Blood Cultures in the Emergency Department Evaluation of Childhood Pneumonia

Samir S. Shah, MD, MSCE,†‡§¶‖ Maria H. Dugan, BA,* Louis M. Bell, MD,*†‡§ Robert W. Grundmeier, MD,** Todd A. Florin, MD,‖†† Elizabeth M. Hines, BA,* and Joshua P. Metlay, MD, PhD¶‖‡‡*

Background: Blood cultures are frequently obtained in the emergency department (ED) evaluation of children with community-acquired pneumonia (CAP).

Objectives: To determine the prevalence of bacteremia in children presenting to the ED with CAP, identify subgroups at increased risk for bacteremia, and quantify the effect of positive blood cultures on management.

Methods: This case–control study was nested within a cohort of children followed up at 35 pediatric practices. Patients from this cohort who were ≤18 years of age, evaluated in the ED in 2006–2007, and diagnosed with CAP were eligible. Cases were those with bacteremia. Controls included those with negative blood cultures and those without blood cultures performed.

Results: A total of 877 (9.6%) of 9099 children with CAP were evaluated in the ED. The mean age was 3.6 years; 53% were male. Blood cultures were obtained from 291 children (33.2%). Overall, the prevalence of bacteremia was 2.1% (95% confidence interval [CI]: 0.8%–4.4%). Bacteremia occurred in 2.6% (95% CI: 1.0%–5.6%) with an infiltrate on chest radiograph and in 13.0% (95% CI: 2.8%–33.6%) with complicated pneumonia. *Streptococcus pneumoniae* accounted for 4 of the 6 cases of bacteremia. Blood culture results altered management in 5 of the 6 bacteremic patients; 1 had an appropriate broadening and 4 had an appropriate narrowing of coverage. The contamination rate was 1.0% (95% CI: 0.2%–3.0%).

Conclusion: Children presenting to the ED for evaluation of CAP are at low-risk for bacteremia. Although positive blood cultures frequently altered clinical management, the overall impact was small because of the low prevalence of bacteremia.

Accepted for publication December 7, 2010.

From the Divisions of *Infectious Diseases and †General Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA; ‡Center for Pediatric Clinical Effectiveness, The Children's Hospital of Philadelphia, Philadelphia, PA; Departments of §Pediatrics and ¶Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia, PA; ‖Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia, PA; **Center for Biomedical Informatics, The Children's Hospital of Philadelphia, Philadelphia, PA; ††Division of Emergency Medicine, The Children's Hospital of Philadelphia, Philadelphia, PA; and ‡‡Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA.

Supported from the National Institute of Allergy and Infectious Diseases (to S.S.S., K01 AI73729) and the Robert Wood Johnson Foundation under its Physician Faculty Scholar Program. Short-term support from the National Heart, Lung, and Blood Institute (to M.H.D.), and supported by the National Institute of Allergy and Infectious Diseases (to J.P.M., K24 AI073957).

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Address for correspondence: Samir S. Shah, MD, MSCE, Division of Infectious Diseases, The Children's Hospital of Philadelphia, Room 1526 (North Campus), 34th Street and Civic Center Boulevard, Philadelphia, PA 19104. E-mail: shahs@email.chop.edu.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.pidj.com).

ISSN: 0891-3668/11/3006-0475
DOI: 10.1097/INF.0b013e31820a5adb

Key Words: child, pneumonia, Bacteremia, *Streptococcus pneumoniae*, epidemiology
(*Pediatr Infect Dis J* 2011;30: 475–479)

Blood cultures are frequently obtained in the diagnostic evaluation of children presenting with community-acquired pneumonia (CAP) to the emergency department (ED). Previous studies reported low rates of bacteremia in children with pneumonia evaluated in the ED with rates ranging from 1.2% to 2.7%.[1–4] However, these studies were performed before widespread use of the heptavalent pneumococcal conjugate[1–4] and the *Haemophilus influenzae* type b vaccines.[2,4] Given the changing epidemiology of childhood pneumonia, the current risk of bacteremia in children evaluated in the ED is unknown.

Blood cultures are not recommended as part of the routine evaluation of adults presenting with CAP to the ED.[5] The decision to perform blood cultures in children evaluated in the ED setting is controversial because few studies have quantified the effect of positive blood cultures on clinical decision-making. Potential advantages of obtaining blood cultures include identification of a causative bacterium, which may allow clinicians to narrow or broaden antibiotic therapy. Potential disadvantages stem from the possibility of a false-positive blood culture result, which may lead to unnecessary diagnostic tests and treatments, or prolonged hospitalization.

Studies of CAP in the adult population conclude that positive blood cultures rarely alter clinical management.[6–9] Data on the utility of blood cultures in the treatment of childhood pneumonia are limited. Hickey et al[1] found no change in clinical management in 11 children with pneumonia whose blood cultures were positive for pathogenic bacteria. The effect of contaminant blood cultures was not investigated in this study. Other pediatric studies examined the role of blood cultures in the ED[10] and, more specifically, in the management of cellulitis[11] and fever.[12–14] These studies reported contamination rates ranging from 0.8% to 7.3%. The 2 studies in this group conducted after licensure of the heptavalent pneumococcal conjugate vaccine found that the proportion of contaminant bacteria exceeded the proportion of pathogenic bacteria in a ratio greater than 3:1.[10,13] Changes in clinical management occurred in fewer than half of the patients with positive blood cultures.[10] Among children with cellulitis, the most common intervention was an additional blood culture obtained to document resolution of bacteremia.[11]

The objectives of this study were to determine the prevalence of bacteremia in children presenting with CAP to the ED, identify subgroups at increased risk for bacteremia, and quantify the implications of positive blood cultures on clinical management.

METHODS

Study Design, Setting, and Participants

This case–control study was nested within the cohort of children followed up at 35 pediatric primary care practices affili-

ated with The Children's Hospital of Philadelphia (CHOP) Pediatric Research Consortium, an Agency for Healthcare Research and Quality (AHRQ)-funded practice-based research network. Children must have had at least 1 well-child visit in the 12 months before diagnosis of CAP to be considered within this cohort. The Pediatric Research Consortium sites span 3 states (Pennsylvania, Delaware, and New Jersey) including urban, suburban, and semirural locations. Patients from this cohort who were ≤18 years of age, evaluated in the CHOP ED between January 1, 2006 and December 31, 2007, and diagnosed with CAP (as defined by a physician-assigned International Classification of Diseases, ninth revision, discharge diagnosis code [481–486] for pneumonia) were eligible for inclusion. Patients were excluded if they required hospitalization ≤14 days before the diagnosis of pneumonia or had an immunocompromising or chronic medical condition predisposing them to severe or recurrent pneumonia (eg, primary or acquired immune deficiency, cystic fibrosis, active chemotherapy for malignancy, sickle cell disease).

Patients with CAP were classified into 3 mutually exclusive groups as follows: those with documented bacteremia (cases), those without bacteremia as documented by a negative or contaminated blood culture (control group 1), and those without a blood culture (control group 2). This study was reviewed and approved by the CHOP Committees for the Protection of Human Subjects.

Data Collection and Study Processes

The following data were abstracted: demographic information including age, race, gender, comorbidities, and vaccination status; clinical and laboratory data from the ED visit; blood culture results; and the presence or absence of pneumonia-associated complications. Among patients with positive blood cultures, the medical records were reviewed further to determine whether culture results led to a change in antibiotic management (eg, broadening or narrowing of therapy) or any additional diagnostic interventions (eg, additional blood cultures, other laboratory testing, radiologic imaging).

All chest radiographs were reviewed by an attending pediatric radiologist as part of routine clinical care. The formal dictated report was further reviewed independently by 2 investigators. Chest radiographs were classified by the presence or absence of any infiltrates (defined as alveolar infiltrates, air bronchograms, and perihilar opacities), bilateral infiltrates, and pleural effusions. Discrepancies in interpretation of the dictated report, which occurred in <1% of items, were resolved by consensus.

Blood cultures were performed at the discretion of the attending physician. Only blood cultures obtained in the ED were included for analysis. Blood cultures were collected by ED nurses, according to standard procedures, using sterile technique. Blood was inoculated into pediatric blood culture bottles (Pedi-Bac T; bioMerieux, Durham, NC) containing supplemented brain heart infusion broth with 0.02% sodium polyanethol sulfonate. Blood cultures are normally delivered to the laboratory within 1 hour of collection through a pneumatic tube system. All blood cultures are then processed in a microbial detection system (BacT/Alert; bioMerieux) which monitors carbon dioxide production within each bottle every 10 minutes, 24 hours per day. Bottles identified as positive were immediately removed by a technician to perform a gram stain and subculture.

Study Definitions

Bacteria defined as pathogenic included *Streptococcus pneumoniae*, *Staphylococcus aureus*, group A beta-hemolytic streptococci, and *H. influenzae*. Bacteria defined as contaminants included coagulase-negative *Staphylococcus* species, α-hemolytic streptococci, *Micrococcus* species, and *Corynebacterium* species. *S. pneumoniae* blood culture isolates were also defined as penicillin susceptible or nonsusceptible according to the minimal inhibitory concentration criteria set by the Clinical and Laboratory Standards Institute.[15] Blood cultures were considered negative if no growth was reported after 5 days. Time to positivity was defined as the interval between specimen collection and result availability.

Pneumonia-associated complications were defined as the presence of one or more of the following: complicated pneumonia, organ dysfunction, metastatic infection, and death. Complicated pneumonia was defined as at least one of the following: lung abscess, parapneumonic effusion/empyema, lung necrosis, or bronchopleural fistula. Organ dysfunction was defined as sepsis, respiratory failure, or dysfunction in cardiovascular, neurologic, hematologic, renal, or hepatic systems according to international consensus guidelines.[16] Metastatic infection was defined as at least one of the following: probable or definite endocarditis,[17,18] mastoiditis, meningitis, pyomyositis, osteomyelitis, or septic arthritis. Asthma was classified as intermittent, mild persistent, or moderate/severe persistent according to national guidelines.[19] Pneumococcal vaccination status was coded as complete (4 doses), partial (1–3 doses), absent (eligible based on age but none received), or not applicable (not eligible based on age).

Statistical Analysis

Continuous variables were described using median, mean, interquartile range, or range values and compared between cases and controls using the Wilcoxon rank sum test. Categorical variables were described using counts and frequencies and compared between cases and controls using the Fisher exact test. Binomial exact 95% confidence intervals (CI) were calculated to determine the precision of estimate of prevalence for bacteremia and contaminated blood cultures.

RESULTS

During the study period, 9099 eligible children from the ambulatory care cohort received a discharge diagnosis of CAP. Of these, 877 (9.6%) were evaluated in the ED (Table, Supplemental Digital Content 1, http://links.lww.com/INF/A721). Among those evaluated in the ED, the mean age was 3.6 years (median, 2 years; range: 0–18 years) and 52.5% were males. Most (69.1%) patients were non-Hispanic blacks. Comorbidities included asthma (40.6%), cerebral palsy (2.6%), and chromosomal abnormalities (1.7%). Pneumonia-associated complications were diagnosed in 81 (9.2%) patients. Complications included organ dysfunction (7.0%), complicated pneumonia (3.7%), and metastatic infection (0.2%); 1.6% (n = 14) had more than one pneumonia-associated complication.

Blood cultures were obtained from 291 children (33.2%). The prevalence of bacteremia among those with blood cultures obtained was 2.1% (95% CI: 0.8%–4.4%) (Table 1). Bacteremia was absent in some subgroups including patients discharged home after evaluation in the ED and patients without an infiltrate on chest radiograph. The prevalence of bacteremia was higher in other subgroups of patients including patients with pneumonia-associated complications (Table 1). Among patients diagnosed with a complicated pneumonia (effusion/empyema, lung abscess, or necrotizing pneumonia) the prevalence of bacteremia was 13% (95% CI: 2.8%–33.6%). *S. pneumoniae* was the most common causative organism accounting for 4 of the 6 cases of bacteremia (Table, Supplemental Digital Content 2, http://links.lww.com/INF/A722). All 4 cases of pneumococcal bacteremia were caused by serotypes not included in the heptavalent pneumococcal vaccine. All 4 *S. pneumoniae* isolates were susceptible to penicillin by current standards for nonmeningeal infections. The remaining 2 cases of bacteremia were caused by *S. aureus* (methicillin-resistant) and *H. influenzae* (nontypable). The contamination rate was 1.0% (95%

CI: 0.2%–3.0%). Contaminants were coagulase-negative staphylococci in all 3 cases.

Compared with children without blood cultures, children with blood cultures were more likely to be >5 years of age (37.8% vs. 13.3%; $P < 0.001$) and have either partial or absent heptavalent pneumococcal vaccination history (44.0% vs. 33.1%; $P < 0.001$). Blood cultures were also more frequently obtained in children with clinical examination findings suggestive of more severe illness including those described as ill-appearing and those with hypoxia. Approximately two-thirds of patients who were eventually diagnosed with pneumonia-associated complications and half of those hospitalized had a blood culture obtained on initial evaluation.

There were no statistically significant differences in demographic, clinical, or laboratory variables at initial presentation between patients with and without bacteremia (Table 2). However, the 6 patients with bacteremia did have a higher rate of pneumonia-associated complications (66.7%) compared with both nonbacteremic patients (16.5%, $P = 0.010$) and patients without blood cultures obtained (5.1%, $P < 0.001$). The most common complications were respiratory failure in bacteremic patients (50%), sepsis in nonbacteremic patients (10.2%), and sepsis in patients without a blood culture obtained (3.6%).

All patients with a positive blood culture were admitted to the hospital on initial presentation. Table, Supplemental Digital Content 2, http://links.lww.com/INF/A722, summarizes the changes in clinical management in patients with positive blood cultures obtained during initial ED evaluation. Blood culture results altered management in 5 of the 6 bacteremic patients of whom 1 had an appropriate broadening of final antibiotic coverage and 4 had an appropriate narrowing of final antibiotic coverage. The only patient (case 2) with a bloodstream infection not sensitive to empiric therapy had methicillin-resistant *S. aureus* infection; this patient had severe back pain and a concomitant epidural abscess diagnosed by magnetic

TABLE 1. Prevalence of Bacteremia in Patients With Blood Culture Obtained

	Bacteremia	95% CI	P*
All patients (n = 291)	2.1%	0.8–4.4	—
Initial chest radiograph			0.436
No infiltrate (n = 50)	0%	0–7.1	
Infiltrate (n = 229)	2.6%	1.0–5.6	
No chest radiograph (n = 12)	0%	0–26.5	
Disposition after evaluation in ED			0.189
Inpatient (n = 227)	2.6%	1.0–5.7	
Outpatient (n = 64)	0%	0–5.6	
Pneumonia–associated complications			0.001
Any complication (n = 51)	7.8%	2.2–18.9	
No complication (n = 240)	0.8%	0.1–3.0	

*χ^2 test.
CI indicates confidence interval; ED, emergency department.

TABLE 2. Characteristics of Bacteremia Patients, Nonbacteremic Patients, and Patients Without Blood Cultures Obtained

	Bacteremic Patients (%) n = 6 Cases	Nonbacteremic Patients (%) n = 285 Control Group 1	P*	Patients Without Blood Culture Obtained (%) n = 586 Control Group 2	P*
Male sex	83.3	52.6	0.220	52.1	0.220
Age			0.940		0.650
≤1 yr	50.0	33.7		40.6	
>1 and ≤5 yr	33.3	28.1		46.1	
>5 and ≤12 yr	16.7	27.0		11.1	
>12 yr	0	11.2		2.2	
Race			1.000		1.000
Non–Hispanic white	16.7	18.6		20.5	
Non–Hispanic black	83.3	68.8		68.9	
Hispanic	0	3.9		3.6	
Other	0	8.8		7.0	
Asthma severity			0.634		0.836
No asthma	83.3	59.3		59.2	
Intermittent	0	9.5		10.2	
Mild persistent	0	11.6		13.5	
Moderate/severe	0	12.3		6.5	
Unknown severity	16.7	7.4		10.6	
Pneumococcal vaccine status			0.357		0.281
None	0	13.3		4.6	
Partial	66.7	30.2		28.5	
Complete	33.3	40.0		64.3	
N/A	0	16.5		2.6	
Fall/winter season	83.3	64.2	0.429	68.9	0.672
Temperature <38.4°C†	33.3	48.8	0.685	45.3	0.695
Percutaneous oxygen saturation <95%‡	33.3	33.6	1.000	20.8	0.610
Ill appearing	16.7	24.2	1.000	13.0	1.000
Respiratory distress (any degree)	66.7	54.0	1.000	40.1	0.303
Chest radiograph			0.686		0.302
No infiltrate	0	17.5		27.5	
Infiltrate	100	78.3		64.0	
No chest radiograph	0	4.2		8.5	
WBC >15,000/mm^3	20.0	37.1	0.654	32.7	1.000

*P-values reflect pairwise comparison with subjects with bacteremia.
†Temperature not recorded in 9 patients.
‡Percutaneous oxygen saturation not recorded in 115 patients.
N/A indicates not applicable; WBC, white blood cell count.

resonance imaging. In this instance, the blood culture result led to an appropriate change in antibiotic therapy and prompted additional diagnostic tests that meaningfully contributed to the diagnosis. The management changed for 1 of the 3 patients with contaminant blood cultures; changes in this patient included a repeat blood culture and 1 day of unnecessary treatment with vancomycin. No adverse events attributable to changes in therapy were reported.

Of the 586 patients without a blood culture obtained in the ED, 28 (5%) had a blood culture obtained within 3 days of presentation. Among those with a delayed blood culture, 1 was positive for pathogenic bacteria (methicillin-sensitive *S. aureus*) and 2 were considered contaminants (*Staphylococcus hominis*; *Staphylococcus epidermidis*). If these patients with delayed blood cultures were included in our overall analysis, the prevalence of bacteremia would be 2.2% (95% CI: 0.9%–4.5%).

DISCUSSION

This study is the first to determine the prevalence of bacteremia in children with CAP evaluated in the ED in the post-pneumococcal conjugate and *H. influenzae* type b vaccine eras. The overall prevalence of bacteremia was low, although patients with complicated pneumonia such as empyema had relatively high rates of bacteremia. Positive blood culture results were often associated with meaningful changes in clinical management; however, the ultimate impact of blood cultures on clinical management was small given the low prevalence of bacteremia.

The prevalence of bacteremia was 2.1% (95% CI: 0.8%–4.4%) in an ambulatory cohort evaluated in the ED setting. Certain subsets of patients had even lower rates of bacteremia including those discharged from the ED and those with a normal chest radiograph. Among the 4 cases of bacteremia caused by *S. pneumoniae*, none of the serotypes were included in the heptavalent pneumococcal vaccine available at the time of the study, but 3 of the serotypes are included in the now available 13-valent pneumococcal conjugate vaccine.[20] Widespread use of this vaccine may further decrease the rate of bacteremia in children with CAP.

Researchers in Italy recently reported the prevalence of bacteremia to be 3.8% among a subset of children with blood cultures obtained nested within a larger study describing the use of real-time polymerase chain reaction for the diagnosis of CAP.[21] However, this study was conducted exclusively in hospitalized patients. Furthermore, despite the fact that it was conducted in the post-pneumococcal vaccine era, the authors noted that vaccination was limited by region and covered <30% of the country. Both of these factors may account for the reported higher prevalence of bacteremia compared with our study.

Most pediatric studies that examined bacteremia and pneumonia-associated complications focused on empyema.[22–24] Byington et al found that approximately one-third of children hospitalized for parapneumonic empyema were bacteremic in 2 different retrospective studies.[22,23] However, both of these studies were conducted in Utah, which was noted by the investigators to have an unusually high rate of empyema and perhaps a unique epidemiology of *S. pneumoniae*. The prevalence of bacteremia was 13.9% in a recent randomized control trial conducted by St Peter et al to compare treatment modalities for empyema.[24] The present study did not distinguish empyema from other types of complicated pneumonia, but we found a similar prevalence of bacteremia among all patients with a complicated pneumonia. We examined the pneumonia-associated complications more broadly than previous studies by including other types of pneumonia-associated complications, including organ dysfunction and metastatic infections in our analysis.

The proportion of contaminants in this study was considerably lower than previous studies conducted in the pediatric ED setting.[10–13] Institutional variability in collection procedures may have resulted in a higher rate of false-positive blood cultures at other institutions. The greater emphasis in the past decade on strategies to decrease contamination rates may also explain the lower rate in our study compared with previous studies. Furthermore, unlike studies that described many unnecessary diagnostic tests, treatments, and hospitalizations as the result of false-positive blood cultures,[12–14] only 1 additional blood culture and 1 day of an unnecessary antibiotic were attributed to a false-positive culture result in this study. Our results suggest that the impact of contaminated blood cultures among patients with CAP, who require hospitalization, may be less important than previously argued.

Given the low yield, blood culture results had a meaningful effect on clinical management in only a small minority of patients from whom a blood culture was obtained. Previous studies conducted in both the pediatric[1] and adult[5,6,9] populations with CAP found that culture results led to changes in management in less than half of patients with blood cultures positive for pathogenic bacteria. In contrast, our study found that culture results led to changes in antibiotic therapy in 5 of the 6 bacteremic patients. Two arguments are proposed in the adult CAP literature[6,9] for why blood cultures infrequently alter management. First, patients often received broad-spectrum empiric antibiotics and a positive culture result rarely necessitated further broadening of antibiotic coverage. Second, physicians were reluctant to narrow antibiotic therapy despite results of susceptibility testing. Our study provides support for the first argument, as nearly all bacteremic patients had pathogens susceptible to empiric therapy started in the ED. However, we found that physicians did appropriately narrow antibiotic therapy in most cases.

This study had several limitations. First, blood cultures were obtained in approximately one-third of patients during initial ED evaluation. Blood cultures were obtained more frequently in children who appeared ill and presumably were at higher risk for bacteremia. Among children without a blood culture obtained, most were discharged home from the ED. Therefore, our study may overestimate the true prevalence of bacteremia among children with CAP evaluated in the ED setting. However, it is likely that in certain subgroups, such as those with pneumonia-associated complications, the prevalence is accurate, as most children in this group had a blood culture obtained on initial evaluation. Second, the volume of blood inoculated for culture was not documented. The detection of bacteremia is improved with larger blood volumes.[25,26] If blood inoculated for culture was inadequate, we would underestimate the prevalence of bacteremia. This scenario is unlikely because standard practice at our institution is to achieve a blood:broth ratio between 1:5 and 1:10 (2–4-mL of blood). Third, because of the retrospective study design, changes in management attributed to blood culture results could not be proven despite best efforts to draw reasonable conclusions from the medical record. It is possible that there were unmeasured or undocumented factors that drove or contributed to changes in management. Fourth, we defined pneumonia by physician-assigned discharge diagnosis codes. It is challenging to distinguish bacterial from nonbacterial pneumonia. It is likely that patients with viral pneumonia were included, causing us to underestimate the true prevalence of bacteremia among children with bacterial pneumonia. Nevertheless, given the lack of a gold standard to diagnosis bacterial pneumonia this limitation is unavoidable and also mirrors clinical practice. Finally, the unique patient population of an ambulatory cohort was both a strength and limitation. We included only children followed up in a large ambulatory care network to

minimize the bias of a tertiary referral center caring for the sickest children. However, for this same reason, these results cannot be broadly generalized to referral-based EDs. Despite the comparatively large sample size, the low prevalence of bacteremia led to relatively wide CI around the prevalence of bacteremia in certain subsets of patients such as those in whom chest radiographs were not obtained.

In summary, children from an ambulatory cohort presenting to the ED for evaluation of CAP are at low-risk for bacteremia. This risk may become even smaller with widespread use of the 13-valent pneumococcal vaccine. Despite the increased frequency of culture directed management changes found in our study, the impact on clinical management among all patients with a blood culture obtained was small because of the low prevalence of bacteremia. Our data do not support the routine use of blood cultures in children with mild CAP evaluated in the ED. Blood cultures may be useful in the evaluation of moderate-to-severe pneumonia requiring hospitalization.

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