Literature Bundle

Fever in the well-appearing infant 8-60 days of age*

*Note: This is NOT a comprehensive literature review

- Bolded studies available on the REVISE II website provided for free

AAP CPG: Pantell RH, Roberts KB, Adams WG, et al. Evaluation and management of well-appearing febrile infants 8 to 60 days old. *Pediatrics*. 2021;148(2):e2021052228.

Background

Evolving bacteriology in febrile infants: transition from Gram Positive to Gram Negative predominance

- Powell EC, Mahajan PV, Roosevelt G, et al. Epidemiology of bacteremia in febrile infants aged 60 days and younger. *Ann Emerg Med*. 2018;71(2):211-216
- Woll C, Neuman MI, Pruitt CM, et al. Epidemiology and etiology of invasive bacterial infection in infants ≤60 days old treated in emergency departments. *J Pediatr*. 2018;200:210-217.e1
- Biondi E, Evans R, Mischler M, et al. Epidemiology of bacteremia in febrile infants in the United States. *Pediatrics*. 2013;132(6):990-996

Age stratification for risk of invasive bacterial infections (bacteremia and meningitis)

- Biondi EA, Lee B, Ralston SL, Winikor JM, Lynn JF, Dixon A, McCulloh R. Prevalence of bacteremia and bacterial meningitis in febrile neonates and infants in the second month of life: a systematic review and meta-analysis. *JAMA Netw Open*. 2019 Mar 1;2(3):e190874.
- Pantell RH, Newman TB, Bernzweig J, et al. Management and outcomes of care of fever in early infancy. *JAMA*. 2004;291(10):1203-1212

Prevalence of UTI, bacteremia, and bacterial meningitis

Infection	Age	Prevalence	Citations
UTI	8-21 days	7-12%	• Biondi EA, Lee B, Ralston SL, Winikor JM, Lynn JF, Dixon A, McCulloh R. Prevalence of bacteremia and bacterial meningitis in febrile neonates and infants in the second month of life: a systematic review and meta-analysis. *JAMA Netw Open*. 2019 Mar 1;2(3):e190874. • **Kuppermann N, Dayan PS, Levine DA, et al. A clinical prediction rule to identify febrile infants 60 days and younger at low risk for serious bacterial infections. *JAMA Pediatr*. 2019;173(4):342-35160** • Blaschke AJ, Korgnski EK, Byington CL. Meningitis in well-appearing febrile infants aged 1-90 days. *Open Forum Infect Dis*. 2018;5(Suppl 1):S133 • Powell EC, Mahajan PV, Roosevelt G, et al. Epidemiology of bacteremia in febrile infants aged 60 days and younger. *Ann Emerg Med*. 2018;71(2):211-216 • Roman HK, Chang PW, Schroeder AR. Diagnosis and management of bacteremic urinary tract infection in infants. *Hosp Pediatr*. 2015;5(1):1-8 • Greenhow TL, Hung YY, Herz AM. Changing epidemiology of bacteremia in infants aged 1 week to 3 months. *Pediatrics*. 2012;129(3):e590-e596 • Pantell RH, Newman TB, Bernzweig J, et al. Management and outcomes of care of fever in early infancy. *JAMA*. 2004;291(10):1203-1212
	22-28 days	7-12%	
	29-60 days	7-12%	
Bacteremia	8-21 days	3.9-5.1% overall 20% with UTI	
	22-28 days	1.6-5% overall 7.5-10% with UTI	
	29-60 days	1.1-2.2% overall 5-10% with UTI	
Meningitis	8-21 days	0.5-1.3%	
	22-28 days	0.4-0.6%	
	29-60 days	0.12-0.32%	

Testing

Validity of using the UA as a screening tool before sending a urine culture

- **Tzimenatos L, Mahajan P, Dayan PS, et al. Accuracy of the urinalysis for urinary tract infections in febrile infants 60 days and younger. *Pediatrics*. 2018;141(2):e20173068**
- Schroeder AR, Chang PW, Shen MW, Biondi EA, Greenhow TL. Diagnostic accuracy of the urinalysis for urinary tract infection in infants <3 months of age. *Pediatrics*. 2015;135(6):965-971

Use of inflammatory markers for risk stratification

- **Burstein B, Alathari N, Papenburg J. Guideline-based risk stratification for febrile young infants without procalcitonin measurement. *Pediatrics*. 2022;149(6):e2021056028**
- **Aronson PL, Shabanova V, Shapiro ED, et al. A prediction model to identify febrile infants ≤60 days at low risk of invasive bacterial infection. *Pediatrics*. 2019;144(1):e20183604**
- **Kuppermann N, Dayan PS, Levine DA, et al. A clinical prediction rule to identify febrile infants 60 days and younger at low risk for serious bacterial infections. *JAMA Pediatr*. 2019;173(4):342-351**
- Milcent K, Faesch S, Gras-Le Guen C, et al. Use of procalcitonin assays to predict serious bacterial infection in young febrile infants. *JAMA Pediatr*. 2016;170(1):62-69
- **Gomez B, Mintegi S, Bressan S, et al. Validation of the "Step-by-Step" approach in the management of young febrile infants. *Pediatrics*. 2016;138(2):e20154381. doi: 10.1542/peds.2015-4381. Epub 2016 Jul 5.**

Use of selective lumbar punctures in febrile infants with positive UAs

- Velasco R, Lejarzegi A, Gomez B, et al. Febrile young infants with abnormal urine dipstick at low risk of invasive bacterial infection. *Arch Dis Child*. 2020 Nov 27:archdischild-2020-320468.
- Burstein B, Sabhaney B, Bone JN, Doan Q, Mansouri FF, Meckler GD. Prevalence of bacterial meningitis among febrile infants aged 29-60 days with positive urinalysis results: a systematic review and meta-analysis. *JAMA Netw Open*. 4(5):e214544.
- **Wang ME, Biondi EA, McCulloh RJ, et al. Testing for meningitis in febrile well-appearing young infants with a positive urinalysis. *Pediatrics*. 2019;144(3):e20183979**
- Young BR, Nguyen THP, Alabaster A, Greenhow TL. The prevalence of bacterial meningitis in febrile infants 29-60 days with positive urinalysis. *Hosp Pediatr*. 2018;8(8):450-457

Use of Oral Antibiotics in Febrile Infants 29-60 days with positive UAs

- **Hoberman A, Wald ER, Hickey RW, et al. Oral versus initial intravenous therapy for urinary tract infections in young febrile children. *Pediatrics*. 1999;104(1 Pt 1):79-86**

Disposition

Discharge from the hospital within 24-36 hours:

- Biondi EA, Mischler M, Jerardi KE, et al. Blood culture time to positivity in febrile infants with bacteremia. *JAMA Pediatr*. 2014;168(9):844-849
- **Aronson PL, Wang ME, Nigrovic LE, et al. Time to pathogen detection for non-ill versus ill-appearing infants ≤60 days old with bacteremia and meningitis. *Hosp Pediatr*. 2018;8(7):379-384**

Discharge from the emergency department with close follow-up:

- Mintegi S, Gomez B, Martinez-Virumbrales L, Morientes O, Benito J. Outpatient management of selected young febrile infants without antibiotics. *Arch Dis Child*. 2017 Mar;102(3):244-249.
- Greenhow TL, Hung YY, Pantell RH. Management and outcomes of previously healthy, full-term, febrile infants ages 7 to 90 days. *Pediatrics*. 2016;138(6):e20160270
- Pantell RH, Newman TB, Bernzweig J, et al. Management and outcomes of care of fever in early infancy. *JAMA*. 2004;291(10):1203-1212

Parent Engagement

- Aronson PL, Politi MC, Schaeffer P, et al. Development of an app to facilitate communication and shared decision-making with parents of febrile infants ≤60 days old. *Acad Emerg Med*. 2021;28(1):46-59.