Risk Assessment and Management of

Febrile Infant (3–60 days)

2025
Minor update

Intermountain Canyons and Desert Regions

This evidence-based care process model (CPM) was revised by Intermountain Healthcare's Children's Health Infectious Diseases Team. It recommends a protocol for assessing, evaluating, and treating infants age 3–60 days who present to the emergency department with a rectal temperature of 38°C or higher or with a reliable history of fever. Note: A separate document, *Neonatal Early-Onset Sepsis (EOS) Guideline*, defines care for neonatal sepsis.

Key Points

Not all febrile infants have the same risk of invasive bacterial infection.

Low-risk infants have approximately a 1.4 % occurrence of either invasive bacterial infection (IBI), such as bacterial meningitis and bacteremia, or urinary tract infection (UTI), which is much lower than high-risk infants.[1-3] Accordingly, they should be subjected to less invasive testing and treatment to avoid the risks and costs of unnecessary procedures.

Procalcitonin or C-reactive protein (CRP), with complete blood count (CBC), and urinalysis (UA) are important in determining an infants risk of IBI or UTI [1,4,5]

- In a study of over 3,000 febrile infants, only 58% of those with bacteremia or bacterial meningitis appeared clinically ill.[6]
- Along with consideration of the infant's age and clinical disposition, procalcitonin or CRP, CBC, and UA can help identify low-risk patients. Approximately 50 % of patients will be low-risk after screening. [1,4,5]

What's new in this update?

- New risk stratification algorithms to help identify low-risk patients.
- Procalcitonin is preferred over CRP in facilities that have the ability to return procalcitonin results within 2 hours.
- Procalcitonin is not a reliable indicator of infection in infants ≤ 48 hours old.
- A dipstick UA positive for LE consists of a trace or greater in infants 3–60 days of age. [13]
- Infants > 60 days of age are no longer included in these algorithms.

Infants 3-28 days

- Observation WITHOUT antibiotics is recommended for low-risk infants 3–28 days old.

Infants 29-60 days

- High-risk infants >28 days that do not have concern of meningitis may be observed at home after single dose of ceftriaxone. [1]
- Some infants 29–60 days of age with outpatient observation of UTIs may ultimately have bacteremia. In these cases, if infant is afebrile and active oral antibiotics are initiated, follow-up blood culture and IV antibiotics are NOT indicated. Management may be continued in the outpatient setting if child is responding to antibiotics. [7,8,9]

What's Inside?

Intermountain Measures

- Improve the proper identification and treatment of febrile infants that have a low-risk of invasive bacterial infection. This will lead to a decrease in:
  - Rates of hospital admission
  - Number of lumbar punctures
  - Amount of antibiotics used
  - Length of hospital stay for those admitted
- Improve suspected serious bacterial infection outcomes by choosing more effective empiric antibiotic therapy.

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Initial Care of the Febrile Infant 3 – 28 Days of Age

Patient age 3–28 days old, with rectal temperature ≥ 38.0 °C (100.4°F) or reliable history of fever

Risk of IBI or UTI ~13%

Are any sepsis criteria (a) present? — yes → See *Septic Shock Recognition Treatment PCH ED Guideline*

no

ABX- antibiotics
CSF- cerebral spinal fluid
CRP- C-reactive protein
HSV- herpes simplex virus
IBI-invasive bacterial infection
LE-leukocyte esterase
LP- lumbar puncture
UTI- urinary tract infection

Assess eligibility for a limited diagnostic workup

- Infant appears well (b)
- No signs of focal infection (c)
- No known risk of HSV (d)
- Infant full term (≥37 weeks)*
- No systemic antibiotics in last 48 hours*
- No chronic medical conditions*

*Note: Outside the NICU data concerning the importance of these factors is limited. For extra caution, use them as criteria for a limited diagnostic workup.

Does patient meet ALL criteria above for limited diagnostic workup?

yes → **Perform LIMITED diagnostic workup (e)**
Urinalysis and Blood Draw (No LP or chest X-ray)

Choose Procalcitonin if can get results in < 2 hrs, otherwise choose CRP. Do NOT order both

ANY of the following present?

If Procalcitonin testing	• Procalcitonin >1.7 ng/mL **OR** • Procalcitonin >0.18 + ANC >4000 cells/mcL?
If CRP testing	• CRP > 2 mg/dL **OR** • ANC >4000 cells/mcL

yes → **Perform FULL diagnostic workup (f)**
- Urinalysis, Blood Draw, and LP. Consider chest x-ray and pathogen PCR testing if indicated.

no → Is UA LE trace or greater? — yes → Perform FULL diagnostic workup (f)

no → **Low risk of IBI (≤0.7%)** [3,10]

Admit for observation

Use shared decision making regarding use of antibiotics during observation.
- If no abx (preferred), no need for LP
- If use abx, perform LP before giving empiric abx (see TABLE 1)

Is CSF >18 WBC/mcL **OR** grossly bloody tap (>10,000 RBC/mcL)?

no → **High risk of IBI or UTI (≥10%)**

Admit for suspected IBI/UTI

Initiate empiric antibiotics per febrile infant power plan 3 – 28 days (see TABLE 1)

yes → **High risk of IBI or UTI (≥10%)**

Admit for suspected CNS IBI
- Send CSF and blood for HSV and enterovirus PCR.
- Initiate empiric abx for meningitis and ADD acyclovir (see TABLE 1).

Proceed to *Continued Management of Febrile infant* (page 6)

Table 1. Empiric Antibiotics and Antivirals for use in Febrile Infants 3 – 28 days of age

Suspected source of Infection	Antibiotic Regimen
Suspected bacterial meningitis OR abnormal CSF	Ampicillin 75 mg/kg/dose IV q 6 hours PLUS ceftazidime 50 mg/kg IV q 8 hours
Suspected UTI with nitrites +	Cefepime 50 mg/kg/dose IV q 12 hours
No known source OR UTI with only LE +	Ampicillin 50 mg/kg/dose IV q 6 hours PLUS ceftazidime 50 mg/kg IV q 8 hours
Ill-appearing neonate OR suspected HSV OR abnormal CSF	Ampicillin 75 mg/kg/dose IV q 6 hours PLUS ceftazidime 50 mg/kg IV q 8 hours PLUS Acyclovir 20 mg/kg/dose IV q 8 hrs
Suspected Staphylococcal infection (e.g. skin soft tissue, omphalitis, osteomyelitis)	To appropriate regimen above ADD: If hemodynamically stable without pleocytosis: Clindamycin 13 mg/kg/dose IV q 8 hrs If hemodynamically unstable or CSF pleocytosis: Vancomycin 20 mg/kg/dose IV q 8 hrs

ALGORITHM NOTES AND ASSESSMENT TOOLS

(a) Sepsis Criteria (ANY)

- Capillary refill time ≥ 3 seconds **OR** flash refill
- Decreased mental status (lethargy, unarousable, inappropriate crying)
- Pulse decreasing/weak OR bounding
- Skin mottled/cool, OR flushed/ruddy
- Tachycardia >205 bpm
- Systolic blood pressure < 60 mmHg

(b) Signs of an ill appearing infant

Ill-appearing infants are often described informally as:

- Irritable
- Septic
- Lethargic
- Toxic

(c) Signs of focal infection

Focal infections are generally of skin and soft tissue origin and can be indicated by:

- Omphalitis
- Mastitis
- Bulging fontanelle
- Abscesses
- Cellulitis

(d) Risk factors for HSV in infants < 29 days

Risk factors include abnormal temperature AND any of the following:

- Vesicles
- Erosions or crusting on skin or mucosa
- Seizure (new)
- Thrombocytopenia (<150,000 / mm^3)

See *HSV Disease in Infants Guideline* for details

(e) Limited diagnostic workup

If patient does not meet sepsis criteria **AND** has met all criteria for a limited workup, only the following tests are recommended:

- Urine testing through catheter
  - Dipstick test (UMAC)
  - Urine culture (UCX)
- Blood draw
  - Procalcitonin (PROCAL) **OR** c-reactive protein (CRP)
  - Blood cultures (BCX)
  - Complete blood count with differential (CBC GPP)
  - Complete metabolic panel (CMP) Although this is not often used in initial risk stratification, elevated transaminases can raise suspicion of disseminated HSV infection. It may also be useful later in management (e.g. bilirubin in antibiotic selection)

(f) Full diagnostic workup

A full diagnostic work up includes all tests that are found in a limited diagnostic workup (e) *PLUS*:

- Lumbar puncture for CSF
  - CSF culture (CSFCX)
  - CSF cell count (CSFCC)
  - CSF glucose (GLUCSF)
  - CSF protein (PRCSF)
- Chest X-ray (CXR) if respiratory symptoms present

Additional testing (if clinically indicated) may include:

- HSV PCR from blood and CSF. Send HSV CSF individually rather than an ME panel.
- Respiratory panel (RFAPCR)
- Enterovirus PCR (ENTPCR) on blood and CSF, particularly June- November and ALWAYS in patients with CSF pleocytosis. [11,12] Send EV CSF individually rather than a Meningitis/encephalitis filmarray (ME) panel.

A CSF ME panel is NOT recommended in routine care of well appearing febrile infants,

Initial Care of the Febrile Infant 29 – 60 Days of Age

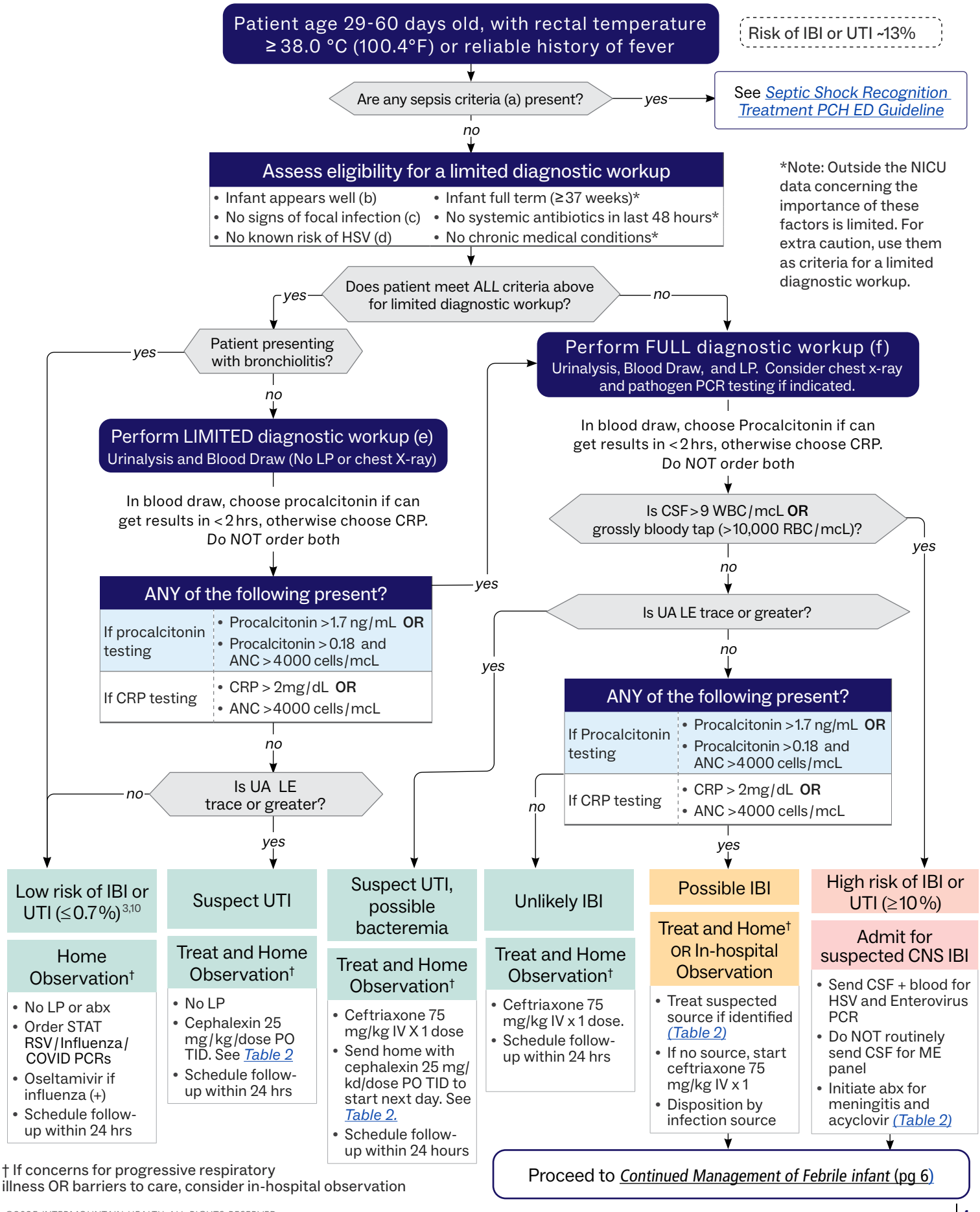

Table 2. Empiric Antibiotics and Antivirals for use in Febrile Infants 29-60 days of age

Suspected source of Infection	Antibiotic Regimen
Meningitis or abnormal CSF	Ceftriaxone 100 mg/kg/dose IV every 24 hrs. Consider adding vancomycin 20 mg/kg/dose q 8 hours if gram stain is positive for gram-positive cocci.
UTI with low inflammatory markers	Cephalexin 25 mg/kg/dose PO TID for 7 days
UTI with elevated inflammatory markers	Ceftriaxone 75 mg/kg/dose IV once then discharge with cephalexin 25 mg/kg PO TID for total duration of 10 days
Unknown source	Ceftriaxone 75 mg/kg/dose IV every 24 hours
Additional Circumstances	**Recommendations**
Suspected HSV infection including abnormal CSF	Ceftriaxone 100 mg/kg/dose IV q 24 hrs. PLUS acyclovir 20 mg/kg/dose IV q 8 hrs. Collect HSV PCR from blood and CSF as recommended in *HSV Disease in Infants Guideline*
Suspect staphylococcal infection (skin soft tissue infection, omphalitis, osteomyelitis, etc.)	To appropriate regimen above ADD: If hemodynamically stable without pleocytosis: Clindamycin 13 mg/kg/dose IV q 8 hrs If hemodynamically unstable or CSF pleocytosis: Vancomycin 20 mg/kg/dose IV q 8 hrs
Influenza positive	Consider oseltamivir 3 mg/kg/dose PO BID

ALGORITHM NOTES

(a) Sepsis Criteria (ANY)

- Capillary refill time ≥ 3 seconds OR flash refill
- Decreased mental status (lethargy, unarousable, inappropriate crying)
- Pulse decreasing/weak OR bounding
- Skin mottled/cool, OR flushed/ruddy
- Tachycardia >205 bpm
- Systolic blood pressure <70 mmHg

(b) Signs of an ill appearing infant

Ill-appearing infants are often described as:

- Irritable
- Lethargic
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(c) Signs of focal infection

Focal infections are generally of skin and soft tissue origin and can be indicated by:

- Omphalitis
- Abscesses
- Mastitis
- Cellulitis
- Bulging fontanelle

(d) Risk factors for HSV in infants > 28 days

Infants >28 days typically have classic HSV symptoms such as :

- Vesicles
- CSF pleocytosis
- Seizure (new)

See *HSV Disease in Infants Guideline* for more detail

(e) Limited diagnostic workup

If patient does not meet sepsis criteria AND has met all criteria for a limited workup, only the following tests are recommended:

- Urine testing through catheter
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(f) Full diagnostic workup

A full diagnostic work up includes all tests that are found in a limited diagnostic workup PLUS:

- Lumbar puncture for CSF
  - CSF culture (CSFCX)
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- HSV PCR from blood and CSF. Send HSV CSF individually rather than an ME panel.
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Continued Management of the Febrile Infant

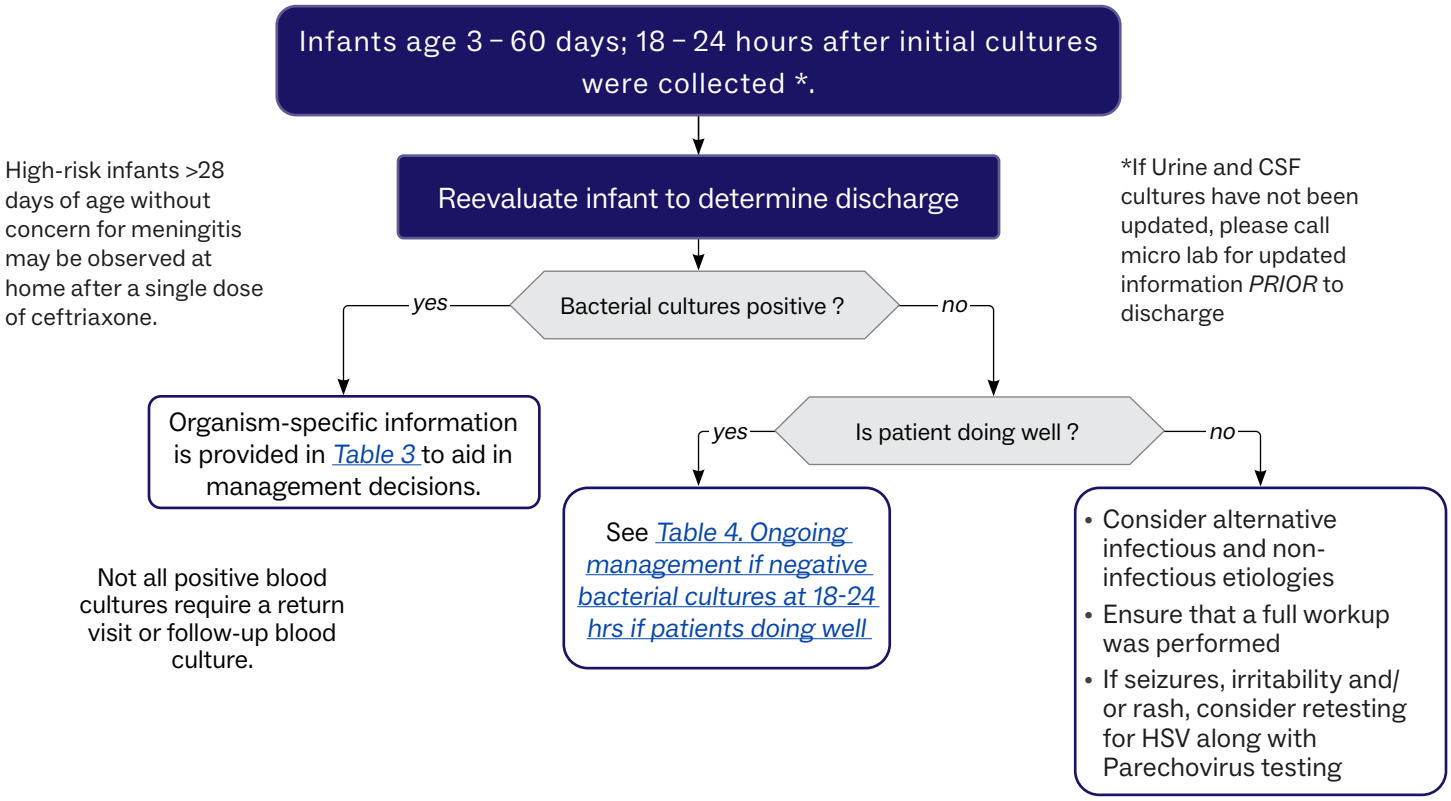

Table 3. Bacterial Cultures Positive: Recommended Actions (continues on next page)

Results*	Recommended action
CSF positive for bacteria	• Consult Infectious Disease for drug recommendations. • Requires IV with CSF penetrating antimicrobials. Likely antimicrobial recommendations from Infectious Disease while awaiting susceptibilities (may change depending on circumstance) – *E. coli* or *Klebsiella spp.*: Ceftriaxone or Ceftazidime – Group B *Streptococcus*: Penicillin G. – *Haemophilus influenzae*: Ceftriaxone. – *Streptococcus pneumoniae*: Ceftriaxone *PLUS* vancomycin.
Blood positive for bacteria	• In admitted patient, **begin antibiotics** if have not already done so, unless it's likely to be a contaminant (below) • If currently on antibiotics, assess current treatment, review susceptibilities, and adjust accordingly. **Specific organism recommendations** **Coagulase-negative *Staphylococcus spp.*** (NOT *S. aureus* or *S. lugdunensis)* – Usually indicative of contamination. – For discharged patients: If patient is clinically well after discussion with family during ED culture call back, and if no hardware (e.g. central line) is present, then no need to bring back in for reevaluation. No follow-up blood culture necessary. – For inpatients: If patient is well clinically and has no hardware (e.g. central line), no antibiotics indicated. Follow-up blood cultures usually not necessary. **Gram-positive bacillus** – Usually indicative of contamination (excluding Listeria). – If patient appears well and has no hardware (e.g. central line), consider as contaminant, no follow-up blood culture necessary. – For discharged patients: If patient is clinically well after discussion with family during ED culture call back, and if no hardware (e.g. central line) is present, then no need to bring back in for reevaluation. – For *Listeria monocytogenes,* consult pediatric infectious disease and start Ampicillin IV.

Table 3. Bacterial Cultures Positive: Recommended Actions (continued)

Results*	Recommended action
Blood positive for bacteria (continued)	***Staphylococcus aureus* (coagulase +)** – Consult Pediatric Infectious Disease. – Obtain follow-up blood culture daily until negative for 48 hours. – Carefully watch movement of arms and legs. Check for focal infection such as skin or soft tissue, osteomyelitis, and rarely UTI. – Treatment. – MSSA (Methicillin-sensitive *S. aureus*): Cefazolin; if suspect CNS, Cefazolin is now recommended for most CNS infections (discuss with ID). – MRSA (Methicillin-resistant *S. aureus*): Vancomycin IV. **Group B streptococcus (e.g. *S. agalactiae*)** – Penicillin G IV. – Discuss with Pediatric Infectious Disease or Antibiotic Stewardship before placing PICC. ***E. coli*, *Klebsiella spp.*** – If accompanied by UTI: Ceftriaxone/ceftazidime, switch to oral antibiotics (e.g. cephalexin) after 1–2 days. – If discharged with cephalexin and child is afebrile and well appearing 24 hours after initial antibiotic dose AND CSF not concerning (e.g. no growth), there is no need to reevaluate in ED and follow-up blood cultures are not indicated. Follow up on susceptibilities and modify if necessary. – Follow-up blood cultures are usually not necessary. Consider if fever continues >24 hours after antibiotic initiation. ***Enterobacter spp.*** – Rarely encountered. – Usually associated with urogenital abnormalities. – Often resistant to cephalexin and occasionally resistant to ceftriaxone. – Preferred antimicrobials include oral levofloxacin or cefepime. – Follow-up blood cultures should be considered. – Reevaluation in the ED should be considered.
Urine positive for bacteria *For uncommon organisms consult with ID	• If patient is catheterized, ≥50,000 CFU/mL of a single uropathogen is indicative of UTI. • When UTI diagnosed a renal ultrasound should be considered *after* the acute phase if the patient improves as expected. • In patients with severe disease or failure to improve as expected, renal ultrasound should be performed *during* acute phase to identify complications such as renal abscesses and pyonephrosis. ***Lactobacillus spp.*, coagulase-negative *Staphylococcus spp.*, and *Corynebacterium spp.*** – These organisms are considered contaminants in infants without complications such as catheterization or immune deficiency and **should NOT prompt treatment.** ***E. coli* (>90% of isolates)** – Transitioning to oral cephalexin is acceptable. If susceptible to ampicillin, amoxicillin is also appropriate. ***Enterobacter spp.*** – When transitioning to oral antimicrobials before discharge, consider fluoroquinolones. Oral beta-lactams generally show low activity. ***Enterococcus spp.*** Transition to amoxicillin.

Table 4: Ongoing Management if Negative Bacterial Cultures at 18 – 24 hrs. (patient doing well)

Results	Recommended action
Focal infection (skin/soft tissue) positive for bacteria	• Treatment can be changed to oral antimicrobials before discharge in most cases • If desired, call Antibiotic Stewardship or Pediatric Infectious Disease for guidance
HSV-positive in blood, CSF, or lesion	• Begin or continue acyclovir (20 mg/kg/dose IV q 8 hrs) • Consider discontinuation of antibacterials AND contact Infectious Disease
Influenza A or B positive	• Consider beginning or continuing oseltamivir • Provide supportive care AND consider discontinuation of antibacterials
Positive for other viral pathogen	• Provide supportive care as indicated • Consider discontinuation of antibacterials
No identified pathogen, but improving	• Ensure urine and CSF cultures have been read by microbiology (it may be necessary to call lab for results before discharge). • Strongly consider discontinuation of antimicrobials

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This CPM presents a model of best care based on the best available scientific evidence at the time of publication. It is not a prescription for every physician or every patient, nor does it replace clinical judgment. All statements, protocols, and recommendations herein are viewed as transitory and iterative. Although physicians are encouraged to follow the CPM to help focus on and measure quality, deviations are a means for discovering improvements in patient care and expanding the knowledge base. Send feedback to Carolyn Reynolds; Executive Clinical Programs Director; Children's Health; carolyn.reynolds@imail.org

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