Routine Penicillin No Longer Needed in Sickle Cell?

BY BRUCE K. DIXON
Chicago Bureau

The incidence of invasive pneumococcal disease among children younger than 5 years with sickle cell disease plummeted during 2001-2004, according to a new study which suggests that credit belongs to the 7-valent pneumococcal conjugate vaccine introduced in 2000.

"Our study clearly demonstrates that the incidence of invasive pneumococcal disease dramatically decreased after the introduction of pneumococcal conjugate vaccine into the routine childhood immunization schedule," Dr. Natasha B. Halasa and colleagues wrote.

The data were derived from the follow-up of 2,026 individuals with sickle cell disease (SCD) enrolled in Tennessee Medicaid (TennCare) from Jan. 1, 1995, through Dec. 31, 2004 (Clin. Infect. Dis. 2007;44:1428-33).

During the study period, 37 individuals (0.6-44 years) with SCD had invasive pneumococcal disease (IPD), and no individuals with SCD had more than one episode of IPD during the study period.

In a comparison of the pre-PCV period (1995-1999) with the post-PCV period (2001-2004), the IPD rate decreased 91% in children aged less than 2 years (from 3,600 to 335 cases per 100,000 person-years) and by 93% in children under 5 years (from 2,044 to 134 cases per 100,000 person-years). In the post-PCV era, a mean 69% of children less than 2 years had evidence of receiving one or more doses of PCV during the prior year.

Although penicillin prophylaxis and pneumococcal polysaccharide vaccine have decreased the rate of invasive pneumococcal disease (IPD) in this high-risk population, breakthrough disease still occurs—most commonly among children younger than 3 years—and IPD continues to be a leading cause of death in children with SCD, the researchers explained.

This study, which showed a mean 92% drop in infection after 2000 among children younger than 5 years, raises important questions about the continued use of penicillin, according to Dr. Martin H. Steinberg, whose accompanying editorial poses the question, "Is prophylactic penicillin needed if conjugate vaccination is so effective?"

"Widespread penicillin use is not risk free. Penicillin-resistant strains of *S. pneumoniae* are increasing in number, and about 40% of isolates associated with sickle cell disease have some measure of resistance," said Dr. Steinberg, with the departments of medicine, pediatrics, and pathology and laboratory medicine at Boston University (Clin. Infect. Dis. 2007;44:1434-5).

'Our study clearly demonstrates that the incidence of invasive pneumococcal disease dramatically decreased after' starting routine PCV vaccination.

Dr. Steinberg believes that the susceptibility of *S. pneumoniae* to penicillin might be decreasing, and he points out that prophylaxis is less effective in carriers of intermediate-resistant and resistant serotypes.

In North America, the 7-valent conjugate vaccine protects against greater than 70% of the serotypes isolated from patients in the preconjugate vaccine era, he said. "However, two-thirds of the serotypes not included in the vaccine were susceptible to penicillin, and the use of this vaccine appeared to decrease the number of antibiotic-resistant, pneumococcal infections (N. Engl. J. Med. 2006;354:1455-63)."

Pending the arrival of a more efficacious 13-valent vaccine, antibiotic prophylaxis could be useful, Dr. Steinberg explained, adding that suboptimal compliance with preventive treatment limits penicillin's effectiveness.

In the Tennessee cohort, only 25% to 30% of the children with SCD who were younger than 5 years had their penicillin prescriptions filled for more than 270 days of a 1-year period. These numbers are similar to those found in an earlier study (JAMA 2003;290:1057-61), Dr. Halasa and colleagues said.

Because ongoing penicillin prophylaxis is difficult to sustain, the effectiveness of this approach in practice appears to be less than that demonstrated in the landmark randomized, clinical trial in which the an-

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Rotavirus G2 Serotypes Are Emerging in Infants

BY PATRICE WENDLING
Chicago Bureau

KANSAS CITY, MO. — Rotavirus G2 serotypes caused an unexpectedly high proportion of rotavirus dehydrating acute gastroenteritis in infants and children during the 2005-2006 epidemic season in Philadelphia, data from an industry-sponsored study show.

Serotype G1P1A[8] is the most common circulating human rotavirus during an epidemic, while G2 serotypes emerge sporadically. Overall, 45% of 2005-2006 rotavirus acute gastroenteritis (AGE) cases at Children's Hospital of Philadelphia (CHOP) were caused by non-G1 serotypes, predominantly G2, Diane Lawley, R.N., and her associates reported in a poster at the National Immunization Conference sponsored by the Centers for Disease Control and Prevention.

Annual surveillance at Children's Hospital of Philadelphia indicates a steady increase in the number of rotavirus AGE cases since the 1994-1995 season. In 2005-2006, there were 306 evaluable cases, compared with 92-185 cases during the preceding 11 consecutive seasons.

Final analysis of 275 community-acquired cases in 2005-2006, after 31 nosocomial cases were removed from analysis, indicated that G2 serotypes caused 101 (37%) cases of AGE, compared with just 1%-11% in the preceding 6 years in the study was conducted by Merck Research Laboratories in West Point, Pa., and CHOP's Clark Laboratory, which receives funding from Merck.

In addition, 21 (8%) serotype G9 cases were identified in 2005-2006.

Data were not available for the entire 11 seasons because only a limited number of samples were tested during the first 5 seasons, Ms. Lawley explained in an interview.

G2 serotypes caused proportionally more gastroenteritis in infants 5 months of age or less (34 cases) and in infants age 12-17 months (15 cases). G2 serotypes also were more common in black infants (80 cases), and in infants from urban versus nonurban homes (66 vs. 34), the authors reported.

The majority of samples in the study were obtained from CHOP inpatients (86%) or patients evaluated in the emergency department (10%), with a smaller percentage (4%) coming from outpatient clinics.

"Although untested, the inability to predict large non-G1 rotavirus outbreaks may favor the use of a multivalent vaccine that specifically protects against G2 infections, which usually do not coexpress P1A[8]," the authors concluded.

Merck's new oral pentavalent rotavirus vaccine (RotaTeq), licensed in the United States in 2006 for children aged 6-32 weeks, contains serotypes G1-4 and G1P1A[8].

GlaxoSmithKline's new monovalent vaccine (Rotarix), licensed in Mexico and numerous other countries, contains the G1P1A[8] serotype. ■

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tibiotic produced an 84% reduction in the rate of IPD among children with SCD the researchers said (N. Engl. J. Med. 1986;314:1593-9).

This study has several limitations, according to Dr. Halasa and her team: The number of individuals with SCD and IPD was small and consisted of patients who lived in surveillance counties in Tennessee and who were enrolled in the Tennessee Medicaid program.

"The pre-PCV era IPD rates in individuals with SCD in this study, however, were nearly identical to those reported from other locations, suggesting that these results are generalizable to others with SCD in the United States," they argue.

A second limitation was that vaccination records, especially from the period prior to the introduction of PCV, may not have captured receipt of all pneumococcal vaccines by persons enrolled in TennCare.

With the universal administration of PCV to all children, both with and without SCD, it is expected that the rates of IPD will continue to decrease among all children, the authors wrote.

"However, ongoing monitoring of these rates and serotyping of all invasive pneumococcal isolates must remain an important priority to monitor whether serotype replacement will occur under continued vaccine pressure. Despite this caution, our data indicate that PCV is effective for reducing the rate of IPD, especially among vulnerable populations," they concluded. ■