BOTTOM LINE RECOMMENDATIONS:

Fever in Young Infants

Neonates (less than or equal to 28 days of age) and young infants (29-60 days of age) with fever account for a significant number of emergency department (ED) visits. At this age, there is an increased risk of **serious bacterial infection (SBI)** in urine, blood or the central nervous system. Most of these infants have self-limited viral illnesses, however up to 10-13% of febrile young infants have SBI (of which greater than 90% are urinary tract infections (UTIs)).[1] Clinical examination can be unreliable in determining the source or severity of infection. The difficulty lies in differentiating the infant with SBI from those without, while minimizing the risks of investigating and/or treating a febrile infant with no SBI. Additionally, young febrile infants are at risk of poor outcomes if SBI is not diagnosed and treated promptly.[2] For further management tools, see the TREKK Sepsis and Critically Ill Neonate PedsPacs.

WHAT IS A FEVER?

- Most experts agree that a temperature of greater than or equal to 38.0°C is a fever.
- A rectal temperature is the most reliable means of obtaining a core temperature in infants. Axillary temperatures may be inconsistent and have no reliable "correction factor".[3] **Any** suspicion of fever in an infant up to 60 days of age warrants a core (rectal) temperature. Even a single temperature recording of greater than or equal to 38.0°C is significant. Consider a period of monitoring with several repeat temperature measurements in an infant with a temperature approaching 38.0°C. Sustained temperatures at or near 38.0°C may more reliably indicate a pathological process. Consultation with Pediatric Referral Centre is advised if there is uncertainty in determining if an infant requires further evaluation.
- If an infant appears unwell, they should be evaluated for serious bacterial infection regardless of presence or absence of fever.
- Other clinical parameters such as presence of lethargy, poor feeding, and irritability are important in the assessment.
- Fever should never be attributed to over-bundling unless SBI has been definitively ruled out. Over-bundling very rarely produces hyperthermia greater than or equal to 38.0°C.[4]

OVERVIEW OF MANAGEMENT

If core temperature is greater than or equal to 38.0°C (as measured by parent or healthcare provider) proceed with urgent evaluation as follows:

- Complete set of vital signs, including a repeat temperature measurement.
- Assess ABCs and intervene as necessary.
- The current standard of care is that all neonates 0-28 days with fever require a full septic workup, empiric antibiotics and admission to hospital. Evidence regarding the management of febrile young infants is evolving. TREKK will continue to monitor any proposed practice change and update guidelines accordingly.
- Neonates with a focal infection identified on physical exam (e.g. skin or soft tissue infection, osteomyelitis, etc.) may require further investigation and pediatric specialist consultation is recommended. Tailor treatment to the source of infection.
- **Do not delay** antibiotics in cases where the infant is too unstable or there are insufficient resources or provider experience to obtain all cultures. Consult with Pediatric Referral Centre to prepare for transport.
- Additional studies may be considered: chest x-ray (respiratory signs/symptoms), viral nasopharyngeal studies (nasal congestion), stool cultures/viral studies (diarrhea).
- Recent evidence supports the use of a clinical prediction rule incorporating procalcitonin (PCT), urinalysis and absolute neutrophil count to identify SBI in infants 0-60 days. Biomarkers (e.g. C-reactive protein (CRP) and/or procalcitonin (PCT)) are superior to white blood cell count and/or absolute neutrophil count for the risk assessment of infants with fever and possible bacterial infection. At present, the availability and turnaround of these tests is variable depending on practice setting.[5]

SPECIFIC MANAGEMENT OF INFANTS WITH FEVER

0-28 DAYS OF AGE OR 29-60 DAYS OF AGE AND ILL-APPEARING

- Complete a full septic work-up by obtaining blood culture, CBC with differential, CRP or PCT (if available), electrolytes, blood glucose, liver enzymes, urinalysis and microscopy, urine culture (catheter sample), cerebrospinal fluid (CSF) studies including culture and viral studies. Include viral nasopharyngeal studies, chest x-ray and stool studies as required.
- Treat with empiric antibiotics and admission to hospital for 36-48 hours, until preliminary cultures are negative. Most blood cultures are positive within 24 hours if it is a true pathogen.
- Assess risk of HSV infection and consider addition of Acyclovir (see Page 2).

Age	Empiric Antibiotics	Route
0-7 days	Ampicillin 300 mg/kg/day divided q6h AND *gentamicin 4 mg/kg/day given q24h **If suspected meningitis, add cefotaxime 200 mg/kg/day divided q6h	IV/IM/IO
8-28 days	Ampicillin 300 mg/kg/day divided q6h AND *gentamicin 5 mg/kg/day given q24h **If suspected meningitis, add cefotaxime 200 mg/kg/day divided q6h	IV/IM/IO
29-60 days	Ampicillin 300 mg/kg/day divided q6h AND cefotaxime 300 mg/kg/day divided q6h Instead of cefotaxime can substitute ceftriaxone 100 mg/kg/day given q24h.	IV/IM/IO

*Aminoglycoside doses vary by renal function; if gentamicin not available use same dose of tobramycin
**Reassess once culture and sensitivity available

29-60 DAYS OF AGE IF STABLE, WELL-APPEARING, NO EVIDENT SOURCE OF INFECTION (LOW RISK CRITERIA)

- Obtain blood culture, CBC with differential, CRP or PCT (if available), urinalysis and microscopy, urine culture (catheter sample).
- Include viral nasopharyngeal studies, chest x-ray and/or stool studies as required.
- Consider discharge only if infant meets **all** low risk criteria. This includes: greater than 37 weeks gestation, no prior hospitalization, no prolonged newborn nursery care, WBC 5-15x10^9/L, bands less than 1.5x10^9/L, urine WBC less than 5/HPF, urine negative for nitrites or leukocyte esterase, CRP less than 20 mg/L (if available), PCT less than 0.5 mcg/L (if available), no chronic illness, no prior antibiotics, no unexplained jaundice.
- If discharged, caregivers must be given clear direction regarding monitoring the infant and when to return. Arrange follow up within 24 hours. Ensure appropriate follow-up of culture results.
- Infants 29-60 days of age with an identified UTI (urinalysis positive for ANY of: leukocyte esterase, nitrites, greater than or equal to 5-10 WBC/hpf, bacteria on microscopy) are typically admitted to hospital. The well appearing infant in this age group with an isolated UTI **may** be discharged home on oral antibiotics or with instructions to return daily for IV antibiotics. Caregivers must be reliable, able to monitor infant and return readily. **Outpatient management should ONLY be done in discussion with Pediatric Referral Centre**. Antibiotic choices include:
  - Oral cefixime (8 mg/kg/DOSE once daily) for 10-14 days, **OR** once daily IV ceftriaxone or aminoglycoside (tobramycin or gentamicin, dose as on Page 1) until afebrile and suitable for change to oral therapy.

0-60 DAYS OF AGE IF SIGNS OF BRONCHIOLITIS (SEE TREKK BRONCHIOLITIS RECOMMENDATIONS)

- Febrile neonates with bronchiolitis have a very low risk of bacteremia and meningitis, but the same rate of UTI as those without bronchiolitis.[6] **All febrile** neonates 0-28 days of age with bronchiolitis should have a full septic work-up.
- Febrile infants 29-60 days of age with bronchiolitis appear to have a lower rate of SBI. It is reasonable to defer further investigation provided they appear well, the fever is low grade (less than 39°C), caregivers can provide close observation, and follow-up can be arranged within 24-48 hours.
- If the infant appears sicker than expected for the severity of bronchiolitis, consider additional evaluation (e.g. CBC with differential, blood culture, CRP or PCT (if available), urinalysis and microscopy, urine culture). Observation in the ED may be appropriate.

HERPES SIMPLEX VIRUS

- Febrile neonates may have herpes simplex virus (HSV) infection, which may have few clinical signs but is associated with significant morbidity and mortality.[7]
- Infants presenting with maternal history of HSV, seizures or focal neurologic abnormalities, diffuse pneumonitis, skin vesicles, mucous membrane lesions, signs of coagulopathy, elevated transaminases, with or without history of exposure to herpes should be evaluated for HSV by obtaining samples in viral transport media from any vesicular skin lesions, all mucous membranes, CSF and blood (if available).
- Fever may not be present in up to 50% of infants with clinical features of HSV infection.[8]
- Start empiric treatment with IV Acyclovir in infants with clinical suspicion of HSV and/or CSF pleocytosis (elevated cell count).
- If the diagnosis of HSV is a consideration, **consult Pediatric Referral Centre**.

INFANTS REQUIRING SPECIAL CONSIDERATION

- Infants appearing severely ill (e.g. lethargy, irritability, signs of shock, evidence of organ dysfunction, coagulopathy) should be evaluated and treated for additional problems beyond infection such as hypoxia, shock, hypoglycemia (serum glucose less than or equal to 2.6 mmol/L). Assess and support airway, breathing and circulation. Provide fluid resuscitation and treat hypoglycemia. For further management tools, see the TREKK Sepsis and Critically Ill Neonate PedsPacs.
- Further evaluation and **Pediatric Referral Centre** consultation is recommended for:
  - Infants with known comorbidities (e.g. congenital disorders, serious illness, indwelling devices)
  - Infants currently on or having recently completed antibiotics
  - Infants who were recently hospitalized (excluding birth hospitalization)
  - Infants with seizures
  - Infants born prematurely (less than 37 weeks gestational age)
  - Infants who have recently travelled outside of the country

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4) Grover G, Berkowitz CD, Lewis RJ, Thompson M, Berry L, Seidel J. The effects of bundling on infant temperature. *Pediatrics.* 1994;94(5):669-673.
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