

Nonsusceptible Pneumococci Up in Replacement Serotypes

BY TIMOTHY F. KIRN
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ASPEN, COLO. — Although the conjugate heptavalent pneumococcal vaccine has decreased penicillin resistance rates in the vaccine's bacterial serotypes, there is some evidence replacement serotypes are emerging, according to a presentation at a conference on pediatric infectious diseases sponsored by Children's Hospital, Denver.

And with those replacement serotypes, penicillin resistance may again be on the increase, warned Dr. Sheldon Kaplan, chief of the infectious disease service at Texas Children's Hospital, Houston.

Serotypes 15 and 33 seem to be the more common serotypes in the vaccine decline, he said.

According to a pneumococci surveillance project of eight children's hospitals, there was a mean of 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 at the hospitals participating in the project have the same blot pattern on a pulse-field electrophoresis gel about 60% of the time. That suggests that different isolates taken from various children are the same clone of the bacteria.

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

Serotype 19A also seems to be on the increase and seems specifically to be replacing 19F, a serotype in the vaccine. According to one report, the annual incidence 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 said. "The CDC is actually reporting increases in these serotypes as well."



Data from a number of surveys have suggested there has been a decrease in antibiotic resistance since the introduction of the conjugate vaccine, but, said Dr. Kaplan, that may no longer be true.

The rate of penicillin nonsusceptible infections may actually be increasing again. Although the number of cases caused by serotypes in the vaccine has declined, the number of cases caused by serotypes not in the vaccine has increased, and it is those serotypes that seem to be acquiring more resistance.

The incidence of invasive disease caused by penicillin nonsusceptible pneumococci in children younger than 2 years has increased since 2002. And, considering only isolates that are 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.

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 serotypes 1, 3, and 19A, which are not in the vaccine.

The Salt Lake City group reported that for the 4 years before the vaccine was introduced, the medical center saw an average of 38 cases of empyema, compared with an average of 72 cases in the first 4 years after its introduction.

Also, pneumococcal parapneumonic empyema represented only 17% of the cases of identified invasive pneumococcal disease seen at that center in the years before the vaccine was introduced, but 32% of the cases afterward (Pediatr. Infect. Dis. J. 2006;25:250-4). Serotype 1 was the most common serotype associated with the empyema both before (46%) and after (34%) the vaccine was introduced. Serotypes 3 and 19A became common after the vaccine (20% and 14%, respectively).

"I can't explain this, but they are seeing more cases with more nonvaccine types," Dr. Kaplan said, noting that the vaccine may have to be updated with at least some of these emerging strains. "How we will address that down the road will have to be seen. It is an expensive vaccine." ■

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DR. KAPLAN

Adacel Shortage Should Resolve by 2007

A temporary shortage in the supply of Adacel—the tetanus-diphtheria-pertussis vaccine marketed by Sanofi-Pasteur—is expected to last until the end of the year.

Boostrix, the Tdap booster vaccine manufactured by GlaxoSmithKline, is in good supply, according to the Centers for Disease Control and Prevention. Adacel (tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed) is indicated as a booster for adolescents and adults aged 11-64 years, while Boostrix is indicated for adolescents aged 10-18 years. For information about Adacel availability, call Sanofi-Pasteur at 800-VACCINE.

The supply shortage of Adacel is expected to be resolved by the end of 2006, said Susan Watkins, a spokesperson for Sanofi-Pasteur.

A new vaccine production facility in Toronto that will provide a sevenfold increase of the supply of vaccines with pertussis components was approved by the Food and Drug Administration in late August.

That facility has already started to manufacture the DTaP vaccine Daptacel, and will begin producing Adacel next, Ms. Watkins said in an interview.

In the meantime, Adacel is being manufactured in another facility, but not in large enough quantities to meet the demand, she added.

—Elizabeth Mechcatie

Updates on the Adacel shortage will be provided on the CDC Web site at www.cdc.gov/nip/news/shortages/default.htm.

Identify Risk Factors to Guide Pneumonia Therapy

BY MARY ELLEN
SCHNEIDER
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DALLAS — Selection of an antibiotic for the treatment of community-acquired pneumonia should be based on the severity of the illness, coverage of common pathogens, and presence of factors that increase the risk for aspiration and/or infection with antibiotic-resistant organisms, Dr. Horace M. DeLisser said at the annual meeting of the National Medical Association.

Physicians shouldn't wait for culture results before treating. Instead, they should rely on the history to identify risk factors that will require modifying the treatment plan, said Dr. DeLisser of the pulmonary, allergy, and critical care division of the University of Pennsylvania, Philadelphia.

To determine whether the patient should be treated on an inpatient or outpatient basis, physicians can use the pneumonia severity index, a widely utilized and rigorously studied prediction rule, he said.

The index is based on 20 parameters that are commonly available at presentation, including demographic information, exam findings, and lab and imaging results. Each parameter is assigned a specific point value that allows physicians to stratify patients into five risk classes.

Classes 1-3 are low risk, class 4 is moderate risk, and class 5 is high risk. Generally, patients in risk classes 1 and 2 are treated on an outpatient basis, those in risk classes 4 and 5 are treated as inpatients, and those in class 3 may be treated as outpatients or admitted briefly, Dr. DeLisser said. "Your clinical judgment should always be used, particularly if there are other psychosocial or emotion factors," he said.

Dr. DeLisser advised physicians not to wait for the culture to come back. Between 40% and 60% of patients will have no pathogens identified, and for inpatients, early administration of antibiotics decreases mortality, he said. Instead, physicians should take into account the modified risk factors for infections, such as residence in a nursing home, underlying disease, and recent antibiotic therapy.

Several organizations in the United States, Europe, and Asia have developed guidelines for the treatment of community-acquired pneumonia. The following treatment recommendations are based on guidelines developed by the American Thoracic Society

(www.thoracic.org/sections/publications/statements/pages/mtpi/commacq1-25.html).

► In otherwise healthy adults without modifying risk factors, use an advanced-generation macrolide, such as azithromycin or clarithromycin. Another option for this group is treatment with doxycycline.

► For outpatients with comorbid disease or modifying risk factors, use a respiratory fluoroquinolone alone, or β -lactam plus an advanced-generation macrolide.

► For otherwise healthy inpatients who are not in the ICU, use an intravenous respiratory fluoroquinolone alone or intravenous azithromycin alone.

► For inpatients with comorbid disease or modifying risk factors, use intravenous respiratory fluoroquinolones alone or a combination of intravenous azithromycin plus intravenous β -lactam.

► Patients in the ICU who do not have risk factors for *Pseudomonas aeruginosa* infection can be treated with intravenous β -lactam plus either intravenous azithromycin or intravenous respiratory fluoroquinolone.

► Those patients at risk for *P. aeruginosa* infection can be treated with intravenous antipseudomonal β -lactam plus intravenous antipseudomonal fluoroquinolone. Another option is treatment with intravenous antipseudomonal β -lactam plus intravenous aminoglycoside plus either intravenous azithromycin or intravenous nonpseudomonal fluoroquinolone.

Most patients will become clinically stable within 3-7 days. Treatment is recommended for a minimum of 5-7 days and for at least 48 hours after reaching clinical stability, Dr. DeLisser said. Longer treatment—between 10 and 14 days—may be required for patients with infections caused by *Staphylococcus aureus*, *P. aeruginosa*, or *Legionella* species.

Patients can be discharged once their vital signs have been stable for a 24-hour period, they are able to take oral antibiotics, they can maintain adequate nutrition and hydration on their own, their mental status is back to baseline, and they have no other active clinical or psychosocial issues.

If the pneumonia does not resolve, consider microbial resistance to the initial antimicrobial regimen, suppurative complications like an abscess or empyema, or subsequent development of nosocomial pneumonia, Dr. DeLisser said. ■