CURRENT CONCEPTS REVIEW

Dental Disease and Periprosthetic Joint Infection

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- The number of patients with end-stage osteoarthritis is increasing, and treatment with hip and knee arthroplasty is expected to increase over the next several decades.
- Dental disease has long been anecdotally associated with increased periprosthetic joint infections, although case-control studies do not support this relationship.
- While most recent guidelines for the prevention of endocarditis have favored treatment of fewer patients, the most recent recommendations for prevention of periprosthetic joint infection have increased the number of patients who would receive antibiotics before a dental procedure.
- Antibiotics given before a dental procedure decrease the risk of bacteremia from the oral cavity, but this is of uncertain clinical importance.
- The number of patients who would require antibiotics before dental procedures to prevent one periprosthetic joint infection greatly outnumbers the number of patients who would experience an adverse event associated with antibiotics given before a dental procedure.

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Arthroplasty in America

The average life expectancy in the United States has risen approximately ten years, from 69.9 years in 1959 to 78.6 years in 1999. With this increased life expectancy comes an increase in chronic medical conditions including end-stage osteoarthritis, with the number of patients requiring hip and knee arthroplasty in the United States growing. In 2005, approximately 200,000 primary hip arthroplasties and 500,000 primary knee arthroplasties were performed. Assuming no change in present-day scientific information to treat osteoarthritis, this number is expected to increase to almost 500,000 hip arthroplasties and 3,500,000 knee arthroplasties by 2030.

Periprosthetic joint infections are an undesired complication of arthroplasty. A periprosthetic joint infection may develop in three distinct time periods: early (within three months after implantation), delayed (three to twenty-four months after implantation), and late (over twenty-four months after implantation). Early infections are generally caused by bacteria seeded in the perioperative period. Delayed infections may be caused by less virulent bacteria seeded perioperatively, virulent organisms that are partially treated, or hematogenous seeding from infections at distant sites. Late periprosthetic joint infections are most often caused by hematogenous bacterial seeding of the prosthesis. The rate of periprosthetic joint infection...
in the first year has been reported to range from 0.58% to 1.6% after knee arthroplasty and from 0.67% to 2.4% after hip arthroplasty.

The most common bacterial causes of periprosthetic joint infection include coagulase-negative staphylococcus (30% to 43%), Staphylococcus aureus (12% to 23%), mixed bacteria (10% to 11%), Streptococcus species (9% to 10%), gram-negative rods (3% to 6%), Enterococcus species (3% to 7%), and anaerobes (2% to 4%). Approximately 11% of periprosthetic joint infections are culture-negative. Bacteria present in the oral cavity account for 6% to 13% of periprosthetic joint infections.

Dental Disease in America
Oral bacteremia refers to transient bacteremia that occurs via translocation of bacteria from the mouth into the bloodstream. It occurs daily as a result of brushing teeth, flossing, and chewing. Bacteremia from an oral source occurs more frequently in patients with income above the poverty line to have seen a dentist in the previous twelve months. The lack of dental insurance is not limited to impoverished patients as many patients with private health insurance often have no dental insurance.

While all states are required to provide dental services to children with Medicaid insurance, states may individually determine what dental coverage will be provided for adult patients with Medicaid. Less than half of the states currently provide comprehensive dental care to these patients. Patients with Medicare insurance have even more limited dental coverage. While Medicare covers hospitalizations for acute dental emergencies, it does not cover routine dental services such as cleanings, fillings, tooth extractions, and dentures.

Oral Flora and Periprosthetic Joint Infections
Given the increasing prevalence of joint replacements and the epidemic of dental decay in the United States, it is imperative to review the relationship between oral bacteremia and periprosthetic joint infection. In this article, we address this relationship, first, by stating the guidelines for antibiotic prophylaxis before dental procedures in patients who have had an arthroplasty. Then, we critically examine the relationship in the published literature between periprosthetic joint infection and dental disease. Finally, we examine the risks and benefits of the most recent guidelines for antibiotic prophylaxis before dental procedures and explore the possible unintended consequences of the increasing emphasis on antibiotic prophylaxis against dental disease in patients undergoing joint arthroplasty.

Guidelines from Professional Societies
Professional guidelines exist to guide health providers in determining which patients require antibiotics before a dental procedure to prevent serious infection, including endocarditis and periprosthetic joint infection. While most recent guidelines for the prevention of endocarditis have favored treatment of fewer patients, the most recent recommendations for prevention of periprosthetic joint infection have increased the number of patients who would receive antibiotics before a dental procedure.

In 2003, the American Dental Association (ADA) and the American Academy of Orthopaedic Surgeons (AAOS) published a joint practice guideline to advise which patients were at highest risk of developing a periprosthetic joint infection after a dental procedure. They concluded that patients undergoing a high-risk dental procedure (defined as dental extraction, periodontal procedures, dental implants, root canals, orthodontic bands, or cleaning of teeth when bleeding is anticipated) should always receive an antibiotic before the dental procedure in the first two years after a joint arthroplasty. The recommendation for all patients to be given antibiotic prophylaxis before dental procedures for the first two years after arthroplasty is simply because most periprosthetic joint infections occur in the first two years after arthroplasty.

Patients who are immunocompromised, such as those with rheumatoid arthritis and systemic lupus erythematosus, or who have comorbidities, such as a previous periprosthetic joint infection, poor nutrition, hemophilia, human immunodeficiency virus, or a malignancy, should receive an antibiotic before high-risk dental procedures regardless of the timing after arthroplasty.

The recommended antibiotic for patients capable of taking oral medication is cephalexin (2 g), cephradine (2 g), or amoxicillin (2 g) given one hour prior to the dental procedure. Clindamycin (600 mg) is recommended for patients with an allergy to penicillin. Patients unable to take oral medications are recommended to receive cefazolin (1 g), ampicillin (2 g), or clindamycin (600 mg), given one hour prior to the dental procedure. Cefazolin and ampicillin can be given either intravenously or intramuscularly, while clindamycin is recommended to be given intravenously only.

The AAOS revised these recommendations with an advisement paper published in 2009. This advisement paper drastically increased the number of patients who were recommended to receive an antibiotic before a dental procedure. It recommended that antibiotic prophylaxis be given before any procedure to all patients with a prosthetic joint, not only those of higher risk, that could potentially lead to bacteremia, regardless of the length of time after the arthroplasty. The rationale for this change is unclear; the references cited to support a change in practice all predate the 2003 joint practice guideline.

In December 2012, the AAOS and ADA released a new clinical practice guideline with three recommendations:

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)
TABLE I Professional Guidelines for Use of Antibiotics Before a Dental Procedure to Prevent Periprosthetic Joint Infection

<table>
<thead>
<tr>
<th>Dental Procedure Risk by Patient Characteristics*</th>
<th>2003 AAOS/ADA Recommendation17†</th>
<th>2009 AAOS Recommendation18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthroplasty done ≤2 yr earlier</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Low</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Arthroplasty done &gt;2 yr earlier</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Low</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Arthroplasty done &gt;2 yr earlier and patient immunocompromised†</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td>ASTM</td>
</tr>
<tr>
<td>Low</td>
<td></td>
<td>ASTM</td>
</tr>
<tr>
<td>Arthroplasty done &gt;2 yr earlier and patient has comorbid medical conditions§</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td>ASTM</td>
</tr>
<tr>
<td>Low</td>
<td></td>
<td>ASTM</td>
</tr>
</tbody>
</table>

*High-risk dental procedures are defined as dental extractions, periodontal procedures, dental implants, endodontic instrumentation beyond the apex of the tooth, subgingival placement of antibiotic fibers or strips, placement of orthodontic bands, intraligamentary local anesthetic injections, cleaning of teeth where bleeding is anticipated. Lower-risk dental procedures are defined as restorative dentistry, local anesthetic injections, intracanal endodontic treatments, placement of rubber dams, postoperative suture removal, placement of removable prosthetic or orthodontic appliances, taking of oral impressions, fluoride treatments, oral radiographs, orthodontic appliance adjustment, and shedding of primary teeth.17†AAOS = American Academy of Orthopaedic Surgeons, and ADA = American Dental Association. Including rheumatoid arthritis, systemic lupus erythematosus, other inflammatory polyarthropathy, or drug or radiation-induced immunosuppression17†. §Including patients with a previous periprosthetic joint infection, malnutrition, hemophilia, human immunodeficiency virus, type-I diabetes, or malignancy17†.

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)

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)

While this guideline recommends that practitioners may consider discontinuation of antibiotics before a dental procedure for patients with a prosthetic joint, it fails to identify low-risk dental procedures or patient characteristics. It also states that "patient preference should have a substantial influencing role" in the decision to discontinue antibiotics before a dental procedure.20. A Shared Decision Making tool, including four multiple-choice questions for the patient, is provided in conjunction with the clinical practice guideline.21

**Bacteremia from the Oral Cavity**

Bacteremia from the oral cavity is common and results from everyday oral activities such as toothbrushing, flossing, and chewing. In patients with healthy dentition, the frequency of oral bacteremia may be as high as 44% after toothbrushing21, 41% after flossing21, and 17% after chewing24,25. A meta-analysis and review by Tomás et al.26 explored the relationship between poor dentition and everyday oral bacteremia. Using the gingival index as a measure of dentition, those authors reported that the risk of bacteremia after toothbrushing was higher in patients with gingival disease (gingival index of >1.5) than in those with healthy gingiva (odds ratio [OR], 2.77 [95% confidence interval (CI), 1.50 to 5.11]; gingival index of 0 to 1.5 versus >1.5)26. The gingival index is measured by pressing a probe to determine the characteristics of the gingiva. It is measured on a scale of 0 to 3, with 0 corresponding to normal gingiva and 3 indicating severe inflammation and ulceration with spontaneous bleeding26.
In addition to everyday oral activities, oral bacteremia occurs because of dental procedures. The risk of bacteremia differs on the basis of the type of dental procedure that is performed; procedures that cause more movement of the tooth within its socket generally have a higher prevalence of bacteremia after the procedure. For example, dental extractions, periodontal procedures, and cleaning when bleeding is anticipated have a higher risk of bacteremia than do fluoride treatments, oral radiographs, and orthodontic appliance adjustments.

It is disconcerting that patients with poor oral hygiene have more frequent bacteremia due to everyday activities. The magnitude of bacteremia that is required to seed a prosthetic joint is not known. In addition, it is unknown if the magnitude or frequency of bacteremia contributes more to periprosthetic joint infections. Some orthopaedic practices have implemented dental evaluations before arthroplasty as a means to decrease oral bacteremia after arthroplasty. With this practice, patients would be required to obtain a dental evaluation and all recommended dental treatments prior to arthroplasty. It is unclear how many facilities have implemented this practice, and its effect on periprosthetic joint infections has not been well studied.

Antibiotics given before a dental procedure decrease the prevalence of oral bacteremia. In an excellent review, Tomás Carmona et al. analyzed the effect of prophylactic antibiotics on the prevention of endocarditis. Of the recommended antibiotics, oral amoxicillin has been studied most rigorously for the prevention of bacteremia after a dental procedure in controlled trials (Table III). Oral amoxicillin administered one hour prior to a dental procedure was found to decrease the risk of bacteremia by approximately 63%, from 73% to 26.7%. Oral clindamycin was found to decrease the risk of bacteremia by 15%, from 88% to 74.9%. Oral penicillin was found to decrease the risk of bacteremia by 49%, from 88.0% to 45.1%. Although oral penicillin has been reported to decrease the risk of bacteremia by just 32%, from 66.7% to 45.1%, intravenous or intramuscular penicillin decreased the risk of bacteremia by 68%, from 56.7% to 18.1%.

To our knowledge, neither oral cephalaxin nor cephradine has been studied in randomized controlled trials for the prevention of bacteremia with dental procedures. Parenteral ampicillin has not been widely studied for the prevention of bacteremia for dental procedures; only one study has described the rate of dental bacteremia after prophylactic intravenous ampicillin, which was found to be 17% (seven of forty-two patients). While parenteral clindamycin and cefazolin have not been specifically studied for this indication, they are antibiotics used extensively for preoperative prophylaxis.

**Bacteremia and Periprosthetic Joint Infections**

What Is the Magnitude of Bacteremia Required to Cause a Periprosthetic Joint Infection?

While everyday oral activities and dental procedures cause bacteremia, the magnitude of bacteremia is quite low. Studies have suggested that the magnitude is on the order of one to thirty-two colony-forming units per milliliter (CFU/mL) to one percent. The inoculum of bacteria required to cause clinically important bacterial disease in humans is unknown.

While the inoculum of bacteria required to cause periprosthetic joint infections in humans is unknown, animal models may provide an estimate. Zimmerli et al. studied the minimum Staphylococcus aureus inoculum required to induce tissue cage infection in guinea pigs. They found that 46 to 210 CFU of bacteria injected into the region of the foreign material was required to induce infection in >95% (forty-four) of the forty-six guinea pigs. Garrison and Freedman intravenously injected rabbits with Staphylococcus aureus and found that 10^6 CFU/mL of Staphylococcus aureus to induce native-valve endocarditis. More recently, Dubé et al. used an inoculum of 10^8 CFU/mL of Staphylococcus aureus to induce native-valve endocarditis in rabbits.

The prevalence of periprosthetic joint infection after Staphylococcus aureus bacteremia has been reported to be 34.1% (fifteen of forty-four patients), 38.7% (twelve of thirty-one patients), and 37.9% (eleven of twenty-nine patients). However, Staphylococcus aureus is among the most virulent bloodstream infections. In contrast, Uğay et al. estimated the risk of periprosthetic joint infection after any hematogenous infection to be 0.1%. Using these data as a guideline, we may hypothesize that any magnitude of Staphylococcus aureus bacteremia could cause periprosthetic joint infection in up to one-third of patients, while either high concentrations or prolonged durations, or both high concentrations and prolonged durations of bacteremia with less virulent organisms, would be required to cause periprosthetic joint infection.

**TABLE III Weighted Average in the Literature of Select Antibiotics Used Before a Dental Procedure and the Relative Decrease in Bacteremia at Five Minutes or Less after the Dental Procedure**

<table>
<thead>
<tr>
<th>Comparison*</th>
<th>Antibiotic Group (no. of patients)</th>
<th>Control or Placebo Group (no. of patients)</th>
<th>Odds Ratio (95% CI)t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin (oral) versus control</td>
<td>26.7% (86 of 322)</td>
<td>73.0% (303 of 415)</td>
<td>0.135 (0.097 to 0.187)</td>
</tr>
<tr>
<td>Clindamycin (oral) versus control</td>
<td>74.9% (149 of 199)</td>
<td>88.0% (139 of 158)</td>
<td>0.407 (0.223 to 0.725)</td>
</tr>
<tr>
<td>Penicillin V (oral) versus control</td>
<td>45.1% (51 of 113)</td>
<td>66.7% (84 of 126)</td>
<td>0.411 (0.244 to 0.695)</td>
</tr>
<tr>
<td>Penicillin G (IV or IM) versus control</td>
<td>18.1% (35 of 193)</td>
<td>56.7% (89 of 157)</td>
<td>0.169 (0.104 to 0.275)</td>
</tr>
</tbody>
</table>

*IV = intravenous, and IM = intramuscular. tCI = confidence interval.
Temporal Relationship Between Periprosthetic Joint Infections and Dental Procedures

A temporal relationship between periprosthetic joint infection and dental procedures has been widely reported in case reports and series although the relationship has not been confirmed in case-control studies.

Berbari et al. performed a single-center prospective case-control study to investigate the relationship between prosthetic hip or knee infections and dental procedures. The investigators enrolled 339 patients with prosthetic hip or knee infection and 339 corresponding control subjects. Dental procedures performed within six months or two years after the hospital admission date were not associated with an increased risk of periprosthetic joint infection. A second case-control study, using Medicare Current Beneficiary Survey data, showed similar results. Forty-two periprosthetic joint infections were identified from the data set, and investigators matched 126 control participants without periprosthetic joint infections. The hazard ratio (HR) for all dental procedures and the risk for periprosthetic joint infection suggested no association (HR, 0.50; 95% CI, 0.12 to 2.18). A subgroup analysis of patients undergoing high-risk dental procedures was also analyzed; no relationship was identified between the high-risk dental procedures and subsequent periprosthetic joint infections (HR, 0.78; 95% CI, 0.18 to 3.39).

Microbiologic Linkage Between Oral Flora and Periprosthetic Joint Infection

While case-control studies do not support a relationship between dental procedures and subsequent periprosthetic joint infections, the frequency at which oral bacteria cause periprosthetic joint infections as a result of everyday oral activities is unknown. Using small numbers of patients, a few authors have evaluated the microbiologic relationship between bacteria isolated from periprosthetic joint infections and bacteria in oral flora. Bartzokas et al. studied the microbiology of four patients with Streptococcus sanguis periprosthetic joint infections. The authors performed pulsed-field gel electrophoresis patterns of Streptococcus sanguis in the oral cavity and at the site of the infection around the prosthetic joints in four patients and found that the bacteria were identical in two patients and differed by just one band in the other two patients. Tamoin et al. extracted bacterial DNA from synovial fluid and gingival plaque in thirty-six patients with either rheumatoid arthritis or osteoarthritis. Nine of these patients had prosthetic joint replacements with clinically aseptic loosening; the others had native joints. Bacterial DNA was isolated from the synovial fluid of two of the nine patients with prosthetic joints, and bacterial DNA from the gingival sample was identical to that of the synovial fluid in one of the patients. Microbiologic studies to definitively link oral bacteria to bacteria from infections around prostheses, such as bacterial DNA analyses and pulsed-field gel electrophoresis, are not readily available in a clinical laboratory. It is certainly plausible that oral bacteria can cause periprosthetic joint infection, but the frequency of this occurrence is unknown.

Risk and Benefit Analyses of Antibiotics Before a Dental Procedure

It has been estimated that there are nearly 7,000,000 people with prosthetic joints in the United States. If we were to assume there is a 2% lifetime risk of periprosthetic joint infection, then there would be approximately 140,000 periprosthetic joint infections (7,000,000 × 0.02) among patients with a prosthetic joint. With 6% to 13% of periprosthetic joint infections being due to oral flora, we would expect 8400 to 18,200 of the periprosthetic joint infections to be secondary to oral bacteremia. Amoxicillin given before a dental procedure decreases oral bacteremia after dental procedures by 63%, and up to one-third of patients with bacteremia may develop a periprosthetic joint infection. If all periprosthetic joint infections secondary to oral bacteremia were caused by dental procedures, which we know is not the case, then amoxicillin given before a dental procedure could decrease the number of periprosthetic joint infections by between 1746 and 3784 cases ([8400 to 18,200] × 0.63 × 0.33) among patients with a prosthetic joint.

On the other hand, we assumed, on the basis of the most conservative estimates in the literature, that up to 2% of patients experience drug reaction or side effects, including Clostridium difficile infection, after oral antibiotics. Hence, we may infer that 140,000 patients (7,000,000 × 0.02) could be harmed by antibiotics given before a dental procedure. By this reasoning, thirty-seven to eighty patients (140,000/1746 to 3784) would experience an adverse antibiotic effect for every one prosthetic joint infection that was prevented by amoxicillin.

Unintended Consequences

There are a number of unintended consequences for the patient and health-care system that should be considered as a result of the increasing emphasis on requiring dental treatments for patients with periprosthetic joint infections. While some patients would have no difficulty scheduling and paying for dental evaluations and treatments, others, particularly the elderly and impoverished, would find obtaining dental evaluations and treatment to be a hardship. If a dental evaluation and treatment were required prior to arthroplasty, some elderly patients living below the poverty line and patients without dental insurance would have a delayed operative date for arthroplasty. This additional waiting time would be associated with a longer period of poor orthopaedic function, longer durations of potentially addicting pain medications, and increased preoperative deconditioning resulting in weight gain and associated complications such as hypertension and diabetes. The health-care system would be unnecessarily taxed with an increased demand for the already thin dental resources, particularly in so-called safety-net dental facilities. The expanded recommendation for antibiotics before a dental procedure for all patients who have had an arthroplasty would not only have an unfavorable balance of risks and benefits for the patients, but it also would lead to an unnecessary increase in pharmacy costs and potential medication interactions.
Overview
The number of patients who require arthroplasty to decrease pain and increase function is increasing exponentially. Dental disease in these patients is common. While bacteremia of oral origin may occur daily, it is generally of low magnitude. There is insufficient evidence to support the practice of requiring dental evaluation and treatment prior to arthroplasty; this practice is in need of research to evaluate its impact on peri-prosthetic joint infection. It has the potential to lengthen practice is in need of research to evaluate its impact on peri-

Case-control studies do not support a relationship between dental procedures and peri-prosthetic joint infections, and few studies have demonstrated microbiologic homology between bacteria found in periprosthetic joint infections and the oral cavity. Antibiotics given before a dental procedure decrease the risk of bacteremia after a dental procedure, but this is of uncertain clinical importance. The number of patients who would need to receive antibiotics before a dental procedure to prevent one potential peri-prosthetic joint infection from oral flora is far greater than the number of patients who would be harmed by these antibiotics; thus, it is reasonable to avoid antibiotics before a dental procedure in most patients after arthroplasty. The existing professional guidelines on this topic are inadequate. While collaborative decision making between patients and clinicians is important, the current AAO/S/ADA clinical practice guideline suggests that patients who have had an arthroplasty should ultimately make the decision to take or decline antibiotics before a dental procedure. Patients do not routinely choose whether they need antibiotics for sinusitis, bronchitis, and other conditions; clinicians use professional judgment to determine the likelihood of bacterial infection and its potential sequelae before prescribing an antibiotic. The same process should be used for antibiotics before a dental procedure for patients who have had an arthroplasty. On the basis of the available literature, we recommend avoidance of antibiotic prophylaxis before a dental procedure for the majority of patients who have had an arthroplasty.

References


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