**FEVER IN INFANTS LESS THAN 60 DAYS**

**Algorithm**

- **For report of tactile fever, you can avoid testing if**:
  - No antipyretics meds were given
  - Infant is well appearing
  - Follow up can be arranged in 12-24 hrs
  - Parents can measure rectal temp at home
  - Patient is not high risk for bacterial infection: premature, maternal group B strep, poor feeding, etc.
  - Caregiver is counseled on return precautions for fever prior to discharge

**Inclusion Criteria**
- Age ≤ 60 days
- Fever ≥ 38.0°C or < 36.0°C or reliable hx of fever at home

**Exclusion Criteria**
- Current gestational age ≤ 37 weeks
- Current weight ≤ 2000 grams
- Need for immediate critical care
- Chronic or underlying illness
- Immunocompromised

**Full Sepsis Workup**
- CBC with diff or point of care CBC
- Procalcitonin (if available)
- LFTs (if suspected HSV)
- Blood cultures (x2)
- UA, urine culture (via cath)
- CSF (culture, cell count, protein, glucose, meningitis encephalitis panel (MEP))
- HSV labs and empiric acyclovir if high risk (see Page 2 for HSV algorithm)
- Start empiric antimicrobials*:
  - <28 days old: ampicillin + gentamicin (If concern for meningitis, use ampicillin + cefotaxime)
  - 29-60 days old: ceftriaxone (if concern for meningitis, add vancomycin)

**Risk Stratification**
- Procalcitonin
- UA, urine culture (via cath)
- CBC with diff or point of care CBC
- Blood cultures (x2)
- HSV labs and antimicrobials if high risk (see page 2 algorithm)

**High Risk for SBI?**
- **Yes**: UA, Urine Culture
- Respiratory viral testing is generally NOT recommended
- Consider: Flu PCR, blood culture, CBC
- Discharge/Admit as appropriate (see page 3 for admission location)

**High Risk for SBI if any of the following:**
- ≤ 28 days old
- Procalcitonin: > 0.3ng/mL
- WBC <5,000 or >15,000/microliter
- Absolute band count ≥1,500/microliter
- CSF: positive gram stain, >9 WBCs/mm³ (29-60 days), or grossly bloody tap at any age (>10,000 RBCs/mm³)

See additional high risk considerations in text on page 5

*Additional Antimicrobial Considerations:*
- If patient has clinical bronchiolitis, complete full sepsis workup, but you can admit and observe off antibiotics
- If cefotaxime is unavailable, use ceftazidime
- If the tap is bloody or unable to obtain LP, treat with meningitic doses (see table on page 6) while awaiting blood and urine cultures, see page 5 for more information
- If patient is high risk for HSV (see page 2), add acyclovir

**No respiratory viral testing unless it will change management**

**Admit**
- see page 3 for location

**Narrow antimicrobial therapy based on culture results**
- Note: you may consider admitting off antibiotics for patients with negative UA, negative inflammatory markers, normal CSF, and temp <38.6°C

**Provider Discretion**
- Discharge or Observe off antibiotics (see pg 3 for admission locations)
- If UA Pos (leuks/nitrites, WBCs >5), Negative PCT, & Temp <38.6°C you can discharge on oral antibiotics after an initial parental antibiotic dose (see pg 6 for details)
ALGORITHM - HSV Testing

High Risk for HSV?
- CSF pleocytosis with a negative gram stain
  1-28 days old: >18 WBCs
  29-60 days old: >9 WBCs
- Seizures
- Altered mental status
- Exposure to HSV lesions (including genital or skin/oral)
- Presence of vesicles
- Elevated ALT
- Leukopenia, thrombocytopenia
- Hypothermia
- Ill appearing

! Higher risk for patients <21 days

HSV Testing:
- MEP (or CSF HSV PCR*)
- HSV multisource PCR (order of collection: eye, nasopharynx, mouth, anus) (or culture if unavailable)
- Vesicle HSV PCR (if vesicle present) (or culture if unavailable)
- Blood HSV PCR
- CMP

*If you are only suspicious of HSV (not enterovirus, parechovirus, or bacterial meningitis), consider HSV PCR testing instead of MEP.

Empiric Treatment
- IV acyclovir
- IV Fluids at 1.5x maintenance
- Admit - see pg 3

Is CSF, multisource, vesicle, AND blood HSV testing negative?
- Yes
- No

Are you still concerned for HSV (seizures, critically ill, etc.)
- Yes
- Continue acyclovir
- Contact ID
- No
- Stop acyclovir

Continue IV acyclovir
- Consult Infectious disease
- Renal function monitoring at 24-48 after starting acyclovir
ALGORITHM - Admission

1. Decision to Admit Patient
2. Age < 28 days or < 44 weeks gestational?
   - Yes → Requires ICU Resources?
     - Yes → Admit to PICU
     - No → Requires ICU Resources?
6. No → Admit to NICU based on Capacity
   - Anschutz Campus: Call NICU first, patient should be admitted to NICU unless space prohibits. (this is to ensure floor bed availability for patients >28days)
   - Network of Care (NOC): admit to NOC inpatient if appropriate or call NICU if there are any concerns or no bed availability

*Note: Kaiser has the option of caring for patients as an attending in the NICU or may request admission to the floor onto the Kaiser service.

Requires ICU Resources
- Advanced Airway Support (includes heated high-flow, apnea, seizures, etc.)
- Hemodynamic Instability
- Concern for bacterial meningitis (ie positive CSF gram stain, CSF pleocytosis)
- Provider Concern

Admit to Floor/Network of Care (NOC) Inpatient
TARGET POPULATION

Inclusion Criteria

- Age less than or equal to (≤) 60 days
- Fever (greater than or equal to (≥) 38.0°C (100.4°F) or less than (<) 36.0°C (96.8°F)
- Parental report of tactile fever should be considered
- Gestational age greater than (> ) 37 weeks AND weight greater than (> )2000 grams

Exclusion Criteria

- Need for immediate critical care
- Chronic or underlying illness
- Immunocompromised

BACKGROUND | DEFINITIONS

- Serious Bacterial Illness (SBI):
  - Includes bacteremia/sepsis, meningitis, and urinary tract infections (UTIs)
  - Febrile infants less than 28 days are at higher risk of SBIs
  - For febrile infants, no universal risk stratification currently exists to identify SBI either by clinical examination, routine laboratory tests, biomarkers or selection criteria.²,³
- Rectal temperature correlates most closely with core body temperature⁵
- Infants with otitis media are at the same risk of bacteremia as patients without an otitis media
- Infants with enterovirus identified in cerebrospinal fluid (CSF) are lower risk for SBI, have decreased length of stay, exposure to antibiotics, and hospital costs.⁶,⁷,⁸,⁹
Table 1: Incidence of SBI in infants

<table>
<thead>
<tr>
<th></th>
<th>Incidence of infection in febrile infants 7-90 days</th>
</tr>
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<tbody>
<tr>
<td>Urinary Tract Infection (UTI)</td>
<td>17%**</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>2%</td>
</tr>
<tr>
<td>Meningitis</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

**10% of patient with UTI will have bacteremia

INITIAL EVALUATION

Thorough history and physical examination including these high-risk considerations:

- Maternal history of intra-partum fever, antibiotic treatment, group B strep infection
- Infant history of prior antibiotic treatment, hospitalization longer than mother, previous hospitalization, unexplained hyperbilirubinemia, prematurity (less than 37 weeks), temp greater than 38.5°C

LABORATORY STUDIES | IMAGING

Procalcitonin

- For well-appearing infants 29-60 days, a normal procalcitonin lowers the risk of serious bacterial infection. (Can consider discharge home without antibiotics after blood and urine cultures are obtained.)
- An elevated procalcitonin warrants further investigation for serious bacterial infection and antibiotic initiation while awaiting blood, urine, and CSF cultures.

Traumatic/Dry Lumbar Punctures

- Interpretation of traumatic or dry taps can be difficult. In general, traumatic lumbar punctures (LPs) are defined as greater than 500 RBCs/hpf and correcting with ratios can be inaccurate. The decision regarding whether or not to treat for meningitis in these situations is influenced by degree of fever, degree of illness, other laboratory studies, cultures, age of the infant, and other factors.

Neonatal Herpes Simplex Virus (HSV)

- See algorithm on page 2
- Early diagnosis and treatment improves outcomes; untreated infections often result in death or serious morbidity
- The vast majority of neonatal HSV cases occur in infants less than 28 days, with few cases reported greater than 6 weeks of age
- Skin, eye, and mucous membrane infection typically presents at 7-14 days of age, CNS infection at 14-21 days, and disseminated disease at 5-12 days

Meningitis Encephalitis Panel (MEP)

- MEP rapidly tests CSF for 14 common causes of central nervous system (CNS) infection but does not rule out meningitis due to other pathogens.
- MEP should be ordered if concern for HSV and enterovirus/parechovirus. If only suspicious of a single organism (or MEP unavailable), consider PCR testing for individual organism(s).
- Consider MEP for enterovirus and parechovirus testing regardless of CSF white blood cell count (WBC) (as most lack pleocytosis).
Viral Testing\textsuperscript{13}

Viral testing indicated in select infants based on season and clinical presentation and only if results will change management.

- Consider flu PCR during influenza season.
- Consider Gastrointestinal Pathogen Panel if bloody diarrhea.

Additional diagnostic studies if indicated:

- Basic metabolic profile (BMP) if concern of dehydration, electrolyte disturbance or if starting acyclovir

THERAPEUTICS

Antibiotic Recommendations

- Obtain all cultures prior to antibiotic administration if possible
- IV route of antibiotic administration is preferred
- If enterovirus or parechovirus is identified in a well-appearing infant, you can discontinue antibiotics
- Duration of antibiotic therapy varies based on diagnosis, culture results, and clinical improvement of the infant

<table>
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<tr>
<th>Focus</th>
<th>Age less than or equal to 7 days</th>
<th>Age 8-28 days</th>
<th>Age 29-60 days</th>
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<tbody>
<tr>
<td>Suspected UTI or SBI</td>
<td>ampicillin 50 mg/kg/dose every 8 hours, max 1000 mg/dose \textit{AND} gentamicin 4 mg/kg every 24 hours</td>
<td>ampicillin 50 mg/kg/dose every 6 hours, max 1000 mg/dose \textit{AND} gentamicin 2.5 mg/kg every 12 hours</td>
<td>ceftriaxone 50 mg/kg/dose every 24 hours, max 2000 mg/dose</td>
</tr>
<tr>
<td>Suspected Meningitis or abnormal CSF</td>
<td>ampicillin 100 mg/kg/dose every 8 hours, max dose 2000 mg/dose \textit{AND} cefotaxime 50 mg/kg/dose every 8 hours, max 2000 mg/dose</td>
<td>ampicillin 100 mg/kg/dose every 6 hours, max 2000 mg/dose \textit{AND} cefotaxime 50 mg/kg/dose every 6 hours, max 2000 mg/dose</td>
<td>vancomycin 10-15 mg/kg/dose IV every 6 hours, max 1000 mg/dose \textit{AND} ceftriaxone 100 mg/kg/dose every 24 hours, max 2000 mg/dose</td>
</tr>
<tr>
<td>Suspected HSV</td>
<td>acyclovir 20 mg/kg/dose IV every 8 hours, max dose 1200mg</td>
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</table>

Alternative to cefotaxime during medication shortage for infants less than or equal to 28 days old: cefazidime 50 mg/kg/dose every 8 hours, max 2000 mg/dose

Outpatient Antibiotic Recommendations for Urinary Tract Infection (UTI)

- For neonates and infants less than 2 months of age with presumed UTI, initiate empiric parenteral antibiotics. Neonates less than 1 month of age must receive parenteral therapy, due to inadequate drug absorption, immature immune system and increased dissemination of infection\textsuperscript{19}. Bacteremia secondary to acute pyelonephritis occurs in 6.1-22.7\% of children less than 2 months of age\textsuperscript{19}. 
For infants 29-60 days old with uncomplicated bacterial UTI and close follow-up, parenteral antibiotics may be switched to oral antibiotics at the discretion of the provider after clinical improvement.

Oral antibiotics should be chosen based on gram stain, culture results and local antibiotic susceptibility patterns.

**Additional Antibiotic Considerations**
- 29-60 days: Antibiotics are not indicated if laboratory results are within normal limits, no concern of SBI/sepsis, or high index suspicion of viral etiology\(^{20,13}\). Select site-specific treatment for minor focal infection in well-appearing child

**DISPOSITION**

**Admission**
- See Admission Algorithm on page 3
- Additional considerations for admission:
  - Unable to confirm follow up in less than 24 hours
  - Lack of telephone or transportation
  - Inadequate home resources
  - Caretaker unable to provide care
  - Notify primary care provider (PCP) and admitting physician

**Discharge Home**
- If the patient is diagnosed with a treatable infection, then manage as appropriate
- Discharge home with good follow up if patient is well-appearing and cultures negative at 24-36 hours, workup for age and appearance is complete and reassuring (including HSV if appropriate).
  - If well appearing infant greater than 7 days with enterovirus or parechovirus identified, can discharge earlier
REFERENCES


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APPROVED BY
Clinical Care Guideline and Measures Review Committee – January 9th, 2018
Pharmacy and Therapeutics Committee – February 1st, 2018

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APPROVED BY
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REVIEW/REVISION SCHEDULE
Scheduled for full review on February 1, 2022.
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