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Original Contributions

EMERGENCY DEPARTMENT EPIDEMIOLOGY OF PNEUMOCOCCAL BACTEREMIA IN CHILDREN SINCE THE INSTITUTION OF WIDESPREAD PCV7 VACCINATION

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☐ **Abstract—Background: The heptavalent pneumococcal conjugate vaccine (PCV7) has produced a shift in the epidemiology of invasive infections from *Streptococcus pneumoniae*. Objective: Our aim was to determine the temporal changes in pneumococcal bacteremia (*Streptococcus pneumoniae bacteremia* [SPB]) in the emergency department (ED) since the introduction of PCV7. Methods: This was a retrospective cohort study of children 0–18 years with SPB evaluated from 1998–2009 in a tertiary-care pediatric ED. The primary outcome was annual proportion of children with SPB from PCV7 serotypes (ie, 4, 6B, 9V, 14, 18C, 19F, and 23F) and nonvaccine serotypes (NVT). Rates of SPB (per 10,000 ED visits) were calculated. SPB was analyzed by time period: before October 2000 was considered "pre-PCV7," November 2000 to October 2003 was considered "peri-PCV7," and after November 2003 was "post-PCV7." Febrile young children (FYC) were defined as children age <36 months and fever without source. Results: A total of 201 episodes of SPB occurred during the study, with a median age of 20.3 months (interquartile range 10.7–49.5 months; range 1.6–215.4 months); 56.7% were male and 69.7% were African American. SPB from PCV7 serotypes decreased more than fourfold, from 82.2% pre-PCV7 to 19.5% peri- and post-PCV7. Most SPB was from NVT serotype 19A (31.3%) peri- and post-PCV7. Annual rates of SPB were 4.01/10,000 ED visits pre-PCV7, decreasing to 2.10 peri-PCV7, and 1.75 post-PCV7. Among the 56 (27.8%) FYC with SPB, NVT were responsible for 11.5% of SPB pre-PCV7, and increased to 80.0% peri- and post-PCV7 ($p < 0.001$). Conclusions: Rates of SPB have decreased since the introduction of PCV7, yet SPB still occurs among children in the ED. NVT are increasing in prevalence, and SPB from PCV7-serotypes have decreased.** © 2013 Elsevier Inc.

☐ **Keywords—bacteremia; pneumococcal disease; pneumococcal conjugate vaccine; epidemiology; emergency department**

INTRODUCTION

Streptococcus pneumoniae (pneumococcus) is among the most common causes of invasive infections in the pediatric population (1–3). Although recommendations for widespread *S. pneumoniae* vaccination with the heptavalent conjugate pneumococcal vaccine (PCV7) were introduced by the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics in June 2000, pneumococcus remains the

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leading cause of bacterial meningitis, pneumonia, and bacteremia in children (4–7).

The current epidemiology of invasive pneumococcal disease is driven by various serotypes that cause infection. Since inclusion of PCV7 in the routine childhood vaccination schedule, numerous studies have described a reduced incidence of invasive infections caused by PCV7-covered serotypes (8–12). Data from the CDC demonstrate a >75% reduction in pneumococcal infections for children <5 years of age since implementation of PCV7 (13,14). More recent data found a 60% reduction in invasive pneumococcal infections across all pediatric ages since 2000 (11). Although reductions in invasive pneumococcal disease have been confirmed, the phenomenon of serotype replacement—emergence of disease due to nonvaccine pneumococcal serotypes in place of vaccine-covered serotypes—has been demonstrated (15). Although pneumococcal infections are less common than before PCV7, nonvaccine serotypes (NVTs) remain prevalent and are capable of causing invasive infection (6,15,16). Importantly, these aforementioned studies have primarily used national surveillance and inpatient data rather than patient-level data for ambulatory patients (7,8,14,17). Patient-level data, such as in this study, will continue to be relevant in the future: a new 13-valent pneumococcal conjugate vaccine (PCV13) has been approved for use in an attempt to negate the effects of serotype replacement. However, with increased serotypes covered in PCV13, it is quite possible additional serotypes will "emerge" and produce disease; therefore, determination of risk factors and characteristics of these children will be of clinical importance.

Pneumococcal infections, specifically bacteremia, are frequently identified in the ambulatory setting, such as the emergency department (ED), rather than as inpatients. In addition, *Streptococcus pneumoniae bacteremia* (SPB) poses a unique clinical challenge for outpatient and emergency clinicians, as these infections can present as an undifferentiated febrile illness that can lead to severe infection (2). The objective of this investigation was to determine the changes in rates of SPB identified in the ED, before and after institution of widespread PCV7 vaccination. Additionally, we sought to assess clinical characteristics among children with SPB, as well as examine the differences in pneumococcal serotype responsible for bacteremia before and after initiation of PCV7 vaccination.

METHODS

Study Design, Setting, and Population

This was a retrospective review of children with SPB identified from the ED of an urban, academic, tertiary-care children's hospital between 1998 and 2009. Subjects included children <18 years of age who had a blood culture obtained as part of their clinical evaluation during their ED visit to our institution; blood cultures that returned positive for *S. pneumoniae* were required for inclusion. Subjects were excluded if their isolate was obtained from any inpatient setting. The study was approved by our Institutional Review Board.

Detection and Serotype Classification of Streptococcus pneumoniae

Study subjects were identified using our hospital microbiology logs and electronic data system (MediTech), which recorded all positive blood cultures for *S. pneumoniae* during the study period. Data pertaining to each pneumococcal isolate were collected for analysis, including date and time of collection and collection method (peripheral venipuncture or central catheter).

Standard ED procedure required inoculation of 0.5–1.0 mL into blood into culture bottles. Throughout the study period, SPB was detected using the BacT/Alert blood culture system (bioMérieux, Durham, NC), which uses carbon dioxide production to automatically monitor for bacterial growth every 10 min, 24 h per day. Cultures were obtained using sterile technique, and inoculated into blood culture bottles (Pedi-BacT; bioMérieux), then transported to the Clinical Microbiology laboratory and loaded into the blood-culture instrument.

Positive isolates were immediately removed and an aliquot was taken for Gram stain and subculture. All pneumococcal isolates were serotyped on the basis of capsular swelling with type-specific antisera (Quellung reaction) using antisera (Statens Seruminstitut, Copenhagen, Denmark). Pneumococcal serotypes were further classified to reflect the serotypes covered in PCV7. Those serotypes included in the PCV7 vaccine (4, 6B, 9V, 14, 18C, 19F, and 23F) were considered vaccine-covered serotypes (VT7), while all others were considered nonvaccine serotypes (NVT7).

Patient Characteristics and Visit Data

Patient and ED-visit data were obtained using our hospital's electronic medical record-keeping system. Patient details, such as demographics and medical history, were collected, including the presence of comorbid conditions such as sickle hemoglobinopathy, intrinsic or acquired immunosuppressive condition (e.g., malignancy), indwelling central lines or other medical apparatus, congenital heart disease, or multiple medical/complex conditions (e.g., severe neurological impairment). ED visit details were collected, including chief complaint, indication for blood culture, and presence of concomitant