Fever Without a Source
Age: 0-28 Day Pathway - Emergency Department
Evidence Based Outcome Center

EXCLUSION CRITERIA
Toxic appearing
No fever
Born < 37 weeks gestational age

ALERT
Patient Toxic/Septic Appearance
Full Sepsis Workup & treat as appropriate.
(LINK TO SEPSIS PATHWAY/GUIDELINE)

INCLUSION CRITERIA
Non-toxic with temperature > 38°C (100.4°F) OR < 36°C (96.5°F) measured in Emergency Department OR reported measurement at home.

Order labs:
- Complete Blood Count with differential
- Blood Culture
- Complete Metabolic Panel
- Urinalysis with Micro
- Urine Culture: Catheter or Suprapubic
- Cerebrospinal Fluid (Hold Tube # 4)
  - Gram stain
  - Culture
  - Cell count with differential
  - Glucose
  - Protein
- Stool culture & Stool WBC (If patient has diarrhea)

Contraindications for Ceftriaxone in patients < 28 days of age:
- Patient expected to or receiving calcium containing IV products.
- Total Bilirubin > 10 (See risk factors for hyperbilirubinemia)

Consider HSV work up and empiric ED treatment for patients with any of the following conditions:

<table>
<thead>
<tr>
<th>Historical and Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe illness / Hypothermia / Lethargy</td>
</tr>
<tr>
<td>Seizures</td>
</tr>
<tr>
<td>Hepatosplenomegaly</td>
</tr>
<tr>
<td>Postnatal HSV contact</td>
</tr>
<tr>
<td>Vesicular rash</td>
</tr>
<tr>
<td>Conjunctivitis</td>
</tr>
<tr>
<td>Interstitial pneumonitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Laboratory Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>CSF pleocytosis</td>
</tr>
<tr>
<td>without clear bacterial infection</td>
</tr>
<tr>
<td>Transaminitis</td>
</tr>
</tbody>
</table>

Normal CSF Values
- 0-20 WBC/mm³
- Protein 0 - 30 days: < 100 mg/dL
- Normal Gram Stain

Order labs:
- HSV DNA PCR of Blood
- Meningitis/Encephalitis PCR Panel of CSF
- Swab/scraping of skin or mucous membrane lesions for HSV DFA AND HSV culture
- Surface HSV cultures in viral transport media tube
  - Conjunctiva
  - Throat
  - Nasopharynx
  - Rectum
  - Skin vesicle (if present)

Start empiric antibiotic treatment:
- Ampicillin x1 + Gentamicin x1

NO

Herpes Simplex Virus (HSV) work-up indicated

YES

NO

Start empiric antibiotic treatment:
- Ampicillin x1 + Gentamicin x1

CSF Pleocytosis and suspicion of meningitis
OR
CSF Gram stain positive

YES

Patient Age: 0-7 Days

Change antibiotic treatment:
1. Confirm meningitic dose of Ampicillin (Redose if needed)
2. Add Cefotaxime (Use Cefepime if supply unavailable)
3. Consider HSV testing and Acyclovir therapy

Patient Age: 8-28 Days

Change antibiotic treatment:
1. Confirm meningitic dose of Ampicillin (Redose if needed)
2. Add Ceftriaxone | Confirm meningitic dosing
   (Use Cefepime if contraindicated ❶)
3. Consider HSV workup and Acyclovir therapy

ADD antiviral treatment: Acyclovir

ADMIT to Inpatient Management Pathway
Fever Without a Source
Age: 29-60 Day Pathway - Emergency Department
Evidence Based Outcome Center

INCLUSION CRITERIA
Non-toxic with temperature > 38°C (100.4°F) OR < 36°C (96.5°F) measured in Emergency Department OR reported measurement at home.

Order labs:
☑ Complete Blood Count with differential
☑ Blood Culture
☑ Basic metabolic panel
☑ Urinalysis with Micro
☑ Urine Culture: Catheter or Suprapubic
☐ Stool culture & Stool WBC (if patient has diarrhea)

Focal bacterial infection

Manage OFF-PATHWAY

YES

NO

Meets Low Risk Criteria

YES

NO

DISCHARGE Home Follow-up in 24 hours
No Antibiotics

CSF Collected

YES

CSF Pleocytosis and suspicion of meningitis OR CSF Gram stain positive

NO

OPTION 1

OPTION 2

OPTION 3

Empiric antibiotic treatment: Ceftriaxone

Empiric antibiotic treatment: Ceftriaxone + Vancomycin

ADMIT for Observation

DISCHARGE Home Follow-up in 24 hours
Patient family & PCP must be in agreement

ADMIT to Inpatient
Manage OFF-PATHWAY

EXCLUSION CRITERIA
Toxic appearing
No fever
Born < 37 weeks gestational age

Low Risk Criteria for Serious Bacterial Infection

Historical and Clinical Features
29-60 days
Full-term (≥ 37 weeks gestation)
No prolonged NICU stay
No chronic medical problems
No systemic antibiotics within 72 hours
Well-appearing and easily consolable
No focal infections on exam

Fecal Leucocytes
Stool WBC ≤ 5 hpf

Blood
WBC ≥ 5,000 AND ≤ 15,000
Immature WBC/neutrophil Ratio < 0.2
Absolute Band Count < 1500/mm³

Standard UA:
WBC < 5/HPF
Negative LE, Nitrite, Bacteria

Chest X-ray (if obtained)
No infiltrate

Normal CSF Values
0-20 WBC/mm³
Protein 0 - 30 days: < 100 mg/dL
Normal Gram Stain

First Updated October 25, 2017
For questions concerning this pathway, Click Here

Last Updated October 25, 2017
Fever Without a Source
Risk Factors for UTI and Screening Recommendations
Evidence Based Outcome Center

<table>
<thead>
<tr>
<th>&gt; 2 months – Not Toilet Trained</th>
<th>Toilet Trained – 18 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of UTI &gt; 1%:</td>
<td>Probability of UTI &gt; 1%:</td>
</tr>
<tr>
<td>2 or more risk factors</td>
<td>Uncircumcised</td>
</tr>
<tr>
<td><strong>Female Risk Factors</strong>*</td>
<td>OR</td>
</tr>
<tr>
<td>Non-black</td>
<td>Circumcised with 3 or more Risk Factors</td>
</tr>
<tr>
<td>( T \geq 39°C )</td>
<td></td>
</tr>
<tr>
<td>Fever ( \geq 2 ) days</td>
<td></td>
</tr>
<tr>
<td>No apparent source of fever</td>
<td></td>
</tr>
<tr>
<td>Age &lt; 12 months</td>
<td></td>
</tr>
</tbody>
</table>

| Probability of UTI > 1%:       | All Patients |
| 2 or more risk factors         | Symptoms referable to urinary tract |
| **Male Risk Factors***         | Prior history of UTI, fever \( \geq 2 \) days |
| Non-black                       | Prolonged fever (\( \geq 5 \) days) |
| \( T \geq 39°C \)               |                           |
| Fever \( \geq 2 \) days        |                           |
| No apparent source of fever    |                           |
| Age < 6 months                  |                           |

*Recommend screening if prior history of UTI, fever \( \geq 2 \) days

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Emergency Department Pathway
0-28 Days  29-60 Days  2-6 Months

Inpatient Pathway

For questions concerning this pathway, 
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Last Updated October 25, 2017
### Low Risk Criteria for Serious Bacterial Infection

#### Historical and Clinical Features
- 29-60 days
- Full-term (≥ 37 weeks gestation)
- No prolonged NICU stay
- No chronic medical problems
- No systemic antibiotics within 72 hours
- Well-appearing and easily consolable
- No focal infections on exam

#### Fecal Leucocytes
- Stool WBC ≤ 5 hpf

#### Blood
- WBC ≥ 5,000 AND ≤ 15,000
- Immature WBC/neutrophil Ratio < 0.2
- Absolute Band Count < 1500/mm³

#### Standard UA:
- WBC < 5/HPF
- Negative LE, Nitrite, Bacteria

#### Chest X-ray (if obtained)
- No infiltrate
Patients with any of the following conditions should be considered for a Herpes Simplex Virus work up and empirical treatment:

### Historical and Clinical Features

- Severe illness / Hypothermia / Lethargy
- Seizures
- Hepatosplenomegaly
- Postnatal HSV contact
- Vesicular rash
- Conjunctivitis
- Interstitial pneumonitis

### Laboratory Findings

- Thrombocytopenia
- CSF pleocytosis
  - without clear bacterial infection
- Transaminitis

**Herpes Simplex Virus Workup Consists of the following labs:**

- [x] HSV DNA PCR of Blood
- [x] Meningitis/Encephalitis PCR Panel of CSF
- [x] Swab/scraping of skin or mucous membrane lesions for HSV DFA AND HSV culture
- [x] Surface HSV cultures in viral transport media tube
  - [x] Conjunctiva
  - [x] Throat
  - [x] Nasopharynx
  - [x] Rectum
  - [x] Skin vesicle (if present)
DCMC Positive Urinalysis (UA) Definition: The presence of Leukocyte Esterase OR Nitrites OR microscopic analysis results positive for leukocytes or bacteria is suggestive of an active UTI. When more than one of these findings is present at the same time, the sensitivity and specificity increase significantly.

Dell Children’s and Seton Family of Hospitals does not currently perform an enhanced urinalysis on urine specimens routinely. The following criteria are guide in diagnosing a UTI in young children using the standard method of collection and processing.

<table>
<thead>
<tr>
<th>Diagnostic</th>
<th>Interpretation</th>
</tr>
</thead>
</table>
| Nitrites            | • Poor sensitivity: Conversion of nitrates to nitrites by bacteria takes approximately 4 hours and not all bacteria reduce nitrate levels combined with frequency of infants voiding.  
                      • Helpful when positive. Few false positives and high specificity.                                                                    |
| Leukocyte Esterase  | • Positive leukocyte esterase is suggestive of a UTI. However, children may have WBC present in their urine in conditions other than a UTI (e.g. Kawasaki Disease) |
| White Blood Cells   | Positive if:  
                      • ≥ 5 WBC per HBF via standard method  
                      Pyuria is absent in approximately 10% of children with a UTI |
| (WBC) - Pyuria      |                                                                                                                                            |
| Bacteriuria         | Presence of bacteriuria alone in the absence of other findings does not define a UTI.                                                                 |

**Culture**

<table>
<thead>
<tr>
<th>Method</th>
<th>Definite*</th>
<th>Indeterminant†</th>
<th>Contaminant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suprapubic</td>
<td>Any growth</td>
<td></td>
<td>Growth of non-pathogens, Mixed culture</td>
</tr>
<tr>
<td>Catheter</td>
<td>≥ 50,000</td>
<td>≥ 10,000</td>
<td>Growth of non-pathogens, Mixed culture, &lt; 10,000 CFU/ml</td>
</tr>
<tr>
<td></td>
<td>CFU/ML</td>
<td>CFU/ML</td>
<td></td>
</tr>
</tbody>
</table>

* If also with presence of pyuria or bacteriuria  
† Consider obtaining repeat specimen  
Mixed Culture = uropathogen + non-pathogen or two uropathogens  
Bag UA specimens should never be sent for urine culture. Only catheter or suprapubic methods are appropriate for culture collection in this age.

**Uropathogens**

<table>
<thead>
<tr>
<th>Gram Negative</th>
<th>Gram Positive</th>
<th>Non-pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli (~80%)</td>
<td>Staphylococcus saprophyticus</td>
<td>Lactobacillus</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>Enterococcus</td>
<td>Coagulase-negative Staph</td>
</tr>
<tr>
<td>Proteus</td>
<td>Staphylococcus aureus</td>
<td>Corynebacterium</td>
</tr>
<tr>
<td>Enterobacter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citrobacter</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For questions concerning this pathway,  
Click Here  
Last Updated October 25, 2017
### Fever Without a Source
Antimicrobial and Antiviral Dose Recommendations

**Evidence Based Outcome Center**

<table>
<thead>
<tr>
<th>Drug[^a,b,c,d]</th>
<th>Dose</th>
<th>Duration[^e]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ampicillin</strong></td>
<td>NON-MENINGITIC ≤ 7 days of age: 50 mg/kg/dose IV q8h&lt;br&gt;NON-MENINGITIC &gt; 7 days of age: 50 mg/kg/dose IV q6h&lt;br&gt;MENINGITIC ≤ 7 days of age: 100 mg/kg/dose IV q8h&lt;br&gt;MENINGITIC &gt; 7 days of age: 100 mg/kg/dose IV q6h</td>
<td>5 doses&lt;br&gt;6 doses&lt;br&gt;5 doses&lt;br&gt;6 doses</td>
</tr>
<tr>
<td><strong>Cefepime</strong></td>
<td>50 mg/kg/dose IV q8h</td>
<td>5 doses</td>
</tr>
<tr>
<td><strong>Cefotaxime</strong></td>
<td>≤ 7 days of age: 50 mg/kg/dose q8h&lt;br&gt;7 days of age: 50 mg/kg/dose q6h</td>
<td>5 doses&lt;br&gt;6 doses</td>
</tr>
<tr>
<td><strong>Ceftriaxone[^d]</strong></td>
<td>If to be admitted: 50 mg/kg/dose IV q12h&lt;br&gt; If to be discharged: 50-100 mg/kg/dose IV (ED ONLY)</td>
<td>3 doses&lt;br&gt;1 dose</td>
</tr>
<tr>
<td><strong>Gentamicin[^b]</strong></td>
<td>4 mg/kg/dose IV q24h</td>
<td>2 doses</td>
</tr>
<tr>
<td><strong>Vancomycin[^c]</strong></td>
<td>≤ 7 days of age: 20 mg/kg/dose IV q8h&lt;br&gt; &gt; 7 days of age: 20 mg/kg/dose IV q6h</td>
<td>5 doses&lt;br&gt;6 doses</td>
</tr>
</tbody>
</table>

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[^a]: Dosing in this table is for patients with normal renal function. Please contact pharmacy for assistance with dosing in renal insufficiency.

[^b]: For gentamicin, serum drug levels are not necessary unless treatment is anticipated or continued for more than 2 doses, SCr is increased more than 0.3 mg/dL from normal value for age, or UOP less than 1 ml/kg/hr.

[^c]: For vancomycin, serum drug levels are not necessary unless treatment is anticipated or continued for more than 2 doses, SCr is increased more than 0.3 mg/dL from normal value for age, or UOP less than 1 ml/kg/hr.

[^d]: Ceftriaxone is contraindicated with calcium containing IV products or hyperbilirubinemia. Meningitic dosing of ceftriaxone is 80-100 mg/kg/day divided every 12-24 hours but CSF concentrations are optimal when dosed at 50mg/kg/dose IV q12h; once daily dosing should be reserved for patients to be discharged from the ED.

[^e]: If cultures become positive at any time, treat specific condition, narrow agent and lengthen antibiotic duration as appropriate.

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### Recommended Dose for UTI

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin</td>
<td>17 mg/kg/dose q8h</td>
<td>7 Days</td>
</tr>
</tbody>
</table>

### Recommended Dose for Antiviral

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>20 mg/kg/dose IV q8h</td>
<td>5 doses OR until HSV surface cultures AND PCR Blood &amp; CSF negative&lt;br&gt;Exceptions: Seizures, Lethargy, or ongoing Fever</td>
</tr>
</tbody>
</table>

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