Pathogen Shift Seen in Post-PCV Ear Infections

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CHICAGO — The trajectory of *Streptococcus pneumoniae*–related otitis media in the United States, which declined dramatically after the introduction of the pneumococcal conjugate vaccine in 2000, is now heading skyward, according to Dr. Michael E. Pichichero.

"Since the PCV vaccine came into play, we've seen a pathogen shift in which the percentage of *S. pneumoniae* bacteria causing ear infections in children, after dropping for the first 3 years, is now rising again," Dr. Pichichero said in an interview.

Although *Haemophilus influenzae* continues to be the predominant pathogen, during the 2005-2006 season there was an upswing in *S. pneumoniae* isolates, with simultaneous increase in the proportion of strains that were penicillin resistant, Dr. Pichichero said.

There was a 20% increase in pneumococcal isolates obtained by tympanocentesis over 3 seasons between 2003 and 2006, according to a poster presented by Dr. Pichichero at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Virtually all the ear infections involved bacterial strains not covered by the vaccine, PCV7 (Prevnar, Wyeth Pharmaceuticals). Among those strains is the "superbug" multidrug resistant form of 19A, which is resistant to all antibacterials approved for pediatric use, said Dr. Pichichero, professor of microbiology and immunology at the University of Rochester Medical Center (URMC) in New York.

The investigators collected and analyzed 267 acute otitis media (AOM) isolates from tympanostomies conducted at URMC, Children's Hospital in Pittsburgh, and an Inova hospital in Fairfax, Va.

Most of the isolates were obtained from children under age 2 years who had been

vaccinated with PCV7, and who had failed antibiotic treatment or had recurrent AOM.

The proportion of *S. pneumoniae* for the respiratory seasons 2003-2004, 2004-2005, and 2005-2006 was 30%, 34%, and 45%, respectively, the authors said, adding that for *H. influenzae* the proportions were 48%, 57%, and 39%; and for *Moraxella catarrhalis,* 6%, 8%, and 12%, respectively.

In 2003, 64% of *S. pneumoniae* isolates were penicillin susceptible, 14% were penicillin intermediate, and 23% were penicillin resistant. Three years later, those proportions were 50%, 23%, and 27%.

The authors explained that the increase in penicillin-resistant *S. pneumoniae* strains was largely due to increased isolation of non-PCV7 serotypes of the bacterium, especially serotypes 6A, 11, 15, 19A, and 35B.

Among the *H. influenzae* isolates, the proportions that produced β-lactamase, indicating resistance to amoxicillin, remained stable over time at about 50%.

After dropping for the first 3 years after the PCV vaccine, *S. pneumoniae* ear infections are now rising again.

DR. PICHICHERO

In the first 3 years after PCV7 was approved, the incidence of *S. pneumoniae*–related AOM appeared to decline, while *H. influenzae*–related AOM increased. In the subsequent 3 years the reverse is occurring and the two incidence lines are intersecting, Dr. Pichichero explained, adding that physicians are faced with a treatment paradox.

"If a family physician sees a child with a difficult-to-treat ear infection tomorrow—the child with recent antibiotic treatment failure or recurrent ear infection—there's a 50% chance that it's *S. pneumoniae* and a 50% chance that its *H. influenzae.* If it's *S. pneumoniae*, there's a 50% chance it's resistant to penicillin and if it's *H. influenzae* there's a 50% chance it's resistant to amoxicillin," he said. In addition, he noted that the treating physician's best option is to follow the American Academy of Family Physicians guidelines.

Only six antibiotic options are advised for empiric treatment, Dr. Pichichero said, including high-dose amoxicillin, high-dose Augmentin, the oral cephalosporins cefpodoxime, cefuroxime, and cefdinir, and injected ceftriaxone.

Levofloxacin, which is not Food and Drug Administration approved for pediatric use and whose safety in children remains unproven, is effective against resistant bacteria.

The AAFP has endorsed levofloxacin for pediatric use only when it's been proven that it's the only antibiotic that will work, according to lab test results, Dr. Pichichero said at the meeting, which was also sponsored by the American Society for Microbiology. The potential for a complication following off-label use of levofloxacin could leave the treating physician open to legal action, he warned.

Dr. Pichichero cautioned that the results of this study may not be generalizable to children with uncomplicated or previously untreated AOM.

A separate analysis from the same study demonstrated that the multiresistant 19A serotype pneumococcal strain is able to evade all approved antibiotics.

In a second study, Dr. Pichichero and his colleagues reported tympanocentesis results from 162 children, three-quarters of whom were under age 2 years, experiencing recurrent AOM or AOM treatment failure. Isolates were obtained during 3 seasons between 2003 and 2006.

Among 34 *S. pneumoniae* with serotypes not included in PCV7, 9 were the multidrug resistant 19A strain.

Dr. Pichichero emphasized the urgent need for the expanded valency vaccine currently in a phase III clinical trial. The vaccine (PCV13), which contains the 19A strain, could become available in late 2009 or early 2010, according to a Wyeth spokesman.

Dr. Stephen I. Pelton commented that previous research has demonstrated that about 30% of children under 7 years of age harbor *S. pneumoniae* in their nasopharynx, and approximately 20% of *S. pneumoniae* are type 19A.

"The multidrug resistant [MDR] 19A is only a small fraction of the 19A isolates currently circulating in the community, and the risk for carriage of an MDR isolate is relatively low, involving about 1% or 2% of children," explained Dr. Pelton, chief of pediatric infectious disease at Boston Medical Center.

The off-label use of levofloxacin may be necessary for children failing therapy.

"Documentation of the presence of MDR 19A in either pneumococcal pneumonia or middle ear disease probably is a good idea before initiating the use of levofloxacin," Dr. Pelton added in an interview.

In fact, if MDR *S. pneumoniae* is suspected, then documentation by tympanocentesis or at a minimum nasopharyngeal culture is a good approach, he said. ■