# PCV7 Herd Immunity Covers Unvaccinated Infants

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The rate of invasive pneumococcal disease among U.S. infants younger than 2 months has declined by 43% since the introduction of the pneumococcal conjugate vaccine in the United States, even though these children are too young to have received the vaccine.

"These data are the first to suggest that neonates and infants too young to receive PCV7 are benefiting from herd immunity," said Dr. Katherine A. Poehling and her coinvestigators. "Although the exact mechanism of herd immunity is uncertain, one hypothesis is that vaccinated children are less likely to have nasal carriage of pneumococcus and hence have less pneumococcal transmission to their contacts."

The biggest decrease occurred in black infants, among whom the rate of invasive disease declined 71% from 1997 to 2004. The change was enough to eliminate the racial disparity in invasive pneumococcal disease between black and white infants, the authors said (JAMA 2006;295:1668-74).

Their population-based study examined rates of confirmed invasive pneumococcal disease in eight states among infants younger than 3 months, from 1997 to 2004.

During that time, there were 170 cases: 89 occurred in the 3 years before the vaccine (PCV7) was introduced, 24 cases during the transition year (2000-2001), and 57 in the 3 years after the vaccine was introduced.

Among all infants younger than 3 months—some of whom would have received at least one dose of the vaccine—the mean rate of disease decreased 42%, from 12 per 100,000 to 7 per 100,000. The rate among infants younger than 2 months—those too young to receive any doses of the vaccine—declined 43%, from 7 per 100,000 to 4 per 100,000.

The largest change occurred among black infants, noted Dr. Poehling, of Vanderbilt University, Nashville, Tenn., and her colleagues.

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In this group, the rate of invasive pneumococcal disease decreased 71%, from 17 per 100,000 to 5 per 100,000.

The precipitous drop in disease echoes that which occurred after the introduction of effective vaccines for other communicable diseases, said Dr. Matthew L. Boulton, professor of epidemiology and director of the preventive medicine residency program at the University of Michigan, Ann Arbor. The challenge now will be to continue reinforcing the importance of vaccination to parents who might hear conflicting messages.

"Paradoxically, the more successful we are in a public health intervention like this, the less people become willing to have their children vaccinated," he said in an interview. This has to do both with misinformation about immunization side effects and complacency about the decrease in disease risk. "It's critical to keep a positive message about the importance of immunization out in the public."

Remind parents of how seriously communicable diseases once affected children's health, and point out the risks of immunization complications in real terms. "Tell them how many millions of doses are given and how very, very few children have true complications," he said. "It's a very tiny number."

The study also examined changes in the pneumococcal serotypes causing the infections. Serotypes resistant to antibiotics decreased 75% from 1998 (the first year of serotyping) to 2004. Antibiotic-susceptible serotypes also decreased, but to a lesser extent (50%).

The study found small increases in disease caused by two serotypes present in the pneumococcal conjugate vaccine (18C and 19F) and in disease caused by a few nonvaccine strains that were not present prior to the introduction of PCV7.

These changes are troubling, according to Moe H. Kyaw, Ph.D., and his associates, whose epidemiologic study arrived at sim-

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ilar conclusions regarding serotype changes after PCV7: Rates of invasive disease caused by antibiotic-resistant bacteria have declined, but rates of resistant disease caused by 19A increased by 238% from 1999 to 2004. The study also found modest increases in invasive disease caused by resistant strains not included in the vaccine (N. Engl. J. Med. 2006; 354:1455-63).

"The increase in resistant disease caused by serotype 19A is a concern," said Dr. Kyaw, of the Centers for Disease Control and Prevention, and his colleagues. "It is difficult to predict whether the increase in resistant serotype 19A or other serotypes not covered by the vaccine will continue. Nevertheless, this replacement disease has the potential to reduce the overall benefit of the vaccine against resistant infections."

Replacement disease with resistant strains, particularly 19A, is a surprise—and not a nice one, Dr. Daniel M. Musher said in an accompanying editorial. "This problem is compounded by the fact that, through genetic transformation, pneumococci can switch capsules." If pneumococcal strains with pandemic potential, such as 6B, 9V, or 23F, acquire a resistant capsule, dangerous new types could emerge.

There is insufficient information to make any predictions about the endemic spread of these replacement serotypes, Dr. Boulton said. "We have seen only cases of disease being caused by these replacement strains, but that's all. It would be a very different situation if we begin to see levels of transmission comparable to what was seen in the serotypes included in the vaccine." ■



# Pneumococcal Vaccine Stops hMPV Infection

Children vaccinated with three doses of pneumococcal conjugate vaccine had a reduced rate of human metapneumovirus-associated infections of the lower respiratory tract, as well as a lower rate of clinical pneumonia than children given placebo, researchers reported.

Dr. Shabir A. Madhi of the University of the Witwatersrand, Bertsham, South Africa, and colleagues performed an analysis of data from nearly 40,000 children—some of whom had been infected with HIV—who had been given three doses of a polysaccharide–protein conjugate vaccine (PCV) or placebo in an ongoing phase III study.

Dr. Madhi and coinvestigators tested nasopharyngeal aspirate samples of the children who had been hospitalized with lower respiratory tract infection (LRTI) for evidence of human metapneumovirus (hMPV), which was discovered only 5 years ago, as well as for HIV and C-reactive protein (J. Infect. Dis 2006;193:1236-43).

They found that for vaccinated children without HIV infection, the hospitalization rate was 46% lower than that of children who received placebo. For HIV-infected children, the reduction was 53% versus placebo. The incidence of clinical pneumonia also was reduced for both HIV-free and HIV-infected children who received vaccine (55% and 65%, respectively).

These results "suggest that bacterial coinfections, particularly pneumococcal infections, are an essential part of the pathogenesis of most severe hMPV infections progressing to pneumonia," they said. This means that children hospitalized with hMPV-associated pneumonia "should be treated with antibiotics."

**—John R. Bell**