**Definition:** An acute febrile illness (temperature ≥100.4°F [38°C]) with uncertain etiology after completion of a thorough history and physical examination. *(1-3)*

**Etiology:** The most common cause of fever without localizing signs (FWLS) is a viral infection. The challenge lies in the difficulty of distinguishing serious bacterial illness (SBI) from viral illness in neonates and early infancy. *(4,5)*

**Inclusion Criteria:**
- Age 0-60 days (Term infants ≥37 weeks gestation)
- Neonates and infants without underlying conditions
- Actual rectal temp ≥100.4°F (38°C) OR reported temp (axillary or rectal) of ≥100.4°F (38°C) in home setting

**Exclusion Criteria:**
- History of prematurity
- Underlying conditions that affect immunity or may otherwise increase risk of SBI
- Toxic/Septic appearance
- Receiving antibiotic treatment for FWLS
- Routine vaccinations given within the previous 48 hours
- Presenting with seizures
- Requiring intensive care management
- Identified focus of infection (e.g., cellulitis, acute otitis media in infants >28 days old)

**Differential Diagnosis:**
- Meningitis
- Bone and joint infections
- Pneumonia
- Urinary tract infection
- Sepsis/Bacteremia
- Enteritis
- Herpes Simplex Virus (HSV) infection
- Enterovirus
- Parechovirus
- SARS-CoV-2 Virus

**Toxic Criteria** *(6,7)*
Infants that meet ANY of the toxic criteria should receive a full sepsis workup and be admitted to the inpatient area for antibiotic therapy and observation (See Tables 1 & 2).

**Signs/Symptoms include:**
- Poor perfusion
- Capillary refill time >2 seconds
- Cyanosis
- Lethargy
- Unable to console
- Tachypnea or bradypnea
- Hypothermia (96.8°F/36°C)

**Table 1. Signs and Symptoms of Shock** *(8,9)*

<table>
<thead>
<tr>
<th>Pulses (central vs. peripheral)</th>
<th>Capillary refill (central vs. peripheral)</th>
<th>Skin</th>
<th>Mental status</th>
<th>Warm Shock</th>
<th>Cold Shock</th>
<th>Non-specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased or weak</td>
<td>≥3 sec</td>
<td>Mottled, cool</td>
<td>Bounding</td>
<td>Decreased, weak</td>
<td>Flash (&lt;1 sec)</td>
<td>Petechiae below the nipple, any purpura</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flushed, ruddy, erythrodema (other than face)</td>
<td>Decreased, irritability, confusion inappropriate crying or drowsiness, poor interaction with parents, lethargy, diminished arousability, obtundation</td>
</tr>
</tbody>
</table>

*† HR followed by ↓ HR with BP changes will be noted as shock becomes uncompensated.*

**Table 2. Vital Sign Changes of Sepsis** *(8,8)*

<table>
<thead>
<tr>
<th>Age</th>
<th>Heart Rate</th>
<th>Respiratory Rate</th>
<th>Systolic BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0d - 1m</td>
<td>&gt;205</td>
<td>&gt;60</td>
<td>&lt;60</td>
</tr>
<tr>
<td>&gt;1m to 3m</td>
<td>&gt;205</td>
<td>&gt;60</td>
<td>&lt;70</td>
</tr>
</tbody>
</table>

†BP changes are late signs of worsening condition. May also present with chills.

**Diagnostic Evaluation:** In this age group, bacterial pathogens associated with FWLS may include Gram-positive organisms (such as group B Streptococcus, Enterococcus, group A Streptococcus, Staphylococcus aureus, Listeria monocytogenes) and Gram-negative organisms (such as Escherichia coli, Enterobacter, Klebsiella). Streptococcus pneumoniae is more likely to occur in infants >30 days old. *(10,11)*

Viral pathogens, such as enterovirus, adenovirus, herpes simplex virus, influenza virus, and parainfluenza virus, are also a concern in this patient population. *(12,13)* There is limited research available on the incidence of SARS-CoV-2 in infants, however preliminary data shows that children, including infants, seem to range from asymptomatic to moderate disease severity. *(14)*
**History: Assess for**

- Onset of fever
- Immunization status (15)
- Irritability
- Poor feeding
- Decreased urine output
- Exposure to infectious agents
  - Other sick contacts/family members
  - Maternal fever at time of delivery
  - Maternal Group B streptococcal vaginal colonization
  - Maternal HSV infection

**Physical Examination:**

Rectal temperatures are preferred to axillary or other methods of temperature measurements. A thorough clinical history and physical examination are essential to determine risk of SBI or identify focus of infection. (16,17)

---

**Table 3. Laboratory Tests**

<table>
<thead>
<tr>
<th>Test</th>
<th>0-28 days</th>
<th>29 to 60 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count (CBC) with differential and platelets</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Blood culture (BC) (obtain prior to antibiotic administration)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>Optional</td>
<td>X</td>
</tr>
<tr>
<td>Enterovirus CSF PCR</td>
<td>X</td>
<td>High risk patients in peak season</td>
</tr>
<tr>
<td>Urinalysis (UA) with micro and culture (obtain specimen via cath or SPA† only)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Lumbar puncture* (LP) [gram stain, culture, cell count and diff, glucose, protein, viral culture‡]</td>
<td>X</td>
<td>Based on risk classification</td>
</tr>
<tr>
<td>HSV testing (blood, CSF, swab specimens, cultures of vesicles)</td>
<td>If HSV risk factors present or worsening condition</td>
<td></td>
</tr>
</tbody>
</table>

**Consider:** (18-26)

- Stool for culture and presence of WBCs (if diarrhea present)
- Viral diagnostic testing or rapid tests (if respiratory symptoms)
- Chest X-ray (if respiratory symptoms; WBC >20,000/mm³ or ANC >10,000/mm³)
- Blood and/or CSF parechovirus PCR during peak season - May to October (if febrile and other viral/bacterial cultures negative)

- † Cath (transurethral catheterization) or SPA (suprapubic aspiration)
- *LP should be performed prior to antibiotic administration
- ‡ Tube #1 Glucose, protein
- Tube #2 Cell count & diff, Gram stain & culture
- HOLD Tube #3 in virology lab

---

**Herpes Simplex Virus**

Evidence shows that there is an increase of the risk of mortality for disseminated HSV with each day of delayed treatment. (25) National guidelines support the consideration of HSV infection as a causative agent for neonates with fever. (26) Laboratory evaluation for neonatal HSV infections should be performed for those with clinical findings suggestive of HSV infection or a maternal history of HSV. (27-30)

**HSV Risk Factors** (29)

- Maternal primary HSV infection
- Maternal fever
- Vaginal delivery
- Prematurity
- Neonatal seizures
- Vesicular rash
- CSF pleocytosis (monocytosis)
- Elevated hepatic enzymes

**Signs/Symptoms of Systemic HSV** (30)

- Skin, eye, and mouth lesions/disease
- Seizures, lethargy, and fever
- Disseminated form - neonate presents with multi-organ failure

The laboratory tests below are recommended if HSV suspected. (26)

- Specimens of skin vesicles for HSV culture or PCR
- CSF sample for HSV PCR
- Whole blood sample for HSV PCR
- Swab specimens from the mouth, nasopharynx, conjunctiva, and anus for HSV culture (completed in-hospital) or PCR (currently a send-out lab)
  - To collect swab specimens for culture, the practitioner may utilize one swab for the eye, mouth, nose and rectum in stated order. Different swabs may be used for each specimen location; however, if this method is used the practitioner should put all swabs in the same transport tube.
**Critical Points of Evidence**

**Evidence Supports**

- Complete HSV testing and administer empiric acyclovir for neonates with no identified bacterial pathogen in CSF and the presence of CSF pleocytosis and/or exam, concern or possible maternal history of HSV, and/or toxic appearance. (25,27,31-34) – Strong recommendation, low quality evidence  
  **Remarks:** Neonates with age less than or equal to 21 days present a heightened concern for HSV.
- Administer empiric antibiotic therapy of ampicillin and gentamicin for all neonates (0-28 days). If there is a concern for meningitis or CSF pleocytosis, cefTAZidime should be administered in lieu of gentamicin. (33,36) – Strong recommendation, low quality evidence
- In well-appearing infants 0 - 60 days of age with fever without localizing signs (FWLS) as well as negative cultures and laboratory assessments, discharge should be considered at 36 hours if not already done. (37-42) – Strong recommendation, low quality evidence
- Enterovirus testing (during peak season) should be utilized in addition to usual care in order to decrease length of stay. (43,44) – Strong recommendation, low quality evidence
- Infants 0-60 days with fever without localizing signs should be tested for enterovirus during peak season regardless of the presence of CSF pleocytosis (*TCH PCR positivity data plus expert consensus indicates that peak season will likely occur from May through October). (44-46) – Strong recommendation, low quality evidence
- Enterovirus PCR CSF should be used for testing when CSF specimen is available. (*This recommendation is also based on rapid turnaround time of CSF PCR as compared to serum PCR at TCH.) (18,48-50) – Strong recommendation, low quality evidence
- Enterovirus-positive infants 0-28 days old should have a minimum of 24 hours of hospital monitoring of bacterial cultures (18,19,48) – Weak recommendation, low quality evidence
- Enterovirus-positive infants 29-60 days old do not need further inpatient monitoring of bacterial cultures once enterovirus result is known. If otherwise meeting discharge criteria, enterovirus positive 29-60 day old infants can be discharged with a dose of ceftriaxone and close pediatrician follow-up. (*Recommendations based on expert consensus plus epidemiologic evidence showing low rates of SBI. SBI seems more common in neonates and those that are high risk.*) (18,19,48) – Weak recommendation, low quality evidence
- Consider CSF parechovirus testing during peak season (May to October) when other viral (e.g., enterovirus, HSV) and bacterial etiologies have been ruled out. (20-23,51,52) – Weak recommendation, low quality evidence
- The diagnostic work-up for neonatal HSV infection should include all of the laboratory tests listed below. (26)
  - Specimens of skin vesicles for HSV culture or PCR
  - CSF sample for HSV PCR
  - Whole blood sample for HSV PCR
  - Swab specimen from the mouth, nasopharynx, conjunctivae, and anus for HSV culture (completed in-house) or PCR (currently a send-out lab)
  - **Remarks:** To collect swab specimens for culture, the practitioner may utilize one swab for the eye, mouth, nose and rectum in stated order. Different swabs may be used for each specimen location; however, if this method is used the practitioner should put all swabs in the same transport tube.
- A modified PECARN rule with the cut-off points below should be used as a predictor for SBI in patients 29 – 60 days old with FWLS. (53-66)
  - Negative urinalysis
  - Absolute neutrophil count (ANC) 1000 – 4000/µL
  - Serum procalcitonin level less than 0.5 ng/mL
  - **Remarks:** The PECARN clinical prediction rule for infants with FWLS should not be utilized in patients with fever duration less than 6 hours. The prediction score was not validated to determine SBI risk in neutropenic patients; therefore, we have included a lower limit for the ANC level.

**Evidence Against**

- AST and/or ALT lab tests should not routinely be used for screening for disseminated HSV in all infants 0-28 days with fever. (30,31,67-70) – Strong recommendation, low quality evidence

**Condition-Specific Elements of Clinical Management**

**Treatment Recommendations** (65,66)

**Table 4. PECARN Low Risk Lab Criteria for 29-60 day old infants with fever duration greater than 6 hours (All three criteria must be met)**

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinalysis with micro (cath or SPA specimen)</td>
<td>Negative</td>
</tr>
<tr>
<td>Absolute Neutrophil Count (ANC)</td>
<td>1000 – 4000 /µL</td>
</tr>
<tr>
<td>Serum Procalcitonin</td>
<td>&lt;0.5 ng/ml</td>
</tr>
</tbody>
</table>

**Table 5. Inpatient Monitoring and Outpatient Management Criteria** (18,19,37-42,48-50)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Inpatient Monitoring</th>
<th>Possible Outpatient Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>All infants ≤28 days old</td>
<td>High risk enterovirus negative 29-60 day old infants</td>
<td></td>
</tr>
<tr>
<td>High risk enterovirus positive 29-60 day old infants</td>
<td><strong>Possible Outpatient Management</strong></td>
<td></td>
</tr>
<tr>
<td>Enterovirus positive 29-60 day old infants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk 29-60 day old infants</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Neonates (≤28 days):
If presenting in clinic setting, refer to EC.
Evaluate with a full sepsis workup and admit to the inpatient area for antibiotic therapy and observation. (18,26,27,31-34,48-50)
Complete HSV testing and administer empiric acyclovir for neonates with no identified bacterial pathogen in CSF and the presence of CSF pleocytosis and/or exam, concern or possible maternal history of HSV, and/or toxic appearance. (26,27,31-34) Neonates with age less than or equal to 21 days present a heightened concern for HSV.
Empiric antibiotic therapy of ampicillin and gentamicin should be initiated on all neonates. If there is a concern for meningitis or CSF pleocytosis, ampicillin and cefTAZidime should be administered. (35,36)
Enterovirus-positive infants 0-28 days old are eligible for discharge after 24 hours of monitoring. (18,19,48)

Infants ≥ 29 days:
If laboratory values do not meet PECARN Rule low risk criteria, an LP is indicated (Table 4). Antibiotics should not be administered until after LP is obtained. If LP is difficult to obtain, do not delay treatment.
Low-risk infants 29 – 60 days old can be managed outpatient if meeting discharge criteria. Enterovirus-positive infants 29-60 days old should be managed outpatient once enterovirus result is known if meeting all other discharge criteria (Table 5). (18,19,48) A dose of ceTRIAXone may be provided.
A penicillin and a third generation cephalosporin are recommended as first-line therapy. For infants >6 weeks old, clinicians may consider third generation cephalosporin monotherapy. Meningitic dosing should be initiated until CSF test results have been reviewed and CNS involvement has been ruled out.

Follow-up Care
Healthcare provider to follow up on blood and urine cultures (if discharged before 48 hours)
Healthcare provider to call lab for CSF culture interpretation prior to discharge.
Follow-up appointment with PCP 12-24 hours post-discharge.
Return to PCP/EC if worsening symptoms

Inpatient/Observation Discharge Criteria
- Decreasing fever curves
- Well-appearing with no evolution of signs/symptoms
- Tolerating oral intake and maintaining hydration status
- Reliable follow-up available 12-24 hours post-discharge
- Caregiver and PCP agree with plan
- Caregiver understands discharge education

<table>
<thead>
<tr>
<th>Patient Criteria</th>
<th>In-hospital Observation Time to Monitor Blood Cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 28 Days Enterovirus Negative</td>
<td>36 hours</td>
</tr>
<tr>
<td>0 – 28 Days Enterovirus Positive</td>
<td>24 hours</td>
</tr>
<tr>
<td>29 – 60 Days High Risk Enterovirus Negative</td>
<td>36 hours</td>
</tr>
<tr>
<td>29 – 60 Days Low Risk OR Enterovirus Positive</td>
<td>Outpatient Treatment</td>
</tr>
</tbody>
</table>

Measures
Outcome
- Length of stay
- # of readmissions for same problem
- Type of follow-up post EC or Inpatient discharge (phone call vs. visit to PCP)
- # of infants >28 days with LP vs. no LP based on risk criteria
- EC treatment plan for infants after LP performed vs. infants without LP performed
- # of call backs for positive blood cultures
- # of call backs for positive urine cultures for patients with negative UA
- # of enterovirus positive patients with concomitant serious bacteria infection

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Table 5. Antibiotic Dose Administration Table (71)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Empirical Parenteral Therapy</strong> (IV)</td>
<td></td>
</tr>
<tr>
<td><strong>Ampicillin</strong></td>
<td>≤7 days: 100 mg/kg/DOSE every 8 h</td>
</tr>
<tr>
<td></td>
<td>&gt;7 days: 75 mg/kg/DOSE every 6 h</td>
</tr>
<tr>
<td></td>
<td>If concern for meningitis: 75 mg/kg/DOSE every 6 hours</td>
</tr>
<tr>
<td><strong>Gentamicin Sulfate</strong></td>
<td>PNA ≤7 days: 4 mg/kg/DOSE every 24 h</td>
</tr>
<tr>
<td></td>
<td>PNA &gt;7 days: 5 mg/kg/DOSE every 24 h</td>
</tr>
</tbody>
</table>

Use in lieu of gentamicin for suspected meningitis or CSF pleocytosis

| **CefTRIAXone** | Neonates: |
| | 0-28 days: 50 mg/kg/DOSE every 8 h |
| | NOTE: Recommended usage to: |
| | - Neonatal patients (defined as ≤44 weeks postmenstrual age OR neonates <1 month of age) |

Treatment of choice for suspected *Staphylococcus* (10)

| **Vancomycin** | <7 days old: |
| | >2,000 g: 10 to 15 mg/kg/DOSE every 8 to 12 hours |
| | ≥7 to 28 days: |
| | >2,000 g: 10 to 15 mg/kg/DOSE every 6 to 8 hours |

Treatment of choice for Herpes Simplex Virus (HSV)

| **Acyclovir** | Neonates and Infants: |
| | 20 mg/kg/DOSE every 8 h |

Table 6. Antibiotic Dose Administration Table (71)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outpatient or Emergency Center Empirical Therapy (IM/IV)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CefTRIAXone</strong></td>
<td>Infants &gt;28 days: 50 mg/kg/DOSE once</td>
</tr>
<tr>
<td><strong>Empirical Parenteral Therapy</strong> (IV)</td>
<td></td>
</tr>
<tr>
<td><strong>Ampicillin†</strong></td>
<td>Infants &gt;28 days and children:</td>
</tr>
<tr>
<td></td>
<td>Mild to moderate infection, IV: 12.5-50 mg/kg/DOSE every 6 hours</td>
</tr>
<tr>
<td></td>
<td>Meningitis or other severe infection, IV: 75-100 mg/kg/DOSE every 6 hours OR 50-67 mg/kg/DOSE every 4 hours</td>
</tr>
<tr>
<td><strong>CefTRIAXone†</strong></td>
<td>Infants &gt;28 days:</td>
</tr>
<tr>
<td></td>
<td>General Dosing, IV: 50 mg/kg/DOSE every 24 hours</td>
</tr>
<tr>
<td></td>
<td>Meningitis, IV: 50 mg/kg/DOSE every 12 hours</td>
</tr>
<tr>
<td></td>
<td>NOTE: Not for use in patients receiving Y-site administration of calcium-containing IV fluids with a single lumen or single IV site</td>
</tr>
<tr>
<td></td>
<td>Not for use in infants &lt;44 weeks postmenstrual age OR neonates &lt;1 month of age</td>
</tr>
<tr>
<td></td>
<td>*Use cefTRIAXone as an alternative</td>
</tr>
</tbody>
</table>

Treatment of choice for suspected *Staphylococcus* (10)

| **Vancomycin** | Infants >28 days to 60 days: |
| | 15 mg/kg/doe every 8 hours |

†Reduce antibiotics to general dosing for suspected infection once meningitis ruled out.
TCH Evidence-Based Outcomes Center Clinical Algorithm
Neonates & Infants with Fever Without Localizing Signs (FWLS) 0-28 days

Begin

Fever ≥ 100.4°F (38°C)

Yes

Well appearing with NO source of infection

Yes

OFF algorithm Manage as appropriate to clinical findings

No

OFF algorithm Manage as appropriate to clinical findings

Exclusion Criteria:
- History of prematurity
- Underlying conditions that affect immunity or may otherwise increase risk of Serious Bacterial Infection
- Toxic/Sepsic in appearance
  - Currently receiving abx for FWLS
  - Received routine immunizations within 48 hours of presentation
  - Presents with seizures
  - Requires ICU management
  - Has an identified focus of infection

Concern for bacterial meningitis (Bacterial Meningitis Score should NOT be used in this population)

Admit to ICU

Administer cefazidime in lieu of gentamicin for antibiotics

OFF Algorithm

Concern for Bacterial UTI

Admit to Acute Care

Manage as appropriate to clinical findings

OFF Algorithm

Concern for HSV

Admit to Acute Care

Administer scheduled Acyclovir

OFF algorithm Manage as appropriate to clinical findings

No concern for bacterial meningitis, UTI and HSV

Admit to Acute Care

Add on Enterovirus CSF PCR if in peak season if specimen available (May - October)

Enterovirus CSF PCR Positive

Yes

Monitor inpatient for 36 hours

Negative Cultures, afebrile and continued well appearance

Yes

Consider discharge if:
- Reliable EC or PCP follow-up in 12-24 h
- Adequate caregiver education
- PCP & caregiver agree with plan

If worsening signs/symptoms, consider additional diagnostic testing for alternate source, and treat as appropriate

OFF algorithm

Recommended HSV Labs:
- HSV PCR from CSF and blood
- Swab specimens from mouth, nasopharynx, conjunctivae, and anus for HSV culture (competed in-hospital) or PCR (currently a send-out lab)
- Specimens of skin vesicles if present for PCR

Further Instructions: To collect swab specimens for culture, the practitioner may utilize one swab for each specimen location; however, if this method is used the practitioner should put all swabs in the same transport tube.

Enterovirus CSF PCR Negative

No

Monitor in hospital with IV antibiotics.
- If bacterial cultures negative at 24 hours, patient may be discharged if:
  - Reliable EC or PCP follow-up in 12-24 h
  - Adequate caregiver education
  - PCP & caregiver agree with plan

- CBC w/ diff
- Blood cultures
- UA with micro & culture
- LP (gram stain, culture, cell count & diff, protein, glucose, HOLD tube #3 in virology if collected)
- IV Antibiotics (Start ampicillin/gentamicin)
- If concerned about HSV*, send recommended HSV labs
- Consider other viral work-ups

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6
TCH Evidence-Based Outcomes Center Clinical Algorithm
Neonates & Infants with Fever Without Localizing Signs (FWLS)
29-60 days

**Low Risk Criteria by PECARN Rule‡:**
- Patients Meeting All Three Criteria Below
  - Negative Urinalysis
  - No leukocyte esterase, nitrite or pyuria (>5 WBC/hpf)
  - ANC 1000 – 4000
  - Serum procalcitonin <0.5 ng/mL

**Low Risk Lab criteria‡ by PECARN Rule:**
- CBC
- Blood Culture
- UA with micro & culture*
- Procalcitonin

**Compare lab results to PECARN Low Risk Criteria‡:**

**Discharge Criteria§:**
- Reliable EC or PCP follow-up in 12-24 h
- Adequate caregiver education
- PCP & caregiver agree with plan

**Septic Shock Criteria:**
Immediately refer to the Septic Shock guideline and intervene rapidly if patient has toxic-appearance, ill-appearance, altered mental status, and/or compromised perfusion with abnormal vital signs

**Exclusion Criteria:**
- History of prematurity
- Underlying conditions that affect immunity or may otherwise increase risk of Serious Bacterial Infection
- Toxic/Septic in appearance
- Currently receiving antibiotics for FWLS
- Received routine immunizations within 48 hours of presentation
- Presents with seizures
- Requires ICU management
- Has an identified focus of infection

**OFF algorithm**
Manage as appropriate to clinical findings

**Well appearing with NO source of infection**

**Fever ≥ 100.4°F (38°C)**

**Begin**

**Administer antibiotics Admit to ICU Off Algorithm**

**Enterovirus positive**
Give a dose of ceftriaxone
Discharge home if meeting all other discharge criteria

**Enterovirus negative**

**Admit to Acute Care Add Enterovirus CSF PCR to labs if in peak season if specimen available (May – October)**

**Concern for Bacterial Meningitis***
*(Bacterial Meningitis Score should NOT be used in this population)*

**Administer empiric antibiotics OR Observe with no antibiotics**

**Clinically well & cx neg ≥ 36 h**

**Consider discharge if meeting criteria§**

**Treat as appropriate OFF algorithm**

**All other patients**

**Perform LP†**

**Concern for Bacterial Meningitis***

**Administer antibiotics Admit to ICU Off Algorithm**

**Enterovirus negative**

**Administer empiric antibiotics**

**Enterovirus positive**

**Give a dose of ceftriaxone Discharge home if meeting all other discharge criteria**

**Discharge Criteria§:**
- Reliable EC or PCP follow-up in 12-24 h
- Adequate caregiver education
- PCP & caregiver agree with plan

**Obtain urine specimen via cath or SPA only**

**†Antibiotics should not be administered until after LP is obtained if needed. If LP difficult to obtain, do not delay treatment.**

**‡Antibiotics should not be administered until after LP is obtained if needed. If LP difficult to obtain, do not delay treatment.**

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References

24. Texas Children's Hospital Pathology Online Lab Catalog. (2011). http://intranet.tch.tmc.edu/catalog/pathcatalog.htm


Clinical Standards Preparation
This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children’s Hospital. Development of this clinical standard is supported by the TCH Quality and Patient Safety Program to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

Fever Without Localizing Signs 0-60 Days Content Expert Team
Joseph Allen, MD, Emergency Medicine
Andrea Cruz, MD, Emergency Medicine
Charlyn Davis, RN, Emergency Medicine Nursing
James Dunn, PhD, Pathology
Catherine Foster, MD, Infectious Disease
Lakshmi Katakam, MD, Neonatology
Lucila Marquez, MD, Infectious Disease
Brent Mothner, MD, Pediatric Hospital Medicine
Aderonke Ojo, MD, Emergency Medicine
Debra Palazzi, MD, Infectious Disease
Minal Patel, MD, Neonatology
Sunjee Patel, MD, Texas Children’s Pediatrics
Autumn Pruette, MD, Texas Children’s Pediatrics
Paula Revell, PhD, Pathology
Emily Rodman, PharmD, Pharmacy
Latissah St Julian, RN, Acute Care Nursing
Joe Tran, MD, Pediatric Hospital Medicine
Sowdhamini Wallace, MD, Pediatric Hospital Medicine
Elizabeth Wuestner, RN, Emergency Center Nursing

Additional EBOC Support
Betsy Lewis, MSN, RN, CNL, Evidence-Based Practice Specialist
Sheesha Porter, MSN, RN, Evidence-Based Practice Specialist
Anne Dykes, MSN, RN, ACNS-BC, Manager
Warren Boudreau, MSN, RN, Director

The following financial and/or intellectual conflict(s) was/were identified and addressed to ensure objectivity: Content Expert Team member A. Cruz, MD author of research on clinical decision rules and management of HSV.

Development Process
This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
   - Management of Infants 0-60 Days with Fever of Unknown Source, Cincinnati Children’s Hospital; Neonatal Fever, Seattle Children’s Hospital; Evaluation/Treatment of Febrile Young Infants (0-56 Days), Children’s Hospital of Philadelphia; Red Book – Report of Committee of Infectious Disease, American Academy of Pediatrics
3. Literature Review of Relevant Evidence
   - Searched: Medline, Cochrane, Cinhahl, AAP, BMJ Clinical Evidence, Google Scholar
4. Critically Analyze the Evidence
   - 2 meta-analyses, 41 non-randomized studies, and 4 review articles
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a FWLS 0-60 Days electronic manual within EBOC.

Evaluating the Quality of the Evidence
Published clinical guidelines were evaluated for this review using the AGREE II criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence in support of or against specific interventions and identifies where evidence is lacking/inconclusive. The following categories describe how research findings provide support for treatment interventions.

- **Evidence Supports** provides evidence to support an intervention.
- **Evidence Against** provides evidence against an intervention.
- **Evidence Lacking/Inconclusive** indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn from the evidence.

The GRADE criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong</td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Weak</td>
<td>Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Very Low</td>
<td>Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence</td>
</tr>
</tbody>
</table>

Recommendations
Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the management of FWLS in infants 0-60 days. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process
Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children’s Hospital. Content Expert Teams are involved in every review and update.

Disclaimer
Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is...
responsible, in consultation with the patient and/or the patient’s family, to make the ultimate judgment regarding care.

<table>
<thead>
<tr>
<th>Date</th>
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</thead>
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<td>Mar 2009</td>
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</tr>
<tr>
<td>Sep 2014</td>
<td>Update</td>
</tr>
<tr>
<td>Jul 2015</td>
<td>Revision</td>
</tr>
<tr>
<td>Jun 2016</td>
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</tr>
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