[2]**

**CSF Normal**

**CSF pleocytosis or other HSV Risk Factors[1]?**

**LP not done/ unsuccessful/ traumatic AND no other HSV Risk Factors[1]**

YES

**Other HSV Risk Factors[1]?**

NO

Collect HSV skin MM swabs, serum PCR, CSF PCR, and enterovirus PCR
Start acyclovir, ampicillin, and cephalosporin (see page 1)
Admit/transfer for observation

YES

NO

Admit/transfer for obs
MAY give ceftriaxone

Start ceftriaxone
Admit/transfer for obs

Observe at home OR in hospital
If D/C, give ceftriaxone and f/u within 24 hrs
If admit, may not give antibiotics and observe
(NNT=50-100 patients treated with antibiotics for one case of occult bacteremia)

[1]**HSV Risk Factors**: Vesicular lesions, Ill appearance, Maternal HSV infection, Exposure to HSV-infected person, Hypothermia, Seizures or abnormal neurological status, Thrombocytopenia, Hepatitis, CSF pleocytosis with negative gram stain

[2]**Traumatic tap** = 10,000 RBC per $mm^3$

# Neonatal Fever / Suspected Sepsis Rationale and Data

## Goals of Clinical Pathway

1. Identification and treatment of infants ≤ 28 days with temperature ≥38 C
2. Create a team-oriented approach to efficient and timely evaluation and work-up
3. Antibiotic administration within 60 minutes for acutely ill/toxic appearing infants

| Data Considerations | Interventions | Rationale |
|---|---|---|
| Fever | Documented rectal temperature | Defined as rectal temperature >38°C (100.4F). Rectal thermometry is the gold standard, and studies have demonstrated greatest discordance in young children between rectal thermometry and temporal measurements. Parental report of tactile fever is likely to be accurate. Range of reported sensitivity 82-89%, specificity 76-86%. Fever above 38.5 does increase the likelihood of invasive bacterial infection according to several recent studies. |
| Urine collection | Catheter specimen collection | Bladder catherization or suprapubic bladder aspiration is the methods of choice for obtaining urine samples according to AAP guidelines. Bag collection sample has an increased risk of contamination, false-positive rate up to 67%. |
| Urine Analyisis | Mandatory urine culture | Urine culture should be obtained in conjunction with dipstick and microscopy if LE is trace or greater, nitrites +,or if > 5WBCs or bacteria present on micro. Historically, UA with micro not felt to be sensitive marker in infants. However, high quality recent studies suggest sensitivity of UA with micro is excellent, with LE of 94% or higher. Pyuria (>5WBCs) adds some incremental sensitivity. |
| White blood cell count, Procalcitonin | Lumbar puncture | Lumbar puncture should be performed in all infants < 22 days regardless of inflammatory markers and in any infant 22-28 days with positive inflammatory markers (ANC>4000 or PCT > 0.5). In the first group, the incidence of meningitis is 0.5-1.3%. |
| Herpes Simplex Testing | Empiric acyclovir | Incidence of neonatal HSV infection is about 2-10/100,000 live births but can have devastating sequelae; disseminated disease has a 1-year mortality of 29% and 70% of patients with CNS disease have abnormal neurologic development. Because the disease is rare, treating all febrile neonates empirically with acyclovir is not cost-effective and most centers use the presence of risk factors as the criteria to test and start empiric treatment. Recommendations based on limited data suggest that if testing is performed due to the presence of symptoms, empiric therapy should be initiated without delay. |

## Invasive Bacterial Infection (SBI) in infants less than 29 days

Infants younger than 29 days have the highest rates of invasive bacterial infection, namely bacteremia and meningitis. Per the new AAP guideline on evaluating fever in infants 8 to 60 days, children aged 22-28 days are at marginally lower likelihood of invasive bacterial infection than children aged 8-21 days (bacteremia rates of 2.8 vs 4.1%, respectively). The above algorithms reflect this differential risk in terms of evaluation strategies and empiric treatment.

## Bacterial Pathogen Consideration

| **Most common pathogens isolated** | Early-Onset | Late-Onset |
|---|---|---|
| Escherichia coli (+++) | +++ | ++ |
| Group B streptococcus (+++) | +++ | +++ |
| Klebsiella (+) | + | + |
| Enterobacter cloacae (+) | + | + |
| Staph aureus (+) | + | +++ |
| Listeria monocytogenes (+) | + | + |
| Other enteric gram-negatives | + | + |
| Non-enteric gram negatives | + | + |
| Enterococcus | - | + |

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