

The Clinical and Economic Impact of Pneumococcal Disease in the Pediatric Population

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This supplement to *The American Journal of Managed Care* features a Special Report on the roundtable conference, "The Clinical and Economic Impact of Pneumococcal Disease in the Pediatric Population," held July 23 and 24, 1999, in Boston, Massachusetts. The panel included experts in pediatrics, infectious diseases, health economics, pharmacy, managed care, and vaccine development.

The need for ongoing multidisciplinary discussions of pediatric pneumococcal disease is clear. Today, *Streptococcus pneumoniae* is the most common cause of invasive bacterial infection in children, contributing to significant morbidity and mortality around the world. Although antimicrobials have significantly reduced mortality within industrialized countries, pediatric hospitalizations and fatalities in the United States caused by pneumococcal meningitis, pneumonia, and bacteremia are still counted in the tens of thousands every year.¹ In addition, the fatality rate from pneumococcal infections among adults has remained unchanged (25%) since the 1950s.

As pointed out by panelist Chris Van Beneden, MD, MPH, children younger than 2 years of age currently have the highest incidence of invasive pneumococcal disease. In fact, with widespread adoption of the *Haemophilus influenzae* type b conjugate vaccine, the pneumococcus has become the leading cause of bacterial meningitis in the United States.¹

In addition to these serious systemic consequences of pediatric pneumococcal infection, this organism causes approximately half of all cases of acute otitis media (AOM), prompting 24 million pediatrician office visits annually in the United States.¹ The emergence of antibiotic-resistant strains of the pneumococcus, including recent reports of resistance to fluoroquinolones, has only added to the urgency of attempts to improve prevention and treatment of pediatric pneumococcal diseases.

Aggressive empiric therapy appears to have prevented any increased mortality associated with pneumococcal antibiotic resistance, but such protection comes at a price. Panelist David Thompson, PhD, demonstrated that treatment of recurrent episodes of AOM typically becomes much more costly than the initial infections. Dr. Thompson indicates that this occurs because of the cost of additional office visits and alternative antibiotics, which are often more expensive than the first-line therapy and are prescribed because of the potential for antimicrobial resistance.

Many of these problems related to pneumococcal infections in children are not new; they have been discussed for decades. In fact, panelist Robert Austrian, MD, has been instrumental in shaping the scientific and clinical course of that debate. And as Dr. Austrian reminded the roundtable panel members, several of the most inscrutable problems related to pneu-

mococcal infections will likely remain with the healthcare community for some time to come.

In an attempt to address some of these problems, pneumococcal vaccines continue to be developed. In fact, the first of the pneumococcal conjugate vaccines will complete its large Phase III trials in early 2000. This new class of conjugate vaccines is significant because the existing 23-valent pneumococcal polysaccharide vaccine fails to induce sufficient immune responses in infants and young children. Several pneumococcal conjugate vaccines currently being tested have been shown to be safe and immunogenic.^{2,3} As reviewed by panelist Stephen I. Pelton, MD, even some children at the highest risk for pneumococcal disease (eg, those with sickle cell disease or human immunodeficiency virus infection) have been shown to display vigorous immune responses to the conjugate vaccines.

This evidence of safety and immunogenicity of the pneumococcal conjugate vaccines as well as preliminary evidence of efficacy in invasive diseases was the real catalyst for this roundtable discussion of the clinical and economic impact of pneumococcal disease in children. The availability of such a pneumococcal conjugate vaccine raises important new questions about immunization guidelines and managed care policies.

The answers to many of these questions will hinge on the efficacy data now emerging from the largest randomized clinical trials. The recently completed 3-year Kaiser Permanente Vaccine study of 38,000 children will likely provide a foundation of data on which many discussions of vaccination protocols and reimbursement will begin. In the Kaiser Permanente Study, the preliminary efficacy of the pneumococcal heptavalent conjugate vaccine (PNCRM7) in preventing invasive disease was extremely high; all 17 of the

first cases of vaccine serotype invasive disease were in controls.

An additional pneumococcal conjugate vaccine efficacy trial among Navajo and Apache Indian infants is expected to be completed by the early part of the year 2000.

Estimates of vaccine efficacy for specific pneumococcal diseases will provide key variables for economists and managed care groups attempting to calculate the costs of widespread pediatric pneumococcal vaccination versus the potential savings. As described by panelist Tracy Lieu, MD, assumptions for vaccine efficacy rates, disease incidence, and disease-related costs will likely be drawn from published data, expert panels, and health plan databases. Outlining a model for such analysis, Dr. Lieu presented preliminary numbers from a

ACRONYM LIST

The following acronyms appear within the pages of this Special Report:

AAP	American Academy of Pediatrics
ABCs	Active Bacterial Core Surveillance
ACIP	Advisory Committee on Immunization Practices
AOM	Acute otitis media
CDC	Centers for Disease Control and Prevention
ELISA	Enzyme-linked immunosorbent assay
Hib	<i>Haemophilus influenzae</i> type b
HIV	Human immunodeficiency virus
HMO	Health management organization
IgG	Immunoglobulin G
PNCRM7	Pneumococcal heptavalent conjugate vaccine
PPV	Pneumococcal polysaccharide vaccine
SCD	Sickle cell disease
TMP-SMX	Trimethoprim-sulfamethoxazole

study she is working on with several experts, which indicates that a conjugate pneumococcal vaccine may prevent more than 1 million cases of pneumococcal disease annually in the United States, including approximately 65,000 cases of serious pneumonia, bacteremia, and meningitis. Dr. Lieu's group has estimated the potential overall savings to society to be approximately \$763 million or \$181 per child vaccinated.

In anticipating the results of the pneumococcal pediatric vaccine trials, the topics raised during this conference very likely mirror the discussions soon to be held, if not already under way, within formulary and immunization guideline committees of many managed care organizations. As always, the recommendations of groups such as the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices will shape most local immunization policies. And within any institution's adoption of national policies, there is ample room for customization,

emphasis, investment, and monitoring. Private and public health organizations will soon need to debate their own policies and procedures regarding many aspects of pneumococcal pediatric vaccination dosing, age limits, schedules, education, reimbursement, and utilization review. As a resource for shaping these important details, the proceedings of this roundtable discussion may provide valuable insights and information.

... REFERENCES ...

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3. Eskola J, Anttila M. Pneumococcal conjugate vaccines. *Pediatr Infect Dis J* 1999; 18:543-551.