ID CONSULT

# Prevnar 13 Expected to Further Reduce Disease

The new 13-valent pneumococcal conjugate vaccine (Prevnar 13) is picking up right where the 7-valent version left off.

It has been 10 years since the introduction of the 7-valent pneumococcal conjugate vaccine (Prevnar). Overall in the United States, the program has had significant success, with an approximate 65%-70% reduction in invasive disease due to *Streptococcus pneumoniae*. We've also seen substantial reductions in acute otitis media (AOM) and community-acquired pneumonia (CAP).

STEPHEN I. PELTON, M.D.

Nonetheless, in the last few years we've started to see a small but real increase in invasive disease due to nonvaccine serotypes, documented by the Centers for Disease Control and Prevention's Active Bacterial Core surveillance (ABCs) system.

At the same time, there has also been documentation of an increase in AOM and a presumption of increases in CAP due to nonvaccine serotypes. These are harder to document, because data are typically obtained from hospital admissions or insurance claims and not from microbiological testing as is done with the ABCs. However, small studies using tympanocentesis have shown high proportions of nonvaccine *S. pneumoniae* serotypes in children with middle ear disease (Pediatr. Infect. Dis. J. 2007;26:S12-6).

Although we can't determine exactly what proportion of CAP and AOM is due to *S. pneumoniae* at any given time – and the longitudinal data are complicated by the secular changes in AOM definition – we do know that for every 1 case of invasive disease there are about 10 cases of CAP and 100 of AOM. So, we're looking at very clinically significant numbers.

In addition to the shift in serotypes, we've seen the emergence of multidrug-resistant pneumococci, particularly strain 19A. While these strains are usually sensitive to vancomycin, linezolid, and fluoroquinolones, they are resistant to the usual first-line antimicrobials, including amoxicillin, clindamycin, and trimethoprim-sulfamethoxazole, as well as ceftriaxone and other cephalosporins. Thus, both CAP and AOM have become more difficult to treat in children who don't respond to initial therapy.

Licensed earlier this year, PCV13 (Prevnar 13) contains all seven of the PCV7 strains (4, 6B, 9V, 14, 18C, 19F, and 23F), plus six more (1, 3, 5, 6A, 7F, and 19A). The serotypes represent either those that have been increasing in some countries using PCV7 (19A, 7F, 3) or that are globally important (1 and 5).

The vaccine was licensed on the basis of immunogenicity for the new serotypes as well as comparability to PCV7 for the seven "old" serotypes and a comparable safety profile.

The 13-valent vaccine is being introduced somewhat differently than was PCV7. The recommendation from the CDC Advisory Committee on Immunization Practices, the American Academy of Pediatrics, and the American Academy of Family Physicians is to administer PCV13 routinely to all children aged 2, 4, 6, and 12-15 months.

For children who previously received one or more doses of PCV7, the series should be completed with PCV13. And for children 15 months through 5 years of age who received only PCV7 (or no vaccine), a single dose of PCV13 is recommended.

In contrast, when PCV7 was licensed, the recommended catchup immunization was through 2 years of age and only high-risk children aged 2-5 years. That's because, in general, the risk for invasive pneumococcal disease begins to decline after 3 years of age.

However, the data on multidrug-resistant strain 19A suggest that it has been producing substantial disease in previously healthy children up through 5 years of age.

In addition, nasopharyngeal carriage of 19A has been seen frequently in children up to age 5. It is hoped that preventing that carriage will reduce the spread to unvaccinated children less than 4-5 months of age, immunocompromised children who don't respond sufficiently to the vaccine, and adults.

Adding indirect protection to a large part of the population should help to reduce the incidence of disease due to the new vaccine serotypes.

Finally, I'd like to address a question that often arises. With new conjugate pneumococcal vaccines, are we simply shifting the serotypes that produce disease and not actually preventing it? I would say no. With each new expansion of the vaccine, not only do we add broader coverage, but we expect to see a further reduction in disease.

It is anticipated that the six new strains of PCV13 will add another 10%-15% reduction in pneumococcal disease beyond the 65%-70% we've already seen with PCV7, so that we will now achieve an approximate 80%-90% disease reduction compared with rates in 1998-1999.

However, I don't think we will entirely eliminate pneumococcal disease. A few other important nonvaccine serotypes, including 22F, 33F, and 15B/C, are likely to continue and possibly increase slightly following the introduction of PCV13. Nonetheless, it will help us to reduce the burden of pneumococcal disease on child health. ■

DR. PELTON *is chief of pediatric infectious disease and also is the coordinator of the maternal-child HIV program at Boston Medical Center. Dr. Pelton said he has received research grants from GlaxoSmithKline, Pfizer, Novartis, and Intercell, and has served on advisory boards for all those companies and for Sanofi-Aventis as part of his professional activities.*

# PCV7 Led to Decline in Penicillin-Nonsusceptible IPD

BY ROXANNA GUILFORD-BLAKE

FROM THE INTERNATIONAL CONFERENCE ON EMERGING INFECTIOUS DISEASES

ATLANTA – Introduction of the 7-valent pneumococcal conjugate vaccine led to a major decline in penicillin-nonsusceptible invasive pneumococcal disease among children younger than age 5 years, according to research from the Centers for Disease Control and Prevention and other public health groups.

These findings were consistent regardless of which definition of susceptibility was used, which illustrates how changing case definitions can affect measured vaccine effects, reported Dr. Lee Hampton of the CDC's Epidemic Intelligence Service.

Using the ABC (Active Bacterial Core) surveillance system, Dr. Hampton and his colleagues analyzed 7,272 cases of serious pneumococcal infections in children younger than age 5 years in 10 ABC areas throughout the United States in 1998-2008.

Isolates were classified as susceptible or nonsusceptible; "nonsusceptibles" were further classified as intermediate or resistant based on both the old and new CLSI (Clinical and Laboratory Standards Institute) standards. CLSI issued new intravenous penicillin resistance break point standards in 2008.

Among cases of all types of IPD in children younger than age 5 years, 10% had intermediate susceptibility and 4% were fully resistant under the new break points. Under the old break points, 14% had intermediate susceptibility and 20% had full resistance, Dr. Hampton and his colleagues found.

Between the 2000 introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) and 2008, children younger than age 5 years experienced a 78% decline in penicillin-nonsusceptible IPD under the old, pre-2008 break points, and a 64% decline under the new break points.

Rates of penicillin-nonsusceptible IPD in 2008 were higher under the old break points (7.4 cases per 100,000 children) than under the new break points (4.4 cases per 100,000).

"We conclude that the introduction of PCV7 was associated with dramatic reductions in penicillin-nonsusceptible invasive pneumococcal disease incidents," regardless of which break point was used, he said. Abruptly switching from the old to the new penicillin break points can create the appearance of a sudden drop in penicillin nonsusceptibility, he added.

Six additional serotypes found in PCV13, but not PCV7, now account for 97% of all penicillin-nonsusceptible IPD under the new break points and 83% of penicillin-nonsusceptible IPD under the old break points, he said. If PCV13 is effective against these additional serotypes, rates of penicillin-nonsusceptible IPD should decrease.

Dr. Hampton identified several limitations to the research, including that the finding may not be generalizable outside the ABC system.

He emphasized the results are preliminary, but that they have significant implications for clinicians. "PCV7 has done a terrific job of reducing penicillin-resistant pneumococcal disease, no matter how you look at it. But doctors still need to avoid prescribing antibiotics when they're not needed, because unnecessary antibiotic use is one of the greatest driving forces behind resistance," he said in an interview.

"Clinicians should understand that more of their patients who need intravenous therapy for non-meningitis pneumococcal disease can now be treated with penicillin. This is great, because penicillin works very well against susceptible pneumococci and promotes less antibiotic resistance than many alternatives," he said. ■

VITALS

**Major Finding:** Between the 2000 introduction of PCV7 and 2008, children younger than age 5 years experienced a 78% decline in penicillin-nonsusceptible IPD under the old, pre-2008 break points, and a 64% decline under the new break points.

**Data Source:** Analysis of 7,272 cases of serious pneumococcal infections in U.S. children younger than age 5 years in 10 ABC areas in 1998-2008.

**Disclosures:** Dr. Hampton reported that he had no conflicts of interest.