Well Appearing Infant with Fever

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Disclosure Statement

- Dr. Frey does not have any significant financial relationship to report.

Objectives

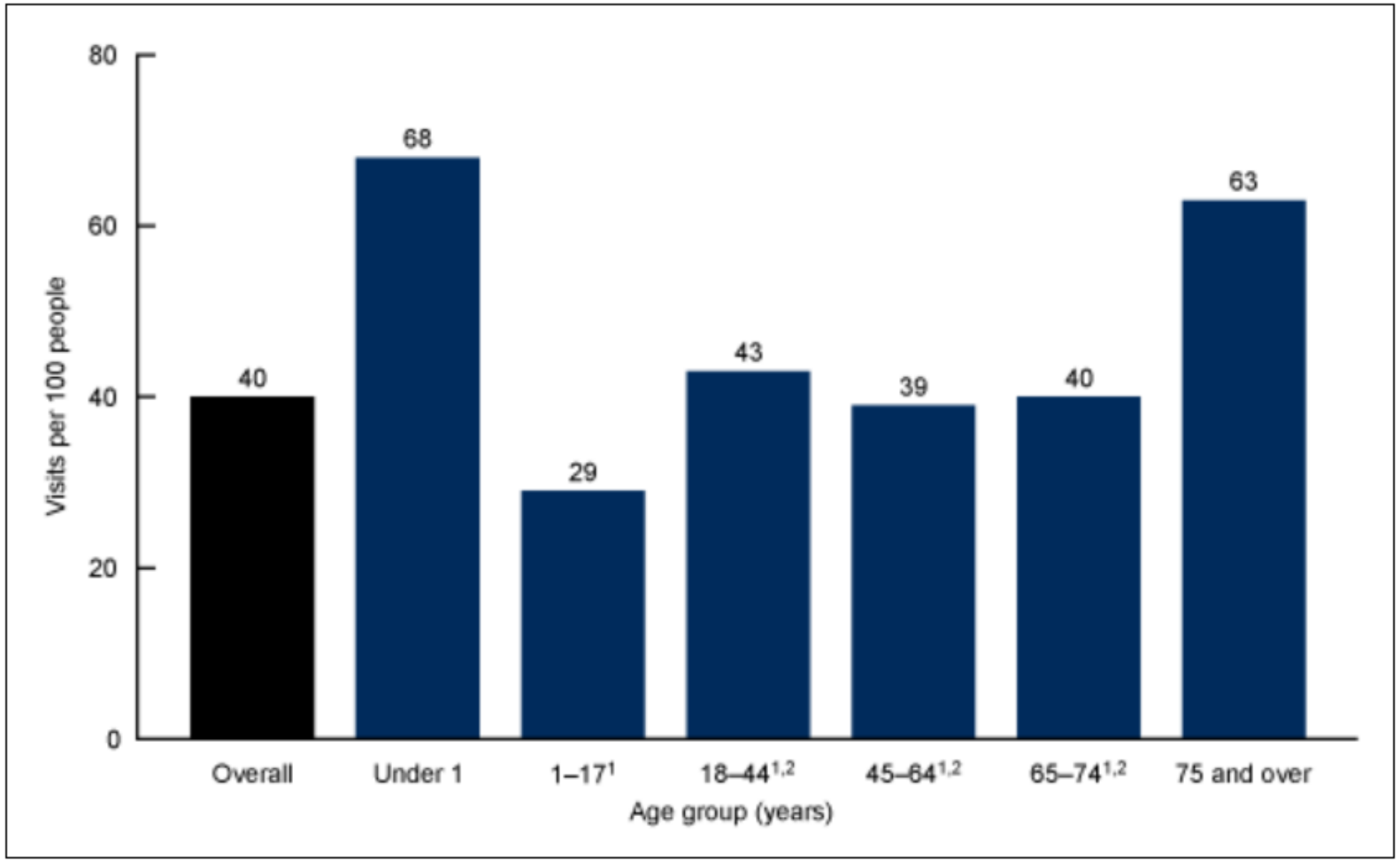
- Review Infant fever statistics
- Review current American Academy of Pediatric guidelines and related literature for febrile infants
- Discuss recent literature regarding viral testing and serious bacterial infections
- Discuss best practice patterns regarding febrile infants

Ten Leadin

tes, 2016-2020

Rank	201	021
1	Stor abd cran spas	omach and odominal pain, amps and spasms
2	Che rela sym refe bod	nest pain and lated symptoms ot referable to dy systems)
3	Feve	nortness of breath
4	Cou	ough
5	Hea in h	ever

Figure 1. Emergency department visit rate, by age group: United States, 2020



CLINICAL PRACTICE GUIDELINE

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old

Robert H. Pantell, MD, FAAP,[a] Kenneth B. Roberts, MD, FAAP,[b] William G. Adams, MD, FAAP,[c] Benard P. Dreyer, MD, FAAP,[d] Nathan Kuppermann, MD, MPH, FAAP, FACEP,[e] Sean T. O'Leary, MD, MPH, FAAP,[f] Kymika Okechukwu, MPA,[g] Charles R. Woods Jr, MD, MS, FAAP[h] SUBCOMMITTEE ON FEBRILE INFANTS

Methods

- AAP guidelines are based on universal agreement or strong consensus among committee members
- Provided with same resources and literature to review
- Goal was to “develop a guideline to improve the diagnosis and treatment of UTIs, bacteremia, and bacterial meningitis”

Eligibility

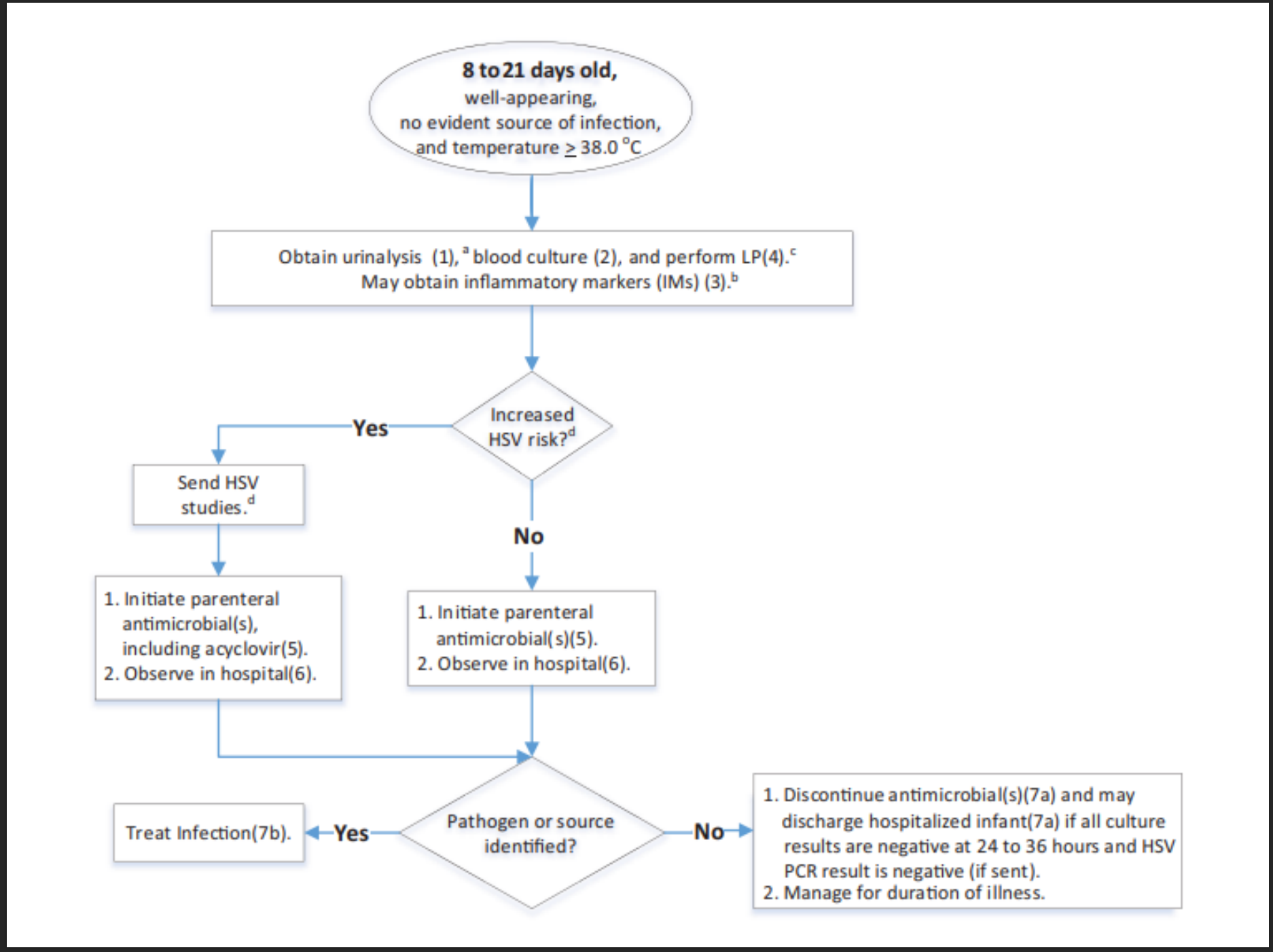
1. Well appearing
2. Rectal temperature of ≥ 38C/100.4F within the last 24 hours
3. Gestation ≥ 37 weeks and < 42 weeks
4. 8-60 days of age

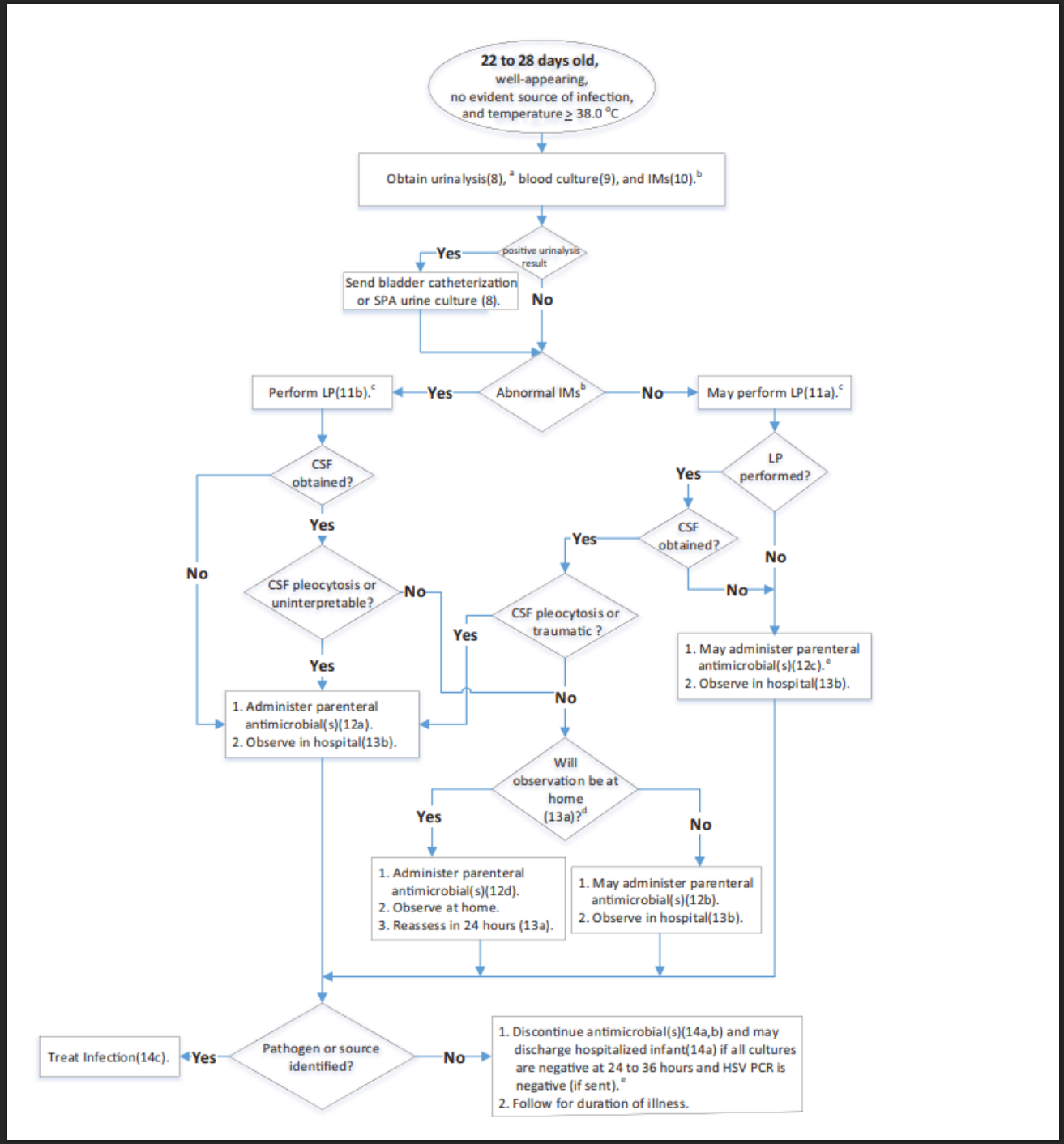
Exclusion

1. Preterm born < 37 weeks
2. Less than 2 weeks of age whose perinatal courses complicated by maternal fever, infection, and or antimicrobial use
3. High suspicion for HSV (vesicles)
4. Focal bacterial infections (cellulitis, omphalitis, septic arthritis, osteomyelitis)
5. **Infants with clinical bronchiolitis**
6. Documented or suspected immune compromise
7. Neonatal course complicated by surgery of infection
8. Infants with congenital or chromosomal abnormalities
9. Medically fragile infants requiring some form of technology or ongoing therapeutic intervention to sustain life
10. Infants receiving immunizations within the last 48 hours

Exclusion

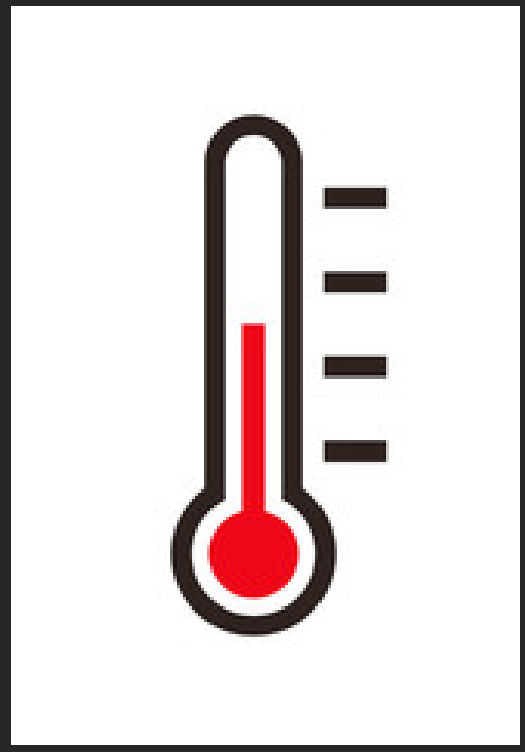
- High risk groups
- High concern for infection based on clinical exam
- **Bronchiolitis****
- Infants receiving immunizations within the last 48 hours


8 to 21 days old,
well-appearing,
no evident source of infection,
and temperature ≥ 38.0 °C
Obtain urinalysis (1),[a] blood culture (2), and perform LP(4).[c]
May obtain inflammatory markers (IMs) (3).[b]
Increased HSV risk?[d]
Yes
No
Send HSV studies.[d]
1. Initiate parenteral antimicrobial(s), including acyclovir(5).
2. Observe in hospital(6).
1. Initiate parenteral antimicrobial(s)(5).
2. Observe in hospital(6).
Pathogen or source identified?
Yes
No
Treat Infection(7b).
1. Discontinue antimicrobial(s)(7a) and may discharge hospitalized infant(7a) if all culture results are negative at 24 to 36 hours and HSV PCR result is negative (if sent).
2. Manage for duration of illness.


22 to 28 days old, well-appearing, no evident source of infection, and temperature ≥ 38.0 °C
Obtain urinalysis(8),[a] blood culture(9), and IMs(10).[b]
positive urinalysis result
Yes
Send bladder catheterization or SPA urine culture (8).
No
Abnormal IMs[b]
Yes
Perform LP(11b).[c]
No
May perform LP(11a).[c]
CSF obtained?
Yes
No
CSF pleocytosis or uninterpretable?
No
Yes
Yes
1. Administer parenteral antimicrobial(s)(12a).
2. Observe in hospital(13b).
LP performed?
Yes
No
CSF obtained?
Yes
No
CSF pleocytosis or traumatic ?
Yes
No
1. May administer parenteral antimicrobial(s)(12c).[e]
2. Observe in hospital(13b).
Will observation be at home (13a)?[d]
Yes
No
1. Administer parenteral antimicrobial(s)(12d).
2. Observe at home.
3. Reassess in 24 hours (13a).
1. May administer parenteral antimicrobial(s)(12b).
2. Observe in hospital(13b).
Pathogen or source identified?
Yes
Treat Infection(14c).
No
1. Discontinue antimicrobial(s)(14a,b) and may discharge hospitalized infant(14a) if all cultures are negative at 24 to 36 hours and HSV PCR is negative (if sent).[e]
2. Follow for duration of illness.

Labs

- Blood Culture
- Inflammatory markers
  - ANC
  - CRP
  - Procalcitonin
  - Fever ≥ 38.5 C



Urinalysis

- Should be done with catheterization or suprapubic aspiration for culture
- Positive
  - Presence of Leukocyte esterase
  - >5 WBCs in centrifuged or > 10 in uncentrifuged urine

Urinalysis Result Is Positive, for Culture. Evidence Quality: A; Strong Recommendation

Benefits	Identification of UTIs Basing culture on urinalysis results reduces likelihood of false-positive result attributable to contamination or misdiagnosis of asymptomatic bacteriuria.
Risks, harm, cost	Requiring positive urinalysis result may miss some true UTIs. Obtaining culture if negative urinalysis result may result in falsely positive culture attributable to contamination or misdiagnosis of asymptomatic bacteriuria leading to inaccurate documentation of a first UTI (which may prompt unnecessary imaging should a UTI occur subsequently). Discomfort of catheterization or SPA. Parent anxiety.
Benefit–harm assessment	Preponderance of benefit based on high rate of UTI.
Shared decision-making	Parents opposed to catheterization should be offered a choice of SPA and informed about the higher rate of ambiguous/false-positive culture results obtained from bagged or voided specimens.[77,78]
Key references	73, 77–93

Lumbar Puncture

- Send for WBC, Protein, Glucose, Gram stain, culture, and possible viral testing

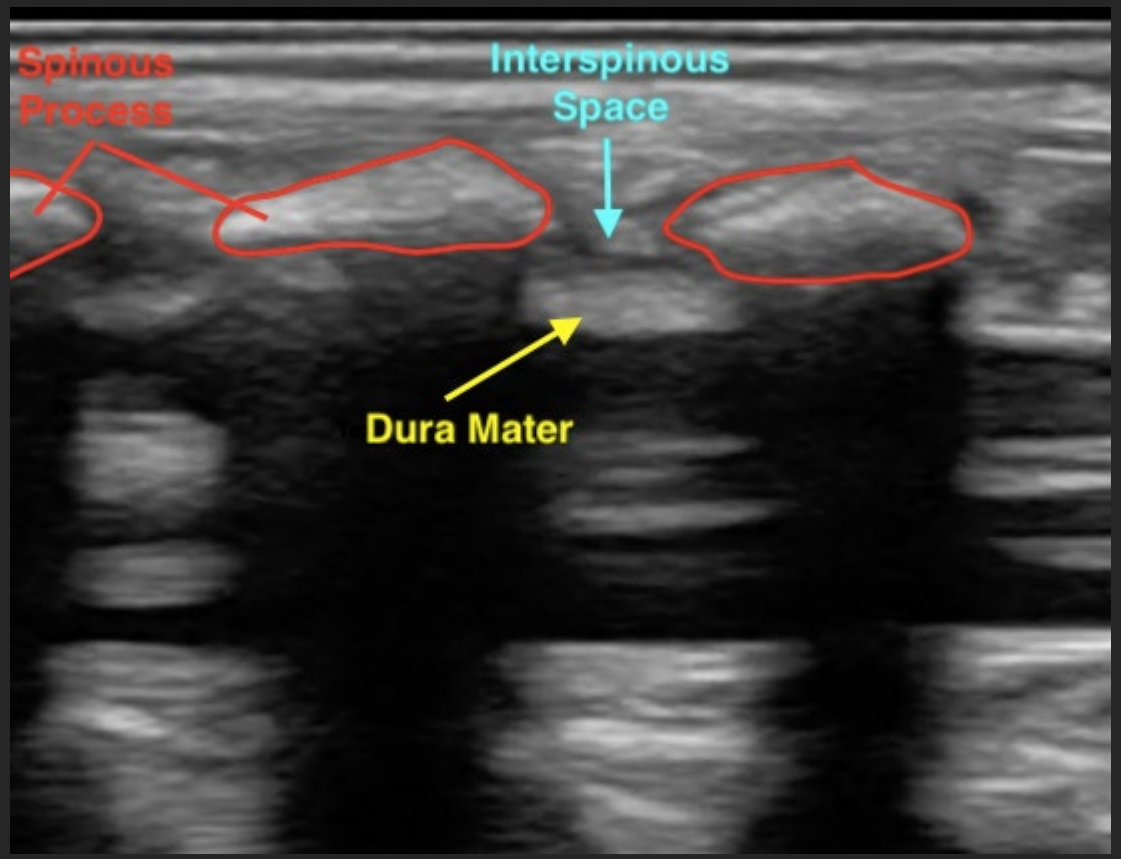


TABLE 2 CSF Values in Febrile Infants Without Evidence of UTI, IBI, HSV, Enterovirus, or Traumatic CSF

	Age, d	*n*	Mean	Median	Range
WBCs per mm^3	1–28	278	6.1	5.0	0–18
	29–60	318	3.1	3.0	0–8.5
Protein mg/dL	1–28	278	75.4	73.0	15.8–131.0
	29–60	318	58.9	54.0	5.5–105.5
Glucose	1–28	278	45.3	46.0	30.0–61.0
Glucose	29–60	318	48.0	48.0	20.6–65.5
RBCs per mm^3	1–28	278	95.5	5.5	0–236
RBCs per mm^3	29–60	318	75.5	2.0	0–64.5

Statistical outliers were removed. Other studies reveal slightly different ranges. Local laboratory tests may provide slightly different upper limits of normal. Adapted from Byington CL, Kendrick J, Sheng X. Normative cerebrospinal fluid profiles in febrile infants. *J Pediatr.* 2011;158(1):130–134.

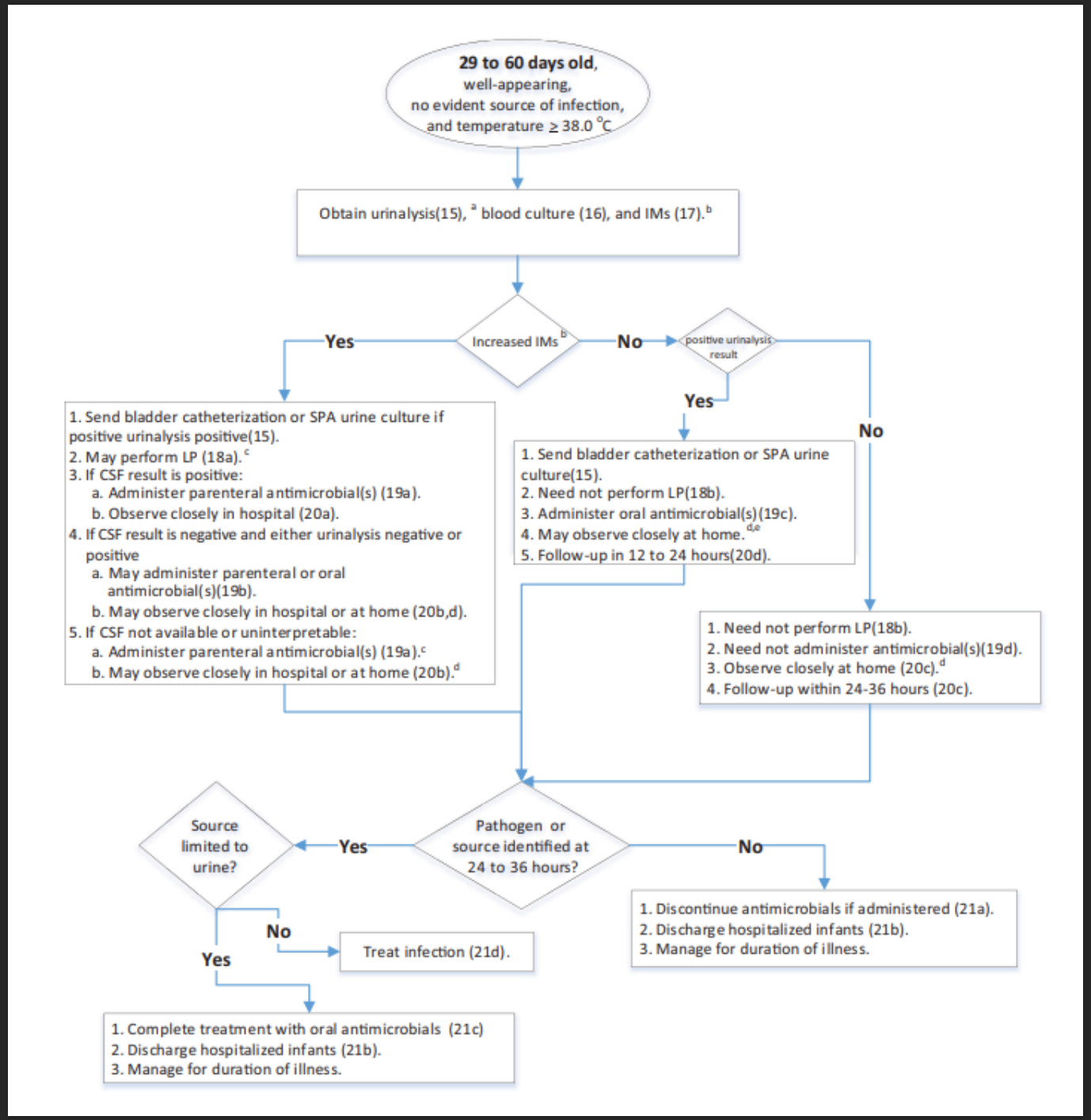
Antibiotics

- Gram negative pathogens (E. coli) are responsible for majority of infections

TABLE 3 Initial Empirical Antibacterial Therapy for Well-Appearing Febrile Infants 7 to 60 Days Old

Suspected Source of Infection	8–21 d Old	22–28 d Old	29–60 d Old
UTI[a]	Ampicillin IV or IM (150 mg/kg per d divided every 8 h) and either ceftazidime IV or IM (150 mg/kg per d divided every 8 h) or gentamicin IV or IM (4 mg/kg per dose every 24 h)	Ceftriaxone IV or IM (50 mg/kg per dose every 24 h)	Ceftriaxone IV or IM (50 mg/kg/dose every 24 h). Oral medications for infants older than 28 d.[b] Cephalexin 50–100 mg/kg per d in 4 doses or cefixime 8 mg/kg per d in 1 dose
No focus identified[c]	Ampicillin IV or IM (150 mg/kg per d divided every 8 h) and either ceftazidime IV or IM (150 mg/kg per d divided every 8 h) or gentamicin IV or IM (4 mg/kg per dose every 24 h)[d]	Ceftriaxone IV or IM (50 mg/kg per dose every 24 h)	Ceftriaxone IV or IM (50 mg/kg/dose every 24 h)
Bacterial meningitis[e]	Ampicillin IV or IM (300 mg/kg per d divided every 6 h) and ceftazidime IV or IM (150 mg/kg per d divided every 8 h)	Ampicillin IV or IM (300 mg/kg per d divided every 6 h) and ceftazidime IV or IM (150 mg/kg per d divided every 8 h)	Ceftriaxone IV (100 mg/kg or d once daily or divided every 12 h) or Ceftazidime IV (150 mg/kg or d divided every 6 h) and vancomycin[f] IV (60 mg/kg or d divided every 8 h)

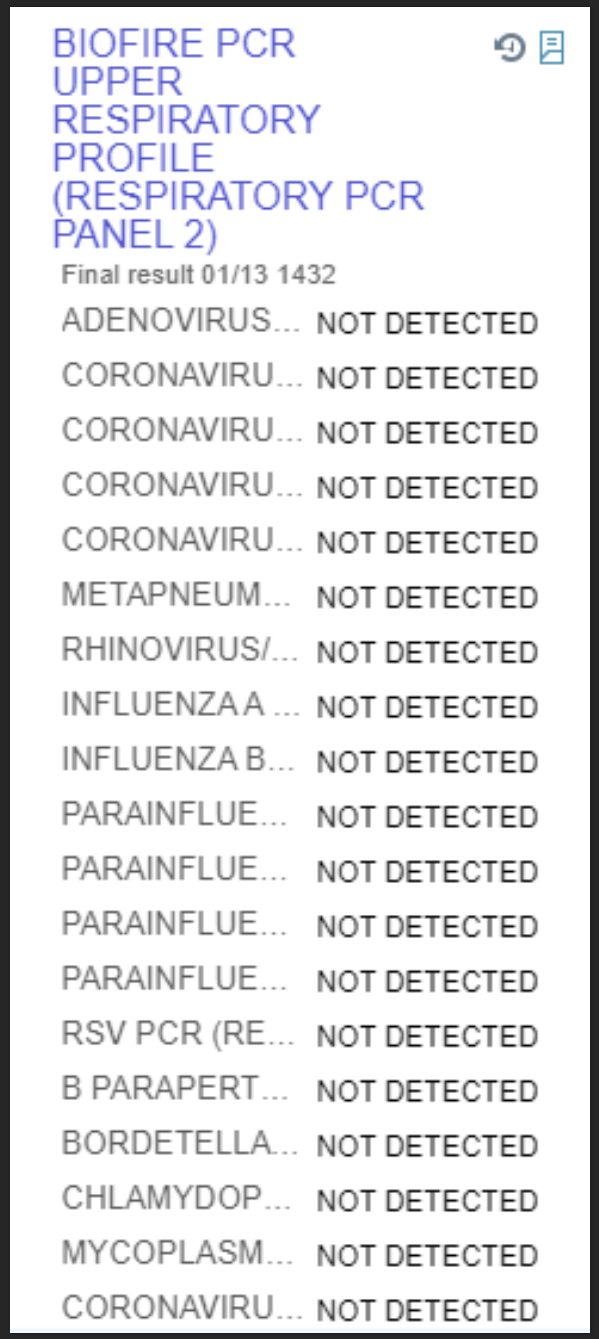
Use of a local antibiogram, if available, can guide choices. Note: If a focus of infection such as pneumonia, cellulitis, gastroenteritis, or musculoskeletal infection is identified, different regimens that cover typical microbial pathogens for the site of infection should be administered. IM, intramuscular; IV, intravenous. Adapted from Bradley JS, Nelson JD, Barnett ED, et al, eds. *2019 Nelson's Pediatric Antimicrobial Therapy.* 25th ed. Itasca, IL: American Academy of Pediatrics; 2019; and Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases.* 31st ed. Itasca, IL: American Academy of Pediatrics; 2018.


29 to 60 days old, well-appearing, no evident source of infection, and temperature ≥ 38.0 °C
Obtain urinalysis(15), [a] blood culture (16), and IMs (17).[b]
Increased IMs [b]
Yes
No
positive urinalysis result
Yes
No
1. Send bladder catheterization or SPA urine culture if positive urinalysis positive(15).
2. May perform LP (18a).[c]
3. If CSF result is positive:
a. Administer parenteral antimicrobial(s) (19a).
b. Observe closely in hospital (20a).
4. If CSF result is negative and either urinalysis negative or positive
a. May administer parenteral or oral antimicrobial(s)(19b).
b. May observe closely in hospital or at home (20b,d).
5. If CSF not available or uninterpretable:
a. Administer parenteral antimicrobial(s) (19a).[c]
b. May observe closely in hospital or at home (20b).[d]
1. Send bladder catheterization or SPA urine culture(15).
2. Need not perform LP(18b).
3. Administer oral antimicrobial(s)(19c).
4. May observe closely at home.[d,e]
5. Follow-up in 12 to 24 hours(20d).
1. Need not perform LP(18b).
2. Need not administer antimicrobial(s)(19d).
3. Observe closely at home (20c).[d]
4. Follow-up within 24-36 hours (20c).
Pathogen or source identified at 24 to 36 hours?
Yes
No
Source limited to urine?
Yes
No
Treat infection (21d).
1. Discontinue antimicrobials if administered (21a).
2. Discharge hospitalized infants (21b).
3. Manage for duration of illness.
1. Complete treatment with oral antimicrobials (21c)
2. Discharge hospitalized infants (21b).
3. Manage for duration of illness.

Limitations

1. Studies used SBI as outcome measure but do not have standard definition
2. Meningitis is uncommon
3. Bacterial species are continually changing
4. Models rely on clinical appearance
5. Clinicians work in different settings
6. Family reliability and comfort levels vary

Viral studies



BIOFIRE PCR UPPER RESPIRATORY PROFILE (RESPIRATORY PCR PANEL 2)

Final result 01/13 1432

ADENOVIRUS...	NOT DETECTED
CORONAVIRU...	NOT DETECTED
CORONAVIRU...	NOT DETECTED
CORONAVIRU...	NOT DETECTED
CORONAVIRU...	NOT DETECTED
METAPNEUM...	NOT DETECTED
RHINOVIRUS/...	NOT DETECTED
INFLUENZA A ...	NOT DETECTED
INFLUENZA B...	NOT DETECTED
PARAINFLUE...	NOT DETECTED
PARAINFLUE...	NOT DETECTED
PARAINFLUE...	NOT DETECTED
PARAINFLUE...	NOT DETECTED
RSV PCR (RE...	NOT DETECTED
B PARAPERT...	NOT DETECTED
BORDETELLA...	NOT DETECTED
CHLAMYDOP...	NOT DETECTED
MYCOPLASM...	NOT DETECTED
CORONAVIRU...	NOT DETECTED

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PMID: 37382957

Urinary Tract Infection, Bacteremia, and Meningitis Among Febrile Young Infants With SARS-CoV-2 and Non–SARS-CoV-2 Viral Infections

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Article Information

Methods

- Secondary analysis of prospective quality improvement data from single center over 2.5 year period
- N of 931
  - Documented rectal temperature of ≥ 38.0 °
  - AAP inclusion and exclusion criteria were included for analysis
- Intervention of Multiplex respiratory testing that included SARS-CoV-2

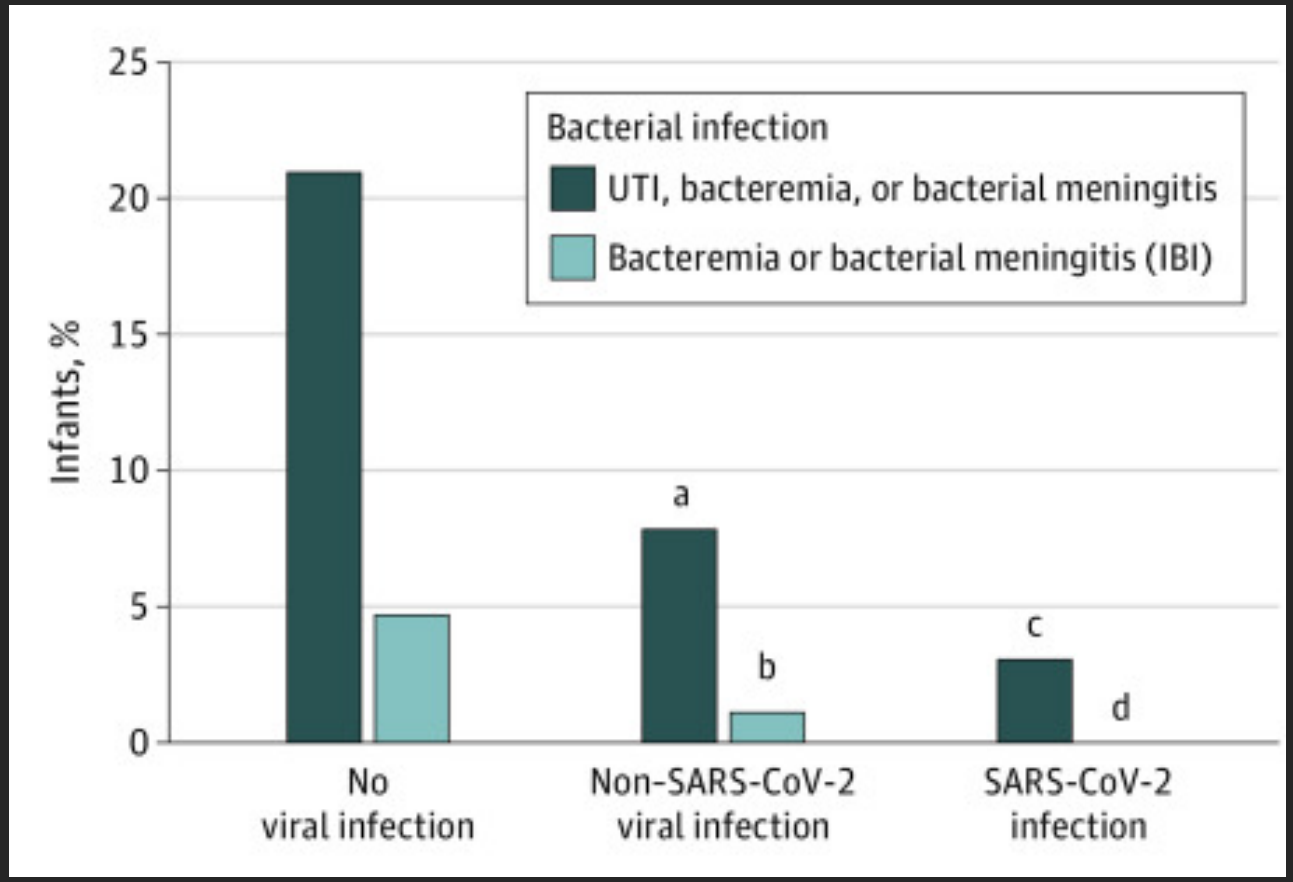
eTable: BioFire Respiratory Panel 2.1 (RP2.1)
Viruses
Adenovirus
Coronavirus 229E
Coronavirus HKU1
Coronavirus NL63
Coronavirus OC43
SARS-CoV-2
Human Metapneumovirus
Human Rhinovirus/Enterovirus
Influenza A
Influenza B
Parainfluenza Virus 1
Parainfluenza Virus 2
Parainfluenza Virus 3
Parainfluenza Virus 4
Respiratory Syncytial Virus
Bacteria
Bordetella parapertussis
Bordetella pertussis
Chlamydia pneumoniae
Mycoplasma pneumoniae

Clinical and Laboratory Characteristics of Infants by Viral Infection Status

Characteristic	Infants, No. (%)			
	Total (N = 931)	No viral infection (n = 320)	Non–SARS-CoV-2 viral infection (n = 448)[a]	SARS-CoV-2 infection (n = 163)[b]
Sex				
Male	547 (58.8)	194 (60.6)	254 (56.7)	99 (60.7)
Female	384 (41.2)	126 (39.4)	194 (43.3)	64 (39.3)
Age, d				
8-21	164 (17.6)	85 (26.6)	58 (12.9)	21 (12.9)
22-28	124 (13.3)	54 (16.9)	55 (12.3)	15 (9.2)
29-60	643 (69.1)	181 (56.6)	335 (74.8)	127 (77.9)
Hospitalized	428 (46.0)	186 (58.1)	199 (44.4)	43 (26.4)
Cerebrospinal fluid culture available	329 (35.3)	165 (55.3)	135 (30.1)	29 (17.8)
Maximal temperature, median (IQR), °C				
All infants	38.3 (38.1-38.7)	38.4 (38.1-38.9)	38.3 (38.1-38.6)	38.4 (38.1-38.7)
Infants with UTI, bacteremia, or bacterial meningitis	38.8 (38.3-39.2)	38.9 (38.5-39.3)	38.5 (38.2-39.0)	38.3 (38.2-39.0)
Procalcitonin, median (IQR), µg/L[c]				
All infants	0.1 (0.1-0.2)	0.1 (0.1-0.4)	0.1 (0.1-0.2)	0.1 (0.1-0.2)
Infants with UTI, bacteremia, or bacterial meningitis	0.7 (0.2-5.1)	1.6 (0.4-7.8)	0.3 (0.1-0.8)	0.1 (0.1-0.2)
C-reactive protein, median (IQR), mg/dL[d]				
All infants	0.31 (0.09-1.12)	0.29 (0.05-2.28)	0.48 (0.16-1.17)	0.14 (0.07-0.28)
Infants with UTI, bacteremia, or meningitis	2.90 (0.94-6.50)	3.94 (1.32-6.91)	2.01 (0.93-6.18)	0.17 (0.14-0.23)
Absolute neutrophil count, median (IQR), cells/µL[e]				
All infants	2700 (1800-4500)	2800 (1800-5300)	3100 (2000-4600)	1900 (1300-2700)
Infants with UTI, bacteremia, or bacterial meningitis	5600 (2900-8400)	6600 (3400-9500)	4600 (2700-6500)	1800 (1600-2200)
Bacterial infections	107 (11.5)	67 (20.9)	35 (7.8)	5 (3.1)

Results

- Prevalence of Any Infection and Invasive Bacterial Infections (IBIs) Specifically Among Febrile Infants According to Viral Status



Discussion

- Findings are similar to previous studies with selective viral testing
- AAP recommendations regarding viral testing
  - Low but not neglible risk in non- SARS-CoV-2
  - No IBIs found in SARS-CoV-2
- Limitations
  - Variant testing limited
  - Low number of IBI
  - Single center
  - Individual practice patterns

How does this change practice?

Resources

- Blaschke AJ, Korgenski EK, Wilkes J, Presson AP, Thorell EA, Pavia AT, Knackstedt ED, Reynolds C, Schunk JE, Daly JA, Byington CL. Rhinovirus in Febrile Infants and Risk of Bacterial Infection. Pediatrics. 2018 Feb;141(2):e20172384. doi: 10.1542/peds.2017-2384. Epub 2018 Jan 17. PMID: 29343585; PMCID: PMC5810600.
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- Estimates of Emergency Department Visits in the United States, 2016-2021 (cdc.gov)
- Estimates of Emergency Department Visits in the United States, 2016-2021 (cdc.gov)
- Products - Data Briefs - Number 452 – November 2022 (cdc.gov)