Application of the Rochester Criteria to Identify Febrile Infants with Bacteremia and Meningitis

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Abstract

Objectives: The Rochester criteria were developed to identify febrile infants aged 60 days at low-risk for bacterial infection and do not include cerebrospinal fluid (CSF) testing. Prior studies have not specifically assessed criteria performance for bacteremia and meningitis (invasive bacterial infection). Our objective was to determine the sensitivity of the Rochester criteria for detection of invasive bacterial infection.

Methods: Retrospective study of febrile infants 60 days old with invasive bacterial infections evaluated at 8 pediatric emergency departments from 7/1/2012 – 6/30/2014. Potential cases were identified from the Pediatric Health Information System using ICD-9 diagnosis codes for

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bacteremia, meningitis, urinary tract infection, and fever. Medical record review was then performed to confirm presence of an invasive bacterial infection and evaluate the Rochester criteria: past medical history, symptoms or ill appearance, results of urinalysis, complete blood count, CSF testing (if obtained), and blood, urine, CSF culture. An invasive bacterial infection was defined as growth of pathogenic bacteria from blood or CSF culture.

Results: Among 82 febrile infants ≤ 60 days old with invasive bacterial infection, the sensitivity of the Rochester criteria was 92.7% (95% CI: 84.9–96.6); 91.7% (95% CI: 80.5–96.7) for neonates ≤ 28 days and 94.1% (95% CI: 80.9–98.4) for infants 29–60 days. Six infants with bacteremia, including one neonate with bacterial meningitis, met low-risk criteria.

Conclusions: The Rochester criteria identified 92% of infants aged ≤ 60 days with invasive bacterial infection. However, one neonate ≤ 28 days old with meningitis was classified as low-risk.

Keywords

Introduction

Febrile infants ≤ 60 days of age are at high-risk for bacterial infections.[1–3] Bacteremia and bacterial meningitis (invasive bacterial infection)[4,5] are less common than urinary tract infection (UTI),[3,6] but are associated with high rates of mortality and neurologic morbidity.[7–10] Clinical appearance alone is not adequate to identify febrile infants with invasive bacterial infection.[11] Therefore, febrile infants often undergo extensive laboratory testing, including lumbar puncture, to evaluate for bacteremia and meningitis.[12] However, the risk of missing a serious bacterial infection must be balanced with risks of this invasive testing which include stress for families[13] and potentially unnecessary hospitalization and parenteral antibiotic treatment if the lumbar puncture is traumatic or unsuccessful.[14]

Clinicians use varied published criteria to identify febrile infants at low-risk for bacterial infection who can safely be discharged home from the emergency department (ED).[15–17] The Rochester criteria were developed for febrile infants ≤ 60 days of age, and are the only published set of criteria that does not include the routine collection of cerebrospinal fluid (CSF).[17,18] The Rochester criteria can therefore be used to identify low-risk infants who may not require lumbar puncture or hospitalization. Prior studies evaluating the Rochester criteria, however, were conducted at single centers and included only a small number of infants with bacteremia or meningitis.[17,19,20] Additionally, the Rochester criteria were developed over 20-years ago and should be reassessed in the era of widespread maternal prophylaxis against Group B Streptococcus (GBS)[21] and conjugate vaccines for *Streptococcus pneumoniae*.[22] A recent executive summary by the Agency for Healthcare Research and Quality also highlighted that there is "insufficient data" on the ability of the low-risk criteria to detect bacteremia and bacterial meningitis in young febrile infants.[23]

Our objective was to describe the clinical characteristics of young infants ≤ 60 days of age with bacteremia and/or bacterial meningitis (invasive bacterial infection) presenting to one

of eight regionally diverse children's hospitals and to determine the sensitivity of the Rochester criteria for detection of invasive bacterial infection among febrile infants.

Materials and Methods

Study Design

We performed a multicenter retrospective cohort study of infants   60 days of age with culture-proven bacteremia and/or bacterial meningitis who were evaluated at one of eight pediatric EDs between July 1, 2012 and June 30, 2014 (see Appendix for list of study sites). Potential cases were identified using the Pediatric Health Information System (PHIS) and confirmed using medical record review at each study site. The study protocol was approved by the Institutional Review Board at each participating site with a waiver of informed consent.

Study Protocol

Each of the eight participating sites contribute data to PHIS, an administrative database affiliated with the Children's Hospital Association (Overland Park, KS) that contains de-identified demographic, diagnosis, and billing data.[24] Potential cases of bacteremia and bacterial meningitis were identified by querying the PHIS database for all infants   60 days of age evaluated at participating EDs with an International Classification of Diseases, 9th revision (ICD-9) discharge diagnosis for bacteremia or sepsis (771.81, 771.83, 790.7, 995.91, 995.92, 785.52, or 038.xx)[12] or bacterial meningitis (036.0, 036.1, 320.0, 320.1, 320.2, 320.3, 320.7, 320.81, 320.82, 320.89, or 320.9).[25] We also queried the PHIS database for all infants with an ICD-9 discharge diagnosis code for UTI or pyelonephritis (590.1, 590.2, 590.8, 599.0, or 771.82)[26] to identify infants with invasive bacterial infection and concomitant UTI. To further identify infants with bacteremia or meningitis who only had a diagnosis code assigned of fever, we additionally identified an equal number of randomly selected infants from the PHIS database over the same 2-year period (using a software-based randomizer) who had an ICD-9 admission or discharge diagnosis code for fever (780.6, 778.4, 780.60, or 780.61)[27] without associated ICD-9 diagnosis code for UTI, bacteremia, or meningitis, and who had culture of urine, blood or CSF obtained during the ED visit or hospitalization. We excluded infants with a complex chronic condition,[28] as these infants may undergo a non-standard evaluation, as well as infants transferred from another hospital as the infant may have undergone testing or treatment prior to transfer. A total of 1057 potential cases were identified using the described search strategy.

We then used medical record review to confirm the presence of culture-positive bacteremia and/or bacterial meningitis among these potential cases. For the infants with confirmed culture-positive bacteremia and/or meningitis on medical record review, data collected included past-medical history, physical exam findings, and results of laboratory testing including urine, blood, and CSF cultures. Data abstraction for medical record review at each of the 8 study sites was performed using the Research Electronic Data Capture (REDCap) tool hosted at the University of Washington.[29]

We abstracted the following demographics from the PHIS database: age, gender, and race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, Asian, or other). To determine the prevalence of infants with invasive bacterial infection among the broader population of infants undergoing diagnostic testing, from the PHIS database we also extracted the total number of infants ≤ 60 days of age in whom a blood culture or CSF testing was performed using the same exclusion criteria described previously.

Rochester Criteria

The Rochester criteria identify febrile infants ≤ 60 days of age at low-risk for bacterial infection if they satisfy all of the following criteria: 1) well-appearing 2) born at ≥ 37 weeks gestation and previously healthy, 3) no source of infection present on exam, 4) peripheral white blood cell (WBC) count 5,000 to 15,000/mm^3, 5) absolute band count ≤ 1500/mm^3, and 6) ≤ 10 WBC on urine microscopy.[17]

We defined fever as a documented temperature ≥ 100.4° F (38.0° C) at home or in the ED.[30] The Rochester criteria were applied to all infants ≤ 60 days of age with fever in the study cohort based on medical record review.

For our study, we defined "Ill appearance" as "symptomatic or ill-appearing" based upon the following medical record review inquiry: "were there any findings on exam to suggest that the patient was symptomatic or ill-appearing? (categorized as yes or no)." If yes, the patients were further categorized based upon the presence or absence of the following features: hypotension, tachycardia (heart rate > 160 beats per minute during ED course), tachypnea (respiratory rate > 50 breaths per minute), increased work of breathing, grunting, mental status changes (somnolence, lethargy, irritability, seizures), or other (with a description).

An infant was determined to not have been previously healthy if any of the following were present: prematurity < 37 weeks gestation at birth, prior antibiotic exposure or hospitalization not including the newborn hospitalization, prior sepsis evaluation for fever, or the presence of immunodeficiency, urinary tract, neurologic, gastrointestinal abnormality, or other severe or chronic condition. Two of the eight participating hospitals do not report bands as a component of the complete blood count (CBC); therefore band count was only reported for infants from 6 hospitals. For sites at which automated differentials were performed, *a priori* the band count was recorded as "not reported" if no bands were reported on the CBC; for the 2 hospitals that do not report bands, "N/A" was documented. Cerebrospinal fluid pleocytosis was defined as ≥ 10 WBC/hpf.[31]

Outcome Measures

Our primary outcome was invasive bacterial infection defined as either bacteremia or bacterial meningitis. We defined bacteremia as growth of a bacterial pathogen from blood culture and bacterial meningitis as growth of a pathogenic species from CSF culture (determined *a priori* by consensus of the two board-certified pediatric infectious diseases physicians in the Febrile Young Infant Research Collaborative).[32] Additionally, cultures that grew common contaminant bacteria were treated as contaminants[32] unless the bacterial species was isolated from two sites (urine, blood, and/or CSF) and treated as a pathogen; these were included as a pathogen species. Infants with bacteremia and CSF pleocytosis, but

with negative CSF culture after antibiotic pretreatment, were defined as bacteremia as per our *a priori* definition.

Statistical Analysis

We described characteristics of infants with bacteremia and/or meningitis overall and in 2 distinct age groups: 28 days and 29–60 days of age. Categorical variables were described using frequencies with 95% confidence intervals (CIs). After retrospective application of the Rochester criteria to the febrile infants 60 days of age, we calculated the sensitivity for invasive bacterial infections.

Results

Patient Characteristics

Of the 5011 infants 60 days of age who underwent blood culture in the 8 EDs during the 2-year study period, 85 (1.7%) had culture-positive bacteremia. Of 3381 infants who had CSF obtained, 10 (0.3%) had culture-positive bacterial meningitis, including 6 with concomitant bacteremia. Fifty-three (59.6%) of the 89 infants with invasive bacterial infection were 28 days of age and 36 (40.4%) were 29–60 days of age. Nine (90.0%) of the 10 infants with meningitis were 28 days of age (Table 1).

Invasive Bacterial Infection

Overall, 43 (48.3%) of the 89 infants with invasive bacterial infection were symptomatic or ill-appearing on presentation; 11 infants had only tachycardia as a symptom. Of the 7 infants who did not have fever on presentation, 6 (85.7%) were symptomatic or ill-appearing including 2 with hypothermia < 36.0°; one well-appearing 3-day old infant was subsequently diagnosed with bacteremia during a hospitalization for hyperbilirubinemia. Of the 82 febrile infants with invasive bacterial infection (including all 10 with meningitis), 58 (70.7%) were either symptomatic/ill-appearing or had an abnormal peripheral WBC or absolute band count as per the Rochester criteria (Table 2). Two febrile neonates 28 days of age had bacteremia with CSF pleocytosis, but negative CSF cultures after antibiotic pretreatment.

Nine of the 10 infants with bacterial meningitis were described as symptomatic or ill-appearing on presentation, including the one infant > 28 days of age who had mental status changes (Table 2 and Table 3). Two infants with meningitis 28 days were determined to be symptomatic or ill-appearing due to tachycardia only, including one 13-day old with GBS bacteremia and meningitis who had a heart rate of 198 with a normal urinalysis and peripheral WBC, with no band cells reported. The one patient that was not symptomatic or ill-appearing was a 19-day old infant with *Paenibacillus* bacteremia and meningitis who had a normal peripheral WBC and absolute band count that met low-risk Rochester criteria (Table 3).

Rochester Criteria

The sensitivity of the Rochester criteria for identification of febrile infants aged 60 days with invasive bacterial infection was 92.7% (95% CI: 84.9–96.6). Among febrile infants

28 days of age, the sensitivity was 91.7% (95% CI: 80.5–96.7), and 94.1% (95% CI: 80.9–98.4) for infants 29–60 days of age.

Four febrile infants, including two 28 days of age (one with meningitis), would not have been classified as low-risk based solely on the presence of tachycardia. Re-classification of these infants as low-risk would lower the sensitivity of the Rochester criteria to 87.8% (95% CI: 80.0–93.2) for invasive bacterial infection.

Six febrile infants with bacteremia, including one with meningitis, would have been classified as low-risk by the Rochester criteria (Table 4). Three of the infants 28 days of age had a CSF pleocytosis, and another had low-level pyuria on urinalysis (6 to 10 WBCs/hpf). The 4 neonates 28 days of age received empiric intravenous antibiotic therapy, while the 2 infants aged 29–60 days received Ceftriaxone prior to ED discharge and were subsequently hospitalized when their blood cultures resulted as positive (Table 4).

Discussion

We performed a multicenter validation of the Rochester criteria for identification of bacteremia and bacterial meningitis. While clinical appearance and CBC alone should not be used to determine the presence of invasive bacterial infection among febrile young infants, with application of the Rochester criteria, 92% of febrile infants 60 days of age with bacteremia and/or meningitis would have been classified as non-low risk. Additionally, 9 of 10 infants with bacterial meningitis were symptomatic or ill-appearing, including the one infant > 28 days of age. However, while the criteria performed similarly among neonates aged 28 days and infants 29–60 days of age, one neonate with meningitis would have missed. As a result, clinicians should be cautious in the application of the Rochester criteria to infants in the first month of life without performance of lumbar puncture.

The majority of infants 60 days of age with bacteremia were described as well-appearing, and nearly one-third of these infants also had no evidence of infection on CBC based upon a WBC of 5,000 to 15,000/mm^3 and an absolute band count 1,500/mm^3 (when obtained). Our findings are consistent with prior investigations that demonstrate that well-appearance[11] and normal serum leukocyte counts[33] are not sensitive for the detection of bacteremia in febrile young infants when used in isolation.

The sensitivity of the Rochester criteria for identification of bacteremia and/or meningitis was 92.7%, similar among infants 29–60 days of age and those aged 28 days. Prior studies of the Rochester criteria reported sensitivity of 92.4% – 96.7%,[17,20] though the majority of the bacterial infections in these studies were UTIs. When only bacteremia and meningitis were included, the sensitivity was 84.6% – 85.7%,[17,20] though there were < 15 cases of bacteremia in each study. Biondi et al recently reported a sensitivity of 80% for bacteremia in a recent multicenter cohort, though their aim was to assess differences in epidemiology based on risk status, not to specifically evaluate the Rochester criteria. Additionally, the performance of the Rochester criteria for detection of meningitis was not assessed.[32] When the 4 febrile infants in our study with tachycardia as their only symptom were re-classified as low-risk, the sensitivity of the Rochester criteria was similar to these prior investigations

at 87.8%. Tachycardia has been reported as a predictor of bacterial infection and sepsis in children, though data is limited for infants < 3 months old.[34,35] The presence of tachycardia as an isolated predictor of invasive bacterial infection should be further explored, as this finding may be commonly observed among febrile infants without bacteremia and/or meningitis and therefore would likely lower the specificity of the Rochester criteria to achieve higher sensitivity.

While the lack of 100% sensitivity of the Rochester criteria for identification of invasive bacterial infection may be of concern to clinicians, the sensitivity reported is similar to or higher than other diagnostic tools being investigated for detection of invasive bacterial infection in young infants, including procalcitonin.[4,5] Additionally, low-risk infants with invasive bacterial infections have been previously reported to do well with outpatient follow-up,[36] though we were unable to meaningfully assess outcomes in this current study as all 6 low-risk infants received empiric antibiotic treatment. Overall, both bacteremia and meningitis were very uncommon among infants who underwent blood culture or CSF testing during the study period, and "missed" infants therefore comprised a low percentage of the entire population. While we were not able to assess the negative predictive value (NPV) of the Rochester criteria, prior studies have demonstrated high NPV among all febrile infants given the rarity of invasive bacterial infections.[17,20] The low, but present, risk of missing a young infant with bacteremia with application of the Rochester criteria must be weighed against the parental stress[13] and potential risks involved with hospitalization and antibiotic administration,[23] particularly for infants aged 29–60 days. Low-risk febrile neonates   28 days of age are routinely admitted and empirically treated.[37–39] Though the Rochester criteria identified most neonates with invasive bacterial infections, further study is needed to examine outcomes of low-risk infants in this age group who are admitted off antibiotics or discharged home with close follow-up. While CSF testing is not part of the Rochester criteria, all 4 infants   28 days of age with bacteremia classified as low-risk would have been identified by CSF pleocytosis with lumbar puncture, which is obtained routinely in this age group,[37,38] or by lower threshold of pyuria on urinalysis as used in prior studies.[40,41]

Among infants who underwent CSF testing during the study period, bacterial meningitis was rare and usually associated with symptoms or ill appearance, especially among infants > 28 days of age. Greenhow et al reported that 10 of 16 infants   90 days of age with bacterial meningitis were ill-appearing, though they used a strict definition of ill appearance and did not specify the age or laboratory values of the 6 infants who were well-appearing.[6] As bacterial meningitis is very rare among infants 29–60 days of age, and the one infant with meningitis in this study had mental status changes, our findings support guidelines of selective CSF testing for these older febrile infants.[39] However, the wide confidence intervals for the sensitivity of the Rochester criteria for detection of bacterial meningitis reflect our small sample size; a larger study would be needed for a more precise estimate of sensitivity. Importantly, one febrile infant   28 days of age with bacterial meningitis would have been missed using the Rochester criteria, and another infant had only tachycardia as a high-risk symptom. These infants and the higher rate of meningitis in this age group support the widely adopted practice of routine CSF testing in neonates.[38,39]

Our study has several limitations. For case identification, we searched an administrative database using ICD-9 diagnosis codes. It is therefore possible that we did not identify all cases of bacteremia and meningitis if an ICD-9 diagnosis code was not attributed to the encounter. However, we used a broad search strategy that included ICD-9 codes for UTI and fever to identify infants with bacteremia or meningitis, in whom an accompanying diagnosis code was not present. Additionally, we excluded patients transferred from another institution, as we were unable to ascertain laboratory testing in these patients. We also excluded children with complex chronic conditions; however, these conditions would often result in a non low-risk classification using the Rochester criteria. Also, our study was conducted within EDs of tertiary care children's hospitals, and our findings may not be generalizable to other practice settings.

The study also has several limitations in the application of the Rochester criteria. First, the presence of fever, as well as clinical appearance and medical history (including prematurity and the Rochester criteria definition of "previous healthy"), may not be accurately documented in the medical record. We also applied the Rochester criteria to infants from all 8 participating hospitals, including 2 hospitals that do not report peripheral bands. However, all but one infant at these 2 hospitals were classified as non-low risk without a reported band count.

Conclusions

Approximately 92% of infants with bacteremia and/or meningitis were accurately identified by the Rochester criteria. Among infants 60 days old, bacterial meningitis was rare and usually associated with symptoms or ill appearance, especially among infants > 28 days of age. However, a few infants 28 days of age with invasive bacterial infections, including one with bacterial meningitis, were well-appearing and classified as low-risk by the Rochester criteria. Clinicians should be cautious in use of the Rochester criteria in febrile neonates 28 days of age without performance of lumbar puncture, pending further investigation on outcomes of low-risk infants with invasive bacterial infections.

Acknowledgements

Appendix

Participating Sites for Medical Record Review

Ann and Robert H. Lurie Children's Hospital of Chicago, Boston Children's Hospital, Children's Hospital of the King's Daughters, Children's Hospital of Philadelphia, Children's

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Abbreviations:

CBC	complete blood count
CI	confidence interval
CSF	cerebrospinal fluid
ED	emergency department
ICD-9	International Classification of Diseases, Ninth Revision
PHIS	Pediatric Health Information System
UTI	urinary tract infection
WBC	white blood cell

References

1. Huppler AR, Eickhoff JC, Wald ER. Performance of low-risk criteria in the evaluation of young infants with fever: review of the literature. Pediatrics. 2010;125:228–233. [PubMed: 20083517]

2. Schwartz S, Raveh D, Toker O, et al. A week-by-week analysis of the low-risk criteria for serious bacterial infection in febrile neonates. Arch Dis Child. 2009;94:287–292. [PubMed: 18977786]

3. Baskin MN. The prevalence of serious bacterial infections by age in febrile infants during the first 3 months of life. Pediatr Ann. 1993;22:462–466. [PubMed: 8414701]

4. Gomez B, Bressan S, Mintegi S, et al. Diagnostic value of procalcitonin in well-appearing young febrile infants. Pediatrics. 2012;130:815–822. [PubMed: 23109682]

5. 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. 2015:1–8. [Epub ahead of print]

6. Greenhow TL, Hung YY, Herz AM, et al. The Changing Epidemiology of Serious Bacterial Infections in Young Infants. Pediatr Infect Dis J. 2014;33:595–599. [PubMed: 24326416]

7. de Louvois J, Halket S, Harvey D. Neonatal meningitis in England and Wales: sequelae at 5 years of age. Eur J Pediatr. 2005;164:730–734. [PubMed: 16136294]

8. Libster R, Edwards KM, Levent F, et al. Long-term outcomes of group B streptococcal meningitis. Pediatrics. 2012;130:e8–e15. [PubMed: 22689869]

9. Tsai MH, Hsu JF, Chu SM, et al. Incidence, clinical characteristics and risk factors for adverse outcome in neonates with late-onset sepsis. Pediatr Infect Dis J. 2014;33:e7–e13. [PubMed: 23899966]

10. Hamer DH, Darmstadt GL, Carlin JB, et al. Etiology of bacteremia in young infants in six countries. Pediatr Infect Dis J. 2015;34:e1–e8. [PubMed: 25389919]

11. Baker MD, Avner JR, Bell LM. Failure of infant observation scales in detecting serious illness in febrile, 4- to 8-week-old infants. Pediatrics. 1990;85:1040–1043. [PubMed: 2339027]

12. Aronson PL, Thurm C, Alpern ER, et al. Variation in Care of the Febrile Young Infant <90 Days in US Pediatric Emergency Departments. Pediatrics. 2014;134:667–677. [PubMed: 25266437]

13. De S, Tong A, Isaacs D, Craig JC. Parental perspectives on evaluation and management of fever in young infants: an interview study. Arch Dis Child. 2014;99:717–723. [PubMed: 24849214]

14. Pingree EW, Kimia AA, Nigrovic LE. The effect of traumatic lumbar puncture on hospitalization rate for febrile infants 28 to 60 days of age. Acad Emerg Med. 2015;22:240–243. [PubMed: 25640087]

15. Baker MD, Bell LM, Avner JR. Outpatient management without antibiotics of fever in selected infants. N Engl J Med. 1993;329:1437–1441. [PubMed: 8413453]

16. Baskin MN, Fleisher GR, O'Rourke EJ. Identifying febrile infants at risk for a serious bacterial infection. J Pediatr. 1993;123:489–490. [PubMed: 8355131]

17. Jaskiewicz JA, McCarthy CA, Richardson AC, et al. Febrile infants at low risk for serious bacterial infection--an appraisal of the Rochester criteria and implications for management. Febrile Infant Collaborative Study Group. Pediatrics. 1994;94:390–396. [PubMed: 8065869]

18. Dagan R, Powell KR, Hall CB, et al. Identification of infants unlikely to have serious bacterial infection although hospitalized for suspected sepsis. J Pediatr. 1985;107:855–860. [PubMed: 4067741]

19. Dagan R, Sofer S, Phillip M, et al. Ambulatory care of febrile infants younger than 2 months of age classified as being at low risk for having serious bacterial infections. J Pediatr. 1988;112:355–360. [PubMed: 3346773]

20. Garra G, Cunningham SJ, Crain EF. Reappraisal of criteria used to predict serious bacterial illness in febrile infants less than 8 weeks of age. Acad Emerg Med. 2005;12:921–925. [PubMed: 16204135]

21. Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). 2010 MMWR Recomm Rep. 2010;59:1–36.

22. Poehling KA, Talbot TR, Griffin MR, et al. Invasive pneumococcal disease among infants before and after introduction of pneumococcal conjugate vaccine. JAMA. 2006;295:1668–1674. [PubMed: 16609088]

23. Hui C, Neto G, Tsertsvadze A, et al. Diagnosis and management of febrile infants (0–3 months). Evid Rep Technol Assess (Full Rep). 2012:1–297.

24. Wood JN, Feudtner C, Medina SP, et al. Variation in occult injury screening for children with suspected abuse in selected US children's hospitals. Pediatrics. 2012;130:853–860. [PubMed: 23071208]

25. Mongelluzzo J, Mohamad Z, Ten Have TR, et al. Corticosteroids and mortality in children with bacterial meningitis. JAMA. 2008;299:2048–2055. [PubMed: 18460665]

26. Tieder JS, Hall M, Auger KA, et al. Accuracy of administrative billing codes to detect urinary tract infection hospitalizations. Pediatrics. 2011;128:323–330. [PubMed: 21768320]

27. Feudtner C, Hays RM, Haynes G, et al. Deaths attributed to pediatric complex chronic conditions: national trends and implications for supportive care services. Pediatrics. 2001;107:E99. [PubMed: 11389297]

28. Aronson PL, Williams DJ, Thurm C, et al. Accuracy of diagnosis codes to identify febrile young infants using administrative data. J Hosp Med. 2015;10:787–793. [PubMed: 26248691]

29. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42:377–781. [PubMed: 18929686]

30. American College of Emergency Physicians Clinical Policies Committee; American College of Emergency Physicians Clinical Policies Subcommittee on Pediatric Fever. Clinical policy for children younger than three years presenting to the emergency department with fever. Ann Emerg Med. 2003;42:530–545. [PubMed: 14520324]

31. Nigrovic LE, Kuppermann N, Macias CG, et al. Clinical prediction rule for identifying children with cerebrospinal fluid pleocytosis at very low risk of bacterial meningitis. JAMA. 2007;297:52–60. [PubMed: 17200475]

32. Biondi E, Evans R, Mischler M, et al. Epidemiology of bacteremia in febrile infants in the United States. Pediatrics. 2013;132:990–996. [PubMed: 24218461]

33. Bonsu BK, Chb M, Harper MB. Identifying febrile young infants with bacteremia: is the peripheral white blood cell count an accurate screen? Ann Emerg Med. 2003;42:216–225. [PubMed: 12883509]

34. Brent AJ, Lakhanpaul M, Ninis N, et al. Evaluation of temperature-pulse centile charts in identifying serious bacterial illness: observational cohort study. Arch Dis Child. 2011;96:368–373. [PubMed: 21233079]

35. Cruz AT, Williams EA, Graf JM, et al. Test characteristics of an automated age- and temperature-adjusted tachycardia alert in pediatric septic shock. Pediatr Emerg Care. 2012;28:889–894. [PubMed: 22929140]

36. Pantell RH, Newman TB, Bernzweig J, et al. Management and outcomes of care of fever in early infancy. JAMA. 2004;291:1203–1212. [PubMed: 15010441]

37. Jain S, Cheng J, Alpern ER, et al. Management of Febrile Neonates in US Pediatric Emergency Departments. Pediatrics. 2014;133:187–195. [PubMed: 24470644]

38. Aronson PL, Thurm C, Williams DJ, et al. Association of clinical practice guidelines with emergency department management of febrile infants 56 days of age. J Hosp Med. 2015;10:358–365. [PubMed: 25684689]

39. Chua KP, Neuman MI, McWilliams JM, et al. Association between Clinical Outcomes and Hospital Guidelines for Cerebrospinal Fluid Testing in Febrile Infants Aged 29–56 Days. J Pediatr. 2015;167:1340–1346.e9. [PubMed: 26477870]

40. Schnadower D, Kuppermann N, Macias CG, et al. Febrile infants with urinary tract infections at very low risk for adverse events and bacteremia. Pediatrics. 2010;126:1074–1083. [PubMed: 21098155]

41. Schroeder AR, Chang PW, Shen MW, et al. Diagnostic accuracy of the urinalysis for urinary tract infection in infants <3 months of age. Pediatrics. 2015;135:965–971. [PubMed: 26009628]

Table 1.

Characteristics of Infants ≤ 60 Days of Age with Bacteremia and Bacterial Meningitis

Characteristic	Bacteremia (n=85)	Meningitis (n=10)[1]
	N (%)	N (%)
Male	50 (58.8%)	5 (50.0%)
Race/Ethnicity		
Non-Hispanic White	36 (42.4)	2 (20.0)
Non-Hispanic Black	16 (18.8)	2 (20.0)
Hispanic	17 (20.0)	2 (20.0)
Asian	4 (4.7)	0 (0)
Other[2]	12 (14.1)	4 (40.0)
Documented temperature ≥ 38.0° C (100.4° F)	78 (91.8)	10 (100)
Age		
0–6 days	8 (9.4)	2 (20.0)
7–14 days	23 (27.1)	2 (20.0)
15–21 days	8 (9.4)	4 (40.0)
22–28 days	11 (12.9)	1 (10.0)
29–60 days	35 (41.2)	1 (10.0)

[1] Includes 6 infants with bacteremia

[2] Other includes patients with Missing race/ethnicity in the Pediatric Health Information System database

Table 2.

Rochester Criteria for Identification of Febrile Infants ≤ 60 days old with Bacteremia and/or Bacterial Meningitis

Age Group	High-Risk PMH[1] N (%)	Symptomatic or Ill-appearing N (%)	UA > 10 WBCs N (%)[2]	Peripheral WBC > 15,000 or < 5,000 N (%)	Absolute Band Count > 1,500 N (%)[3]	Symptomatic or Ill-appearing or abnormal WBC/band count[4] N (%)	Non low-risk per Rochester criteria[5] N (%, 95% CI)
Bacteremia							
Overall[6] (n=78)	21 (26.9)	33 (42.3)	42/75 (56.0)	35 (44.9)	17/63 (27.0)	54 (69.2)	72 (92.3, 95% CI: 84.2–96.4)
28 days (n=45)	10 (22.2)	18 (40.0)	25/42 (59.5)	22 (48.9)	13/40 (32.5)	32 (71.1)	41 (91.1, 95% CI: 79.3–96.5)
29–60 days (n=33)	11 (33.3)	15 (45.5)	17/33 (51.5)	13 (39.4)	4/23 (17.4)	22 (66.7)	31 (93.9, 95% CI: 80.4–98.3)
Bacterial Meningitis							
Overall[6] (n=10)	4 (40.0)	9 (90.0)	1/8 (12.5)	4 (40.0)	2/8 (25.0)	9 (90.0)	9 (90.0, 95% CI: 60.0–98.2)
28 days (n=9)	4 (44.4)	8 (88.9)	1/7 (14.3)	4 (44.4)	2/7 (28.6)	8 (88.9)	8 (88.9, 95% CI: 56.5–98.0)
29–60 days (n=1)	0 (0)	1 (100)	0/1 (0)	0 (0)	0/1 (0)	1 (100)	1 (100, 95% CI: 20.6–100.0)

[1] Gestational age < 37 weeks, prior hospitalization or antibiotics, prior sepsis evaluation for fever, immunodeficiency, urinary tract abnormality prior to ED visit, neurologic abnormality, gastrointestinal abnormality, other severe or chronic condition

[2] 3 patients did not have a urinalysis obtained, including 1 with bacterial meningitis

[3] 2 of 8 hospitals do not report band count; denominator comprises all infants at the remaining 6 hospitals, including those infants with band count "not reported"

[4] Abnormal WBC/band count defined as peripheral WBC > 15,000 or < 5,000 or absolute band count > 1500

[5] Any positive finding in the preceding categories, separately calculated for bacteremia and bacterial meningitis

[6] Includes infants with temperature of ≥ 38.0° C (100.4° F) at home or in ED

Abbreviations: PMH, Past Medical History; UA, Urinalysis; WBC, White Blood Cell; CBC, Complete Blood Count

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Table 3.

Bacterial Meningitis Cases

Age (days)	Symptomatic or Ill Appearance (Y/N)	Peripheral WBC	Absolute Band Count	CSF WBC	CSF RBC	Urine culture	Blood culture	CSF culture
3	Y	1,730	27.7	Not obtained	Not obtained	E. Coli	Salmonella enteriditis	Salmonella enteriditis
6	Y	9,000	1980	26,875	10,000	No growth	GBS	GBS
7	Y	5,900	N/A[2]	1,009	95,025	No growth	E. Coli	E. Coli
13	Y	14,000	Not reported[1]	1,220	17	No growth	GBS	GBS
15	Y	12,000	2640	53	53,805	S. aureus	S. aureus	S. aureus
19	N	6,900	1035	1,385	16	No growth	Paenibacillus	Paenibacillus
20	Y	16,800	Not reported[1]	1,460	280	No growth	No growth	GBS
21	Y	16,100	N/A[2]	40	56,100	No growth	No growth	Klebsiella oxytoca
28	Y	4,870	Not reported[1]	2	0	No growth	Not obtained	GBS
37	Y	5,160	258	Not obtained	Not obtained	No growth	No growth	GBS

[1] Hospital includes band count on CBC; no bands reported on automated differential

[2] Band count not included on CBC at this hospital

Abbreviations: CSF, Cerebrospinal Fluid; WBC, White Blood Cell; RBC, Red Blood Cell

Table 4.

Febrile Infants 60 Days of Age with Bacteremia/Bacterial Meningitis Meeting Low-Risk Rochester Criteria (n=6)

Age (days)	Urinalysis WBC	Peripheral WBC	Absolute Band Count	CSF WBC	Urine culture	Blood culture	CSF culture	ED discharge[1]
3	3–5	8,610	Not reported[2]	35	No growth	Enterococcus	No growth	No
12	6–10	13,800	Not reported[2]	3	Enterococcus[5]	Klebsiella	No growth	No
14	2–5	13,400	Not reported[2]	17	E. Coli	E. Coli	No growth	No
19	0–5	6,900	1,035	1,385	No growth	Paenibacillus	Paenibacillus	No
53	Not reported	7,540	N/A[3]	1[4]	No growth	S. pneumoniae	No growth[4]	Yes
56	0–5	11,100	1,221	80[4]	No growth	GBS	No growth[4]	Yes

[1] Discharge from ED on initial visit

[2] Hospital includes band count on CBC; no bands reported on automated differential

[3] Band count not included on CBC at this hospital

[4] Obtained on index visit

[5] <10,000 CFU/ml, treated as a contaminant

Abbreviations: WBC, White Blood Cell; CSF, Cerebrospinal Fluid; ED, Emergency Department