Vaccine May Fuel Resistant *S. pneumoniae* 19A

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CHICAGO — The multidrug-resistant *Streptococcus pneumoniae* serotype 19A continues to spread across the United States, according to Dr. David J. Farrell.

"We believe that that the emergence of this 19A clone has been driven by the 7-valent pneumococcal conjugate vaccine," Dr. Farrell said in an interview during a poster presentation at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Dr. Farrell, director of clinical microbiology at G.R. Micro Ltd., a London-based company doing contract research for pharmaceutical firms, and his colleagues collected more than 21,000 *S. pneumoniae* samples from 103 U.S. centers during the 4 years of the global PROTEKT (Prospective Resistant Organism Tracking and Epidemiology for the Ketolide Telithromycin) study.

In all, 562 of the isolates were the multidrug resistant (MDR) 19A strain, Dr. Farrell said at the meeting, which was sponsored by the American Society for Microbiology. Sources of the isolates included blood, sputum, bronchoalveolar lavage fluid, middle-ear fluid, sinus aspirates, and nasopharyngeal swabs or aspirates.

Between 2002 and 2006, the proportion of isolates that were MDR 19A increased from 1% to 6%. The largest proportion was in the group aged 0-2 years (rising from 4% to 15%), followed by the group aged 3-14 years (1% to nearly 9%).

In the group of those aged at least 65 years, MDR 19A accounted for 3% of all isolates in 2005-2006, said Dr. Farrell in an interview. "So we've got this 19A serotype that's not in the vaccine, it's being driven by the vaccine, and it's becoming more prevalent and spilling over to older children and adults, including the elderly population."

Although serotype data are incomplete for the group aged 15-64 years, genotype analysis suggested the same upward trend is occurring, and at the same rate, he said.

A second study of antimicrobial resistance patterns in *S. pneumoniae* isolated from children showed the experimental oral penem antibiotic faropenem was the most potent oral β-lactam based on in vitro activity.

During the 2005-2006 respiratory season, *S. pneumoniae* isolates were prospectively collected from 104 participating institutions distributed across the United States as part of the faropenem surveillance (FAMOUS) study. In total, 393 isolates were collected from children aged 6-14 years, 3-5 years, and younger than 2 years. The isolates were then tested for susceptibility to faropenem, meropenem, amoxicillin/clavulanate, cefdinir, cefuroxime, penicillin, azithromycin, levofloxacin, and trimethoprim/sulfamethoxazole.

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DR. FARRELL

Multidrug resistance was defined as resistance to either two or three of these agents, said Ian A. Critchley, Ph.D., director of microbiology at Replidyne Inc., Louisville, Colo., which is evaluating faropenem. Of the 393 *S. pneumoniae* isolates from children younger than age 14 years, half were penicillin susceptible, a quarter were penicillin intermediate, and another quarter were penicillin resistant.

Faropenem was the most active β-lactam against all pediatric isolates, with a minimum inhibitory concentration required to inhibit the growth of 90% of organisms (MIC_{90}) of 1 mcg/mL. The MIC_{90} of both amoxicillin/clavulanate and cefdinir was 8 mcg/mL. The least effective agents were penicillin, azithromycin, and trimethoprim/ sulfamethoxazole, with percent-susceptible rates of 49, 55, and 57, respectively.

Antimicrobial resistance was generally higher in isolates from children aged younger than 2 years, compared with isolates from those aged 6-14 years. Penicillin resistance ranged from 15% in isolates from children aged 6-14 years to 31% in isolates from children younger than 2 years.

"In children under 2 years, [in whom] there's been wide use of β-lactams and macrolides, the penem compound holds out favorably in our in vitro minimum inhibitory concentration profile, compared with amoxicillin/clavulanate and cefdinir," said Dr. Critchley. In the *S. pneumoniae* re-

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sistant to three classes of agents, only 29% were susceptible to amoxicillin/clavulanate, and none of the isolates was susceptible to cefdinir, he added.

In a separate comment, Dr. Stephen I. Pelton said MDR 19A should be suspected in children with persisting signs and symptoms of acute otitis media despite antimicrobial therapy. "Some of these isolates will be susceptible to high-dose Augmentin or a three-dose regimen of intramuscular ceftriaxone, but others may not," said Dr. Pelton, chief of pediatric infectious disease at Boston Medical Center.

Tympanocentesis with or without tube insertion will offer symptomatic benefit for those with treatment failure or persistent earache, irritability, or other symptoms, Dr. Pelton said in an interview.

In addition, the PCV7 vaccine should not bear all the blame for the increase in the resistant 19A strain, he added. "The 19A strain was intermediate resistant in 2000, and it is both the vaccine's lack of cross-reactivity and the presence of resistance that has selected for the increase in 19A. So there are two processes: selection of 19A already [intermediate] resistant to penicillin, and the introduction of new 19A strains with even higher resistance. Switching to 19A may be the result of the vaccine, but continued use of antibiotics is the selection driving this clone increase," he said. ■

ACIP Approves FluMist for Kids Aged 2-5 Years

ATLANTA — The live, attenuated influenza virus vaccine can be used in children 2-5 years of age with no wheezing in the past 12 months, the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices recommended at their fall meeting.

LAIV vaccine, manufactured as FluMist by MedImmune Inc., should not be administered to individuals with asthma or to children younger than age 5 with recurrent wheezing, ACIP said.

Acknowledging the difficulty in identifying recurrent wheezing in young children, the committee suggested physicians ask parents of 2- to 5-year-olds (children aged 24-59 months) the following question before administering FluMist: "In the past 12 months, has a health care provider ever told you that your child had wheezing or asthma?" The vaccine is not recommended for children whose parents answer yes to the question or for those with wheezing noted in their chart within the past year.

For healthy 2- to 49-year-olds, either trivalent inactivated virus (TIV) vaccine or LAIV vaccine can be used for flu immunization.

The Food and Drug Administration approved FluMist for children aged 24 months up to 59 months, on Sept. 19, 2007.

Dr. Joseph Bocchini of Louisiana State University, Shreveport, the American Academy of Pediatrics liaison at the meeting, said the approval "expands our ability to provide vaccine to 2- to 5-year-olds" and provided a choice of which vaccine to give.

—Melinda Tanzola