

Controversy in Otitis Media Management: Should We Follow the CDC Recommendations?

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In recent years, physicians have been moving toward using evidence-based, patient-oriented outcomes data to guide the management of a variety of medical conditions. Because of this evidence-based medicine approach, the treatment of acute otitis media has become controversial in the USA. Discussion in the medical literature has centered on inappropriate use of antibiotics in the treatment of acute otitis media and upper respiratory tract infections. Current antibiotic usage patterns are thought to contribute to the increasing patterns of antimicrobial resistance in common pathogens of the middle ear. In response, the Centers for Disease Control and Prevention instituted a nation-wide effort to address the problem of emerging infectious diseases and define patterns of antimicrobial resistance. More specifically, the Drug-Resistant *Streptococcus Pneumoniae* (DRSP) Therapeutic Working Group has recommended doubling the dosage of amoxicillin to 80 to 90 mg per kg per day in the empiric treatment of acute otitis media, along with recommending earlier use of broader spectrum antibiotics for treatment "failures" after three days. These recommendations are of concern because they are not based on any patient-oriented outcomes evidence.

A brief review of the evidence in the approach to otitis media would be helpful. Three essential questions must be answered: Does acute otitis media need to be treated with antibiotics? If so, which antibiotic should be used? How long should treatment be continued? Four systematic reviews analyze the literature on these topics. These reviews provided the following conclusions:

- More than 80 percent of cases of acute otitis media resolve spontaneously.
- The only short-term advantage of using antibiotics to treat otitis media is a modest decrease in the number of children with continued pain at two to seven days from diagnosis. Use of antibiotics has not affected the long-term outcomes.
- Narrow-spectrum antibiotics are still the recommended and effective treatment for acute otitis media and, in most children, a shortened course (five days) is adequate treatment with no negative impact on clinical outcomes.

These conclusions are based on patient-oriented evidence, but the CDC guidelines are based on laboratory data (disease-oriented evidence) and consensus opinion. Guidelines developed using a nonsystematic approach can be misleading and, in this case, imply that all children with garden-variety otitis media require increased dosages of antibiotics. Whether intended or not, the implication of the CDC guidelines are already widely communicated by editorials, newsletters and the pharmaceutical industry. Despite the large amount of in vitro data cited, there is little correlation between the Petri dish and how a child responds to antibiotic treatment.

What are the costs of recommended antibiotic regimes to the health care system and to patients and their families? Combinations of amoxicillin and amoxicillin-clavulanate will likely challenge patient adherence. Three daily doses of intramuscular ceftriaxone are expensive and are not likely to be an acceptable regimen for infants and children. The authors state that "... (in) the absence of any significant dose-related toxicity, it seems reasonable to use amoxicillin at 80 to 90 mg per kg per day..." However, antibiotic treatment of acute otitis media is associated with a doubling of the risk of rashes, vomiting and diarrhea. Will doubling the antibiotic dose further increase the risk of drug reaction? If so, this will translate into more physician office visits, more time off from work for parents, and more missed days of school for children. Are these acceptable risks in a condition that resolves spontaneously in 80 percent of the time without antibiotics.

The focus of the DRSP Therapeutic Working Group is to address increasing antibiotic resistance with increased doses of amoxicillin and the earlier use of broad-spectrum antibiotics. In the Netherlands and Iceland, however, the rate of antibiotic use for acute otitis media is one-third of that in the USA, and the rate of antibiotic resistance is much lower. No clinical evidence shows that increasing the dosage of amoxicillin or using broad-spectrum antibiotics will overcome antibiotic resistance - and it may make it worse.

These recommendations by the CDC and the DRSP Therapeutic Working Group may be useful in some patient subpopulations, but we believe that they should not be generalized to primary care and family practice populations without solid, clinical, patient-oriented outcomes data to support them. Rather than throwing more antibiotics at ear infections, we should be focusing efforts on reducing their indiscriminate use and identifying subsets of children who truly need antibiotics.

Acute Otitis Media Caused by Resistant Pneumococci

Scott F. Dowell

McConaghy and Smith are to be congratulated for their carefully reasoned review of the importance of reducing inappropriate and broad-spectrum antimicrobial treatment of acute otitis media, which concludes that "we should be focusing efforts on reducing indiscriminate use and identifying subsets of children who truly need antibiotics". We agree wholeheartedly with these sentiments and have published principles of judicious use of antimicrobial agents for otitis media, as they cite.

The task of the Drug-Resistant *Streptococcus pneumoniae* (DRSP) Therapeutic Working Group, however, was different. This group was charged with providing advice for the management of acute otitis media, given an identified subset of children for whom antibiotics were truly needed. In 1999, resistant pneumococci were of primary concern in this subgroup of children, and few clinical, patient-oriented outcome studies were available to guide clinicians in making the best treatment decisions for their patients. In fact, none of the 18 drugs currently labeled for treatment of acute otitis media has gained US Food and Drug Administration approval

for use against resistant pneumococci, primarily because the clinical evidence for efficacy against these pathogens is so hard to come by.

Nevertheless, ample evidence shows that resistant pneumococci are of real clinical concern and that adequate treatment is important for good clinical outcomes. Of the major pathogens causing acute otitis media, pneumococci are not only the most common but are the least likely to resolve in the absence of appropriate therapy. For example, 50 percent of *Haemophilus influenzae* infections will resolve even if the patient is treated with a placebo, but only 20 percent of *Streptococcus pneumoniae* infections will resolve. Clinical outcome is in fact well correlated with bacteriologic eradication of pathogens of the middle ear fluid, and pneumococcal resistance is directly correlated with clinical failure and bacteriologic persistence.

What, then, is the family physician to do after careful examination of the child and determination that all criteria for acute otitis media requiring antimicrobial therapy have unequivocally been met? If resistant pneumococci are not a concern, any of the 18 approved drugs might appropriately be selected, but this is no longer the case for most areas of the USA. For pneumococci that are not susceptible to treatment with penicillin, drugs such as cefaclor, loracarbef, cefixime and ceftibuten are inactive and more likely to fail, clinically and bacteriologically. Therefore, in the absence of controlled, patient-oriented outcome studies, the DRSP Therapeutic Working Group document was an attempt to provide some guidance for antimicrobial treatment in the era of resistant pneumococci.

Fortunately, amoxicillin remains an excellent first-line choice because it is effective, safe, inexpensive and convenient to administer. The higher dosage provides expanded coverage of resistant pneumococci, McConaghy and Smith ask if this will increase the risk of adverse drug reactions, and the answer is no, so far as we are aware. For those children with clinically documented treatment failures, the most likely pathogens are beta-lactamase-producing *H. influenzae* and drug-resistant *S. pneumoniae*. The alternative agents identified are all effective against drug-resistant *S. pneumoniae* and are beta-lactamase stable. It is true that each has shortcomings for some patients (eg, amoxicillin-clavulanate is expensive, cefuroxime axetil has a bitter taste and ceftriaxone must be injected). Most of the alternatives, however, are slightly yet measurably more likely to lead to treatment failure.

In summary, we are pleased to see that the DRSP Therapeutic Working Group document has generated such thought and criticism and heartily endorse the call for more patient-oriented outcomes studies and publications. We do not agree that "there is little correlation between the Petri dish and how a child responds to antibiotic treatment". Rather, we hope that the available bacteriologic and clinical efficacy data summarized in the document provide a rational interim approach for treating the subset of children with true acute otitis media.