

The American Heart Association 2007 endocarditis prophylaxis guidelines: A compromise between science and common sense

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The new American Heart Association (AHA) guidelines on antimicrobial prophylaxis for endocarditis published in 2007 represent a major step in the evolution of these guidelines (1). Antimicrobial prophylaxis is recommended for use in fewer patients and for a smaller number of invasive procedures. Because antimicrobial prophylaxis for endocarditis has been a standard and routine part of the management of patients with heart disease, and because its use involves several different specialties, such as cardiology, infectious disease and dentistry, it is noteworthy that these guidelines were not received with the same rancour that greeted similar guidelines from the British Society for Antimicrobial Chemotherapy (BSAC), which were published one year earlier (2). "Defying explanation" was the headline of the letter by the British Congenital Cardiac Association and the British Cardiovascular Society expressing concerns about the BSAC guidelines (3). We believe that the new AHA guidelines were more readily accepted because they have previously been circulated to and endorsed by scientific bodies, including the American Dental Association, the Infectious Diseases Society of America and the Pediatric Infectious Diseases Society, and because there is an increasing awareness that medical practice needs to be evidence-based. Nonetheless, there are still concerns regarding these new guidelines from physicians and patients, despite the fact that the 2007 guidelines were built on the foundation of previous guidelines. In this brief commentary, we summarize the major changes since the 1997 guidelines and provide suggestions on incorporating these changes into clinical practice.

The provision of antimicrobial therapy to prevent bacterial endocarditis has long been considered an essential part of the management of persons with cardiac lesions, because the consequences of bacterial endocarditis in either a native or prosthetic valve can be grave. Since the initial inception of the AHA recommendations for antibiotic regimens for the prevention of infective endocarditis in 1955, these guidelines have gradually been evolving, as nicely summarized in the 2007 recommendations (1,4). The previous AHA guidelines, published in 1997, contained what was considered to be a significant change in endocarditis prophylaxis recommendations for high-risk procedures: the provision of a single 2 g oral amoxicillin dose 1 h before a dental or respiratory procedure (5). This was heralded as a significant modification because it eliminated the postprocedure dose. Furthermore, cardiac lesions were categorized into low, moderate and high risk for endocarditis. Antimicrobial prophylaxis was recommended for patients at moderate or high risk. The low-risk lesions were considered to be of such negligible consequence that antimicrobial prophylaxis was not recommended (5).

CONCEPTUAL PROBLEMS WITH PROPHYLAXIS

The fundamental problem common to all previous guidelines, including the current one, is that they were based more on consensus than on solid evidence. The key principles underpinning all the previous

AHA guidelines are as follows (1):

- Infective endocarditis is an uncommon albeit life-threatening condition for which prevention is preferable over the treatment of an established infection.
- Specific cardiac conditions predispose to endocarditis.
- Bacteremias with microorganisms known to cause endocarditis can occur in association with invasive dental, gastrointestinal or genitourinary tract procedures.
- In experimental animal models, antimicrobial prophylaxis has been shown to prevent endocarditis.
- Antimicrobial prophylaxis is likely effective in the prevention of endocarditis in patients who undergo dental, gastrointestinal and genitourinary tract procedures.

Although the first four principles outlined above are valid, there is no good evidence to support the last principle, which is the main reason for the provision of prophylactic antibiotic therapy. There are other arguments against the practice of antimicrobial prophylaxis. Infective endocarditis is more likely to result from exposure to random bacteremias occurring with activities of daily living than from bacteremias due to dental, gastrointestinal or urinary tract procedures. Antimicrobial prophylaxis likely prevents an exceptionally small number of cases of endocarditis, if any, in persons undergoing dental, gastrointestinal or urinary tract procedures. Episodes of bacteremia from daily activities may be reduced by the maintenance of optimal oral health, which is likely more effective in preventing endocarditis than prophylactic antimicrobial therapy for dental procedures. Antimicrobial agents are not benign drugs, and complications such as anaphylactic reactions or *Clostridium difficile* colitis have been reported with antimicrobial prophylaxis for dental procedures (6). The risk of adverse events associated with antibiotic use may exceed the benefit from prophylactic antibiotic therapy.

BSAC GUIDELINES

It is important to note that based on similar reasoning, the BSAC challenged the existing guidelines for the prevention of endocarditis and recommended that "despite the lack of evidence of the benefit for prophylactic antibiotics to prevent endocarditis associated with dental procedures, the Working Party considered that many clinicians would be reluctant to accept the radical, but logical step of withholding antibiotic prophylaxis for dental procedures. It was therefore agreed to compromise and recommend prophylaxis only for those patients in whom the risk of developing endocarditis is high and, if infected, would carry a particularly high mortality" (2). The authors rightfully acknowledged that the vast majority of practitioners would find it exceptionally difficult to make this dramatic modification in clinical practice from providing antimicrobial prophylaxis for high-risk procedures to not providing any at all. In the BSAC recommendations, the

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TABLE 1
Comparison of patients who require antimicrobial prophylaxis for the prevention of infective endocarditis before dental procedures

| American Heart Association (1) | British Society for Antimicrobial Chemotherapy (2) |
|---|---|
| <ul style="list-style-type: none"> • Prosthetic cardiac valves • Previous endocarditis • Congenital heart disease <ul style="list-style-type: none"> ◦ Unrepaired cyanotic congenital heart disease, including palliative shunts and conduits ◦ Completely repaired congenital heart defects with prosthetic material or device whether placed by surgery or catheter intervention during the first 6 months after the procedure (prophylaxis is recommended because endothelialization of prosthetic material may be incomplete within 6 months of the procedure) ◦ Repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device • Cardiac transplantation recipients who develop cardiac valvulopathy | <ul style="list-style-type: none"> • Previous endocarditis • Cardiac valve replacement surgery (mechanical or biological prosthetic valve) • Surgically constructed systemic or pulmonary shunt or conduit |

TABLE 2
American Heart Association regimens for prophylaxis of infective endocarditis before dental procedures

| Patient group | Antibiotic | Route | Single dose before procedure | |
|---|--------------------------------|-------------------------------|------------------------------|-----------|
| | | | Adults | Children |
| Usual antibiotic | Amoxicillin | Oral | 2 g | 50 mg/kg |
| Unable to take oral medication | Ampicillin | Intravenous or intramuscular* | 2 g | 50 mg/kg |
| | Cephazolin or ceftriaxone† | Intravenous or intramuscular | 1 g | 50 mg/kg |
| Allergic to penicillin/ampicillin | Clindamycin | Oral | 600 mg | 20 mg/kg |
| | Cephalexin | Oral | 2 g | 50 mg/kg |
| | Azithromycin or clarithromycin | Oral | 500 mg | 15 mg/kg |
| Allergic to penicillin/ampicillin and unable to take oral medications | Clindamycin | Intravenous | 600 mg | 200 mg/kg |
| | Cefazolin or ceftriaxone | Intravenous or intramuscular | 1 g | 50 mg/kg |

*Intramuscular injections should be avoided in persons receiving anticoagulants; †Cephalosporins should be avoided in persons with a history of anaphylaxis to beta-lactam-related antibiotics. Data from reference 1

high-risk patients include individuals with previous endocarditis, cardiac valve replacement surgery (mechanical or biological prosthetic valves), and surgically constructed systemic or pulmonary shunt or conduit (2). Dental procedures that require antibiotic prophylaxis included those involving dentogingival manipulation. The BSAC guidelines did not receive prior endorsement from the British cardiac societies, which, not unexpectedly, refused to accept the guidelines, resulting in confusion among physicians and patients.

AHA GUIDELINES

The AHA working group involved and obtained endorsement from related societies. The arguments for modifying the guidelines are persuasive and well-referenced. There are many similarities between the AHA and BSAC guidelines in terms of high-risk patients (Table 1). In both guidelines, 'high risk' refers to the very high likelihood of severe adverse outcome should the patient develop endocarditis, and not to the patient's lifetime risk of developing the disease. In the AHA guidelines, patients with congenital heart disease requiring prophylaxis are better defined, and transplant valvulopathy is included as a high-risk feature. Neither guideline recommends prophylaxis in patients with valvular heart disease with or without regurgitation. The acceptance of this guideline alone will lead to a considerable reduction in the use of antimicrobial prophylaxis. Antimicrobial regimens that are recommended for prophylaxis in dental procedures are listed in Table 2.

As to the risk of endocarditis arising from respiratory tract procedures, the authors of the AHA guidelines believe that a conclusive link between these procedures and endocarditis does not exist (1). In

patients with high-risk cardiac lesions, antibiotic prophylaxis with the regimens in Table 2 may be considered for those undergoing procedures that involve incision or biopsy of the respiratory mucosa, such as tonsillectomy or adenoidectomy (1). Antibiotic prophylaxis for bronchoscopy is not recommended unless the procedure entails incision of the respiratory mucosa. However, if the invasive respiratory tract procedure is to manage an established infection, such as drainage of an abscess or empyema, antibiotic prophylaxis is warranted as outlined in Table 2. The authors also suggest that if *Staphylococcus aureus* is a potential consideration, an anti-staphylococcal agent should be used, and that if methicillin-resistant *S aureus* is suspected, vancomycin should be the drug of choice (1).

The 2007 AHA guidelines also include sweeping recommendations with regard to endocarditis prophylaxis for persons undergoing gastrointestinal or genitourinary tract procedures. The administration of prophylactic antibiotic solely to prevent endocarditis in persons undergoing these procedures, including colonoscopy and esophagogastroduodenoscopy, is deemed unnecessary (1). The rationale for this recommendation is based on the relative absence of data demonstrating a conclusive link between these procedures and the development of infective endocarditis. In addition, the administration of antimicrobial prophylaxis has not been shown to prevent endocarditis in association with these procedures (1). Enterococci are part of the normal gastrointestinal tract and are the only microorganisms likely to cause infective endocarditis in the setting of gastrointestinal procedures. With the increased prevalence of antimicrobial resistance among enterococci, the previously recommended prophylaxis is likely of limited benefit. In

patients with high-risk cardiac lesions with known colonization or infection of the genitourinary tract who are undergoing surgery or manipulation in these areas, prophylaxis may be considered and should include an agent effective against the enterococci (penicillin, ampicillin, piperacillin, vancomycin). However, no published reports have demonstrated that such therapy may prevent enterococcal endocarditis.

With regard to procedures involving infected skin, skin structure and musculoskeletal tissues in persons with high-risk cardiac lesions as listed in Table 1, prophylaxis for endocarditis with an agent effective against staphylococci and beta-hemolytic streptococci (Table 2) may be of benefit. Vancomycin or clindamycin may be administered in patients unable to tolerate beta-lactam agents or in situations when methicillin-resistant *S aureus* is speculated.

The 2007 AHA guidelines acknowledged the relative absence of high-quality data on which the previous recommendations were established. Table 3 summarizes the highlights of the new 2007 recommendations. While the new guidelines may appear wide sweeping and very restrictive in not recommending antimicrobial prophylaxis in many patients with cardiac lesions, they provide a pragmatic and reasonable approach supported by the best available evidence. The guidelines are based on consensus and compromise, balancing the absence of solid evidence with the catastrophic consequences of endocarditis in the high-risk patients. We may only know with time whether these recommendations have appropriately targeted the correct risk groups and procedures. It is important for all of us, as clinicians, to document cases of endocarditis that occur in patients in whom prophylaxis would have been administered according to previous guidelines. This will allow for a re-evaluation and future modification of the current recommendations. Canada may be able to play a key role in this regard because of the well-developed provincial health databases that can track the prevalence of endocarditis over time.

ADVICE TO PATIENTS

When dealing with patients who have received antibiotic prophylaxis in the past and no longer require antibiotic prophylaxis according to the current guidelines, the physician should have a detailed discussion with them emphasizing that discontinuing antibiotic prophylaxis according to the current guidelines does not mean that the clinical characteristics that increase their risks of developing endocarditis have changed. They continue to be at an increased risk of developing endocarditis. They should be advised about the importance of good dental hygiene. They also need to be educated regarding the signs and symptoms of endocarditis so that they seek prompt medical attention early in the course of the disease. Early diagnosis with prompt initiation of effective antimicrobial therapy is the best way to minimize the mortality and morbidity of endocarditis.

CONCLUSION

We strongly support and endorse the 2007 AHA guidelines for the prevention of endocarditis, which is a major step forward in the management of patients with heart disease and will decrease the widescale use of antimicrobials (5). The risk for the development of endocarditis is more related to the clinical characteristics of the patient than to any specific invasive procedures. Antimicrobial prophylaxis to prevent procedure-related endocarditis is likely of limited benefit, and it is a more effective strategy to minimize the intrinsic risks associated with patients. In light of growing concerns about antimicrobial resistance and development of *C difficile* infection with the use of antimicrobial therapy, we caution readers that relying on the old adage 'better safe than sorry' to justify the administration of antimicrobial therapy may lead to more harm to our patients. We should adhere to the 2007 AHA guidelines because they are a reasonable compromise between solid science and common sense.

TABLE 3
Highlights of the 2007 American Heart Association guidelines for the prevention of infective endocarditis

- Bacteremias resulting from activities of daily living are more likely to result in infective endocarditis than bacteremias from dental procedures
- Even if prophylaxis were completely effective, only an extremely small number of cases of infective endocarditis may be prevented with antibiotic prophylaxis
- Recommendation of antibiotic prophylaxis is not based exclusively on an increased lifetime risk of developing endocarditis
- Prophylaxis of infective endocarditis is recommended only in patients with conditions that put them at the highest risk of adverse outcomes should they develop endocarditis (Table 1)
- Antibiotic prophylaxis is no longer recommended for patients with other forms of cardiac conditions not listed in Table 1
- Antibiotic prophylaxis is recommended only for the dental procedures that involve manipulation of the gingival tissues or periapical tissue of teeth or perforation of the oral mucosa in patients with underlying high-risk cardiac conditions (Table 1)
- Antibiotic prophylaxis is recommended for procedures involving the respiratory tract or infected skin, skin structures or musculoskeletal tissues only in patients with the underlying cardiac abnormalities outlined in Table 1
- Antibiotic prophylaxis exclusively to prevent endocarditis is not recommended for gastrointestinal or genitourinary tract procedures
- The recommendation as to the procedures for which endocarditis prophylaxis was not recommended in the 1997 guidelines remains in effect, including ear or body piercing, tattooing, vaginal delivery and hysterectomy

Data from reference 1

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