

Pneumococcal Vaccine: Beyond 13 Serotypes

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EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

SAN FRANCISCO – Hard on the heels of approval of the 13-valent pneumococcal conjugate vaccine in early 2010, tests of a 15-valent pneumococcal conjugate vaccine are underway, and researchers are looking for new strategies beyond adding more and more pneumococcal serotypes to the vaccine.

“We can’t keep adding new serotypes. There are 92 serotypes,” Dr. Sheldon L. Kaplan said at the meeting. One target may be a vaccine that’s directed against noncapsular epitopes, suggested Dr. Kaplan, professor of pediatrics and head of the pediatric infectious diseases section at Baylor College of Medicine, Houston.

Meanwhile, the experimental 15-valent pneumococcal conjugate vaccine (PCV15) would add serotypes 22F and 33F – two of the five most common serotypes seen in invasive pneumococcal disease today. Since the introduction of



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the first 7-valent pneumococcal conjugate vaccine (PCV7) in 2000, invasive disease from those seven serotypes (4, 6B, 9V, 14, 18C, 19F, and 23F) has nearly disappeared, but disease from non-PCV7 serotypes has been on the rise since at least 2004.

In 2006-2007, 5% of isolates from invasive pneumococcal disease in children younger than 5 years old contained serotype 22F, and 5% contained 33F, which promoted these isolates to candidates for the PCV15 vaccine (*J. Infect. Dis.* 2010;201:32-41).

The most important serotype accounting for nearly half of invasive pneumococcal disease since introduction of the PCV7 vaccine – serotype 19A – was added to the 13-valent pneumococcal vaccine (PCV13) that was licensed in early 2010. The 2006-2007 data showed that 47% of invasive pneumococcal infections in children under 5 years of age was due to serotype 19A. Other data show that perhaps half of 19A isolates are resistant to three or more classes of antibiotics.

The PCV13 vaccine (Prevnar 13, made by Wyeth Pharmaceuticals Inc. and marketed by Pfizer Inc.) also added serotypes 1, 3, 5, 6A, and 7F. “Serotypes 1 and 3 are very important causes of pneumonia, especially pneumonia with empyema. We don’t see much serotype 5 in the United States, so it’s not going to make much of an impact there,” Dr. Kaplan said.

The success of PCV7 stokes hopes that PCV13 could have an equally dra-

matic impact. “I think we’re going to see a major decline in invasive disease due to adding these nonvaccine serotypes to the PCV13,” perhaps reducing the current numbers of invasive pneumococcal disease by 70%, he added.

The Advisory Committee on Immunization Practices (ACIP) and the Red Book by the American Academy of Pediatrics’ Committee on Infectious Diseases recommend administering PCV13 rou-

tinely to children at 2 months of age and suggest a catch-up schedule for children with incomplete vaccination histories.

Centers for Disease Control and Prevention monitoring after introduction of the PCV7 vaccine showed a 70%-75% reduction in overall invasive pneumococcal disease, Dr. Kaplan said.

His institution is part of a coalition of eight children’s hospitals that have been monitoring invasive pneumococcal dis-

ease since 1994, covering a surveillance population of around 19 million people. Cases of invasive pneumococcal disease decreased from an average of 400-500 cases per year before the PCV7 vaccine to a nadir of 100-200 cases per year in 2004, but the number has slowly crept up since then to 221 cases in 2009, he said (*Pediatrics* 2010;125:429-36).

As in CDC data, serotype 19A accounts for about half of invasive pneu-

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Important Safety Information

Contraindications

Humalog is contraindicated during episodes of hypoglycemia and in patients sensitive to Humalog or one of its excipients.

Important Safety Information, continued

Warnings

Humalog differs from regular human insulin by its rapid onset of action as well as a shorter duration of action. Therefore, when used as a mealtime insulin, Humalog should be given within 15 minutes before or immediately after a meal.

Due to the short duration of action of Humalog, patients with type 1 diabetes also require a longer-acting insulin to maintain glucose control (except when using an insulin pump).

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The safety and effectiveness of Humalog in patients less than 3 years of age have not been established. There are no adequate and well-controlled clinical studies of the use of Humalog in pregnant or nursing women.

Starting or changing insulin therapy should be done cautiously and only under medical supervision.

mococcal disease cases in the network's surveillance, he added.

The network data also show that the most prominent type of infection before PCV7, bacteremia, fell from approximately 60% of cases to around 40% of cases post-PCV7. Pneumonia increased from 20% of cases to 30%, and the proportion of isolates associated with bacterial meningitis remained relatively steady, between 11% and 17%.

"In our multicenter study, cases of culture-proven pneumococcal pneumonia declined from 80-100 kids per year to about 40-50 cases/year in 2004, and have

slowly climbed back up to more than 60 cases per year," entirely due to serotypes not included in PCV7, Dr. Kaplan said. Other data have shown a rise in rates of complicated pneumonias, such as empyema, he added.

Although PCV7 was associated with a modest decline in cases of acute otitis media and in the use of an-

tibiotics to treat AOM, at least until 2004, multidrug-resistant serotype 19A is playing a larger role in AOM. "In our studies, 19A accounts for about 60% of pneumococcal isolates recovered from children who have draining ears, myringotomies," and pressure equalization tubes, he said.

In one study, cases of pneumococcal pneumonia increased from 40-50 per year in 2004 to more than 60 per year because of serotypes not included in PCV7.

"As a result, we're seeing an increasing number of kids with pneumococcal mastoiditis," he added. Mastoiditis cases declined from around 5-10 cases per year before PCV7 to 3-4 cases per year, but have totaled 15-25 cases per year in the past few years.

Dr. Kaplan has received grants from Pfizer Inc. and Sanofi Pasteur for investigator-initiated studies, and is a member of pediatric advisory committees for Pfizer, Novartis, and Sanofi Pasteur. He said he has received honoraria from Pfizer, Novartis, GlaxoSmithKline, and Sanofi Pasteur. ■



Important Safety Information, continued

Warnings, continued
Hypoglycemia

Hypoglycemia is the most common adverse effect associated with insulins, including Humalog. Hypoglycemia can happen suddenly, and symptoms may be different for each person and may change from time to time. Severe hypoglycemia can cause seizures and may be life-threatening.

Other Side Effects

Other potential side effects associated with the use of insulins include: hypokalemia, weight gain, lipodystrophy, and hypersensitivity. Systemic allergy is less common, but may be life-threatening. Because of the difference in action of Humalog, care should be taken in patients in whom hypoglycemia or hypokalemia may be clinically relevant (eg, those who are fasting, have autonomic neuropathy or renal impairment, are using potassium-lowering drugs, or taking drugs sensitive to serum potassium level).

Important Safety Information, continued

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