Preschool-Aged Children Are First to Get Influenza

BY MIRIAM E. TUCKER
Senior Writer

Emergency department data demonstrate that preschool children are the first to come down with influenza each year and could play an important role in the infection's spread, according to John S. Brownstein, Ph.D., of Children's Hospital Boston, and his associates.

Data collected from four emergency departments and one ambulatory care setting in Massachusetts during 2000-2004 suggest that children aged 3-4 years are consistently the first to seek care for respiratory illness during each influenza season, and that the temporal pattern of illness in that group strongly predicts mortality due to influenza and pneumonia among people of all ages.

The results bolster arguments in favor of universal vaccination of all preschool-aged children in addition to the 6- to 23-month-olds for whom the vaccine is currently recommended, the investigators said (Am. J. Epidemiol. 2005;162:686-93).

Among patients presenting to the different health care settings—including one pediatric emergency department, one adult emergency department, and two that treat both adults and children—children aged 3-4 years presented earliest in the season, with a mean lead time of 34 days prior to the peak in overall mortality. Children of that age group presenting to pediatric emergency departments had the longest lead time of all, with a mean of 50 days. In contrast, adults aged 18 years and older in the ambulatory care and emergency department settings had a mean lead time of just 12 days.

Prediction of influenza and pneumonia mortality varied by age. Children younger than 3 years were the best predictors, explaining 41% of the deviance, while those aged 3-4 years explained 37%, the investigators reported.

"Although this finding does not necessarily prove that preschool-aged children are driving the yearly influenza epidemics, they intriguingly suggest that preschool-aged children are the initial group infected and may be important in the subsequent spread," they wrote.

These and other data point to the idea that targeting yearly influenza vaccination to younger children may benefit the entire community. The idea is currently under consideration by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices. ■

Invasive Pneumococcal Disease Curbed by Seven-Valent Vaccine

BY PATRICE WENDLING
Chicago Bureau

Routine use of seven-valent pneumococcal conjugate vaccine in young children has dramatically reduced the incidence of vaccine-type and overall invasive pneumococcal disease in children and adults, the Centers for Disease Control and Prevention reported.

Vaccine-type IPD also declined outside the target population, with the largest absolute rate reduction in persons 65 years and older.

The most substantial decline in the rate of vaccine-type disease has been in the target population of children less than 5 years old, according to an analysis comparing disease rates in 2003 with those in 1998-1999, when the Prevnar vaccine was not available.

In this age group, vaccine-type invasive pneumococcal disease (IPD) decreased 94% from 80 cases per 100,000 population to 4.6 cases (MMWR 2005;54:893-7).

Incidence rates of vaccine-type IPD also declined substantially among individuals outside the target population, with the largest absolute rate reduction occurring in those 65 years and older.

The routine use of the vaccine prevented 29,599 expected vaccine-type IPD cases in 2003, according to the analysis conducted by the Active Bacterial Core surveillance of the Emerging Infections Program Network in cooperation with the CDC.

An estimated 9,140 cases of vaccine-type IPD were directly prevented by vaccinating children less than 5 years old. An additional 20,459 cases (69%) were prevented through indirect effects of the vaccine across all ages.

"This is not the first vaccine to be shown to have a herd immunity effect, but the magnitude of the effect being so large is what makes this vaccine important," Deron C. Burton, M.D., of the CDC's division of bacterial and mycotic diseases, said in an interview.

Among children less than 5 years old and adults aged 40 years or older, the reduction in vaccine-type IPD was offset by an increase in disease caused by pneumococcal serotypes not included in the seven-valent vaccine. There were a total of 4,721 projected additional cases of nonvaccine-type IPD across all age groups in 2003, compared with baseline.

Dr. Burton said ongoing surveillance will be required to determine if the replacement disease effect stays small or if it increases in magnitude and begins to erode some of the benefits of the vaccine. ■

Most U.S. Measles Cases in 2001-2004 Were Preventable

BY MIRIAM E. TUCKER
Senior Writer

More than half of all the cases of measles reported among United States residents during 2001-2004 were preventable, according to the Centers for Disease Control and Prevention.

Although endemic measles has been eliminated from the United States, cases continue to be imported from other parts of the world, and infected travelers can transmit the disease to susceptible contacts, the CDC said (MMWR 2005;54:817-20).

Of the 251 measles cases reported to the CDC during 2001-2004, 71% occurred among U.S. residents and 29% among nonresidents. Of the 177 cases among U.S. residents, 100 (56%) were considered preventable, which means that they occurred in persons for whom vaccination against measles is recommended by the Advisory Committee on Immunization Practices, but those individuals had not received one or more doses of measles-containing vaccine.

Among the 177 U.S. residents, 52% (92) were aged 0-19 years and 48% (85) were aged 20 years or older. Nearly one-third (31%) had traveled abroad, while the other 69% were infected in the United States. More than three-fourths (77%) of the total group had not been vaccinated. Of those 136, only 7 cases (5.1%) were considered not preventable, because the individuals were born before 1957 and measles vaccination is not recommended for that age group, the CDC said.

Current recommendations for travelers include vaccination for infants 6-11 months of age and two doses of measles-containing vaccine for travelers aged 12 months and above. Yet the 100 preventable cases in this report included a total of 43 travelers: 17 infants aged 6-15 months, 11 children and adolescents aged 16 months to 19 years, and 15 adults aged 20 and older.

One of these cases was an 11-year-old girl who developed a rash 3 days after returning to the United States from the United Kingdom. She had not been vaccinated because of her parents' religious beliefs. She had close contact with an 11-month-old infant, who subsequently had contact with up to 234 persons at a summer camp 2 days before he also developed a rash. After extensive investigation and control efforts, no further cases were subsequently identified.

Measles cases among persons born before 1957 are rare. However, individuals in this age group who travel internationally might wish to consider vaccination to minimize their risk of measles, the CDC advised. Information on vaccination recommendations for travelers is available at www.cdc.gov/travel. ■

Susceptibility Gene Identified For Acute Rheumatic Fever

BY BRUCE JANCIN
Denver Bureau

VIENNA — A polymorphism in the gene coding for toll-like receptor 2 seems to constitute a powerful susceptibility gene for acute rheumatic fever, H. Hakan Aydin, M.D., Ph.D., said at the annual European Congress of Rheumatology.

Indeed, 56 of 61 unselected Turkish children who met diagnostic criteria for acute rheumatic fever were heterozygous for the simple polymorphism, in which arginine is replaced by glutamine at position 753 in the toll-like receptor 2 (TLR-2) gene, according to Dr. Aydin of Ege University, Izmir, Turkey.

In contrast, just 9 of 91 ethnically matched healthy pediatric controls and 12 of 116 healthy adult controls were heterozygous for TLR-2 *Arg753Gln*. Not a single patient or control was homozygous for *Arg753Gln*.

Genetic differences in host susceptibility to acute rheumatic fever as reflected in the TLR-2 polymorphism go a long way toward explaining why only 0.3-3.0% of patients with acute group A streptococcal pharyngitis go on to develop acute rheumatic fever. Some investigators have also argued that certain strains of group A strep may be more selectively rheumatogenic than others, although to date the evidence supporting this proposition is sketchy, he added at the meeting sponsored by the European League Against Rheumatism.

TLRs play a key role in host immunity, initiating the full range of both adaptive and innate immune responses against all manner of foreign microbes. Stimulation of the TLRs results in production of proinflammatory cytokines, adhesion molecules, chemokines, antibodies, costimulatory molecules, and the major histocompatibility complex, as well as the nuclear transcription factor–kappa-B.

Thus, a polymorphism in TLR-2 rendering affected individuals hyporesponsive to bacteria that contain TLR-2 agonists—as do gram-positive group A strep—could have important clinical consequences. Dr. Aydin and his coinvestigators have also studied polymorphisms in TLR-4 but saw no association with acute rheumatic fever.

The finding that a TLR-2 polymorphism is strongly associated with increased susceptibility to rheumatic fever should eventually lead to a simple genetic test to risk-stratify patients for a disorder the World Health Organization says is still a major health problem, particularly in developing countries. It also opens the door to pharmacologic manipulation of TLR-2 for therapeutic purposes, Dr. Aydin predicted. ■

Pages 56a—56b