The purpose of this clinical update is to present the revised 2007 guidelines by the American Heart Association (AHA) on the prevention of infective endocarditis.

**Background**

Infective endocarditis (IE) is a microbial infection that is very rare but life-threatening. Despite the advancements in technology to diagnose and treat this disease, it carries a high risk of mortality and morbidity. IE typically occurs in individuals with underlying structural cardiac defects who develop bacteremia with certain organisms known to cause endocarditis. Therefore, primary prevention of IE is very important.

Antibiotic prophylaxis for the prevention of IE has been recommended with various regimens by the American Heart Association (AHA) for more than 50 years. The fundamental principles for the development of such guidelines were: 1) prevention is preferable to treatment of IE; 2) certain cardiac conditions have been associated as risk factors for IE; 3) bacteremia known to cause IE occurs with invasive dental procedures; 4) antibiotic prophylaxis was shown to be effective for prevention of IE in animal studies; and 5) antibiotic prophylaxis was thought to be effective in humans. Based on evolving epidemiological and clinical data, the recommendations for dental prophylaxis have been repeatedly updated. To understand the rationale for the current revision, it is prudent to review the pathogenesis and presentation of IE.

**Pathogenesis**

The development of IE typically begins at a site of damaged endothelial surface in close proximity to an anatomic defect or prosthesis. Endothelial surface damage is a result of alterations of blood flow produced by certain types of congenital or acquired heart disease. For example, a high velocity jet striking the endothelium or blood flow from a high to a low pressure chamber can traumatize the surface. A condition known as nonbacterial thrombotic endocarditis (NBTE) occurs when fibrin and platelets adhere to the damaged endothelial surface. Transient bacteremia allows bacteria to seed onto and adhere to the NBTE mass. The frequency and intensity of this bacteremia are directly 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 flora that colonize the traumatized site. IE results from this interaction between the blood-borne pathogen and the fibrin platelet matrix at sites of endocardial cell damage.

**Etiology**

Viridans group streptococci associated with the oral microflora have been found to be the most common isolates among patients with IE. One study reported the identification of 98 bacterial species, 32 of which were reported to cause endocarditis related to bacteremias associated with tooth brushing and dental extractions. Ten of the 32 (31%) IE-associated bacterial species were viridans group streptococci. Another study found 86% of 107 IE cases were caused by either streptococcal or staphylococcal species. Viridans group streptococci were the most common causative organisms and were isolated in 47 cases (44%); *Staphylococcus aureus* was identified in 28 cases (26%). While streptococci continue to be the common finding of IE cases, staphylococci species are becoming increasingly recognized as an etiology. Fowler et al. conducted a prospective observational cohort study in 39 medical centers from 16 countries and found *Staphylococcus aureus* to be the leading cause of IE in many regions of the world.

**Bacteremias from routine activities in comparison with dental procedures**

Bacteremias have been found to occur often with activities of daily living such as tooth brushing or chewing. Poor dental hygiene and periodontal infections may produce bacteremias even in the absence of dental procedures. Evidence points to an association of periodontal disease in relation to clinical and subclinical vascular disease.

Although it does not have the same incidence and nature of bacteremia as a dental extraction, there was a 23% incidence of bacteremia of IE-causing species with tooth brushing. Tooth brushing caused a small amount of bleeding but had positive cultures 38% of the time. In comparison, extractions associated with a large amount of bleeding had positive cultures 54% of the time. The frequency and cumulative duration of exposure to bacteremia from routine daily events over 1 year is likely to be much higher than those resulting from dental procedures. The cumulative exposure to bacteremia over 1 year from routine daily activities may be as high as 5.6 million times greater than a single deciduous tooth extraction. This may be explained as tooth brushing affecting a larger surface area of gingival crevicular tissue.

The focus on the frequency of bacteremia associated with a specific dental procedure has resulted in an overemphasis on antibiotic prophylaxis and an underemphasis on maintenance of good oral hygiene and routine dental care. Good oral hygiene and eradicating dental disease will decrease the frequency of bacteremia from routine daily activities.

**Risk of adverse reactions of antibiotic prophylactic therapy**

There are no prospective, randomized, placebo-controlled studies on the efficacy of antibiotic use for the prevention of IE in patients who undergo a dental procedure. Despite the lack of well-controlled studies addressing the impact of the AHA-recommended antibiotic protocols on the incidence, nature, magnitude, and duration of bacteremia, a vast majority of providers recommend antibiotic prophylaxis to patients with known valvular disease. In a survey, it was shown that 24% of providers indicated medico-legal concerns for prescribing antibiotics.

Nonfatal adverse reactions, such as rash, diarrhea, and GI upset, occur commonly with the use of antibiotics. These common adverse reactions are usually not severe and are self-limiting since only a single-dose therapy is recommended for dental prophylaxis. True risk of death caused by fatal anaphylaxis has been documented with various antibiotics. It was estimated that 20 fatalities per million patients receiving oral amoxicillin or IV ampicillin sodium and 1 fatality per 1 million patients receiving cephalaxin or cefazolin for prophylaxis were due to anaphylaxis.
The current AHA guidelines have determined that a single dose of amoxicillin/amoxicillin is safe and the preferred agent for those who do not have a history of type 1 hypersensitivity reaction to penicillin.

Revised AHA guidelines on prophylaxis for infective endocarditis

In the 2007 guidelines, the AHA recommended that bacteremia resulting from daily activities is much more likely to cause IE than bacteremia associated with a dental procedure. It also stated that an exceedingly small number of IE cases may be preventable through the use of antibiotic prophylaxis.1 Strom et al. found that dental procedures were not a risk factor for IE, even in patients with underlying cardiac valvular abnormalities.14

Patients with highest risk of adverse outcomes

The major changes to the revised guidelines include the following: antibiotic prophylaxis for dental procedures is recommended only for patients associated with the highest risk of adverse outcome from IE.1 (Table 1) Antibiotic prophylaxis is no longer recommended for the moderate risk group such as individuals with acquired valvular dysfunction (e.g. due to rheumatic heart disease) and hypertrophic cardiomyopathy.15 Prophylaxis should not be based solely on an increased lifetime risk for acquisition of infective endocarditis.

Prophylaxis is recommended for dental procedures involving the manipulation of gingival tissue, the periodical region of teeth or perforation of the oral mucosa. Prophylaxis is no longer needed for the following procedures: routine anesthetic injections through non-infected tissue, dental radiographs, placement of removable prosthetic 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.1 (Table 2)

The recommended choice of antibiotic for dental procedures has remained unaltered from the previous AHA guideline. Because amoxicillin is well absorbed in the GI tract and provides high sustained serum concentration, it is the preferred choice for oral therapy. However, it is recommended that individuals who are allergic to penicillin or amoxicillin use cephalaxin or another first-generation oral cephalosporin- clindamycin, azithromycin or clarithromycin. Patients who cannot tolerate oral antibiotic may be treated with ampicillin, ceftriaxone, or cefazolin administered intramuscularly or intravenously. (Table 3)

Conclusion

It has long been assumed that dental procedures cause IE in patients with underlying cardiac risk factors and that antibiotic prophylaxis is effective. However, there are no published data demonstrating that administration of prophylactic antibiotics prevents IE associated with bacteremia from an invasive procedure. The literature does suggest that an exceedingly small number of IE cases are caused by dental procedures. The majority of cases may have resulted through bacteremia from routine daily activities such as chewing, tooth brushing, flossing, and other activities. Therefore, antibiotic therapy should be restricted to patients with the highest risk of adverse outcomes from IE.

References


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The opinions and assertions contained in this article are the private ones of the authors and are not to be construed as official or reflecting the views of the Department of the Navy.
Table 1. Cardiac conditions with the highest risk of adverse outcome from endocarditis for which prophylaxis with dental procedure is reasonable

<table>
<thead>
<tr>
<th>Category</th>
<th>Prophylaxis Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic cardiac valve or prosthetic material used for cardiac valve repair</td>
<td>Previous IE</td>
</tr>
<tr>
<td>Congenital heart disease (CHD)*</td>
<td>• Unrepaired cyanotic CHD, including palliative shunts and conduits</td>
</tr>
<tr>
<td></td>
<td>• 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</td>
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<tr>
<td></td>
<td>• Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)</td>
</tr>
<tr>
<td>Cardiac transplantation recipients who develop cardiac valvulopathy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>* Antibiotic prophylaxis is only recommended for these forms of CHD</td>
</tr>
</tbody>
</table>

Table 2. Dental procedures for which endocarditis prophylaxis is reasonable for patients in Table 1

All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa*

*The following procedures and events do not need prophylaxis:
• routine anesthetic
• injections through non-infected tissue
• taking dental radiographs
• placement of removable prosthodontic or orthodontic appliances
• adjustment of orthodontic appliances
• placement of orthodontic brackets
• shedding of deciduous teeth
• bleeding from trauma to the lips or oral mucosa

Table 3. Regimens for a dental procedure (single dose 30 to 60 min before procedure)

<table>
<thead>
<tr>
<th>Category</th>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Amoxicillin</td>
<td>2g</td>
</tr>
<tr>
<td>Unable to take oral medication</td>
<td>Ampicillin or Cefazolin/ceftriaxone</td>
<td>2g IM or IV</td>
</tr>
<tr>
<td></td>
<td>1g IM or IV</td>
<td>50mg/kg IM or IV</td>
</tr>
<tr>
<td>Allergic to penicillins or ampicillin—oral</td>
<td>Cephalexin or Clindamycin or Azithromycin/clarithromycin</td>
<td>2g</td>
</tr>
<tr>
<td></td>
<td>600mg</td>
<td>20mg/kg</td>
</tr>
<tr>
<td></td>
<td>500mg</td>
<td>50mg/kg IM or IV</td>
</tr>
<tr>
<td>Allergic to penicillins or ampicillin and unable to take oral medication</td>
<td>Cefazolin/ceftriaxone or Clindamycin</td>
<td>1g IM or IV</td>
</tr>
<tr>
<td></td>
<td>600mg IM or IV</td>
<td>20mg/kg IM or IV</td>
</tr>
</tbody>
</table>