President’s Page: Antimicrobial Prophylaxis to Prevent Infective Endocarditis: Why Did the Recommendations Change?

It has been more than 50 years since the American Heart Association (AHA) first made recommendations for the use of antimicrobial agents to prevent infective endocarditis (IE). The first AHA document on this subject was published in 1955 and has been followed by 9 revisions outlining which patients, which procedures, and what antibiotics should be used to prevent IE. Since that time, there have been extensive efforts by physicians, dentists, and patients to ensure that everyone at risk for developing endocarditis would follow these guidelines and receive the proper regimen of antibiotics prior to selected dental or surgical procedures.

However, in 2007 the AHA issued guidance for IE prophylaxis that greatly simplified the recommendations and proposed substantive changes—changes that would affect hundreds of thousands of patients in the U.S. alone (1). Since then, we, and most likely all of you, have been barraged by our surgical and dental colleagues and patients with inquiries—“Are you sure this is the right thing to do? Would you mind putting the recommendation in writing before I proceed?”

What Evidence for Change?

Why were these significant changes introduced, and why wasn’t there a heads up that such a dramatic change was coming? It helps to remember that the prior rationale for using antimicrobial prophylaxis was that antibiotics would control bacteremia at the time of the procedure and thus prevent IE. However, this treatment rationale was based primarily on expert opinion and support from a few case-controlled and descriptive studies. There has never been a controlled, randomized study that evaluated this strategy.

In contrast, some have noted the lack of consistent association between having an interventional procedure and the development of IE, and they have questioned the clinical effectiveness of antibiotic prophylaxis. Some have asked whether the risk of giving antibiotics outweighed the small, perhaps nonexistent benefit. It has even been suggested that the risk of a serious allergic reaction to amoxicillin is greater than the risk of contracting IE.

A report from the Cochrane Collaboration in 2004 concluded, “There is no evidence about whether penicillin prophylaxis is effective or ineffective against IE in people at risk who are about to undergo an invasive dental procedure. There is lack of evidence to support published guidelines in this area, and it is not clear whether the potential harm and costs of penicillin administration outweigh any beneficial effect” (2).

Evidence is now moving from “procedure-related bacteremia” toward “cumulative bacteremia” as the more likely cause of most cases of IE. For instance, daily activities such as tooth brushing are estimated to produce bacteremia 6 million times higher than a single tooth extraction. Thus, continued episodic bacteremia due to poor dentition may pose a much greater risk for the development of IE than a single dental procedure.
A final impetus for change was that the guidelines themselves had become more complicated with each revision, with ambiguous recommendations for which specific patient and which particular procedure required the prophylaxis.

Recommendations Shift Emphasis

On the basis of these controversies, the AHA Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee convened a group of national and international experts in the field, including cardiologists, infectious disease specialists, pediatricians, and dentists. This writing group analyzed relevant literature regarding procedural-related bacteremia and IE, in vitro susceptibility data of the organisms causing IE, and results of prophylactic studies and animal models of experimental IE, as well as any retrospective or prospective studies in the prevention of IE. After several years of discussion and debate within the writing group combined with input from experts from other learned societies, the new recommendations were released. The recommendations were clear, simple, and to the point:

- **Infective endocarditis prophylaxis should be given only to a high-risk subgroup of patients prior to dental procedures that involve manipulation in gingival tissue or periapical region of the teeth or perforation of the oral mucosa.**
- **High-risk patients include only those with a: 1) prosthetic cardiac valve; 2) previous infective endocarditis; 3) complex congenital heart disease; and 4) valvulopathy following cardiac transplantation.**
- **Infective endocarditis prophylaxis is not recommended prior to gastrointestinal or genitourinary procedures.**

These recommendations represented a major departure from the traditional practice of IE prophylaxis. The committee wanted to shift emphasis away from a focus on antibiotic prophylaxis prior to a single procedure to recommendations that place a much greater emphasis on improved access to dental care and oral health in patients with underlying cardiac conditions. “High-risk” patients were defined not on the basis of an increased risk for IE, but rather on an increased risk of an adverse outcome should they develop endocarditis.

The new guideline, which generated considerable controversy among physicians, dentists, and patients, represented a paradigm shift from traditional dogma and was based on expert consensus rather than on any compelling new data or evidence. In fact, one might argue that it was really a consensus document—and not an evidence-based guideline.

Health care providers have been reluctant to stop a practice that they had been taught was necessary to prevent a devastating event and that they have ingrained in their patients who have underlying structural heart disease. Even the experts in this practice area have been unable to reach agreement or comfort with these new recommendations. Other societies, such as the British Society for Antimicrobial Chemotherapy, have also recommended simplified guidelines, although not at the magnitude of change suggested by the AHA (3).

The American College of Cardiology (ACC)/AHA Task Force on Practice Guidelines is providing an update on IE prophylaxis for the 2006 ACC/AHA Guidelines for the Management of Patients with Valvular Heart Disease (VHD) (4), and we should probably anticipate that the soon-to-be-published Adult Congenital Heart Disease Guidelines will also include some sort of update. The ACC/AHA VHD Guidelines, as well as several others, have always referenced the AHA IE Prophylaxis Guide- line. The writing committees for the VHD Focused Update and Guidelines, which comprise physicians selected for their expertise in VHD, were asked to comment on the new IE recommendations released by the AHA. Based on their review of the initial 2007 AHA document, the AHA published an errata document in April 2008 that changed some of the language in order to clarify the recommendations. The ACC/AHA Focused Update, which will be published in JACC and Circulation soon, addresses the recommendations as they apply to the management of VHD.

Controversy or Different Expectations?

Among many physicians and experts, controversy continues over these changes. Some firmly believe that the new recommendations should clearly be followed without exception. However, others argue that for antibiotic prophylaxis “the lack of evidence of benefit is not necessarily the same as lack of benefit” and that insufficient new evidence exists to justify such a radical change in policy. It has been argued that there is an illogicality of the fudge in continuing to recommend prophylaxis for very high risk patients, as endocarditis is always dangerous. If antibiotic prophylaxis is ineffective, why select only a high-risk group for prophylaxis?

Despite the controversy and angst that these new recommendations have generated, there have been some beneficial outcomes. The document has raised awareness that meticulous oral hygiene and routine preventive care by dentists are of utmost importance in preventing IE in patients at increased risk. Other sources of contin-ued bacteremia, such as nail biting, intrauterine devices, acne, and body piercing, are now being recognized and addressed.

The situation we face revolves in part around our expectations about what represents a guideline. We have become less comfortable in endorsing consensus as a guideline and have come to expect evidence-based data to guide our clinical decision-making. Thus, there is no correct recommendation, and a state of equipoise currently exists around this question, which begs for a properly designed
clinical trial. Perhaps, the AHA and our own committees should have eliminated the “guideline,” simply explained the issues, and recommended that you and your patients make the final decision regarding treatment while we await real evidence.

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REFERENCES


