Prevention of Infective Endocarditis: Revised Guidelines from the American Heart Association and the Implications for Dentists

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ABSTRACT

Infective endocarditis is a rare but life-threatening microbial infection of the heart valves or endocardium, most often related to congenital or acquired cardiac defects. The American Heart Association (AHA) recently updated its recommendations on prophylaxis during dental procedures. The revisions will have a profound impact on both the patient and the dental practitioner. The purpose of this paper is to review the pathogenesis and clinical presentation of infective endocarditis and discuss the 2007 AHA guidelines and their implications for dentists.

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Infective endocarditis is an uncommon but potentially life-threatening microbial infection of the heart valves or endocardium, most often related to congenital or acquired cardiac defects. High morbidity and mortality rates remain associated with the infection despite advances in diagnosis, antimicrobial therapy, surgical techniques and management of associated complications. Since the American Heart Association (AHA) produced guidelines on the prevention of infective endocarditis in 1997,[1] many groups have questioned the efficacy of antimicrobial prophylaxis in patients who undergo dental procedures and have suggested that this recommendation be revised.[2–6]

The AHA appointed a writing group, including experts in the prevention and treatment of infective endocarditis from the American Dental Association, the Infectious Diseases Society of America and the American Academy of Pediatrics, to review input from national and international experts on the disease. The recommendations of this group culminated in the 2007 AHA guidelines on prophylaxis for infective endocarditis, which will have a profound impact on both patients and dental practitioners.

The purpose of this paper is to review the pathogenesis and clinical presentation of infective endocarditis and discuss the new guidelines on prophylaxis and their implications for dentists.

Pathogenesis of Infective Endocarditis

Turbulent blood flow produced by certain types of congenital or acquired heart disease may traumatize the endothelium and result

Table 1 Diagnosis of infective endocarditis[7]

Major criteria
Positive blood culture
Echocardiogram evidence of endocardial involvement
New valvular regurgitation
Minor criteria
Predisposing heart condition
Intravenous drug use
Fever
Vascular phenomena (emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, Janeway lesions)
Immunologic phenomena (glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor)
Isolated blood culture or serologic evidence of active infection
Echocardiogram findings consistent with endocarditis but not diagnostic of the disease

in the deposition of platelets and fibrin on the damaged endocardium or endothelial surface. This may result in the formation of sterile vegetations, a condition known as nonbacterial thrombotic endocarditis.[6,7] Invasion of the bloodstream by microbes that can colonize this damaged site may result in infective endocarditis.

Odontogenic Sources of Transient Bacteremia

In 1909, Horder discovered an association between dental health and infective endocarditis, when he noted that "infection is grafted upon a previously sclerosed endocardium... the source of the infecting agent, in most of the cases, is the mouth."[8] Oral mucosal surfaces are populated by a dense endogenous microflora. Trauma to these surfaces, particularly the gingival crevice around teeth, releases these microbial species transiently into the bloodstream.

Transient bacteremia caused by the viridans group of streptococci and other oral microflora commonly occurs during dental extractions, other procedures and even during routine daily activities.[6,7] The frequency and intensity of the resulting bacteremias is related to the nature and magnitude of the tissue trauma, the density of microbial flora and the degree of inflammation or infection at the trauma site. The species entering the bloodstream depends on the endogenous microflora that colonize the traumatized site.

Microbial Adherence

The focus of infection is determined by the ability of various microbial species to adhere to specific anatomic sites.[6] Mediators of bacterial adherence serve as virulence factors in the pathogenesis of infective endocarditis. Some streptococci in the viridans group contain a lipoprotein receptor antigen I (LraI) that acts as a major adhesin to the fibrin platelet matrix of nonbacterial thrombotic endocarditis.[6,9]

Microbial Proliferation within a Vegetation

Once attached to an anatomic focus, these microorganisms stimulate further deposition of fibrin and platelets on their surface. Thus buried, the microorganisms can multiply rapidly, apparently uninhibited by host defenses.[6] More than 90% of the microorganisms in mature valvular vegetations are unresponsive to antibiotics as they are metabolically inactive.[6,10]

Thus, infective endocarditis arises from complex interactions between the bloodstream microbial pathogen and the matrix molecules and platelets at sites of endocardial cell damage.

Clinical Presentation of Infective Endocarditis

Signs and Symptoms

The classic symptoms of infective endocarditis include fever, anemia, positive blood cultures and heart murmur.[7] However, diagnosis must always involve a high level of clinical suspicion, as these classic findings may not always be present (**Table 1**). Other symptoms may include fatigue, weight loss, night sweats, anorexia and arthralgia. Emboli may result in chest pain, abdominal pain, blindness, paralysis and hematuria. Petechiae may occur on skin or mucosal tissues and linear hemorrhages may be visible under the nails. Osler's (subcutaneous) nodes, Janeway lesions (flat, nontender, red spots on palms and soles that blanch on pressure) and retinal hemorrhages may also be noted.

Laboratory Findings

- Leukocytosis with neutrophilia
- Increased erythrocyte sedimentation rate
- Positive C-reactive protein
- Increased levels of serum immunoglobulins
- Blood cultures positive for pathogen
- Positive rheumatoid factor

Electrocardiogram Findings

- Prolonged PR interval (caused by abscess)
- Silent myocardial infarction (caused by emboli in coronary artery)

Echocardiography

- Vegetations
- Valvular perforations
- Other abnormalities (e.g., abscesses, pericarditis)

Box 1 Cardiac conditions with the highest risk of adverse outcome from infective endocarditis and for which prophylactic dental procedures are recommended[6]

- Prosthetic cardiac valve
- Previous infective endocarditis
- Congenital heart disease[a]
  - Unrepaired cyanotic congenital heart disease, including palliative shunts and conduits
  - Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure[b]
  - Repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)
- Cardiac transplantation with subsequent cardiac valvulopathy

[a]*Except for the conditions listed here, antibiotic prophylaxis is no longer recommended for any other form of congenital heart disease.*
[b]*Prophylaxis is recommended because endothelialization of prosthetic material occurs within 6 months after the procedure.*

Prophylaxis for Infective Endocarditis during Dental Procedures

Rationale for Prophylaxis

The 1997 AHA guidelines[1] recommended antimicrobial prophylaxis to prevent infective endocarditis among patients with underlying cardiac conditions who must undergo bacteremia-producing procedures. The recommendation was based on the following factors: infective endocarditis is an uncommon but life-threatening disease and prevention is preferable to treatment of established infection; certain underlying cardiac conditions predispose patients to infective endocarditis; bacteremia with organisms known to cause infective endocarditis is common during invasive dental procedures; antimicrobial prophylaxis is effective in preventing infective endocarditis in animals; and antimicrobial prophylaxis was thought to be effective in preventing infective endocarditis associated with dental procedures in humans.

Primary Reasons for Revision of the Guidelines

Although the rationale for prophylaxis of infective endocarditis remains valid, it does not compensate for the lack of data demonstrating a benefit. Moreover, antibiotic prophylaxis is not risk free. Penicillins cause allergic reactions among 1%–10% of patients. The risk of death from anaphylactic reaction is 5 times greater than that from treating infective endocarditis.[11] Maintenance of optimal oral health and hygiene may reduce the incidence of bacteremia from daily activities and is more important than prophylactic antibiotics for a dental procedure in reducing the risk of infective endocarditis.

Revised AHA Guidelines on Prophylaxis for Infective Endocarditis

In its 2007 guidelines,[6] the AHA concluded that bacteremia resulting from daily activities is much more likely to cause infective endocarditis than bacteremia associated with a dental procedure. Moreover, they concluded that only an extremely small number of cases of infective endocarditis might be prevented by antibiotic prophylaxis even if prophylaxis is 100% effective. Thus, antibiotic prophylaxis is not recommended based solely on an increased lifetime risk of acquisition of infective endocarditis.

As a result, the revised guidelines were greatly simplified. The major changes include the following: infective endocarditis prophylaxis for dental procedures is recommended only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from infective endocarditis (**Box 1**). Antibiotic prophylaxis is no longer recommended for those with any other form of congenital heart disease.

Prophylaxis is recommended for all dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa *only* for patients at highest risk of adverse outcome from infective endocarditis (**Box 1**). Prophylaxis is no longer needed for routine anesthetic injections through noninfected tissue, dental radiographs, placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of deciduous teeth or bleeding from trauma to the lips or oral mucosa.

The recommended antibacterial regimens for dental procedures remain unchanged (**Table 2**).

Discussion

The vast majority of cases of infective endocarditis caused by oral microflora likely result from random bacteremias caused by routine daily activities, such as chewing food, brushing teeth, flossing, use of water irrigation devices and other activities.[6,7] These transient bacteremias usually clear within 10 minutes.[7] For example, tooth brushing was found to introduce bacteria into the bloodstream in about 40% of people tested[7]; similarly, chewing paraffin or oral irrigation produced transient bacteremias in 50% of people.[7] Guntheroth[12] estimated that with normal physiologic use of the oral cavity, about 5,376 minutes of transient bacteremias occur each month in the average person. Thus based on the high frequency of physiologic bacteremias and the low incidence of dental procedures preceding the onset of infective endocarditis, the odds of a case of infective endocarditis occurring from physiologic "seeding" of oral bacteria is 1,000 times

Table 2 Prophylactic antibiotic regimens before a dental procedure[6]

Patient group	Antibiotic	Dose (single, 30–60 min before procedure)	
		Adults	Children
Able to take oral medication	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin **OR** Cefazolin or ceftriaxone	2 g IM or IV 1 g IM or IV	50 mg/kg IM or IV 50 mg/kg IM or IV
Allergic to penicillins or ampicillin and able to take oral medication	Cephalexin[a,b] **OR** Clindamycin **OR** Azithromycin or clarithromycin	2 g 600 mg 500 mg	50 mg/kg 20 mg/kg 15 mg/kg
Allergic to penicillins or ampicillin and unable to take oral medication	Cefazolin or ceftriaxone[b] **OR** Clindamycin	1 g IM or IV 600 mg IM or IV	50 mg/kg IM or IV 20 mg/kg IM or IV

Note: IM = intramuscular, IV = intravenous.
[a]*Or other first- or second-generation oral cephalosporin at equivalent adult or pediatric dose.*
[b]*Cephalosporins should not be given to a patient who has a history of anaphylaxis, angioedema or urticaria with penicillins or ampicillin.*

greater than after a dental procedure.[12] However, the presence of dental disease may increase the risk of bacteremia associated with these routine activities.

As health care providers, dentists must consider the benefits of infective endocarditis prevention along with the risks of administering antibiotics: adverse drug events, the financial cost of antibiotics, the development of bacterial drug resistance and medicolegal concerns. But no matter how we weigh the risks and benefits of prophylaxis for infective endocarditis, until prospective clinical trials are conducted, its true efficacy will remain unclear.

Based on the revised 2007 AHA guidelines,[6] substantially fewer patients will meet the criteria for infective endocarditis prophylaxis before dental procedures. The new recommendations may understandably cause concern at multiple levels. There will be concern among patients who have previously received antibiotic prophylaxis to prevent infective endocarditis before dental procedures and are now advised that such prophylaxis is unnecessary. Moreover, there may be concerns amongst physicians, who in the past have supported antibiotic prophylaxis and may not be aware of the recent changes to the guidelines. There may be concern on the part of regulators who now must decide whether to modify their practice guidelines to mirror those of the current AHA recommendations. Similarly there may be initial resistance within certain hospitals to follow the new recommendations.

It is thus important for dentists to be familiar with both the AHA guidelines and the rationale behind them. This will allow them to alleviate their own concerns, re-educate their patients about the changes and communicate effectively with their medical colleagues to optimize the continued safe delivery of patient care.

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