Floating Hospital for Children at Tufts Medical Center

INFANT SEPSIS CLINICAL PRACTICE GUIDELINE

Guideline for Suspected Occult Infection in Young Infants (0-60 days of life)

Target Population

Non-toxic, previously healthy infants 0-60 days of age with fever (≥38°C by rectal measurement) without signs of focal infection. In this age group hypothermia, poor feeding, lethargy, irritability without fever should also be considered for occult infection.

EXCLUSIONS

1. Premature infants (gestational age less than 37 weeks at birth).
2. Infants who appear toxic, have focal signs of infection or who are at high risk for serious bacterial infection due to known exposures.
3. Infants of families for whom follow-up cannot be assured.
4. Infants with condition that may affect immune system or increase risk for serious infection.
5. Infants receiving any current or recent antimicrobial therapy.
6. Infants who have received an immunization within 48 hours.
7. Infants presenting with seizures.

SCOPE

Most common cause of fever in this age group is a viral illness but the incidence of serious bacterial illness (SBI) with T ≥38°C (100.4°F) is higher in this age group, estimated to be 9-13%. Serious bacterial illness includes the following: bacteremia, bacterial gastroenteritis, cellulitis, omphalitis, osteomyelitis, septic arthritis, meningitis, pneumonia, and urinary tract infection (UTI). UTI is the most common SBI. Bacterial meningitis has been identified in alert, mildly ill infants under three months of age without meningeal signs or fever. Multiple screening tools have been studied to determine infants at low risk for serious bacterial illness. None of these tools are reliable in infants 0-28 days so this age group is not appropriate for outpatient management of fever.

DIAGNOSTIC APPROACH (see also algorithm)

0-28 days

Admission required; obtain the following in the emergency room:

1. Blood: CBC with diff, blood culture, glucose, ALT
2. Urethral catheterization: urinalysis with microscopic, urine culture
3. Lumbar puncture: CSF cell count, protein, glucose, culture (Tube 1: protein and glucose; Tube 2: gram stain, culture; Tube 3: cell count and differential; Tube 4: hold for additional studies

Consider the following based on presentation and exam: chest x-ray, RSV antigen, influenza a/b, stool rotavirus and/or WBC smear, HSV workup (HSV PCR blood and CSF, swab conjunctiva/mouth/rectum for HSV culture or PCR)

29-60 days

Same evaluation as 0-28 days or initial diagnostic workup to assess the "risk" of serious bacterial infection which includes CBC with diff, blood culture, urinalysis with microscope. If over 6 weeks of age with RSV bronchiolitis can consider only UA and urine culture.

Febrile infants 29-60 days can be classified as low risk if they meet all of the following criteria. The low risk classification equates to a 98.9% negative predictive value (NPV) for having a serious bacterial infection (if include CSF, CXR if symptomatic, stool culture if diarrhea then 99.7%).

-Well appearing infant
-Previously healthy with no previous antibiotic use
-WBC between 5,000 and 15,000
-absolute band count ≤ 1500 cells/µL, band neutrophil ratio 0.2 or less
-UA with less than 5-10 WBC/hpf

} 98.9% NPV for SBI

Addition of CSF studies in this age group will increase NPV and should be strongly considered. Some institutions perform LP on all febrile infants 0-60 days. Decision to not initially perform LP can be a left to discretion of provider if preference is to obtain CBC with diff, urinalysis with microscope and blood culture first but should be performed if low risk criteria not met or antibiotics started for any reason.

-CSF less than 8 WBC/µL
-CXR (if needed/obtained) with no focal infiltrate
-Stool cx (if needed/obtained) with no RBC or WBC

} 99.7% NPV for SBI

If patients are over 4 weeks of age and CBC, UA and initial CSF studies are normal, the patient may be discharged to home if he or she is well appearing and there is follow up assured within 24 hours.

EMPIRIC TREATMENT

0-28 days

Ampicillin PLUS cefotaxime
Consider acyclovir if HSV suspected

29-60 days

Cefotaxime or ceftriaxone
Add vancomycin if CSF pleocytosis or gram positive diplococcic on gram stain

Dexamethasone for suspected pneumococcal meningitis

"For infants and children 6 weeks of age and older, adjunctive therapy with dexamethasone may be considered after weighing the potential benefits and possible risks. Some experts recommend use of corticosteroids in pneumococcal meningitis, but this issue is controversial and data are not sufficient to make a routine recommendation for children. If used, dexamethasone should be given before or concurrently with the first dose of antimicrobial agents." (Red Book, 2012).

BACKGROUND INFORMATION

There are multiple protocols for evaluation of infantile fever. If these criteria are used within 0-28 days of life studies have shown missed SBI which has decreased controversy in work up in this age group. Over 28 days there is variation on expert opinion mostly with respect if lumbar puncture is necessary. Below is a summary of some study protocols. In the Boston criteria all infants 28-89 days had lumbar puncture, if met low risk criteria were given ceftriaxone 50mg/kg IM as outpatient and followed up in 24 hours. Philadelphia age range was 29-60 days and all patients had lumbar puncture, unlike Boston if meet low risk criteria which includes CSF results did not receive antibiotics. The Rochester criteria, clinician to assess SBI risk prior to obtaining lumbar puncture. If infant does not meet low risk criteria then empiric antibiotics are given which necessitates lumbar puncture.

	Rochester	Boston	Philadelphia	Milwaukee
Age	<60 d	28-89 d	29-60 d	30-60 d
Temp	>38.0°C	>38.0°C	>38.2°C	
History	• Term infant • No perinatal antimicrobial therapy • No underlying disease • Not hospitalized longer than the mother	• No immunizations within preceding 48 hours • No antimicrobial within 48 hours • Not dehydrated	• Not specified	
Physical exam	• Well-appearing • Unremarkable examination	• Well-appearing • No ear, soft tissue or bone infection	• Well-appearing • No ear, soft tissue or bone infection	• Well-appearing • No ear, soft tissue or bone infection
Labs	• WBC >5000 and <15000/mm3 • Absolute band count <1500/mm3 • UA <10 WBC/hpf • <5 WBC/hpf stool smear with diarrhea	• CSF <10/mm3 • UA <10 WBC/hpf • Chest radiograph: no infiltrate • WBC <20,000/mm3	•WBC <15,000/mm3 • Band-neutrophil ratio <0.2 • UA <10 WBC/hpf • Urine gram stain negative • CSF <8 WBC/mm3 • CSF gram stain negative • Chest radiograph: no infiltrate • Stool: no blood, few or no WBCs on smear	• CSF total WBC <10/mm3 • CBC total WBC <15,000/mm3 • Urinalysis WBC <10/HPF, negative for bacteriuria/ leukocyte esterase/nitrite • No pulmonary infiltrate on chest radiograph if performed
Fail low risk criteria	Hospitalize + empiric antibacterial agent(s)	Hospitalize + empiric antibacterial agent(s)	Hospitalize + empiric antibacterial agent(s)	Hospitalize + empiric antibacterial agent(s)
Meet low risk criteria	• Home • No antibacterial therapy • Follow-up required	• Home • Empiric antibacterial therapy • Follow-up required	• Home • No antibacterial therapy • Follow-up required	• Reliable caretaker follow-up required • Empiric antibacterial therapy
Reported statistics	Sensitivity 92% (83-97%) Specificity 50% (47-53%) Positive predictive value 12.3% (10-16%) NPV 98.9% (97-100%)	Sensitivity - NA Specificity 94.6% Positive predictive value - NA NPV - NA	Sensitivity 98% (92-100%) Specificity 42% (38-46%) Positive predictive value 14% (11-175) NPV 99.7% (98-100%)	

Adapted Feld 2005

ETIOLOGIC AGENTS

In the last 25 years, group B streptococcus has been the most common cause of meningitis in children 2 to 6 weeks of age, followed by *Escherichia coli*, *Listeria monocytogenes, Haemophilus influenzae,* and *Streptococcus pneumoniae.* Beyond the neonatal period, *Streptococcus pneumoniae* and *Neisseria meningitidis* represent the most common causes of bacterial meningitis. Today the most common cause of outpatient bacterial sepsis or meningitis is *S. pneumoniae*. Recent studies have demonstrated that the rate of bacterial sepsis has declined substantially since the introduction of *Haemophilus* conjugate vaccines.

INPATIENT MANAGEMENT

After an appropriate evaluation in an outpatient setting or emergency department (ED), which would include cultures of blood, urine, and CSF, antibiotic therapy is usually initiated especially 0-28 days. These infants have been admitted for observation and continued antibiotic therapy. If serious bacterial infection has been ruled out by negative blood, CSF and urine cultures; appropriate continuing care can be assured; infant is well-appearing and afebrile, consider discharge within 48-72 hours. In many hospitals blood cultures are assessed continuously but CSF and urine only once per day therefore will need to confirm at time of discharge if urine and CSF are negative.

Discharge planning should begin on admission. The family should be informed prior to discharge of the possible need for reexamination and the remote possibility of readmission and will need to be available by phone for 48 hours following discharge, should a positive culture be reported.

DIAGNOSTIC CONSIDERATIONS

- Traumatic lumbar puncture. Frankly bloody CSF should not be used to make clinical decisions, and lumbar puncture should be attempted again in such situations. Although methods for evaluating CSF obtained from a traumatic lumbar puncture are described in the literature (e.g., correcting the cells by assuming 1 WBC/1,000 red blood cells),we do not recommend using these formulas to guide clinical decisions (Pediatrics in Review, 2008).
- Lumbar puncture after empiric antibiotics. CSF should be obtained in all patients in whom bacterial meningitis is suspected when it is medically safe to do so, regardless of antibiotic exposure. Testing for bacterial DNA by 16S rDNA PCR or using latex agglutination if available may be considered in treated patients with sterile CSF.

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Practice guidelines do not necessarily apply to every patient. A provider's clinical judgment is essential. As always, clinicians are urged to document management strategies.

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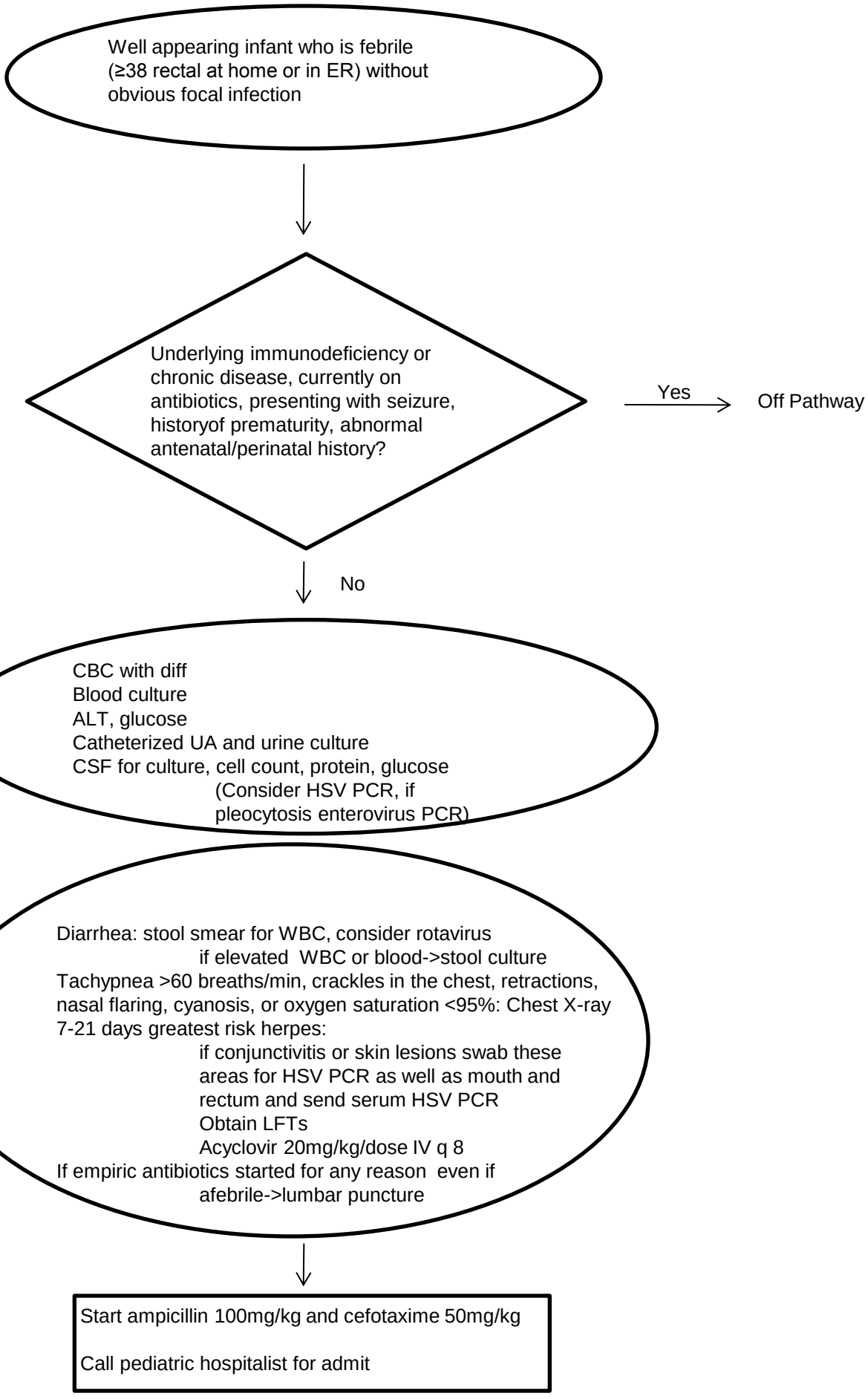
Fever 0-28 days



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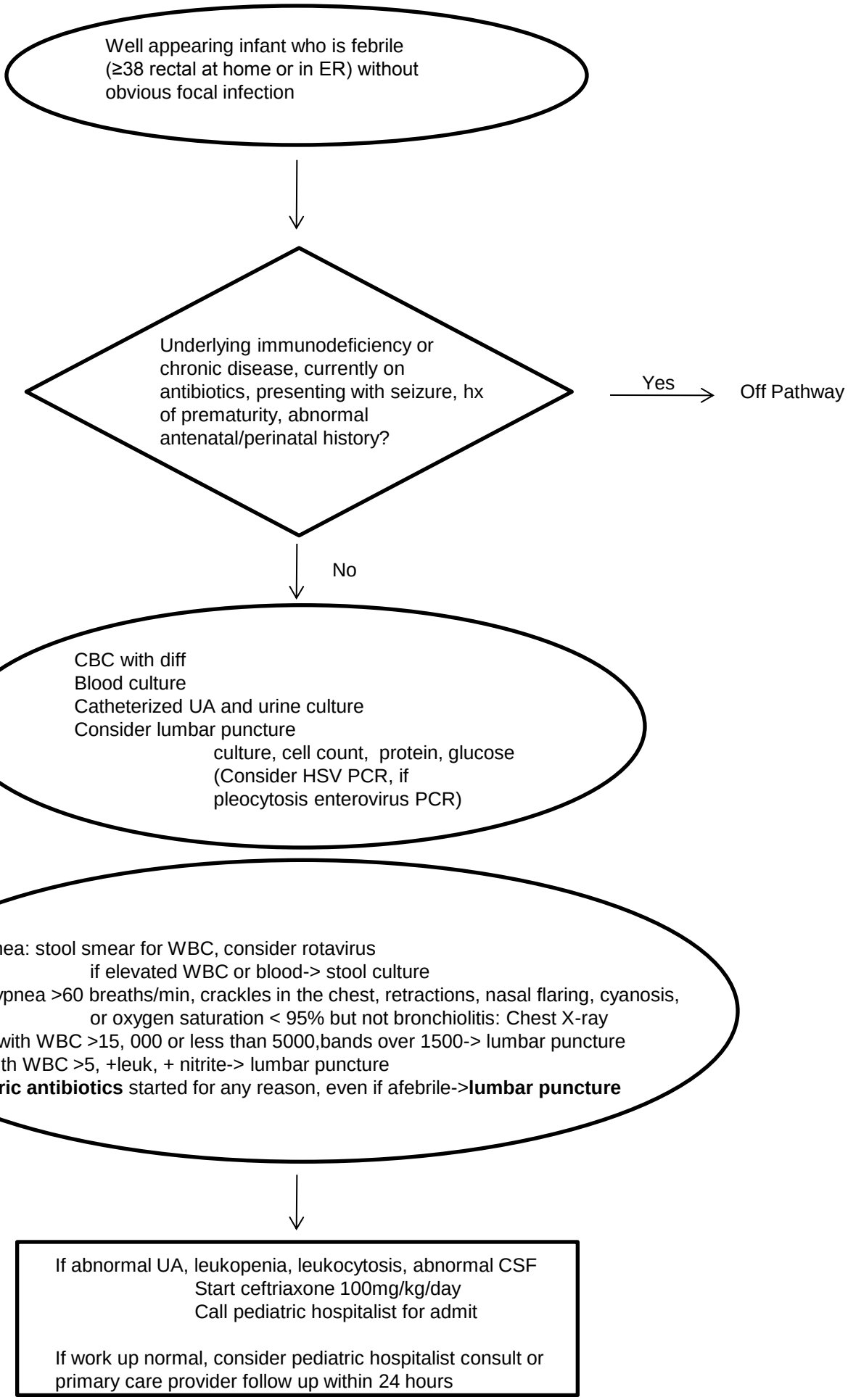
Fever 29-60 days



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Fever 2-3 months