

Expert: Antibiotics-for-AOM Study Is Year's Best

BY BRUCE JANCIN
Denver Bureau

ASPEN, COLO. — A Dutch meta-analysis addressing the long-controversial issue of antibiotics for acute otitis media tops one expert's list of the most important studies in the field of pediatric infectious diseases during the past year.

The Dutch study earned No. 1 status because it was rigorously well conducted and provided the last key piece of missing information needed to make a fully informed decision about whether to prescribe antibiotics for this common condition, Dr. Michael Radetsky explained at a conference on pediatric infectious diseases sponsored by Children's Hospital, Denver.

"This is it. No further information will ever come out in the future that will help you in your decision making," said Dr. Radetsky, a pediatric infectious diseases consultant at the University of New Mexico, Albuquerque.

Maroeska Rovers, Ph.D., and colleagues at Wilhelmina Children's Hospital, Utrecht, the Netherlands, scoured the world literature and found 10 randomized, placebo-controlled clinical trials that met their quality standards and addressed the issue of antibiotics for acute otitis media in children up to age 12 years. They contacted the principal investigators, got their raw data, and recalculated the results using advanced statistical methods.

Their conclusion? Antibiotics are in fact useful—but only in two specific settings: in children with acute otitis media and otorrhea, and in children less than age 2 years with bilateral disease (Lancet 2006; 368:1429-35).

The number of children fitting either such description who would need to be treated with antibiotics in order for one additional child to obtain benefit was three to four, which Dr. Radetsky deemed "very reasonable." However, the degree of clinical benefit in terms of reduction of pain and/or fever at 3-7 days was modest, he added at the conference, also sponsored by the University of Colorado.

Coupling the Dutch findings with those from earlier studies in the United Kingdom and United States that demonstrated the efficacy and practicality of deferred antibiotics, Dr. Radetsky said that the paradigm for office-based treatment should be to defer antibiotics, with a prescription handed to the parent to be filled only if the child doesn't improve in the next day or 2.

And while deferred antibiotics should be the default position, there is a role for immediate antibiotic therapy in the two specific settings identified by the Dutch pediatricians. In addition, Dr. Radetsky said, there is solid evidence from earlier studies that standard-dose amoxicillin is the drug of choice (Pediatrics 2006;117:1087-94) and that 5 days of treatment are as good as 10 (JAMA 1998;279:1736-42).

Sharing the podium with the Dutch acute otitis media study were the following runners-up:

► **Once- vs. twice-daily amoxicillin for streptococcal pharyngitis.** Dr. Herbert W. Clegg of Estover Pediatrics, Charlotte, N.C., and his coinvestigators there and at University of Minnesota, Minneapolis, randomized 652 children aged 3-18 years to 10 days of once- or twice-daily amoxicillin. The dosing was weight adjusted. Patients who weighed less than 40 kg got either 375 mg twice daily or 750 mg once daily. Those weighing more than 40 kg received 500 mg twice daily or 1 g once daily.

Microbiologic failure was defined as culture-proven infection with or without symptoms, and by the same M-type microorganism as at baseline. Rates were similar in the two study arms at 15%-20%. Likewise, clinical recurrence rates weren't significantly different at 8% and 10% in the two groups (Pediatr. Infect. Dis. J. 2006;25:761-7).

► **Antibiotics for acute purulent rhinitis.** Investigators at the University of Auckland (New Zealand) conducted a meta-analysis

of seven high-quality randomized, placebo-controlled, blinded clinical trials and concluded antibiotic therapy conferred a statistically significant—albeit modest—18% increased relative likelihood

of symptomatic benefit in terms of the amount of purulent discharge present at days 5-8. But the number needed to treat in order to benefit 1 patient, which was estimated at 7-15, overlapped the number needed to harm, which was 12-78 (BMJ 2006;333:279-81).

It's never a good situation when those two numbers overlap, Dr. Radetsky said. Moreover, there's no way to predict which patients might benefit from antibiotics.

"So don't do it," he urged. "But if you must do it, if you're going to cave in to pressure—if the mother is weeping, the father is hitting his head against the wall, the child can't get back into day care—you know how it is—then please only do it for 3-5 days."

► **Use of C-reactive protein and WBC to distinguish bacterial from viral infections.** Investigators at Turku (Finland) University Hospital reviewed their long-term experience and concluded that a single result using either test is of only limited clinical value in making a distinction between bacterial and viral infections.

Both the CRP and WBC values were generally substantially higher in confirmed bacterial than in viral infections. The trouble was that there were important exceptions to that broad trend that seriously compromised the lab tests' predictive value.

For example, the WBC in confirmed infections with *Staphylococcus aureus*—one of the two most common pathogens causing bacteremia—was only one-third to one-fourth the level seen in infections caused by *Streptococcus pneumoniae* or *Escherichia*

coli. In fact, the WBC in *S. aureus* infections was similar to levels associated with most of the key viral infections. The viral outlier was adenovirus, which produced WBCs and CRPs in the bacterial infection range (J. Pediatr. 2006;149:721-4).

"This is a very well-done study—and these are results that can be used in real life," Dr. Radetsky commented.

He added that the best role for CRP in his view is in following the progress of antibiotic treatment and deciding when to discontinue it.

"In my part of the world now, virtually all of the go home on oral antibiotics types of diseases [are] treated exactly the same way: You treat until the patient is better and the CRP is normal," the pediatrician continued.

► **Standard- vs. double-dose amoxicillin for nonsevere pneumonia in young children.** Investigators at the Pakistan Institute of Medical Sciences, Islamabad, randomized 876 children aged 2-59 months who had nonsevere pneumonia to 3 days of amoxicillin at either the standard dose of 45 mg/kg per day or to 90 mg/kg per day. Nonsevere pneumonia was defined using World Health Organization criteria: an elevated respiratory rate with no retractions.

On day 5, clinical resolution of the respiratory illness was observed in 98.4% of patients, with no difference between the two study arms. On follow-up on day 14, there was a 2% relapse rate, again with no difference between the two treatment groups (Arch. Dis. Child. 2007;92:291-7).

The Pakistani investigators treated for just 3 days with antibiotics on the basis of two earlier randomized trials conducted in more than 4,100 young children in India and Pakistan, which demonstrated 3 days of treatment was as good as 5.

► **The questionable value of chest x-rays in acute bronchiolitis.** Dr. Suzanne S. Schuh and colleagues at the Hospital for Sick Children, Toronto, prospectively studied 265 children aged 2-23 months who had a clinical diagnosis of acute bronchiolitis. All were given a chest x-ray. Comparison of the pre- and postradiography patient management plans revealed that the imaging study led to an alteration in treatment plan in a mere 2.6% of cases (J. Pediatr. 2007;150:429-33).

"Chest x-rays may not be necessary at all, because they rarely give rise to information [that] would require a change in your management," Dr. Radetsky observed.

► **Negative blood cultures: How reliable are they?** They are not very reliable, according to pediatricians at Royal Children's Hospital, Melbourne. They conducted a prospective study of all 1,358 blood culture bottles obtained during a 6-month period. The culture-positive rate was 5.2% in bottles deemed of adequate volume, significantly better than the 2.2% positive rate in bottles of insufficient volume.

The Australians defined adequate blood sample volume as at least 4 mL in children aged 36 months and up, at least 0.5 mL in those 1 month of age or younger, and at least 1 mL in all those in-between. Fifty-

four percent of bottles were judged to be of inadequate volume, a rate that declined to 36% following a staff education campaign (Pediatrics 2007;119:891-6).

► **Accuracy of rapid influenza tests.** A multicenter study involving 270 children under age 5 years hospitalized for acute respiratory symptoms or fever who underwent influenza culture and/or reverse transcriptase-polymerase chain reaction testing as well as one of four rapid influenza tests concluded that the rapid tests were moderately accurate, with an overall sensitivity of 65% and a specificity of 97%.

But the investigators from the New Vaccine Surveillance Network and the Centers for Disease Control and Prevention noted that the accuracy of the rapid tests varied considerably week by week over the course of flu season, as a function of the local background influenza prevalence at the time of testing.

They concluded that when the local prevalence was less than 10%, the false-positive test rate was so high that rapid tests were of little value (Pediatrics 2007;119:e6-11).

"Many people may argue that in areas of high prevalence, the rapid tests are not necessary, and in areas of low prevalence, they are not accurate," according to Dr. Radetsky.

► **Scalp ringworm disease patterns in preschoolers.** Susan M. Abdel-Rahman, Pharm.D., and colleagues at Children's Mercy Hospital, Kansas City, Mo., prospectively followed 446 children at a single urban preschool for 2 years. On a monthly basis, they performed scalp exams and gathered scalp samples for genotyping of *Trichophyton tonsurans* isolates. Their goal was to learn the natural course of preschool infection with *T. tonsurans*, by far the No. 1 cause of tinea capitis in the United States.

In older children and adults, it's known that the background *T. tonsurans* carriage rate is low, around 5%. Symptoms occur at the time the fungal infection is acquired. Isolation of symptomatic patients and treatment with antifungal agents are routine.

The picture in preschoolers described by Dr. Abdel-Rahman and colleagues was quite dissimilar. They documented a high background colonization rate, ranging from 14% to 44% on a monthly basis. Symptomatic disease occurred at any time, not in conjunction with acquisition of infection or particular strain types.

The investigators identified three carriage patterns. Most common was persistent carriage of a single exclusive strain. Another common pattern was carriage of a predominant strain month after month, with transient appearance of additional strains.

Least common was carriage of random strains. Symptomatic disease appeared to represent activation of a single persistent strain present on a child's scalp (Pediatrics 2006;118:2365-73).

"If you're in preschool, it's a different illness," Dr. Radetsky observed. "It is chronic background colonization with periodic symptomatic disease that gets better on its own and may not even require isolation." ■



'This is it. No further information will ever come out in the future that will help you' in decision making.

DR. RADETSKY