Antibiotic Prophylaxis for Dental Procedures: Are We Drilling in the Wrong Direction?

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The possibility that bacteremia from the mouth could cause infective endocarditis (IE) was first suggested over a hundred years ago, and it was later reinforced by others who targeted the viridans group streptococcus (VGS) from poor oral hygiene and dental extractions. These observations, along with the advent of antibiotics, eventually led to the first guidelines from the American Heart Association (AHA) in 1955. Antibiotic prophylaxis (AP) became the primary focus for prevention of IE, and a standard of care for countries around the world. Controversy concerning efficacy and safety issues has existed for over 30 years and there has been a progressive reduction in the patient populations and the procedures suggested for AP since that time. Of concern, and in spite of a decreasing emphasis on AP for cardiac patients, upwards of 25 non-cardiac patient populations are recommended for AP by some clinicians out of concern for systemic infections that might originate from dental procedures (e.g., prosthetic joints).

Significant differences in recommendations from experts in the U.S., United Kingdom, and other countries over the years highlight the lack of convincing data to either support or reject this practice. The National Institute for Health and Clinical Excellence (NICE) in the U.K. issued new recommendations in 2006, which took the bold step of eliminating AP all together. Current (2007) AHA guidelines narrow the focus to only four cardiac groups at “higher” risk for a “bad outcome” from IE, but who represent approximately 10% of all people at risk for IE. The AHA-defined “moderate” risk groups represent approximately 90% of people at risk for IE, all of whom were recommended for AP prior to 2007. There are, therefore, no preventive guidelines for the millions of people in the U.S. at risk for contracting IE but who are not felt to benefit from AP.

Although there is understandable concern on the part of some cardiologists and some patients about eliminating AP, a recent retrospective study by Thornhill et al suggests that AP
has no significant impact on the incidence of, or death from IE. The authors point out that these findings may not apply to patients in the higher risk groups since approximately 20% of physicians in the U.K. may continue to use AP in spite of NICE guidelines that mandate a cessation for this practice, unless the patient requests it. This group did find a modest increase in the incidence of IE over their 10 year period due to both streptococci and staphylococci.

Support for the role of oral bacteria as a significant cause of IE comes largely from two sources. The best evidence for this association is the frequency with which specifically oral bacterial species are cultured from the blood of patients with community-associated (CA-IE). The literature suggests that 20% to 65% of cases of IE worldwide result from bacteria that can be found in, or are exclusive to the mouth. This wide range of cases of IE attributed to oral bacteria stems, in part, from the use of standard biochemical rather than molecular methods of bacterial identification. For example, reports of VGS are not specific enough to implicate the mouth as the source. Other supporting documentation comes from over 75 years of bacteremia studies of dental procedures and other manipulations of gingival tissues. These studies suggest a wide range of incidence of bacteremia from species known to cause IE, and one must conclude that oral bacteremia is likely to occur with the vast majority of dental office visits. These studies employ surrogate measures of risk for IE (i.e., incidence, duration, nature, and magnitude of bacteremia) but they have driven the focus on AP for dental procedures since the 1950’s.

Retrospective case-control studies provide a closer look at this relationship. Strom et al contacted patients who had been hospitalized (cases) for IE at one of 54 hospitals in the Philadelphia area and compared them with matched community residents (controls). His group found that recent dental treatment was no more frequent in cases than in controls, and they concluded that dental treatment did not seem to be a risk factor for CA-IE. The study by
DeSimone et al in this issue of Circulation moves us one step closer to a better understanding of this question of efficacy for AP by conducting the first population-based study in the U.S. to determine the impact of the 2007 AHA guidelines. They focused on cases of IE from presumed oral streptococci over a 12 year period, and found no increase in VGS IE in the two plus years since 2007. Of interest, two of the three patients who developed IE from VGS after 2007 had not been to the dentist in the previous six months, and the third patient had AP prior to a recent dental office procedure.

Case-control, population-based, and other epidemiologic investigations often have methodological weaknesses that soften their impact, for example: i) small sample size and power; ii) subject recall bias; iii) demographics that may not be representative of the general population; iv) incubation time frames that are too long for IE; v) the imperfect nature of hospital and national data bases on admission and discharge coding; and, ICD-9 coding of bacterial species. Nevertheless, results from well-designed studies are important because they provide additional evidence that the well intentioned focus on AP may be misdirected.

The AHA, Institute of Medicine, NICE and other professional groups have called for studies that would resolve this longstanding question concerning the efficacy of AP, and clarify the role of poor oral hygiene and resulting periodontal disease in the pathogenesis of IE. Although there have been calls for a prospective, randomized, double blind study of AP in people at risk for CA-IE, significant obstacles exist, for example: i) there are ethical and legal concerns about randomizing people in the AHA higher risk group to a placebo; ii) such a trial would only address the 10% of people currently recommended for AP in the U.S.; and, iii) given the rarity of IE, it has been estimated that upwards of 30,000 people at risk would be needed to detect a clinically important AP treatment effect, and the cost of this trial would be prohibitive.
Transient bacteremia frequently occurs as a result of dental plaque accumulation, evolving to a dense mat of oral bacteria around the teeth which cross the inflamed periodontal pocket tissues to the circulation. Clearly, this must be the main source and portal of entry for the oral bacterial species that cause upwards of 25% of cases of CA-IE. Current science strongly suggests that poor oral hygiene and periodontal disease are far greater risk factors for the development of oral bacteria-related IE than invasive dental procedures. The largest study to date compared tooth extraction, a highly invasive dental procedure, with tooth brushing as a common, naturally-occurring source of bacteremia.\textsuperscript{14, 15} This group found that the incidence of bacteremia from tooth brushing (32%) was high enough to strongly suggest that bacteremia from various activities of daily living (chewing food as well) may occur hundreds of times more often than bacteremia from dental office procedures. Indeed, it has been suggested that some individuals may generate bacteremia for 90 hours each month from such “physiologic” causes,\textsuperscript{16} by comparison with dental office procedure-generated bacteremia of one to two times per year on average. This study provides unique documentation of a strong association between three oral hygiene and gingival disease parameters and the incidence of bacteremia with IE-related species.\textsuperscript{17} These associations strengthened with higher levels of dental plaque and calculus and gingival disease.

DeSimone and colleagues have provided further data to reinforce the trend towards a greatly decreased number of cardiac patients recommended for AP, as well as support for a more definitive study to determine the extent to which oral hygiene, periodontal disease and oral bacteria are associated with CA-IE. These data would improve our understanding of risk factors, and re-focus efforts on prevention of IE to improving oral hygiene and preventing periodontal disease. This information has the potential to reduce the overall incidence of CA-IE, it would be
immediately transferable to everyday clinical practice, and it would inform future AHA and other international guidelines on preventive strategies for IE.

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**References:**


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