



Official reprint from UpToDate®

www.uptodate.com©2013 UpToDate®

**Medline® Abstracts for References 4,29,30,32,43,49,62,63
of 'Fever without a source in children 3 to 36 months of age'**

4

TI Practice guideline for the management of infants and children 0 to 36 months of age with fever without source. Agency for Health Care Policy and Research.

AU Baraff LJ, Bass JW, Fleisher GR, Klein JO, McCracken GH Jr, Powell KR, Schriger DL

SO Ann Emerg Med. 1993;22(7):1198.

STUDY OBJECTIVE: To develop guidelines for the care of infants and children from birth to 36 months of age with fever without source.

PARTICIPANTS AND SETTING: An expert panel of senior academic faculty with expertise in pediatrics and infectious diseases or emergency medicine.

DESIGN AND INTERVENTION: A comprehensive literature search was used to identify all publications pertinent to the management of the febrile child. When appropriate, meta-analysis was used to combine the results of multiple studies. One or more specific management strategies were proposed for each of the decision nodes in draft management algorithms. The draft algorithms, selected publications, and the meta-analyses were provided to the panel, which determined the final guidelines using the modified Delphi technique.

RESULTS: All toxic-appearing infants and children and all febrile infants less than 28 days of age should be hospitalized for parenteral antibiotic therapy. Febrile infants 28 to 90 days of age defined at low risk by specific clinical and laboratory criteria may be managed as outpatients if close follow-up is assured. Older children with fever less than 39.0 C without source need no laboratory tests or antibiotics. Children 3 to 36 months of age with fever of 39.0 C or more and whose WBC count is 15,000/mm³ or more should have a blood culture and be treated with antibiotics pending culture results. Urine cultures should be obtained from all boys 6 months of age or less and all girls 2 years of age or less who are treated with antibiotics.

CONCLUSION: These guidelines do not eliminate all risk or strictly confine antibiotic treatment to children likely to have occult bacteremia. Physicians may individualize therapy based on clinical circumstances or adopt a variation of these guidelines based on a different interpretation of the evidence.

AD UCLA Emergency Medicine Center.

PMID 8517575

29

TI Intramuscular versus oral antibiotic therapy for the prevention of meningitis and other bacterial sequelae in young, febrile children at risk for occult bacteremia.

AU Fleisher GR, Rosenberg N, Vinci R, Steinberg J, Powell K, Christy C, Boenning DA, Overturf G, Jaffe D, Platt R

SO J Pediatr. 1994;124(4):504.

Because studies of the treatment of children with occult bacteremia have yielded conflicting results, we compared ceftriaxone with amoxicillin for therapy. Inclusion criteria were age 3 to 36 months, temperature \geq 39 degrees C, an acute febrile illness with no focal findings or with otitis media (6/10 centers), and culture of blood. Subjects were randomly assigned to receive either ceftriaxone, 50 mg/kg intramuscularly, or amoxicillin, 20 mg/kg/dose orally for six doses. Of 6733 patients enrolled, 195 had bacteremia and 192 were evaluable: 164 *Streptococcus pneumoniae*, 9 *Haemophilus influenzae* type b, 7 *Salmonella*, 2 *Neisseria meningitidis*, and 10 other. After treatment, three patients receiving amoxicillin had the same organism isolated from their blood (two *H. influenzae* type b, one *Salmonella*) and two from the spinal fluid (two *H. influenzae* type b), compared with none given ceftriaxone. Probable or definite infections occurred in three children treated with ceftriaxone and six given amoxicillin (adjusted odds ratio 0.43, 95%

confidence interval 0.08 to 1.82, $p = 0.31$). The five children with definite bacterial infections (three meningitis, one pneumonia, one sepsis) received amoxicillin (adjusted odds ratio 0.00, 95% confidence interval 0.00 to 0.52, $p = 0.02$). Fever persisted less often with ceftriaxone (adjusted odds ratio 0.52, 95% confidence interval 0.28 to 0.94, $p = 0.04$). Although the difference in total infections was not significant, ceftriaxone eradicated bacteremia, prevented significantly more definite focal bacterial complications, and was associated with less persistent fever.

AD Department of Pediatrics, Harvard Medical School, Boston, Massachusetts.
PMID151462

30 [Check for full text availability](#) [Department of the Navy PubMed](#)

TI Incidence of occult bacteremia among highly febrile young children in the era of the pneumococcal conjugate vaccine: a study from a Children's Hospital Emergency Department and Urgent Care Center.

AU Stoll ML, Rubin LG

SO Arch Pediatr Adolesc Med. 2004;158(7):671.

BACKGROUND: The optimal diagnostic approach to and management of well-appearing, highly febrile young children has been a matter of debate owing to the possibility of clinically inapparent, or occult, bacteremia (OB). The most common causative organism of OB is *Streptococcus pneumoniae*. Universal immunization with a heptavalent pneumococcal conjugate vaccine (PCV7) has recently been implemented, but there are limited data on the impact of this vaccine on the incidence of OB.

OBJECTIVE: To evaluate the incidence of OB in the era of routine use of PCV7.

METHODS: We conducted a retrospective cohort study of highly febrile (temperature, 39 degrees C) children between the ages of 2 months and 36 months who had blood cultures performed in the emergency department or urgent care center between December 11, 2001, and March 5, 2003, and were discharged to home at the time of the initial visit.

RESULTS: Of 329 blood cultures obtained from children who met inclusion criteria and did not meet exclusion criteria, 3 (0.91%; 95% confidence interval, 0%-1.9%) yielded a pathogenic bacterium; all were *S pneumoniae*. Neither an elevated total white blood cell count, an elevated absolute neutrophil count, nor an increased percentage of bands was highly predictive of OB. Blood cultures positive for organisms were more commonly due to contaminants (4; 95% confidence interval, 0%-2.4%) than pathogens.

CONCLUSIONS: In the PCV7 era, OB is uncommon in highly febrile children 2 to 36 months of age. With continued use of PCV7, the routine practice of obtaining blood cultures and complete blood cell counts may no longer be indicated in previously healthy, well-appearing, highly febrile children 2 to 36 months of age, particularly those who have received at least 1 dose of PCV7.

AD Division of Infectious Diseases, Schneider Children's Hospital of the North Shore-Long Island Jewish Health System, Albert Einstein College of Medicine, New Hyde Park, NY 11040, USA.

PMID15237067

32 [Check for full text availability](#) [Department of the Navy PubMed](#)

TI Changing epidemiology of outpatient bacteremia in 3- to 36-month-old children after the introduction of the heptavalent -conjugated pneumococcal vaccine.

AU Herz AM, Greenhow TL, Alcantara J, Hansen J, Baxter RP, Black SB, Shinefield HR

SO Pediatr Infect Dis J. 2006;25(4):293.

BACKGROUND: The introduction of routine vaccination with heptavalent conjugated pneumococcal vaccine has changed the overall incidence of bacteremia in children 3 months-3 years old.

OBJECTIVE: To describe the changing incidence and etiology of bacteremia in previously healthy toddlers presenting to outpatient clinical settings.

METHODS: Retrospective case series of all blood cultures obtained between September 1998 and August 2003 in Kaiser Permanente Northern California outpatient clinics and emergency departments from previously healthy children 3 months-3 years old.

RESULTS: Implementation of routine vaccination with the conjugated pneumococcal vaccine resulted in an 84% reduction of *Streptococcus pneumoniae* bacteremia (1.3-0.2%) and a 67% reduction in overall bacteremia (1.6-0.7%) in the study population. The rate of blood culture isolation of contaminating organisms remained unchanged at 1.8%;

therefore, by the end of the study, >70% of organisms identified in blood cultures were contaminants. During the 5 study years, total blood cultures drawn decreased by 35% in outpatient pediatric clinics but remained unchanged in emergency departments. By 2003, one-third of all pathogenic organisms isolated from blood cultures were *Escherichia coli*, one-third were non-vaccine serotype *S. pneumoniae*, the majority of the remaining one-third were *Staphylococcus aureus*, *Salmonella* spp., *Neisseria meningitidis* and *Streptococcus pyogenes*. In our population of children routinely immunized with the conjugated pneumococcal vaccine, a white blood cell count >15,000 by itself is a poor predictor of bacteremia in the febrile toddler (sensitivity, 74.0%; specificity, 54.5%; positive predictive value, 1.5%; negative predictive value, 99.5%).

CONCLUSION: In the United States, routine vaccinations with *Haemophilus influenzae* type b and *S. pneumoniae* vaccines have made bacteremia in the previously healthy toddler a rare event. As the incidence of pneumococcal bacteremia has decreased, *E. coli*, *Salmonella* spp. and *Staphylococcus aureus* have increased in relative importance. The use of the white blood cell count alone to guide the empiric use of antibiotics is not indicated. New guidelines are needed to approach the previously healthy febrile toddler in the outpatient setting.

AD Department of Pediatrics and Pediatric Infectious Disease, Kaiser Permanente, Hayward, CA 94545, USA.
arnd.herz@kp.org

PMID16567979

43 [Check for full text availability](#) [Department of the Navy PubMed](#)

TI Risk of bacteremia for febrile young children in the post-*Haemophilus influenzae* type b era.

AU Lee GM, Harper MB

SO Arch Pediatr Adolesc Med. 1998;152(7):624.

OBJECTIVES: To determine the risk for bacteremia, in the post-*Haemophilus influenzae* type b era, in a prospective cohort of well-appearing febrile children 3 to 36 months of age with no obvious source of infection; and to compare the predictive abilities of objective criteria in identification of children with occult pneumococcal bacteremia from those at risk.

DESIGN: All children seen from 1993 through 1996, 3 to 36 months of age with a temperature of 39.0 degrees C or higher, no identified source of infection (except otitis media), and discharged to home were considered to be at risk for occult bacteremia and included in the study.

SETTING: Urban pediatric emergency department.

RESULTS: Of 199868 patient visits to the emergency department, 1911 children were considered to be at risk for occult bacteremia. Blood cultures were obtained from 9465 (79%). A total of 149 blood cultures contained pathogenic organisms, indicating a rate of occult bacteremia of 1.57% (95% confidence intervals: 1.32%-1.83%). White blood cell count and absolute neutrophil count were the best predictors for occult pneumococcal bacteremia. Using a white blood cell count cutoff value of 15 cells x 10⁹/L (sensitivity, 86%; specificity, 77%; and positive predictive value, 5.1%) would result in the treatment of approximately 19 nonbacteremic children for each bacteremic child treated.

CONCLUSIONS: The prevalence of occult bacteremia in children 3 to 36 months old with temperatures of 39.0 degrees C or higher and no obvious source of infection is 1.6%. The white blood cell and absolute neutrophil counts are the most accurate predictors of occult pneumococcal bacteremia and when available should be used if presumptive antibiotic therapy is being considered.

AD Department of Medicine, Children's Hospital, Boston, Mass 02115, USA.

PMID9667531

49 [Check for full text availability](#) [Department of the Navy PubMed](#)

TI Occult bacteremia from a pediatric emergency department: current prevalence, time to detection, and outcome.

AU Alpern ER, Alessandrini EA, Bell LM, Shaw KN, McGowan KL

SO Pediatrics. 2000;106(3):505.

OBJECTIVE: To evaluate selected characteristics of occult bacteremia in the post-*Haemophilus influenzae* type b (HIB) vaccine era.

METHODS: A retrospective cohort study was performed involving 5901 children 2 to 24 months old with fever \geq 39.0 degrees C evaluated with a blood culture at an urban tertiary care children's hospital emergency department (ED) between February 1993 and June 1996. Patients were excluded if immune-suppressed, diagnosed with a focal

infection, evaluated by lumbar puncture, or admitted to the hospital during initial evaluation. Prevalence of occult bacteremia, distribution of current pathogenic organisms, and time to positive culture in a continuously monitored system were determined. All patients with cultures positive for pathogenic bacteria were reevaluated and serious adverse outcomes were documented.

RESULTS: The prevalence of occult bacteremia was 1.9% (95% confidence interval: 1.5%-2.3%). *Streptococcus pneumoniae* accounted for 82.9% of all pathogens and *H influenzae* was not a causative organism in this cohort. The mean time to positive culture was significantly shorter for pathogens compared with contaminants (14.9 hours vs 31.1 hours). A culture that was positive in ≤ 18 hours was 13.0 (6.3-26.6) times more likely to contain a pathogen than a contaminant. The average time from positive culture notification to reevaluation in the ED was 10.6 hours and over half of the patients recalled to the ED for positive cultures were admitted to the hospital. Of patients with occult pneumococcal bacteremia, 95.7% had resolution of their bacteremia without the use of parenteral antibiotics. Two patients had serious adverse outcomes. The rate of meningitis or death was .03% (.004%-12%). The contamination rate of blood cultures was 2.1% (1.7%-2.5%). Most (85%) of these patients were reevaluated in the ED and more than one third were admitted to the hospital before full identification of the organism.

CONCLUSIONS: Prevalence of occult bacteremia in the post-HIB vaccine era is lower than previously reported. *S pneumoniae* is the most common causative organism and resolves without parenteral antibiotics in the vast majority of cases. Continuously monitoring blood culture systems allow for early identification and can aid in differentiating contaminated from true pathogenic cultures by time to positive culture. Serious adverse outcome is an uncommon result of occult bacteremia. Updated epidemiology and microbiologic technology may impact the evaluation and treatment of children at risk for occult bacteremia.

AD Division of Emergency Medicine, Children's Hospital of Philadelphia, Pennsylvania 19104, USA.
alpern@email.chop.edu

PMID|0969095

62

TI Management of fever without source in infants and children.

AU Baraff LJ

SO Ann Emerg Med. 2000;36(6):602.

Twenty percent of febrile children have fever without an apparent source of infection after history and physical examination. Of these, a small proportion may have an occult bacterial infection, including bacteremia, urinary tract infection (UTI), occult pneumonia, or, rarely, early bacterial meningitis. Febrile infants and young children have, by tradition, been arbitrarily assigned to different management strategies by age group: neonates (birth to 28 days), young infants (29 to 90 days), and older infants and young children (3 to 36 months). Infants younger than 3 months are often managed by using low-risk criteria, such as the Rochester Criteria or Philadelphia Criteria. The purpose of these criteria is to reduce the number of infants hospitalized unnecessarily and to identify infants who may be managed as outpatients by using clinical and laboratory criteria. In children with fever without source (FWS), occult UTIs occur in 3% to 4% of boys younger than 1 year and 8% to 9% of girls younger than 2 years of age. Most UTIs in boys occur in those who are uncircumcised. Occult pneumococcal bacteremia occurs in approximately 3% of children younger than 3 years with FWS with a temperature of 39.0 degrees C (102.2 degrees F) or greater and in approximately 10% of children with FWS with a temperature of 39.5 degrees C (103.1 degrees F) or greater and a WBC count of 15,000/mm³ or greater. The risk of a child with occult pneumococcal bacteremia later having meningitis is approximately 3%. The new conjugate pneumococcal vaccine (7 serogroups) has an efficacy of 90% for reducing invasive infections of *Streptococcus pneumoniae*. The widespread use of this vaccine will make the use of WBC counts and blood cultures and empiric antibiotic treatment of children with FWS who have received this vaccine obsolete.

AD Department of Pediatrics and Emergency Medicine, University of California, Los Angeles Emergency Medicine Center, Los Angeles, CA, USA. lbaraff@ucla.edu

PMID|1097701

63

TI Reevaluation of outpatients with *Streptococcus pneumoniae* bacteremia.

AU Bachur R, Harper MB

SO Pediatrics. 2000;105(3 Pt 1):502.

BACKGROUND: The reevaluation process for outpatients recalled for *Streptococcus pneumoniae* bacteremia has not been standardized. Children who return ill or with new serious focal infections require admission and parenteral

antibiotic therapy. Limited data exist to guide the follow-up management of those patients identified as having occult pneumococcal bacteremia.

OBJECTIVES: Characterize the outcomes of outpatients with pneumococcal bacteremia based on their evaluation at follow-up. For patients who are well-appearing without serious focal infection, propose a management scheme for reevaluation.

METHODS: Retrospective review of outpatients with pneumococcal bacteremia. Patients with immunocompromise, those identified with focal bacterial infection at the initial visit, or those admitted at the initial visit were excluded. Data were collected from the initial visit (when blood culture drawn) and follow-up visit with regard to clinical parameters, laboratory data, diagnoses, and any antibiotic treatment. Decision tree analysis was used to generate a model to predict children at high risk for persistent bacteremia (PB).

RESULTS: A total of 548 episodes of pneumococcal bacteremia were studied. Seventy-three children received no antibiotic, 239 oral antibiotic, and 236 parenteral antibiotic at the initial visit. Median age, temperature, and white blood cell (WBC) count were 13.5 months, 40.0 degrees C, and 20 400/mm³. Forty-one patients had PB or new focal infections (15 with PB alone, 4 had focal infection and PB). Eight patients had meningitis at follow-up. Ninety-two percent returned because of notification of the positive blood culture result. A repeat blood culture was obtained in 92%, 23% had a lumbar puncture, 33% had a chest radiograph, and 12% were admitted. PB was associated with the antibiotic treatment group, elevation of temperature, and WBC count at follow-up. A simple management scheme using 2 sequential decision nodes of antibiotic treatment (none vs any) and then temperature at follow-up (>38.8 degrees C) would have predicted 16/19 patients with PB (sensitivity = .84 and specificity = .86).

CONCLUSIONS: All patients with pneumococcal bacteremia need prompt reevaluation. For well-appearing patients without new focal infection, the utility of diagnostic testing (specifically repeat blood cultures) and the need for admission may be determined by the use of antibiotics at the initial evaluation and the presence of fever at follow-up. The majority of patients can be managed as outpatients entirely. Patients who did not receive antibiotics at the initial evaluation and those treated with oral antibiotics but remain febrile are at the highest risk for persistent bacteremia.

AD Division of Emergency Medicine, Children's Hospital, Boston, MA 02115, USA. bachur@a1.tch.harvard.edu
PMID10699100