Replacement Serotypes Spur Resistance Fears

Despite pneumococcal vaccine successes, penicillin nonsusceptible infections may be increasing again.

BY TIMOTHY F. KIRN
Sacramento Bureau

ASPEN, COLO. — Although the conjugate heptavalent pneumococcal vaccine has decreased penicillin resistance rates among those serotypes of the bacteria included in the vaccine, there is already some evidence that "replacement" serotypes are appearing.

And among those replacement serotypes, penicillin resistance may be on the increase, Dr. Sheldon Kaplan said at a conference on pediatric infectious diseases sponsored by Children's Hospital, Denver.

This is a situation that deserves watching, said Dr. Kaplan, chief of the infectious disease service at Texas Children's Hospital, Houston.

Two serotypes that seem to be emerging as the more common ones contained in the vaccine decline are serotypes 15 and 33, Dr. Kaplan reported.

'We're not the only people who are seeing this. CDC is actually reporting increases.'

DR. KAPLAN

According to a pneumococci surveillance project of eight children's hospitals, there was a mean five cases of invasive disease caused by serotype 15 in 1994-2000.

In 2002, there were 14 cases.

For serotype 33, the mean number of cases was less than one during the 1994-2000 period.

In 2002, there were nine cases, said Dr. Kaplan, whose hospital is part of the surveillance project (Pediatrics 2004; 113:443-9).

Specific isolates of serotype 15 collected by the project have been found to have the same blot pattern on a pulsefield electrophoresis gel about 60% of the time.

That suggests the different isolates taken from various children are the same clone of the bacteria.

About 80% of the serotype 33 isolates appear to be the same clone.

Serotype 19A also appears to be on the increase, and 19A appears specifically to be a serotype that is replacing 19F, a serotype in the vaccine.

According to one report, the annual incidence rate of invasive disease in children less than 2 years of age caused by serotype 19A has increased from 1 case per 100,000 population in 2001 to more than 6 cases per 100,000 in 2004 (J. Infect. Dis. 2005;192:1988-95).

There also has been a 2.5-fold increase in cases in children older than 5 years of age.

"We're not the only people who are seeing this," Dr. Kaplan commented. "CDC is actually reporting increases in these serotypes as well."

Moreover, as is well known, a number of surveys have suggested there has been a decrease in antibiotic resistance since the introduction of the conjugate vaccine.

That was true, but it may not be anymore, Dr. Kaplan said. The rate of penicillin nonsusceptible infections may actually be increasing again.

Although the number of cases caused by serotypes in the vaccine has declined precipitously, the number of cases caused by serotypes not in the vaccine has increased, and those serotypes appear to be acquiring more resistance.

The incidence rate of invasive disease caused by penicillin nonsusceptible pneumococci among children younger than 2 years has increased overall since 2002. And, considering just isolates not in the vaccine, it has increased from 51% in 1999 to 68% in 2004, Dr. Kaplan said.

"It looks like these nonvaccine serotypes are more likely to be penicillin nonsusceptible today than they were 5 years ago," he said.

In addition, a group from Salt Lake City has seen an increase in pediatric cases of pneumococcal pneumonia complicated with empyema since the introduction of the vaccine. Moreover, the serotypes associated with these cases tend to be those not in the vaccine—serotypes 1, 3, and 19A.

The Salt Lake City group reported that for the 4 years prior to the vaccine, their medical center saw an average of 38 cases of empyema, compared with an average of 72 cases in the first 4 years after the vaccine's introduction.

Also, pneumococcal parapneumonic empyema represented only 17% of the cases of identified invasive pneumococcal disease seen at that center in the years prior to the vaccine, but 32% of the cases after the vaccine (Pediatr. Infect. Dis. J. 2006;25:250-4).

Serotype 1 was the most common serotype associated with the empyema both prior to the vaccine (46%) and afterward (34%). Serotypes 3 and 19A became common after the vaccine (20% and 14%, respectively).

"I can't explain this, but they are clearly seeing more cases, with more nonvaccine types," Dr. Kaplan said.

He noted that the vaccine may have to be updated with at least some of these emerging strains.

"We do see these emerging serotypes. How we will address that down the road will have to be seen," Dr. Kaplan added. "It is an expensive vaccine." ■

Despite Vaccine, Some at Risk for Invasive Pneumococcal Disease

BY DOUG BRUNK
San Diego Bureau

SAN FRANCISCO — The highest rates of invasive pneumococcal disease were seen in children younger than 2 years of age in a Massachusetts study, Dr. Katherine K. Hsu reported during a poster session at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

The results also showed that black and Hispanic children remain especially vulnerable to nonvaccine-type invasive pneumococcal disease (IPD), compared with white children.

Higher risk of IPD in black and Hispanic children could not be attributed to unequal vaccination.

DR. HSU

"The implications in Massachusetts are that despite advances with pneumococcal conjugate vaccine and huge declines in invasive pneumococcal disease, there still are some children at risk," Dr. Hsu said in an interview.

Using microbiology reports of pneumococcal isolates from the Massachusetts Department of Public Health, the researchers identified 357 cases of IPD in children younger than 18 years of age between Oct. 1, 2001, and Sept. 30, 2005. Demographic data was confirmed with follow-up telephone interviews with primary care providers and/or adult caregivers. Incidence rates were derived using Census 2000 denominators.

Dr. Hsu and her associates found that the relative risk of IPD was 15.9 for children younger than 6 months, 16.8 for those aged 6-12 months, and 12.7 for those aged 12-24 months, compared with a relative risk of only 4.5 for children aged 24-60 months. Dr. Hsu did not give any data on older children.

The researchers also found that black and Hispanic children were two times more likely than their white counterparts to have IPD, particularly the nonvaccine type. Dr. Hsu, of the section of pediatric infectious diseases at Boston Medical Center, noted that these differences could not be attributed to unequal vaccination coverage rates. "Are these children perhaps more at risk because they're colonized more in the nasopharynx?" she asked. "Are they from different socioeconomic classes where there's more crowding or more smoking, or are there other risk factors for invasive disease such as HIV infection that are more dominant in those populations? We don't know the answer."

The study was supported by Wyeth. ■

No Benefit of Antihistamines, Decongestants Found in OME

BY DOUG BRUNK
San Diego Bureau

Antihistamines and/or decongestants serve no benefit for children who have otitis media with effusion, a Cochrane review of medical literature has concluded.

In fact, children who used them experienced an 11% spike in side effects such as gastrointestinal upset and drowsiness, compared with those who did not use them.

"Because we found no benefit for any of the studied interventions for any of the outcomes measured and we found harm from the side effects of the interventions, we recommend that practitioners not use antihistamines, decongestants, or antihistamine/decongestant combinations to treat otitis media with effusion in children," wrote the researchers, who were led by Dr. Glenn Griffin of Quinte West Medical Center in Trenton, Ont.

They noted that the findings mirror the current joint guidelines on the management of otitis media with effusion (OME) from the American Academy of Family Physicians, the American Academy of Otolaryngology–Head and Neck Surgery, and the American Academy of Pediatrics (Pediatrics 2004;113:1412-29).

For the review, which appears in the Oct. 18 issue of the Cochrane Database of Systematic Reviews (2006, Issue 4), Dr. Griffin and his associates studied 15 randomized, controlled trials of 1,516 children with OME that compared antihistamines, decongestants, or a combination of the two and that appeared in the medical literature through March 2006. Studies that randomized children based on acute otitis media were not included in the analysis (Epub doi:10.1002/14651858.CD003423).

The researchers found no benefit of taking decongestants alone or in combination with antihistamines in terms of being cured within 1 month, lessening hearing loss, risk of OME recurrence, development of otitis media, and the need for tympanostomy.

Six of the studies in the analysis measured side effects of medications. In these, 17% of children who received decongestants alone or in combination with antihistamines suffered side effects such as gastrointestinal upset and drowsiness, compared with only 6% of children who took placebo, a difference of 11%. The researchers estimated that for every nine children treated with the drugs, one would be harmed.

The investigators acknowledged that a key limitation of the review was the small number of studies found, but "the studies were so consistent in their findings that even if we missed a study, the summary results are unlikely to be overturned." ■