

Fever of Unknown Source in Infants



FAST FACTS

8–12.5%

of febrile young infants will have an SBI, with a prevalence of up to 20% in infants less than 28 days old

44%

of cases of bacteremia in infants 0–90 days old are caused by *E. coli*

Given the broad differential diagnosis, infants with fever of unknown source (FUS) pose challenges to clinicians across inpatient and outpatient settings. Viral infections remain the most common cause of FUS in this vulnerable age group. However, a systematic approach is key to evaluating, identifying and managing infants with a high risk for serious bacterial infection (SBI). These include bacteremia, gastroenteritis, cellulitis, meningitis, pneumonia and UTIs.

ASSESSMENT

Perform a detailed history and physical exam (HPE) with probing questions around the timing and degree of fever, as well as the infant's feeding and activity levels. Also obtain a detailed family history regarding exposures and sick contacts in the home and/or daycare settings.

HPE (HISTORY AND PHYSICAL EXAM) RED FLAGS

- Infant is less than 28 days old
- Decreased tone, inconsolable, lethargic
- Stridor, grunting, wheezing, retractions or nasal flaring
- Mottling, pallor or cyanosis of the skin
- Poor feeding

MANAGEMENT/TREATMENT

Obtain these studies in infants less than 28 days old: CBC with differential, including absolute neutrophil count (ANC); blood culture; CSF analysis; and urinalysis (UA) with urine culture (use straight catheterization instead of bagged specimens due to contamination risk).

Obtain these studies in infants 29–60 days old: CBC with differential, focusing on the ANC; blood culture; UA and urine culture via straight catheterization; and procalcitonin* (PCT). Lumbar puncture (LP) is only necessary if the infant meets certain high-risk criteria (see reverse).

Consider viral testing for enterovirus, RSV, etc. based on HPE, season, sick contacts and community infection patterns. A confirmed virus doesn't exclude concomitant bacterial infection.

Continued primary care management is considered reasonable if low-risk clinical and lab criteria are met (see reverse); the infant is scheduled to be seen again within 24 hours; and the family understands when to go to the ED.

WHEN TO REFER

You can forgo the outpatient workup and refer directly to Cincinnati Children's Emergency Department if the infant has a chronic illness, presents with HPE red flags (see above) or is deemed abnormal based on the Pediatric Assessment Triangle (see reverse). Also refer to the ED if the infant meets intermediate or high-risk lab criteria for an SBI (see reverse).

**PCT is only run at base and Liberty labs. If stat labs are ordered, recommend sending the patient/family to base with the option of waiting at base for results. Average time approximately 90–120 minutes.*

If you would like additional copies of this tool, or would like more information, please contact the Physician Outreach and Engagement team at Cincinnati Children's.

If you have questions about a patient referral, call the Physician Priority Link® at 513-636-7997 and ask for the ED or hospital medicine physician on call.

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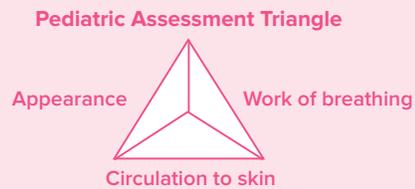
Patient Presents

Standard Workup

- Situational History
 - Family History
 - Physical Exam
- Viral infections remain the most common cause of FUS in this vulnerable age group. However, a systematic approach is key to evaluating, identifying and managing infants with a high risk for serious bacterial infection (SBI).*

HPE (HISTORY AND PHYSICAL EXAM) RED FLAGS

- Infant is less than 28 days old
- Abnormal Pediatric Assessment Triangle (decreased tone, lethargic, stridor, nostril flaring, mottling, cyanosis, etc.)
- Poor feeding



Any Red Flags?

Yes | No

Perform full workup, including lumbar puncture**

Infants less than 28 days old: CBC with differential, including ANC; blood culture; UA and urine culture; CSF analysis

Infants 29–60 days old: CBC with differential, including ANC; blood culture; UA and urine culture; procalcitonin PCT*

**See risk stratification below

Continue primary care outpatient management, as long as:

- Low-risk lab criteria are met (see below)
- The infant is scheduled to be seen again within 24 hours **and**
- The family understands all reasons to go to the ED (including, but not limited to, HPE red flags)

You can forgo the outpatient workup and refer directly to Cincinnati Children’s Emergency Department if the infant has a chronic illness, presents with HPE red flags or is deemed abnormal based on the Pediatric Assessment Triangle. Also refer to the ED if the infant meets intermediate or high-risk lab criteria for an SBI (see below).

RISK STRATIFICATION BASED ON LAB RESULTS

Low Risk

- Negative UA (UA with <10 WBC per hpf) **AND**
- Biomarkers below threshold:
 - PCT ≤0.5 ng/mL,
 - ANC ≤4,000/ mm³

ACTION

- No antimicrobials, discharge home with close follow up with PCP in next 24 hours
- Family knowledgeable of when to call/return

Intermediate Action

- Negative UA
- PCT ≤0.5 ng/mL **BUT** ANC >4,000/ mm³

ACTION

- **Option 1: Proceed with LP, send CSF studies and consider empiric antimicrobials**
- **Option 2: Defer LP and admit for observation OFF antimicrobials**

High Risk

- Negative UA with
- PCT >0.5 ng/ml regardless of ANC value

ACTION

- Proceed with LP and CSF studies
- Start empiric antimicrobials and admit to hospital

Abnormal UA

- Positive UA: (WBC ≥10 per hpf)

ACTION

- **Option 1: Defer LP and treat empirically for presumed UTI if: PCT ≤0.5 ng/mL regardless of ANC value; consider admission**
- **Option 2: Consider LP and sending CSF studies if: PCT >0.5 ng/mL regardless of ANC value; admit to hospital**