

# Vaccine May Fuel Resistant *S. pneumoniae* 19A

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Chicago Bureau

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

"We believe 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 Inter-

science 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 mul-

tidrug 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  $\beta$ -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,



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DR. FARRELL

amoxicillin/clavulanate, cefdinir, cefuroxime, penicillin, azithromycin, levofloxacin, and trimethoprim/sulfamethoxazole.

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  $\beta$ -lactam against all pediatric isolates, with a minimum inhibitory concentration required to inhibit the growth of 90% of organisms (MIC<sub>90</sub>) of 1 mcg/mL. The MIC<sub>90</sub> 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  $\beta$ -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-

Continued on following page

## AzaSITE™

(azithromycin ophthalmic solution) 1%

### Sterile topical ophthalmic drops

#### BRIEF SUMMARY

Before prescribing, please consult the full prescribing information.

#### INDICATIONS AND USAGE

AzaSite is indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following microorganisms:

CDC coryneform group G\*  
*Haemophilus influenzae*  
*Staphylococcus aureus*  
*Streptococcus mitis* group  
*Streptococcus pneumoniae*

\*Efficacy for this organism was studied in fewer than 10 infections.

#### DOSAGE AND ADMINISTRATION

The recommended dosage regimen for the treatment of bacterial conjunctivitis is:  
Instill 1 drop in the affected eye(s) twice daily, eight to twelve hours apart for the first two days, and then instill 1 drop in the affected eye(s) once daily for the next five days.

#### CONTRAINDICATIONS

None

#### WARNINGS AND PRECAUTIONS

##### Topical Ophthalmic Use Only

NOT FOR INJECTION. AzaSite is indicated for topical ophthalmic use only and should not be administered systemically, injected subconjunctivally, or introduced directly into the anterior chamber of the eye.

##### Anaphylaxis and Hypersensitivity With Systemic Use of Azithromycin

In patients receiving systemically administered azithromycin, serious allergic reactions, including angioedema, anaphylaxis, and dermatologic reactions including Stevens Johnson Syndrome and toxic epidermal necrolysis have been reported rarely in patients on azithromycin therapy. Although rare, fatalities have been reported. While these reactions have not been observed with topical ophthalmic use of AzaSite, the potential for anaphylaxis or other hypersensitivity reactions should be considered, since patients with a known hypersensitivity to azithromycin or erythromycin were excluded from study.

##### Growth of Resistant Organisms With Prolonged Use

As with other anti-infectives, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit-lamp biomicroscopy, and where appropriate, fluorescein staining.

##### Avoidance of Contact Lenses

Patients should be advised not to wear contact lenses if they have signs or symptoms of bacterial conjunctivitis.

#### ADVERSE REACTIONS

The most frequently reported ocular adverse reaction in patients receiving AzaSite was eye irritation. This reaction occurred in approximately 1% to 2% of patients. Other adverse reactions associated with the use of AzaSite were reported in

less than 1% of patients and included burning, stinging and irritation upon instillation, contact dermatitis, corneal erosion, dry eye, dysgeusia, nasal congestion, ocular discharge, punctate keratitis, and sinusitis.

#### USE IN SPECIFIC POPULATIONS

##### Pregnancy

**Pregnancy Category B.** Reproduction studies have been performed in rats and mice at doses up to 200 mg/kg/d. The highest dose was associated with moderate maternal toxicity. These doses are estimated to be approximately 5000 times the maximum human ocular daily dose of 2 mg. In the animal studies, no evidence of harm to the fetus due to azithromycin was found. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, azithromycin should be used during pregnancy only if clearly needed.

##### Nursing Mothers

It is not known whether azithromycin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when azithromycin is administered to a nursing woman.

##### Pediatric Use

The safety and effectiveness of AzaSite solution in pediatric patients below 1 year of age have not been established. The efficacy of AzaSite in treating bacterial conjunctivitis in pediatric patients one year or older has been demonstrated in controlled clinical trials.

##### Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

#### STORAGE AND HANDLING

Store unopened bottle under refrigeration at 2°C to 8°C (36°F to 46°F). Once the bottle is opened, store at 2°C to 25°C (36°F to 77°F) for up to 14 days. Discard after the 14 days.

#### PATIENT COUNSELING INFORMATION

Patients should be advised to avoid contaminating the applicator tip by allowing it to touch the eye, fingers, or other sources. Patients should be directed to discontinue use and contact a physician if any signs of an allergic reaction occur.

Patients should be told that although it is common to feel better early in the course of the therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by AzaSite or other antibacterial drugs in the future.

Patients should be advised not to wear contact lenses if they have signs or symptoms of bacterial conjunctivitis. Patients are advised to thoroughly wash hands before using AzaSite.

#### Rx only

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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

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