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**Medline ® Abstracts for References 15,30-37
of 'Fever without a source in children 3 to 36 months of age'**

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TI The accuracy of clinical symptoms and signs for the diagnosis of serious bacterial infection in young febrile children: prospective cohort study of 15 781 febrile illnesses.

AU Craig JC, Williams GJ, Jones M, Codarini M, Macaskill P, Hayen A, Irwig L, Fitzgerald DA, Isaacs D, McCaskill M

SO BMJ. 2010;340:c1594.

OBJECTIVES: To evaluate current processes by which young children presenting with a febrile illness but suspected of having serious bacterial infection are diagnosed and treated, and to develop and test a multivariable model to distinguish serious bacterial infections from self limiting non-bacterial illnesses. Design Two year prospective cohort study. Setting The emergency department of The Children's Hospital at Westmead, Westmead, Australia.

PARTICIPANTS: Children aged less than 5 years presenting with a febrile illness between 1 July 2004 and 30 June 2006.

INTERVENTION: A standardised clinical evaluation that included mandatory entry of 40 clinical features into the hospital's electronic record keeping system was performed by physicians. Serious bacterial infections were confirmed or excluded using standard radiological and microbiological tests and follow-up. Main outcome measures Diagnosis of one of three key types of serious bacterial infection (urinary tract infection, pneumonia, and bacteraemia), and the accuracy of both our clinical decision making model and clinician judgment in making these diagnoses.

RESULTS: We had follow-up data for 93% of the 15 781 instances of febrile illnesses recorded during the study period. The combined prevalence of any of the three infections of interest (urinary tract infection, pneumonia, or bacteraemia) was 7.2% (1120/15 781, 95% confidence interval (CI) 6.7% to 7.5%), with urinary tract infection the diagnosis in 543 (3.4%) cases of febrile illness (95% CI 3.2% to 3.7%), pneumonia in 533 (3.4%) cases (95% CI 3.1% to 3.7%), and bacteraemia in 64 (0.4%) cases (95% CI 0.3% to 0.5%). Almost all (>94%) of the children with serious bacterial infections had the appropriate test (urine culture, chest radiograph, or blood culture). Antibiotics were prescribed acutely in 66% (359/543) of children with urinary tract infection, 69% (366/533) with pneumonia, and 81% (52/64) with bacteraemia. However, 20% (2686/13 557) of children without bacterial infection were also prescribed antibiotics. On the basis of the data from the clinical evaluations and the confirmed diagnosis, a diagnostic model was developed using multinomial logistic regression methods. Physicians' diagnoses of bacterial infection had low sensitivity (10-50%) and high specificity (90-100%), whereas the clinical diagnostic model provided a broad range of values for sensitivity and specificity.

CONCLUSIONS: Emergency department physicians tend to underestimate the likelihood of serious bacterial infection in young children with fever, leading to undertreatment with antibiotics. A clinical diagnostic model could improve decision making by increasing sensitivity for detecting serious bacterial infection, thereby improving early treatment.

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PMID20406860

30

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.

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PMID15237067

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TI An analysis of pediatric blood cultures in the postpneumococcal conjugate vaccine era in a community hospital emergency department.

AU Sard B, Bailey MC, Vinci R

SO *Pediatr Emerg Care.* 2006;22(5):295.

OBJECTIVE: Blood cultures are commonly included in the evaluation of febrile children younger than 3 years without focal source of infection. Clinicians treat patients with a positive blood culture before final identification of the organism. Their treatment might include reevaluation in the emergency department (ED), additional tests, parenteral antibiotics, and hospital admission even for children who ultimately have false-positive (FP) blood cultures. The advent of pneumococcal conjugate vaccine (PCV) has made occult bacteremia less common, decreasing the likelihood that a positive blood culture result before final organism identification will be a true pathogen. This study will identify the characteristics of patients with FP blood cultures in the post-PCV era.

METHODS: Charts were reviewed of all children ages 1 to 36 months with a temperature of at least 38.08 degrees C who had a blood culture obtained in our community hospital ED from January 1997 to January 2005.

RESULTS: Bacteria grew in 106 (3.5%) out of 2971 blood cultures. True positives (TPs), defined as true pathogens, had a prevalence of 0.7%, representing 19.8% of positives. FPs, defined as contaminants, occurred in 2.8% of cultures, representing 80.2% of positives. Patients with FP cultures had lower mean white blood cell (WBC) counts ($10.51 \times 10^9/L$ vs. $16.95 \times 10^9/L$; $P = 0.0001$) and lower mean presenting temperatures (38.8 degrees C vs. 39.4 degrees C; $P = 0.005$). FPs had longer time to positivity (34.6 vs. 17.7 hours; $P = 0.001$) than TPs. A culture with a Gram stain suggestive of a contaminant, time to positivity greater than 24 hours and a WBC of less than $15 \times 10^9/L$ had a PPV for an FP of 97%. When analysis was restricted to well-appearing children age 2 to 36 months with temperature of more than 39 degrees C without focal source of infection who were discharged from the ED, these three criteria had a PPV for an FP of 100%. In these highly febrile children, the FPs had significantly lower WBCs ($9.14 \times 10^9/L$ vs. $22.84 \times 10^9/L$; $P = 0.0001$) and longer time to positivity (33.4 vs. 19.8 hours; $P = 0.007$) than TPs. The likelihood of obtaining FP cultures increased after the introduction of PCV from 62.5% to 87.8% odds ratio, 4.3; 95% confidence interval, 1.44-13.38).

CONCLUSIONS: In the post-PCV era, the majority of blood culture results will be FPs. FP cultures are predictable in febrile children with WBC counts less than $15.00 \times 10^9/L$, time to positivity of more than 24 hours, and a Gram stain result suggestive of a contaminant. Prospective studies applying these criteria to the at-risk population for occult bacteremia are indicated.

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PMID16714955

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- 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.

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PMID16567979

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- TI Pneumococcal bacteremia in febrile infants presenting to the emergency department before and after the introduction of the heptavalent pneumococcal vaccine.
- AU Carstairs KL, Tanen DA, Johnson AS, Kailes SB, Riffenburgh RH
- SO *Ann Emerg Med.* 2007;49(6):772.

STUDY OBJECTIVE: Fever is among the most common presenting complaints of infants and children younger than 3 years who present to the emergency department (ED). The evaluation and management of the febrile child is evolving rapidly. We compare the proportion of pneumococcal bacteremia between febrile infants and children younger than 3 years who had and had not received the heptavalent pneumococcal vaccine and who had received blood culture tests in our ED.

METHODS: We performed a non-concurrent prospective observational cohort study, with a standardized medical record review to collect data of patients treated in the ED of a tertiary care military hospital during 24 months. Patients were eligible if they were younger than 36 months and had a temperature greater than or equal to 100.4 degrees F (38 degrees C). A data collection sheet was used to abstract age, temperature, and whether CBC count and blood cultures were obtained. Heptavalent pneumococcal vaccine status and blood culture results were obtained through review of the computerized medical record. Descriptive analysis was used for comparing the 2 groups. Group size analysis was based on the prevalence of occult bacteremia caused by *Pneumococcus* before the introduction of heptavalent pneumococcal vaccine. Interobserver variation was assessed by independent review of 10% of abstracted records. The main outcome measure was the proportion of positive pneumococcal blood cultures in infants and children younger than 3 years who had received at least 1 vaccination of heptavalent pneumococcal vaccine versus those who had not.

RESULTS: Three thousand five hundred seventy-one patients met entry criteria; 1,428 had blood cultures obtained, and 833 of them received at least 1 immunization of heptavalent pneumococcal vaccine. All groups were similar in age, sex, and temperature. Positive blood culture results, including probable contaminants, were obtained for 4.2% (58/1,383) of the patients. In the heptavalent pneumococcal vaccine group, there were 0 of 833 (0%) positive pneumococcal blood cultures compared with 13 of 550 (2.4%) in the unimmunized group ($P < .001$; 95% confidence interval 1.4% to 3.3%).

CONCLUSION: Pneumococcal bacteremia was found to be lower in our patients who had received the heptavalent pneumococcal vaccine than in the patients who had not.

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PMID17337092

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TI Outcomes of febrile children without localising signs after pneumococcal conjugate vaccine.

AU Waddle E, Jhaveri R

SO Arch Dis Child. 2009;94(2):144.

BACKGROUND: Evaluation of children with fever without localising signs (FWLS) has barely changed in the USA since 1993 despite reduced invasive disease after the introduction of Haemophilus influenzae type b conjugate vaccine and conjugate pneumococcal vaccine (PCV7). PCV7 is now recommended in the UK for children under 2 years of age, and new NICE guidelines have been issued for managing feverish children in the UK in anticipation of PCV7's efficacy. We compared rates of bacterial infections in children aged 3-36 months with FWLS in the pre- and post-PCV7 eras to define current trends and evaluate existing guidelines.

METHODS: We identified all paediatric blood cultures performed in an emergency department before and after PCV7. We subsequently identified all children aged 3-36 months with FWLS and reviewed their medical records.

RESULTS: We identified 148 patients with FWLS in the pre-PCV7 period and 275 patients after PCV7. There were 17 positive cultures before PCV7 (10 pathogens and seven contaminants) and 14 positive cultures (but only one pathogen) after PCV7. This represented a 94.6% decrease overall ($p = 0.009$) and a 100% decrease in Streptococcus pneumoniae. Rates of urinary tract infections (UTIs) were unchanged (6.8% vs 7.6%); UTIs are now the most prevalent bacterial infection in this group. Over 50% of patients still received empirical antibiotics.

CONCLUSIONS: Based on our data, the emphasis in managing children with FWLS should be on diagnosing UTI. Guidelines for evaluating children with FWLS in countries using PCV7 should emulate the NICE model and reflect the trends identified in this study.

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PMID18539684

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TI Prevalence of occult bacteremia in children aged 3 to 36 months presenting to the emergency department with fever in the postpneumococcal conjugate vaccine era.

AU Wilkinson M, Bulloch B, Smith M

SO Acad Emerg Med. 2009;16(3):220.

OBJECTIVES: The goal of this study was to identify the prevalence of occult bacteremia (OB) in well-appearing, previously healthy children aged 3 to 36 months who present to the emergency department (ED) with fever without source in the post-pneumococcal conjugate vaccine (PCV) era.

METHODS: This was a retrospective cohort study of children presenting to an urban pediatric ED between July 1, 2004, and June 30, 2007. Children were included if they were aged 3 to 36 months, febrile, and previously healthy; had no source of infection on examination; had a blood culture drawn; and were discharged from the ED. Outcome measures were rates of OB and contaminant rates.

RESULTS: A total of 8,408 children met all inclusion criteria. There were 21 true-positives, yielding an OB rate of 0.25% (95% confidence interval [CI]= 0.16% to 0.37%). There were 159 contaminant cultures yielding a contaminant rate of 1.89% (95% CI = 1.61% to 2.19%), or a ratio of 7.6 contaminants for each true-positive. There were 14 included patients who grew Streptococcus pneumoniae from the blood, for a rate of 0.17% (95% CI = 0.09% to 0.27%).

CONCLUSIONS: Given the current rate of OB in the post-PCV era, it may no longer be cost-effective to send blood cultures on well-appearing, previously healthy children aged 3 to 36 months who have fever without source.

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PMID19133844

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TI Pneumococcal bacteremia in febrile infants presenting to the emergency department 8 years after the introduction of pneumococcal conjugate vaccine in the Basque Country of Spain.

AU Benito-Fernández J, Mintegi S, Pocheville-Gurutza I, Sánchez Etxaniz J, Gómez Cortés B, Hernández Almaraz JL

SO *Pediatr Infect Dis J.* 2010;29(12):1142.

We included 3088 well-appearing infants aged between 3 and 36 months with fever without a source with a blood culture done as part of their study of fever. Rate of positive blood cultures for *Streptococcus pneumoniae* occult bacteremia (OB) was 0.58%. Rate of OB caused by PCV7-serotypes and nonvaccine serotypes were 0.16% and 0.42%, respectively. A total of 18 cases of *S. pneumoniae* OB were identified between January 1, 2006 and December 31, 2009. None of the 5 infants who had *S. pneumoniae* OB caused by vaccine serotypes had received PCV7. The decline in pneumococcal OB rates observed after PCV7 introduction in our area (Basque Country, Spain) continues 8 years later. There is no evidence of an OB rate increase caused by non-PCV7 serotypes.

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PMID20592642

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TI Bacteremia in feverish children presenting to the emergency department: a retrospective study and literature review.

AU Bressan S, Berlese P, Mion T, Masiero S, Cavallaro A, Da Dalt L

SO *Acta Paediatr.* 2012 Mar;101(3):271-7. Epub 2011 Oct 15.

AIM: To evaluate the incidence of bacteremia, and the isolated pathogens, in well-appearing children with fever without source (FWS) presenting to the pediatric emergency department (PED), after pneumococcal conjugate vaccine - 7 valent (PCV-7) widespread introduction in the Veneto region of north-eastern Italy, and to review the main literature contributions on the subject.

METHODS: Blood cultures performed at the PED of Padova from 1 June 2006 to 31 January 2009 in febrile children aged 1-36 months were retrospectively retrieved. Medical records of previously healthy well-appearing children with FWS were identified and reviewed.

RESULTS: The study finally included 392 patients. Bacteremia rate was 0.34% (95% CI 0-1) in the age group 3-36 months and 2% (95% CI 0-4.7) in infants 1-3 months. No *Streptococcus pneumoniae* was isolated. The literature review identified 10 relevant studies carried out in the USA and Spain showing an overall bacteremia rate <1% for feverish children aged 3-36 months, with values <0.5% in settings with high PCV-7 coverage.

CONCLUSION: Overall bacteremia rate is currently <0.5% in well-appearing children aged 3-36 months with FWS attending the PED in areas with PCV-7 widespread vaccination and is sufficiently low to preclude laboratory testing in favour of close follow-up. Further research is needed to evaluate a more conservative approach in infants 2-3 months of age.

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