

## Perspectives on the American College of Cardiology/American Heart Association Guidelines for the Prevention of Infective Endocarditis

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In 2007, the American Heart Association published a guideline statement dramatically changing its previous position on the use of antibiotic prophylaxis in patients at risk of infective endocarditis (IE). This year, these views were incorporated in an update of the 2006 American College of Cardiology/American Heart Association Guidelines for the Management of Patients With Valvular Heart Disease. The new recommendations represent a dramatic shift with regard to which patients should receive antibiotic prophylaxis for prevention of IE and for what procedures. The shift in recommendations is striking in that the recommendations are based not on new data, but on no data. (There are no large, prospective, randomized double-blind trials testing the efficacy of IE prophylaxis.) However, available data suggest that there may be no real risk associated with IE prophylaxis. Even if few cases of IE are successfully prevented using antibiotic prophylaxis, those few cases may represent a favorable risk-benefit ratio. On an individual basis, patients with organic heart valve disease who are trying to delay or avoid surgical intervention have something very real to risk if they develop IE, and a very real benefit if they avoid it. Pending data from prospective randomized trials, a strategy of individual decision-making by informed patients may be best. (J Am Coll Cardiol 2009;53:1852-4) © 2009 by the American College of Cardiology Foundation

In 2007, the American Heart Association (AHA) published a guideline statement (1) dramatically changing its previous position on the use of antibiotic prophylaxis in patients at risk of infective endocarditis (IE). This year, these views were incorporated in an update (2) of the 2006 American College of Cardiology (ACC)/AHA Guidelines for the Management of Patients With Valvular Heart Disease (3). As these 2 revisions have pointed out, the new recommendations represent a dramatic shift with regard to which patients should receive antibiotic prophylaxis for prevention of IE and for what procedures. The AHA statement and subsequent ACC/AHA guideline update were not published in isolation; multiple other cardiac and noncardiac organizations have in the past several years published recommendations (4-9) that dramatically limit the scope of patients for whom antibiotic prophylaxis is recommended, as well as the types of procedures for which designated patients should receive prophylaxis. What is striking about these new recommendations is that the dramatic shift is based not on new data, but on no data.

**Historical perspective.** Since 1955, the AHA has recommended antibiotic prophylaxis for the prevention of IE

among patients at increased risk of disease (10). In 1972, existing recommendations for prophylaxis during oral procedures were expanded (11) to include gastrointestinal (GI) tract and genitourinary (GU) tract procedures. Subsequent recommendations published in 1977 (12), 1984 (13), 1990 (14), and 1997 (15) included more specific content regarding patient risk and procedures that should be covered. Notably, the original recommendations and all subsequent revisions were based not on data from randomized trials but on consensus opinion weighing risks and benefit. In publishing past guidelines, note was made that guidelines for prophylaxis against IE could pose a medical-legal risk (14) and that many cases of IE can be attributed to randomly occurring bacteremia rather than to an invasive procedure (15).

**Current recommendations.** The current guidelines (1,2) shift the recommendation for antibiotic prophylaxis from all patients with an increased lifetime risk of developing IE to only patients with an underlying cardiac condition that increases the risk of an adverse outcome from IE (and therefore would derive the greatest benefit from preventing IE). Antibiotic prophylaxis for dental procedures is now recommended only in patients with a prosthetic heart valve; previous IE; cyanotic congenital heart disease that is unrepaired, within 6 months of a repair procedure, or repaired but with residual defect at or near the location of prosthetic material; or in cardiac transplant recipients with cardiac

valvulopathy. Antibiotic prophylaxis is not recommended in conjunction with GI tract or GU tract procedures.

Citing a rationale for the change in recommendations, the current guidelines (1,2) note the absence of data supporting the efficacy of antibiotic prophylaxis in the prevention of IE. A limited potential benefit of prophylaxis is cited in that IE is felt most likely to result from frequent exposure to random bacteremia associated with daily activities than from bacteremia caused by a dental, GI tract, or GU tract procedure, suggesting that prophylaxis may prevent only a small number of cases of IE. A potential risk of antibiotic prophylaxis is cited in the AHA document (1) as a risk of anaphylaxis and in the ACC/AHA guideline update (2) as a more general risk of antibiotic-associated adverse effects. Of note, however, the AHA guideline statement (1) discloses that during the 50 years that the AHA had recommended penicillin as the preferred prophylaxis to prevent IE, no case of fatal anaphylaxis was reported for a patient receiving penicillin administered for IE prophylaxis.

The AHA statement (1) explicitly notes that potential consequences of the revised recommendations include reduced malpractice claims related to IE prophylaxis and stimulation of prospective research on IE prophylaxis. The latter outcome is echoed in the ACC/AHA guideline update (2), noting that fewer patients receiving IE prophylaxis will stimulate prospective studies on IE prevention.

**Absence of evidence-based medicine.** Practitioners in cardiology have become accustomed to medical decisions based largely on evidence-based medicine. In diseases such as coronary artery disease and heart failure, the presence of large numbers of patients with a potentially life-threatening medical condition, and medical interventions that lend themselves to randomization, allow the performance of prospective randomized clinical trials using “hard” end points such as mortality, with results that may dramatically affect future patient management. In the past few decades, a variety of large, prospective, randomized clinical trials with a creative array of acronyms have redefined (among other things) intervention for acute coronary syndromes, medical therapy for coronary artery disease and heart failure, and medical and device therapy for a variety of lethal and nonlethal cardiac arrhythmias.

What should we do in the absence of evidence-based medicine? Some aspects of cardiology do not readily lend themselves to randomized controlled trials owing to limited patient numbers, therapies that are not easy to randomize (e.g., mitral valve repair), or outcomes that are meaningfully measured only years and even decades after intervention. These limitations affect most decisions for patients with heart valve disease, and the published guidelines for the management of such patients rely heavily on results of small nonrandomized trials and on expert opinion. Notably, most recommendations in the 2006 ACC/AHA guidelines for the management of patients with valvular heart disease are made with Level of Evidence B or C (3), reflecting the absence of large, prospective randomized clinical trials.

## Weighing risks and benefit.

The current conundrum in IE prophylaxis recommendations is not unique in medicine, but it is unusual in the field of cardiology. Data do not exist from large, multicenter, prospective, randomized, double-blinded trials. In this setting, it seems appropriate to weigh as best we know the risks and benefit of therapy and try to make an informed (or at least a best-guess) decision.

Are there really risks associated with IE prophylaxis? If the experience of the individual practitioner is that serious adverse reactions to antibiotic prophylaxis are extremely rare, the experience of the AHA is that they may be nonexistent (1). If anaphylaxis is not a real risk, neither is antibiotic resistance; resistant organisms are not created with rare and isolated exposure to an antibiotic. The financial cost of 2 g of oral amoxicillin twice yearly is negligible. Finally, although the medical-legal “cost” of guideline recommendations is admittedly impossible to calculate, there is no precedent in medicine to write medical practice guidelines with the specific goal of avoiding malpractice claims when guidelines are not followed.

What about benefit? Even if it is only the rare case of IE that is successfully prevented with antibiotic prophylaxis, this is a very real benefit to that patient. On an individual basis, patients with organic heart valve disease who are trying to delay or avoid surgical intervention have something very real to risk if they develop IE (and a very real benefit if they avoid it), even if they are not in the cited groups with the highest risk of an adverse outcome of IE. If the risk of prophylaxis is essentially nonexistent, even a very small potential benefit favors the use of IE prophylaxis in patients at risk.

**An alternative strategy.** The AHA and ACC/AHA statements (1,2) do a good job describing the rationale for change in IE prophylaxis guideline recommendations. But these are only guidelines, and all practitioners in all circumstances need not necessarily follow them. The notion of individually weighing risks and benefit is not irrational, especially in a setting where there are no data that refute a time-honored standard of care (and, admittedly, no data to support them).

I have personally adopted an approach with my patients of informed decision-making. For patients with organic heart valve disease (including both those for whom IE prophylaxis had been an established norm and those with a new diagnosis and so not accustomed to IE prophylaxis), I discuss the history of IE prophylaxis, the previous guideline recommendations, the new recommendations, the rationale for change, and the absence of data to either support or refute their use. Informed patients seem capable of making intelligent decisions about their own care. (It is perhaps paternalistic to think, especially in a scenario in which

## Abbreviations and Acronyms

<b>ACC</b>	= American College of Cardiology
<b>AHA</b>	= American Heart Association
<b>GI</b>	= gastrointestinal
<b>GU</b>	= genitourinary
<b>IE</b>	= infective endocarditis

controlled studies have not been performed, that patients should not be involved in a decision about their medical care.) After discussing the basis of the new recommendations, and when given a choice, most of my patients remain comfortable continuing to use antibiotic prophylaxis. If and when prospective, randomized trials are performed, rethinking individual decisions will again make sense.

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**Key Words:** infective endocarditis ■ prophylaxis ■ antibiotics ■ guidelines ■ prevention.