



Editorial

What to Think About Antibiotic Prophylaxis and Infective Endocarditis

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See article by Mackie et al., pages 942–948 of this issue.

The practice of using antibiotic prophylaxis before dental procedures dates back to the early days of antibiotics, when Northrop and Crowley—2 oral surgeons—were interested in the relationship of dental procedures to infective endocarditis (IE).¹ They found that only a minority of patients with IE had a preceding dental procedure. However, they also demonstrated that antibiotics preceding dental procedures could reduce the incidence of bacteremia. In what now can only be considered a leap of faith, they concluded that there was a “responsibility” to administer antibiotics before dental procedures in individuals at risk for IE. The rest, as the saying goes, was history. Multiple authoritative guidelines starting in the 1940s went on to consistently recommend antibiotic prophylaxis for the prevention of IE. The only problem: the evidence supporting these recommendations was no stronger than that found by Northrop and Crowley, and whenever anyone looked for evidence to support the practice, they came up disappointed.² Dental (and other bacteremia-inducing) procedures just do not seem to be strongly correlated with IE.

In 2001, after summarizing the evidence that failed to support antibiotic prophylaxis for IE before dental procedures, we called on organizations and guideline authors to reconsider their positions in a *Heart* editorial that was subtitled “Back to the Future.”³ Fast forward to 2015 (8 years after the American Heart Association tempered their recommendations) and we are in “the future.” What has this future wrought?

In 2007, after much delay, the American Heart Association (AHA) dramatically tempered their recommendations for antibiotic prophylaxis—recognizing the paucity of supporting evidence—recommending them only for dental procedures and only for patients at the highest risk of the development of IE.⁴ The British National Institute for Health and Care

Excellence (NICE) took an even more aggressive approach to the available evidence and stopped recommending antibiotic prophylaxis for IE altogether, heralding the dawn of the postprophylaxis era.⁵ Other international guidelines have taken positions more closely resembling those of the AHA.⁶ Canadian physicians and dentists have adopted the AHA guidelines.

Remarkably, attention to prevent this important (albeit rare) condition has not been adorned with the highest-quality evidence. There has yet to be a randomized trial comparing prophylaxis vs no prophylaxis in even the highest-risk patients, so the true benefits and risks associated with IE prophylaxis are unknown.

Population-based studies to understand the effects of scaled-back IE prevention in the United Kingdom have yielded contradictory conclusions. Thornhill et al.⁷ performed a before and after population-based study to examine the effects of the NICE guidelines on antibiotic prescribing and IE incidence. They found a 79% reduction in IE prophylaxis prescribing and no evidence of an increase in IE cases or deaths. However, a more recent study took a broader and long-term look at the incidence of IE in the United Kingdom after the NICE guidelines and found that they were associated with an increased risk of IE that was temporally associated with the introduction of the NICE guidelines.⁸ The results of this study were almost certainly confounded by population-based changes in the prevalence of IE risk factors (especially the presence of implantable cardiac electronic devices). Indeed, the increased incidence of IE that they observed (0.45 cases per 10 million people per month; 0.28 cases per 10 million per month if outlier data is removed) cannot be explained by changing practices in dental prophylaxis: a minority of cases of IE is caused by oral organisms. Even if antibiotic prophylaxis were 100% efficacious, the rise in cases is beyond what we would expect epidemiologically. Nevertheless, publication of this study pressured NICE to reconsider their original recommendations, which have subsequently remain unchanged.

Looking at IE epidemiology in France, where approaches to IE prophylaxis closely mirrored efforts in the United States, Duval et al.⁹ found that there has been no appreciable rise in

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the incidence of streptococcal IE but rather an increase in staphylococcal IE.⁹

Similar efforts to examine the effects of the AHA 2007 IE prophylaxis guidelines on the incidence of IE in the United States have yielded (what might appear to be) conflicting results. Using the Nationwide Inpatient Sample database, Pant et al.¹⁰ showed that IE incidence rose steadily from 2000-2011, with an increased incidence of streptococcal IE (but not of staphylococcal IE) after publication of the AHA guidelines.¹⁰ However, hospitalization rates for IE were unchanged over that period, and roughly one-third of IE cases in 2000 were not associated with an identified organism (compared with only 10% of those cases in 2011), suggesting that at least some of the increase in incidence could be explained by ascertainment bias. DeSimone et al.¹¹ made similar arguments. In a careful (and perhaps most insightful) exploration of IE incidence related to changes in antibiotic prophylaxis, DeSimone et al. explored streptococcal IE in particular and found no increased incidence in relation to the AHA guidelines.

It is on this background that Mackie et al.¹² present their nicely executed study of IE incidence in relation to changes in AHA recommendations. Using the Canadian Institute for Health Information (CIHI) Discharge Abstract Database over an 11-year period beginning April 2002, they found a progressive increase in IE incidence that preceded the 2007 guidelines, with no significant change in the incidence rate after publication of the AHA guidelines. Although IE incidence increased, streptococcal IE incidence decreased.

This study faces challenges similar to previous efforts to understand IE epidemiology. It relies solely on diagnostic coding (and therefore physician documentation), and there is no published evidence informing us of the reliability of CIHI data for IE. Because IE is primarily a clinical diagnosis, there are risks of both over- and underdiagnosis. Additionally, these data provide hospital-based information, and thus there is no concomitant information on outpatient IE prophylaxis, and at-risk conditions (such as intravenous drug use, prosthetic valves, and implantable cardiac electronic devices) might not be reliably reported. In particular, understanding the population-based temporal epidemiology of pacemakers and defibrillators (identified as increasingly prevalent risk factors) would put the results in greater context. Despite these caveats, this study does tell us that increasing rates of IE were not associated with the AHA guidelines on IE prophylaxis.

Were we and the guideline authors right? We think so. There remains no strong association with IE and dental procedures and no reliable evidence that antibiotic prophylaxis prevents IE. IE incidence might change over time, but it is likely related to a variety of factors, not the least of which includes a population with increased risk factors (such as age, the presence of implantable cardiac electronic devices, prosthetic heart valves, and surgically reconstructed congenital heart disease). When an increased incidence of IE is observed, it likely results from the increasing prevalence of at-risk patients becoming infected with primarily staphylococci. Oral organisms continue to be an important cause of IE, but reducing or eliminating antibiotic prophylaxis before dental

procedures has had no appreciable effect on this incidence. In the current era of “antimicrobial stewardship,” cardiologists, dentists, and other health care practitioners should resist the urge to prescribe antibiotics with no substantive evidence of benefit.

Disclosures

The authors have no conflicts of interest to disclose.

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