Antibiotic Resistance after Licensure of Pneumococcal 7-Valent Conjugate Vaccine

To the Editor—We have some concerns regarding the conclusions reached by Steenhoff et al. [1] in their article about antibiotic resistance patterns occurring in pneumococcal isolates after the licensure of pneumococcal 7-valent conjugate vaccine (Prevnar; Wyeth). Our criticism of their conclusions focuses on their description of increasing rates of antibiotic resistance. They insist that antibiotic resistance is increasing among Streptococcus pneumoniae isolates. An article in the 6 April 2006 issue of the New England Journal of Medicine noted that, as the total number of cases of pneumococcal bacteremia has decreased sharply, the absolute number of isolates not susceptible to penicillin has markedly decreased [2]. Steenhoff et al. [1] attempted to demonstrate increases in the rate of antibiotic resistance using relative risk. The data displayed in table 4 of their article [1] include 89 samples obtained during the years 1999–2000 (44.5 samples per year), but the 5 years of samples obtained during 2001 to 2005 include 99 samples (19.8 samples per year). This correlates with the decreases that we know occurred in the number of cases of pneumococcal disease. Instead, they conclude that the prevalence of nonsusceptibility to penicillin increased during the same period. This cannot be stated; without a denominator for the data presented in this table (e.g., the number of resistant organisms per unit of patient population), it is impossible to compare the 2 columns of data.

Perhaps a better presentation of their results would echo the recent article in the New England Journal of Medicine [2]. These data suggest large decreases in total numbers of all of their 28,000 isolates, with larger decreases among isolates susceptible to penicillin, leaving the remaining proportion of cases of pneumococcal disease as being slightly more resistant. Such a portrayal is perhaps more reflective of the current state of pneumococcal disease.

Acknowledgments


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References


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Reply to Robertson et al.

To the Editor—We thank Drs. Robertson and Rasnake for their thoughtful comments and the opportunity to clarify our findings [1]. In describing our results, we correctly reported that there was “an increase in the proportion of penicillin-resistant isolates between 1999 and 2005” [2, p. 910]. However, later in the article, we stated that the prevalence rather than the proportion of nonsusceptible isolates had increased during the study period. We agree that our single use of the word...
“prevalence” in this context was suboptimal.

Robertson and Rasnake [1] also express concern about our use of “relative risk.” Relative risk represents the ratio of the risk of disease for persons with the risk factor to the risk of disease for persons without the risk factor [3]. In our study, the risk factor is the occurrence of pneumococcal bacteremia in the postlicensure period, whereas the outcome, or “disease,” is the presence of an isolate not susceptible to penicillin. In such a context, the term “relative risk” represents the risk of having a nonsusceptible isolate in the postlicensure period, compared with the risk in the prelicensure period, among the cohort of children who already have pneumococcal bacteremia; it does not refer to a population estimate of risk in an uninfected child [2]. The benefit of presenting relative risk in this instance is a clinical one. It informs the clinician who asks, “When faced with a child with a high likelihood of pneumococcal bacteremia, is my decision-making regarding empiric antibiotic therapy different now than what it was in the prelicensure period?” Our data suggest that, in the population served by our emergency department, the relative risk of having an isolate with nonsusceptibility to penicillin among children with pneumococcal bacteremia is higher after the introduction of heptavalent pneumococcal conjugate vaccine than in the years 1999–2000.

Additionally, a comparison is made between our data regarding pediatric pneumococcal bacteremia and those of Kyaw et al. [4]. The population-based study by Kyaw et al. [4] describes the effect of the introduction of the pneumococcal conjugate vaccine on drug-resistant Streptococcus pneumoniae isolated from any normally sterile site from 1996 to 2004. Although the overall rate of penicillin-nonsusceptible disease decreased between 1996 and 2004, there was substantial regional variation; one site did not experience a statistically significant decrease in the number of isolates not susceptible to penicillin during the study period [4]. Such dramatic geographic variation in drug susceptibility of pneumococcal isolates is known to occur [5]. In fact, awareness of substantial geographic variation in the proportion of drug-resistant S. pneumoniae has prompted some groups to recommend consideration of regional susceptibility patterns in the choice of empirical therapy for community-acquired pneumonia [6]. Therefore, our results should be interpreted in the context of the known regional variability of drug resistance.

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