Antibiotic prophylaxis (AP) refers to the practice of the administration of antibiotics to patients without signs of infection in order to reduce subsequent postoperative or post-treatment complications by the prevention of bacterial colonization. In dentistry, the main indications for antibiotic prophylaxis have been to prevent infective endocarditis (IE) and prosthetic joint implant infection (PJI).

Patients at risk of infective endocarditis
Infective endocarditis (IE) is an infection caused by pathogens that enter the bloodstream and settle in the heart lining, one or more heart valves or blood vessels. Patients with certain predisposing conditions may have a greater risk of developing IE. In the past, patients with nearly every type of congenital heart defect received antibiotics before dental procedures based on recommendations by the American Heart Association (AHA). For non-penicillin allergic patients, oral penicillin was recommended from 1955 until 1990. In 1990, 3g amoxicillin became the oral regimen of choice, to be taken one hour before dental procedures (1). In 1997 the recommended amoxicillin dose was reduced to 2g (2).

In 2007, the AHA developed revised guidelines by using an evidence-based approach to reduce ambiguities about the patient for whom AP may be indicated and under what conditions, as well as what antibiotics to use (3). The Council on Scientific Affairs of the American Dental Association (ADA) approved these guidelines, which were also published in the association's dental journal (4). The major change was that antibiotics prior to dental procedures would only be recommended for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from IE. The following cardiac conditions for which AP with dental procedures would be reasonable were identified as:

- Prosthetic cardiac valve or prosthetic material used for cardiac valve repair
- Previous infective endocarditis
- Congenital heart disease (CHD)
  - Unrepaired cyanotic CHD, 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 six months after the procedure
Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)

Cardiac transplantation recipients who develop cardiac valvulopathy

In 2017, the AHA and American College of Cardiology (ACC) published a focused update (5) to their previous guidelines on the management of valvular heart disease. This reinforced their previous recommendations that AP is reasonable for the subset of patients at increased risk of developing IE and at high risk of experiencing adverse outcomes from IE (5). Their key recommendations were:

“Prophylaxis against IE is reasonable before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa in patients with the following:

1. Prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts.
2. Prosthetic material used for cardiac valve repair, such as annuloplasty rings and chords.
3. Previous IE.
4. Unrepaired cyanotic congenital heart disease or repaired congenital heart disease, with residual shunts or valvular regurgitation at the site of or adjacent to the site of a prosthetic patch or prosthetic device.
5. Cardiac transplant with valve regurgitation due to a structurally abnormal valve.”

The 2017 AHA/ACC report also noted that, based on limited data, IE appears to be more common in heart transplant recipients than in the general population; the risk of IE is highest in the first six months after transplant because of endothelial disruption, high-intensity immunosuppressive therapy, frequent central venous catheter access, and frequent endomyocardial biopsies (5).

Elsewhere, concerns about overprescribing AP have also received attention. In Europe, similar guidelines to those in the U.S. restricting AP to only patients with the highest risk of IE were issued in 2009 (6). In contrast, complete restrictions were placed in the United Kingdom (UK) in 2008, the recommendation being: “Antibiotic prophylaxis against infective endocarditis is not recommended for people undergoing dental procedures” (7).

While the increase in incidence of IE was significant both for individuals at high risk of infective endocarditis and those at lower risk, the authors noted that their data do not establish a “causal association”. NICE guidelines were revised to: “Antibiotic prophylaxis against infective endocarditis is not recommended routinely for people undergoing dental procedures” (10).

A recurring theme in the relevant literature is that there is an absence of robust data about the effectiveness of AP to prevent IE. A systematic review and meta-analysis published in 2017 concluded: “the evidence base for the use of AP is limited, heterogeneous and the methodological quality of many studies is poor. Post-procedural bacteremia is not a good surrogate endpoint for IE. Given the logistical challenges of a randomized trial, high quality case–control studies would help to evaluate the role of dental procedures in causing IE and the efficacy of AP in its prevention” (8).

As part of its Oral Health Topic series in March 2017 (20), the ADA recommended that dental professionals continue to follow the AHA guidelines (3, 4), including the dosage regimens for a dental procedure reflected in the 2008 AAE Quick Reference Guide as follows:
<table>
<thead>
<tr>
<th>Situation</th>
<th>Agent</th>
<th>Regimen: Single Dose 30 to 60 min. Before Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Amoxicillin 2 g</td>
<td>50 mg/kg</td>
</tr>
<tr>
<td>Unable to take oral medication</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Allergic to penicillins or ampicillin—oral</td>
<td>Cephalexin φ OR Clindamycin OR Azithromycin or clarithromycin 2 g 600 mg 500 mg 50 mg/kg 20 mg/kg 15 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Allergic to penicillins or ampicillin and unable to take oral medication</td>
<td>Cefazolin or ceftriaxone δ OR Clindamycin 1 g IM or IV 600 mg IM or IV 50 mg/kg IM or IV 20 mg/kg IM or IV</td>
<td></td>
</tr>
</tbody>
</table>

*IM: Intramuscular
*IV: Intravenous
φ Or other first- or second-generation oral cephalosporin in equivalent adult or pediatric dosage.
δ Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillins or ampicillin.

In these situations, clindamycin, azithromycin or clarithromycin would be recommended for AP. Alternatively, if possible, treatment should be delayed until at least 10 days after completion of the antibiotic to allow re-establishment of usual oral flora. In situations where patients are receiving long-term parenteral antibiotic for IE, the treatment should be timed to occur 30 to 60 min after delivery of the parenteral antibiotic. It is considered that parenteral antimicrobial therapy is administered in such high doses that the high concentration would overcome any possible low-level resistance developed among oral flora (3, 4).

**Patients at risk of prosthetic joint implant infection**

Patients with prosthetic joints have been considered to be at increased risk of developing PJI subsequent to receiving dental care. Since 1997, several advisory statements or clinical practice guidelines have been published by the ADA and/or the American Academy of Orthopaedic Surgeons (AAOS) to address AP to prevent PJI (11-17).

In 2009, the AAOS released an information statement regarding AP for dental patients with total joint replacements recommending “that clinicians consider AP for all total joint replacement patients prior to any invasive procedure that may cause bacteremia” (16). The 2009 information statement generated considerable controversy and confusion (18, 19).

In 2012, the AAOS/ADA jointly released revised clinical practice guidelines for AP for patients with PJs based on a comprehensive analysis of the available literature by a physician and dentist volunteer work group and experts in systematic reviews; the final review was further subjected to peer review by several independent organizations (15). These guidelines were summarized as follows:

“1. The practitioner might consider discontinuing the practice of routinely prescribing prophylactic antibiotics for patients with hip and knee prosthetic joint implants undergoing dental procedures.

**Grade of Recommendation:** Limited

**Definition:** A Limited recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.

**Implications:** Practitioners should be cautious in deciding whether to follow a recommendation classified as Limited, and should exercise judgment and be alert to emerging publications that report evidence. Patient preference should have a substantial influencing role.

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2. We are unable to recommend for or against the use of topical oral antimicrobials in patients with prosthetic joint implants or other orthopaedic implants undergoing dental procedures.

**Grade of Recommendation:** Inconclusive

**Definition:** An Inconclusive recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

**Implications:** Practitioners should feel little constraint in deciding whether to follow a recommendation labeled as Inconclusive and should exercise judgment and be alert to future publications that clarify existing evidence for determining balance of benefits versus potential harm. Patient preference should have a substantial influencing role.

3. In the absence of reliable evidence linking poor oral health to prosthetic joint infection, it is the opinion of the work group that patients with prosthetic joint implants or other orthopaedic implants maintain appropriate oral hygiene.

**Grade of Recommendation:** Consensus

**Definition:** A Consensus recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria.

**Implications:** Practitioners should be flexible in deciding whether to follow a recommendation classified as Consensus, although they may set boundaries on alternatives. Patient preference should have a substantial influencing role.

In 2014, an expert panel was assembled by the Council on Scientific Affairs (CSA) of the American Dental Association (ADA) to update the 2012 evidence report and guidelines. The subsequent systematic review concluded that there were no statistically significant association between dental procedures and PJI, and the following evidence-based clinical practice guidelines were published in 2015 (13). Key recommendations were:

- “In general, for patients with prosthetic joint implants, prophylactic antibiotics are not recommended prior to dental procedures to prevent prosthetic joint infection.”

- “The practitioner and patient should consider possible clinical circumstances that may suggest the presence of a significant medical risk in providing dental care without antibiotic prophylaxis, as well as the known risks of frequent or widespread antibiotic use. As part of the evidence-based approach to care, this clinical recommendation should be integrated with the practitioner’s professional judgment and the patient’s needs and preferences.”

- “In cases where antibiotics are deemed necessary, it is most appropriate that the orthopedic surgeon recommend the appropriate antibiotic regimen and when reasonable write the prescription.”

The clinical rationales for the 2015 recommendations were based upon evidence that: (i) dental procedures are not associated with PJI, (ii) antibiotics provided before care do not prevent PJI, (iii) there are potential harms of antibiotics including risk for anaphylaxis, antibiotic resistance, and opportunistic infections like *Clostridium difficile*, (iv) the benefits of AP may not exceed the harms for most patients, and (v) the individuals circumstances and preferences should be considered when deciding whether to prescribe prophylactic antibiotics prior to dental procedures (13).

In February 2017, a guest editorial by the American Dental Association Council on Scientific Affairs Antibiotic Prophylaxis Working Group published in the Journal of the American Dental Association reaffirmed the 2015 recommendations: “The 2015 ADA clinical practice guideline is valid and should continue to inform clinical decisions for dental patients in ambulatory settings.” (14)

**Organ and stem cell transplant patients**

These patients require special treatment when being provided dental care both before and after the transplant because they take immunosuppressive medications. There is currently no evidence to suggest that prophylactic antibiotics would offer the patients benefits that outweigh the risks of the antibiotics. However, the endodontic provider should consult with the patient’s medical team before providing dental care.
REFERENCES


