

## ID CONSULT

## Embrace Short-Course Therapy for Strep



BY MICHAEL E. PICHICHERO, M.D.

I'd like to clear up some of the controversy regarding short-course antibiotic therapy for streptococcal tonsillopharyngitis versus longer-term therapy.

A meta-analysis published this summer from a group in Athens is the latest to call into

question the wisdom of using antibiotics for less than 10 days in the treatment of group A  $\beta$ -hemolytic streptococcal (GABHS) tonsillopharyngitis. They examined 11 randomized controlled trials (including one of mine) comparing short-course (7 days or less) versus long-course (at least 2 days longer than short course) treatment.

The investigators concluded that short-course therapy produced inferior bacteriologic cure rates, even though the results were only statistically significant among the studies that compared short vs. long courses of penicillin (Mayo Clin. Proc. 2008;83:880-9).

In fact, in the study from my group that they included, 5 days of twice-daily treatment with cefpodoxime was as efficacious in bacteriologic eradication and clinical response (defined as cure plus improvement) as 10 days of cefpodoxime therapy, and both regimens produced superior bacteriologic efficacy, compared with a 10-day regimen of penicillin V three times daily in the treatment of GABHS tonsillopharyngitis in children (Arch. Pediatr. Adolesc. Med. 1994;148:1053-60).

Indeed, the Food and Drug Administration has approved three oral antibiotics for 5-day strep throat treatment in both children and adults: cefdinir (Omnicef), cefpodoxime (Vantin), and azithromycin (Zithromax). With the FDA approval, use of these three agents is considered a standard of care and therefore medicolegally safe. Nonetheless, the American Academy of Pediatrics continues to recommend 10 days of penicillin as the treatment of choice, and many practitioners are reluctant to embrace the short-course concept.

When I advocate in favor of short-course therapy, I'm speaking only of those that have the FDA labeling to back it up. I wouldn't use first-generation cephalosporins such as cephalexin (Keflex) or cefadroxil (Duricef) in short course, for example, even though those generics are nearly as cheap as penicillin and might be more effective than 10 days of penicillin or as effective as 5 days of one of the approved agents (although they probably aren't). Without

the FDA indication for 5-day use, the medicolegal risk is too great.

But with cefdinir, cefpodoxime, and azithromycin, the literature clearly supports 5-day efficacy—defined by the FDA as 85% or better bacterial eradication at the end of treatment—in treating strep throat. Cefdinir and cefpodoxime have recently become available as generics and thus are less costly than they were before, although they are still more expensive than the first-generation cephalosporins.

In a meta-analysis Dr. Janet Casey and I conducted of 22 trials involving a total of 7,470 patients, short-course second- and third-generation cephalosporins produced a bacterial cure rate superior to 10 days of penicillin, with an odds ratio of 1.47 and cure rates of 90% vs. 70%. On the other hand, we found that 5 days of penicillin is inferior to 10 days of penicillin, just as the Mayo group did (Pediatr. Infect. Dis. J. 2005;24:909-17).

The Athens group lumped together studies using different types of comparisons in making their overall conclusion, which I don't think is a helpful way of reporting meta-analysis data. Moreover, as Dr. Casey and I pointed out in our article, in the real world few children complete 10 days of treatment anyway. When you factor that in, the 5-day option looks even better.

Another important issue affecting the results of these studies is whether strep carriers were excluded. Penicillin does not do a good job of eradicating carrier status, whereas cephalosporins do. In addition, a strep carrier who has symptoms caused by a virus would be mistakenly recorded as a clinical failure.

We separately analyzed the nine studies that excluded strep carriers in our 2005 meta-analysis, as well as in another meta-analysis that we published in 2004 in which we showed that the likelihood of bacteriologic and clinical failure of GABHS tonsillopharyngitis in children is significantly less with 10 days of treatment with an oral cephalosporin than with oral penicillin for 10 days (Pediatrics 2004;113:866-82). In both analyses, the cephalosporins still came out ahead.

Finally, cure rates for azithromycin should not be lumped into the same category as rates for the cephalosporins, because azithromycin has a half-life of about 96 hours, compared with 2-4 hours with the cephalosporins. Thus, when you give azithromycin for 5 days, it stays in the body as long as 10 days of another antibiotic.

The issue here is in the dosing, which often causes

confusion among practitioners. For strep throat, the 5-day dose of azithromycin for children is a single 10- to 12-mg/kg per day dose for each of the 5 days. This is different from the dosage given for otitis media or sinusitis, which is 10-12 mg/kg per day for just the first day, followed by 5 mg/kg per day for the next 4 days. It's easy to forget that, because we write far more prescriptions for ear and sinus infections.

Dr. Casey and I have shown that the otitis media dose of azithromycin is inferior for the treatment of strep throat (Clin. Infect. Dis. 2005;40:1748-55). If you accidentally prescribe the lower dose for strep throat and the child develops rheumatic fever, you may have a lawsuit on your hands.

In adolescents and adults with strep throat, this means that you need two of the standard "Z-PAKs" in order to give a high enough dose for eradication. The Z-PAKs label doesn't say this because our data showing inferiority weren't published until after the product was approved for treating strep throat. Thus, in this case you won't get sued if you just prescribe one pack, ... but there's a better chance the patient will be cured if you prescribe two.

I hope I've convinced you that 5-day treatment is a viable option for strep throat, because the guidelines from AAP and other organizations aren't likely to change any time soon. Guidelines should be based on data, but the current guideline writers prefer to harken back to penicillin studies done in the 1940s and 1950s, when rheumatic fever was still prevalent. However, a recommendation for 10 days of cephalosporin or amoxicillin for treating strep throat is currently under discussion. It stands to reason: The only way to prevent rheumatic fever is to eradicate strep, and these drugs do that better than penicillin!

Keep in mind too that at the time those old studies were done, penicillin cured 95% of strep bacteria. Today that number is just 65%, because of the bombardment of antimicrobials we've been using for the last several decades. The newer literature suggests it's time for change.

I have performed clinical trials, received honoraria, and/or served as a consultant for Abbott Laboratories and Pfizer Inc. ■

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## Study Finds Cleaning Fails to Disinfect Pediatric Office Toys

BY HEIDI SPLETE  
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WASHINGTON — Parents are right to suspect that pediatric waiting room toys are germ: Researchers found viral RNA on 20% of toys in a sick child waiting room, based on samples from three different days in different seasons.

"Mothers in waiting rooms across the country are very concerned that their children play with these toys and will pick up something, although this belief has never been confirmed," said Dr. Diane Pappas of the University of Virginia, Charlottesville.

"Our study was set up to look for respiratory viral RNA on toys in the waiting room," she said at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

The researchers took 20 swab samples from the sick and well waiting rooms in a

general pediatric office on three occasions: October 2006, January 2007, and March 2007. These time periods corresponded with a high community prevalence of rhinovirus, respiratory syncytial virus, and influenza viruses, respectively. "We tested a little differently depending on what was in the community at the time," Dr. Pappas said.

Overall, 12 (20%) of 60 samples were positive for viral RNA. Of these, 11 were picornavirus and 1 was influenza B. When the results were broken down by location, 3 (30%) of 10 new toys in the "grab bag" (in which packages were



After being wiped down with a disinfectant cloth, 4 of 15 toys in a sick waiting room still tested positive for viral RNA.

handled repeatedly by children in the process of selecting 1 toy), were positive, as were 6 (20%) of 30 toys in the sick child waiting room, and 2 (17%) of 12 toys in the well child waiting room. And one of

three (33%) samples from a pediatrician's stethoscope was positive.

The researchers also tested the effectiveness of the office cleaning protocol, which involved wiping the toys with a disinfectant cloth, and they collected 15 samples from the sick waiting room before and after cleaning.

Before cleaning, viral RNA was found on 6 (40%) of 15 toys in the office waiting room, including the yellow dump truck and the "very popular stegosaurus," said Dr. Pappas. After cleaning, 4 (27%) of the 15 toys were still positive for viral RNA.

The results suggest that pediatric office toys often are contaminated with viral RNA, even when they are cleaned. But the presence of viral RNA does not mean that the virus is infectious—whether viral remnants left on toys can cause infections in children who play with the toys remains unknown, Dr. Pappas said.

Dr. Pappas stated that she had no financial conflicts of interest to disclose. ■