



## INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN YOUNGER THAN 2 YEARS LOS ANGELES COUNTY, 2004

### BACKGROUND

Invasive pneumococcal disease (IPD) is a leading cause of bacterial illness in young children and causes considerable illness and death in the elderly. The infectious agent, *Streptococcus pneumoniae*, also has become increasingly resistant to antibiotics during the last decade. ACDC has conducted (IPD) surveillance for IPD since late and the Los Angeles County Department of Health Services (LAC DHS) added IPD to its list of reportable diseases in October 2002.

IPD can be prevented by two types of available vaccines: the 23-valent pneumococcal polysaccharide vaccines (Pnu-Imune<sup>®</sup>23 and Pneumovax<sup>®</sup>23), which are effective for adults and children over age 2 years; and the heptavalent pneumococcal conjugate vaccine (Prenvar<sup>®</sup>), which was approved in February 2000 for use in infants and protects against the seven most common strains of *S. pneumoniae* in infants. The Advisory Committee on Immunization Practices (ACIP) recommends that infants receive four doses as part of their routine vaccinations at 2, 4, 6, and 12–15 months [1]. Since the introduction of Prenvar<sup>®</sup>, a significant reduction in the number of IPD cases has been seen in children less than 5 years old in Los Angeles County (LAC) as well as in other populations [2]. Until March 2005, the Respiratory Diseases Branch of the Centers for Disease Control and Prevention (CDC) had been monitoring IPD cases in this age group to identify possible vaccine failures. When pneumococcal vaccine histories could be obtained and isolates were available, ACDC reported these cases to the CDC through a pneumococcal conjugate vaccine failure case report form and forwarded the isolates for serotyping. The data obtained was utilized for monitoring distribution of serotypes, host risk factors, and vaccine lot effectiveness.

In 2004, a nationwide shortage of Prenvar<sup>®</sup> resulted in ACIP recommending a suspension of the fourth dose beginning mid-February and later the third dose beginning March. A mid-year review of cases through May 2004 in LAC showed a rise in IPD cases among those less than 5 and especially less than 2 years old. There were 22 reports of IPD in children less than 2 years old from January through May 2004 compared to 6 reported cases during the same time period in 2003. ACDC was concerned that the shortage was leading to increases in IPD, through vaccine failures or a replacement of serotypes not covered by Prenvar<sup>®</sup>, and initiated an investigation of cases occurring in children less than 2 years old from January through May 2004.

### METHODS

Cases were defined as children less than 2 years old reported to LAC DHS with a positive culture for *S. pneumoniae* in a normally sterile site dated between January and May 2004. ACDC is notified of cases through a standardized IPD reporting form that includes variables for age, gender, residence, race/ethnicity, hospitalization, outcome, culture site and date, antibiotic susceptibility results, and vaccination status. Penicillin non-susceptible *S. pneumoniae* (PNSP) strains are defined as strains that are determined to be intermediate or resistant by the reporting facility's antibiotic susceptibility testing. All data from the case report forms initially submitted to ACDC were abstracted. ACDC investigators contacted the infection control professionals and/or medical records units of the reporting facilities by telephone to request the cases' discharge summaries and to obtain contact information of the primary physician and the parent/guardian. If the reporting facility could not provide the primary physician information, the parent/guardian of the cases was requested by telephone or letter to provide the name of the physician or clinic that vaccinated the child. The primary physician or clinic was then contacted by telephone and asked to provide the vaccination history of the child.

Vaccination histories were reviewed to determine if the case children had received the age-appropriate number of doses of Prenvar<sup>®</sup> as recommended by the ACIP before the date of culture and if any missed doses coincided with the period of shortage. For this report, the first, second, and third doses were



considered late if they were given more than 1 month after the recommended ages of 2, 4, and 6 months, respectively; the fourth dose was considered late if not given by 13 months of age. Available medical records, including discharge summaries and history and physicals (H&P), were reviewed for risk factors and missing demographic and hospitalization data. The ZIP codes of the cases' reported residences were mapped using ArcView.

The laboratories used by the reporting facilities were contacted to request available isolates to be forwarded to the LAC Public Health Laboratory. Isolates were sent for serotyping through the California Department of Health Services to the CDC's Respiratory Disease Branch.

## RESULTS

None of the 22 IPD cases reported to ACDC initially included immunization status. Complete vaccination histories were obtained for 20 of 22 cases. In the two cases where the histories were not obtained, medical records and case reports did not list a primary physician and the parents could not name the physician or clinic that vaccinated the child. Discharge summaries or other medical records were received for 16 cases and 6 were not available.

The median age of all cases was 12.5 months and ranged from 1 to 21 months. Most (57%) were Latino and most (59%) were male. Mapping of cases did not show any geographic clustering. In six cases *S. pneumoniae* was cultured from cerebrospinal fluid (CSF) or blood and CSF while the rest were culture positive in blood. Half (50%) were hospitalized, but all cases survived the infection. A few of the cases (14%) were infected with PNSP strains.

All but one child, who was younger than the recommended age for the first dose, had at least one dose of Pevnar<sup>®</sup> by the date of positive culture. 7 of 19 (37%) children were late with their Pevnar<sup>®</sup> vaccinations. Nevertheless, when their vaccinations were administered, they occurred within a month of the recommended ages for routine administration of currently licensed childhood vaccinations (i.e. 2,4,6, and 12–15 months) [3]. Of these seven, only one child's last dose was withheld due to the shortage. Another's was withheld because she was on chemotherapy. Two children, one of whom had been born premature (gestational age 27 weeks), had late vaccinations as a result of receiving the first dose at 4 months. The remaining three had visited their physicians for scheduled immunizations several months before the shortage without receiving Pevnar<sup>®</sup> and became ill before the next scheduled immunization. They had no risk factors for pneumococcal disease.

Isolates were available for only 6 cases. Serotyping results for 5 of the 6 isolates indicate that the strains were not covered by Pevnar<sup>®</sup>. The sixth isolate could not be typed.

## DISCUSSION

This study did not reveal anything unusual about this cohort of IPD cases nor did it show an association between the Pevnar<sup>®</sup> shortage and the increase of cases seen in the beginning of 2004. The demographics of the children were representative of the population of children <2 years old in LAC. Almost all were vaccinated despite the shortage, many of them appropriately for their age, and the majority had no risk factors for pneumococcal disease. One child may have received his vaccinations 2 months late due to a premature birth at 27 weeks. However, it is important to reiterate that Pevnar<sup>®</sup>, as well as other childhood vaccinations, should not be delayed because of prematurity.

The rate of PNSP strains is slightly lower than the overall rate for cases of all ages (22%) through May 2004. However, this is to be expected if the children were indeed protected by Pevnar<sup>®</sup> against the more resistant strains of *S. pneumoniae*. Moreover, continued surveillance after May showed a characteristic seasonal drop in IPD cases in children less than 2 years old to baseline levels.

Nevertheless, this study indicates that there is good pneumococcal vaccination coverage in LAC—all children were eventually vaccinated with at least 2 doses by the time of data collection and the majority of children were appropriately vaccinated for their age at the time of their illness. It also demonstrates that



national vaccine failure surveillance had been severely limited in case identification as all 22 cases were reported to ACDC with unknown vaccination status. The CDC requested through February 2005 that IPD in children less than 5 years old with at least one dose of Prevnar<sup>®</sup> be reported as a potential vaccine failure. Because active follow-up is not routine, the 20 cases eventually found to be vaccine failures would have slipped through normal surveillance procedures.

#### REFERENCES:

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