

## Lessons From The International Primary Care Network

The report in this issue by Bartelds, et al. entitled "Acute Otitis Media in Adults: A Report from the International Primary Care Network" demonstrates, as did previous work by the same group,<sup>1</sup> that primary care research which transcends national boundaries is an important and feasible strategy for enhancing our understanding of common and important clinical issues. This research uniquely enlarges our perspective and helps us call into question our accepted ways of understanding and managing problems. In the same way that practice-based research will lead to new insights and methods compared with research based on the dominant referral center model, practice-based international research will lead to new insights compared with research confined to a single medical culture.

As do many interesting reports, findings from this study raise additional questions, and in these questions lies much of the study's value. It has been said that the first step to wisdom is knowing that we do not know. Not only is it important to find out what we do not know, but for many of us the intellectual excitement provided by charting the unknown is often greater than that provided by describing the known. The importance of discovering what we do not know should not be underestimated. Not too many years ago, we "knew" that tonsillectomies helped to prevent recurrent pharyngitis in young children. We "knew" that all urinary tract infections had to be treated with antibiotics for a full 10 days — and heaven help the noncompliant patient who did not finish all of his or her pills!

Turning now to the treatment implications of this study, we all "know" that antibiotics are useful in the treatment of acute otitis media caused by bacterial infections. This study, however, as does the previous one by Froom, et al.,<sup>1</sup> suggests that the basis for our knowledge is more shaky

than we had supposed; no treatment effect is demonstrated. Both studies leave open the hypothesis that antibiotic use does not necessarily improve outcome. The lack of a demonstrable relation between antibiotic usage and clinical response stands in contrast to the only two placebo-controlled studies of antibiotic use for treating acute otitis media.<sup>2,3</sup> Both show a modest short-term benefit. Neither of these studies involved adults. A recent meta-analysis report also supports the idea that antibiotic use in children is helpful, as the authors found a 23 percent difference in the percentage of ears free of effusion at the first posttreatment assessment.<sup>4</sup>

One additional study<sup>5</sup> illustrates (in children) that even when presumably inappropriate antibiotics are used, there is still a 74 percent favorable clinical response rate compared with an 89 percent clinical response rate when an appropriate antibiotic is used. This study suggests that demonstrating an effect greater than 15 percent in clinical outcome is going to be very difficult, even with appropriate antibiotic use. Further, this effect would diminish in any population where the rate of viral acute otitis media is relatively higher than that of bacterial acute otitis media.

What do we make of the apparent lack of effect of antibiotics? Is it real, or was the study power inadequate? Inadequate power might be the case, because a 15 percent difference in clinical response rate would require more than 1200 patients divided between the antibiotic and control groups to show an effect of antibiotics at the  $P = 0.05$  level. If the difference were 25 percent, then more than 500 patients divided between experimental and control groups would still be required. Was there a difference in prescribing patterns, with those patients who were from the outset more likely to have had persisting problems receiving the antibiotics? To what extent, in terms of clinical findings, were the 16 percent of patients who were lost to follow-up different from the other patients who were not lost to follow-up? How were the results affected by the fact that most

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Address reprint requests to John W. Beasley, MD, University of Wisconsin Medical School, Department of Family Medicine, 777 South Mills Street, Madison, WI 53715.

of the nonantibiotic management occurred in three of the nine participating countries?

The value of international studies is illustrated precisely by these unanswered questions. Despite this need for further study, in the United States our belief that antibiotics are useful in acute otitis media management is so certain that to get any proposal for a placebo-controlled trial of antibiotics in patients with acute otitis media approved by an institutional review board would be nearly impossible. Differences in treatment effect for acute otitis media (and, of course, for many other conditions) will probably have to be investigated across national boundaries for two reasons: the first is that significant deviation from a standard treatment ("known" to be efficacious) for research purposes might not be possible within this country. The second reason is that we might not even think of certain diagnostic or management options, used in other countries, that are worthy of controlled examination. The catchment of other diagnostic and management options would be further enhanced by involving non-Western countries in any further expansion of the International Primary Care Network.

As illustrated in the article by Bartelds, et al., the methodological problems involved in conducting transnational studies are great and indeed suggest studies of their own. Does the complaint of ear pain mean the same thing in Switzerland as it does in the Netherlands? Does a red tympanic membrane mean the same thing in Belgium as it does in the United States or Israel? What in the various countries determines whether patients return for follow-up?

We must not be put off by these problems because of the important heuristic value of these studies. They have great potential for expanding the range of potentially researchable questions and developing additional useful methodologies. As we develop better skills for controlling variables (e.g., entry criteria), for defining management and outcome, and for improving follow-up, we will begin to answer — as well as ask — questions, and the answers will greatly affect the way we deal with common and important problems. We will be seeing more studies from both domestic and international networks addressing such common problems as back pain, asthma, bronchitis, and coronary artery disease. As we

develop more sophisticated methods for primary care research and the necessary funding sources and expertise that allow us to conduct controlled trials and observational studies, we will see increasingly valuable clinical information emerging from these international efforts.

John W. Beasley, MD  
University of Wisconsin Medical School  
Madison, WI

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## Answers In Search Of Questions

There is a sense in which practicing comprehensive care resembles being a contestant on the television game show, "Jeopardy." Winning requires asking correct questions in response to given answers. Stakes and risks rise the longer the game is played until final jeopardy, when contestants must make a clever wager on their ability to state the appropriate question after a topic is announced, but before the answer has been given.

The game show analogy loses simplicity and precision in real-life family practice, but our capacity and willingness to ask revealing ques-

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