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PERIODONTAL DISEASE, BACTEREMIA, AND ORTHOPEDIC SURGERY

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Abstract
The current literature in both dentistry and orthopedic surgery indicates a need for better collaboration between dental and medical professionals concerning the management of patients with orthopedic joint replacements. Although rare, joint prosthesis infections that emanate from oral bacteremias are potentially devastating. Prophylactic antibiotic treatment in patients at high risk for systemic complications from oral bacteremia has become the standard of care in dentistry; however, routine antibiotic prophylaxis is not recommended for patients who are not at risk. Given the virulent nature of the microbes associated with inflammatory periodontal disease and the potential for bacteremia, it is recommended that patients be evaluated by a dental professional prior to any elective joint replacement surgery.

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Key Words: Antibiotic prophylaxis, bacteremia, inflammation, orthopedic surgery, periodontal disease, prosthetic joint replacement

Introduction

The total population of the oral microflora of the human mouth has been estimated at 6 billion microbes.[1] This number includes approximately 140 taxonomic groups and 700+ different species, although it is unlikely that any one individual harbors more than 200 species.[2,3] It appears that at least 30 species participate in the inflammatory periodontal diseases, although this is likely an underestimate, as many microbes in the periodontal pocket remain uncultivated and uncharacterized.[4] However, the 30 known species have several factors in common: namely, most are gram-negative and anaerobic, and produce endotoxins and other antigens capable of eliciting a profound host immune response.[5,6]

Given the dense and diverse population of oral microbes, it should not be surprising that dental patients are subjected to periodic episodes of transient bacteremias of oral origins. Numerous reports have identified bacteremia in patients after dental treatment procedures such as extractions,[7] scaling,[8,9] periodontal probing,[10] suture removal,[11] orthodontic treatment,[12] restorative dentistry,[13] and nonsurgical endodontic therapy.[14] In addition, normal everyday activities such as mastication,[15] tooth brushing,[16] and dental flossing[17] have been associated with bacteremia. Both Roberts[18] and Guntheroth[15] have suggested that everyday events are more significant than dental procedures in the production of bacteremia. In fact, Guntheroth[15] has suggested that normal everyday activities may result in bacteremia for 90 hours per month, compared with 6 minutes for the average dental extraction.

Several articles have noted that patients with periodontal disease experience a greater incidence and magnitude of bacteremia than do those with a healthy periodontium.[10,19,20] Indeed, Forner and colleagues[19] report that among patients with chronic periodontitis, the magnitude of bacteremia is directly associated with the level of gingival inflammation (i.e., higher gingival and plaque index scores and a higher num-

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ber of sites with bleeding on probing). Interestingly, the authors found no relationship between probing depth and the magnitude of bacteremia, indicating that active inflammation, not the extent of periodontal attachment loss, is the more important of the 2 variables.

Hujoel and colleagues[21] estimated that the total surface area of diseased and ulcerated periodontal pocket epithelium can range from 8 to 20 cm^2, depending on the severity of periodontal disease. Obviously, epithelium ulcerated to this extent offers ample opportunity for connective tissue invasion by bacteria and/or their endotoxins, leading to bacteremia and endotoxemia. Bacteremia and endotoxemia have been implicated in a variety of systemic responses, such as altered platelet function and increased intravascular clotting, and also in synthesis of prostaglandins.[22] The localized inflammatory event of periodontal disease is also implicated in the systemic inflammatory response, leading to the production of acute-phase proteins by the liver (i.e., C-reactive protein, serum amyloid A, haptoglobin, and fibrinogen).[22-24] All of these systemic responses, in turn, may have varying degrees of impact on systemic diseases, including cardiovascular disease,[22,23] ischemic stroke,[22,23] diabetes,[25] adverse pregnancy outcomes,[26] and possibly dementia and Alzheimer's disease.[27]

Total joint arthroplasty

Periodontal disease may play a role in several systemic conditions, including diabetes, adverse pregnancy outcomes, and clinical problems, such as malnutrition related to masticatory problems, generally associated with older age groups (>65 years).[28] The practice of preventive dentistry has allowed more individuals to retain functional dentition into their elderly years. The paradox of this success is that these same individuals are exposed to the risk of periodontal disease while in an age group that accounts for a large percentage of total joint arthroplasty.[29] In the United States, for example, it is estimated that more than 500,000 total joint arthroplasties are performed annually.[30-32] The majority of such surgeries involve knee and hip joint prostheses in patients 50 years of age or older.[31,33] However, joint replacements in younger patients are being done with increased frequency as total joint component technology advances.

Prosthetic joint infections

Total joint replacement has a 10-year success rate of >90%,[34] yet failures do occur. Infection of a newly positioned joint prosthesis can be a devastating complication, resulting in significant morbidity, pain, loss of function, and possibly total failure requiring surgical revision and long-term antibiotic therapy. Infections involving prosthetic joint replacements are classified as *early* or *late*.[35] Early infections are defined as those occurring within 3 months after implantation surgery and generally result from the introduction of an infectious agent at the time of surgery.

Although the incidence of early periprosthetic sepsis is quite low, on the order of 0.39%,[36] the unreported incidence in the community setting, where most joint replacements are performed, is likely higher. The infection rate is also higher in revision surgery for worn out or failed, but noninfected joint replacements. Overall, the rate of infection for joint prosthetic surgery is generally <2%. One study[36] of 6,489 primary and revision total knee surgeries reported an infection rate of 1.8%.

Late or delayed infections of a total joint arthroplasty occur more than 3 months after surgery and are usually secondary to bacteremia. Interestingly, the incidence of late-occurring infections is also relatively low, generally <1%.[37] The 2 years after prosthetic joint placement are considered to be the most hazardous in terms of potential bacterial seeding of the implant site via the hematogenous route.[38] It has been suggested that enhanced vascularity of the surgical site during the 2 years of wound healing enhances the possibility of hematogenous seeding of bacteria.[39] However, in spite of the potential for infection, several articles have noted that the risk of a joint prosthesis becoming infected from bacteremia of oral origin is exceedingly low.[32, 39-42]

Most joint infections appear to be caused by *Staphylococcus aureus, Staphylococcus epidermidis*, or other coagulase-negative staphylococci.[43] The predominant oral microbes implicated in both endocarditis and septic prosthetic joints belong to the viridans (α-hemolytic) streptococci family (i.e., *Streptococcus mitis, Streptococcus oralis, Streptococcus gordonii, Streptococcus sanguis*, and *Streptococcus mutans*).[39-42] In addition to being α-hemolytic, all of the viridans streptococci are aerobic, gram-positive microbes. Pallasch and Slots[41] analyzed data from 6 studies and determined that roughly 66% of 281 bacteria isolated from prosthetic joint infections were staphylococci, but only 5% were classified as viridans streptococci.

The viridans streptococci and some gram-negative, anaerobic periodontal pathogens express virulence factors that facilitate their ability to promote infection. Such factors include expression of cell-wall adhesion molecules that allow adherence to host cells or the surface of implanted biomedical devices. In addition, both staphylococci and viridans streptococci are capable of complex biofilm formation with a characteristic extracellular matrix that, in turn, promotes microbial colonization and adherence to biomaterial surfaces, renders the biofilm resistant to penetration by antibiotics, and enables evasion of the

host immune response.[43,44] In general, bacteria involved in soft tissue infections are capable of producing leukotoxins and hemolysins, both of which facilitate destruction of host tissues.[43]

It is well established that infection, tissue necrosis, or invasive surgery can be triggering factors that stimulate macrophages, fibroblasts, endothelial cells, and other host cell types to produce and release a variety of inflammatory cytokines.[45] Infection of prosthetic joints may also involve the localized production and release of inflammatory cytokines (e.g., interleukins 1, 6, and 8, and tumor necrosis factor α), prostaglandins, and host-cell enzymes, specifically the matrix metalloproteinases (e.g., collagenase, elastase, and gelatinase), all of which may promote inflammation-mediated destruction of connective tissue and bone.[43-46]

Orthopedic infections resulting from bacteremia of oral origin are rare, yet common sense would seem to dictate that the time, energy, and money spent preventing prosthetic joint infection is likely more effective than that expended in treating an established infected joint.[29] Thus, 3 questions arise: 1) What are the responsibilities of the dentist and orthopedic surgeon regarding prevention of infection before and during surgery? 2) What are the conditions for prescribing antibiotics for prophylaxis and treatment of patients with existing joint prostheses? 3) What are the responsibilities of the dentist and orthopedic surgeon regarding collaborative treatment of patients prior to and after joint replacement?

Collaborative treatment prior to and after joint replacement

The mutual responsibilities of the dentist and orthopedic surgeon are to reduce the incidence of dental bacteremia-related total joint sepsis by providing collaborative antibiotic prophylaxis and treatment of patients requiring joint replacement. Close collaboration regarding both the treatment of existing oral infections prior to joint surgery and the use of antibiotic prophylaxis after placement of a joint prosthesis is crucial for providing optimal care for the orthopedic surgery patient.

Prosthetic total joint infection is a catastrophic surgical complication. Routine surgical clearance to prevent complications from other organ systems is normally required preoperatively and often includes evaluations by subspecialists such as internists and cardiologists. One of the few absolute contraindications to total joint arthroplasty is a pre-existing focus of infection elsewhere.[47] Patient dental history is unreliable, and the orthopedic preoperative checklist historically has not included a documented risk of perioperative dental bacteremia. Prevention of total joint infection from exogenous sources typically receives a great deal of attention, unlike surveillance and correction of endogenous sources of bacteremia. Preoperative collaboration should take the form of a dental evaluation and clearance prior to total joint replacement to minimize this source of sepsis.

Dental clearance can be documented with a simple form that can be sent via facsimile or e-mail by the patient's dentist to the orthopedic surgeon. Patients who have received a complete dental examination within 6 months prior to surgery should easily obtain dental clearance. In the authors' experience, a substantial portion of patients needing joint replacement have not had regular dental care. These patients require dental examination and correction of sources of bacteremia prior to clearance for joint replacement surgery. Occasionally extensive preoperative dental procedures are required for patients who have neglected routine dental care.

For the first postoperative year, antibiotic prophylaxis is recommended prior to all dental manipulations except routine cleanings. After the first year, antibiotic prophylaxis is required only for "high-risk" procedures, such as extraction or root canal, that cause bleeding. Dental-related antibiotic prophylaxis in patients not allergic to penicillin should include cephalexin, cephradine, or amoxicillin in a dose of 2 g given 1 hour prior to the dental procedure. For patients allergic to penicillin, clindamycin 600 g should be given 1 hour prior to the dental procedure.[48,49]

Patients who have received a joint prosthesis should be seen on a regular basis for routine dental care. It is well known that periodontal disease is related to bacteremia that may feature a wide variety of microbes, both aerobic and anaerobic. Thus, to reduce the risk of bacteremia of oral origin, patients with an orthopedic prosthesis should be free of inflammatory periodontal disease. To ensure the least possible risk for the patient, the dentist and orthopedic surgeon should maintain an open line of communication, with each clinician emphasizing to the patient the importance of good oral hygiene and dental care. Although infection from periodontal pathogens may be rare, the occurrence of an infected prosthetic joint can have a devastating impact on the patient.

Prior to scheduling any joint replacement surgery, the patient should be examined to assess periodontal health, and appropriate treatment completed as necessary. The orthopedic physician must have a working knowledge of periodontal diseases, their diagnoses, and various modalities of treatment. More specifically, the orthopedic physician must understand that periodontal therapy to control oral bacterial loads and inflammation can require either surgical or nonsurgical treatment, may involve systemic or localized delivery of antibiotics, and is likely to involve

a significant amount of time. Indeed, the treatment of inflammatory periodontal disease requires a minimum of 4 to 6 weeks, and should include intensive patient education to maintain the health of the periodontal tissues. Except for cases of trauma, joint replacement surgery is generally an elective procedure and can usually be delayed until the patient has consulted with a dentist and/or periodontist and completed the treatment required to establish an oral cavity free of infection and inflammation. After completion of periodontal therapy, the dentist/periodontist should document the patient's oral health, including any potential problems, and consult with the orthopedic surgeon before joint replacement surgery is scheduled.

Once joint replacement surgery is approved and scheduled, responsibility then shifts to the surgical staff to prevent surgery-related infection. Guidelines promoted by the Patient Safety Committee of the American Academy of Orthopedic Surgeons[50] have been organized in an "outside-to-in" concept of environmental control that includes the operating room environment, the patient environment, and the wound environment.

Guidelines for the operating room environment include maintaining positive air pressure in the conventional operating room, with more than 15 volume exchanges per hour.[50] Despite decades of experience with clean-air operating rooms, no uniform methods for efficiently preventing infections have been developed. However, laminar flow statistically reduces airborne contamination, and body exhaust suits, in combination with other infection control measures, also appear to improve infection rates. Use of scrubs, masks, and gloves and sterilization of all surgical instruments should follow published guidelines. Ethylene oxide has been classified as a carcinogen and is being replaced by H_2O_2 sterilization procedures. Operating room doors should remain closed and needless traffic, activity, and personnel eliminated. Strict adherence to operating room discipline and Universal Precautions should be maintained. Hand washing with soap and water is highly effective in preventing nosocomial spread of organisms. Newer alcohol and chlorhexidine gluconate-based hand lotions appear to provide more effective antisepsis than standard scrub and are recommended in the absence of visible soiling. In addition, healthcare personnel are more likely to comply with hand hygiene procedures if surgeons, senior medical staff, and peers are seen to be compliant.

Maintaining the optimal patient environment includes monitoring and maintenance of normal glycemia, normothermia, and administration of antimicrobial prophylaxis.[50] The initial dose of the appropriate antimicrobial should be given within 1 hour preceding incision, and repeated during surgery as needed to maintain blood levels. Antimicrobial prophylaxis should be ceased within 24 hours, even if catheters or drains are still in place. Protection of the wound environment includes hair removal with an electric shaver or depilatory (not a safety razor) just prior to surgery, and proper skin preparation of the surgical field with alcohol, povidones, iodophors, or chlorhexidine gluconate. As much as possible, operative time should be minimized, tissue handled gently, and dead space and tissue eradicated. Whether to drain to reduce the risk of hematoma is questionable, because it raises concern regarding tract drainage, creates a potential passageway for infection, and increases transfusion requirements. There is no evidence that antibiotic irrigation is effective in prophylaxis for infection in orthopedic procedures.

Antibiotic prophylaxis and treatment in patients with joint prostheses

Dentistry has successfully implemented, and accepted as the standard of care, the recommendations of the American Heart Association[51] that antibiotic prophylaxis be provided for those patients at risk of developing adverse systemic problems as a result of bacteremia caused by oral tissue manipulation. In at-risk heart patients, the low incidence of complications from dental procedure-related bacteremia is the result of good communication among patients, cardiologists, and dentists.

Figure 1

Severe infection of a hip prosthesis occurring several years after placement as a result of bacteremia. Based on patient's dental history, the bacteremia had a high probability of oral origin.

The problem of antimicrobial prophylaxis in orthopedic implant surgery will become increasingly important and complex as the general population ages and requires more arthroplasty procedures. Given the low rate of prosthetic joint infection from bacteremia of oral origin and the fact that such bacteremia is transient and, for most dental procedures, of low magnitude,[19] one must conclude that the prescribing of prophylactic antibiotics for patients with an existing joint prosthesis is based on anecdotal, historical, and legal concerns. However, infection, should it occur, can be devastating to the patient and require additional surgeries, lengthy recovery time, and additional medical expenses (Figure 1). Despite this, some authors have proposed that the risk of adverse reaction to the antibiotic prophylaxis is greater than the risk of infection.[39,52-55] Statistically, it has been estimated that 30 of every 100,000 patients

Table 1: Guidelines for prophylactic antibiotics in patients at increased risk of hematogenous total joint infection

Patients at High Risk for Total Joint Infection, for Whom Antibiotic Prophylaxis is Recommended

- All patients during the first 2 years after prosthetic joint replacement
- Patients who are immunocompromised or immunosuppressed, as a result of the following:
  - Inflammatory arthropathies (e.g., rheumatoid arthritis, systemic lupus erythematosus)
  - Drug-induced immunosuppression
  - Radiation-induced immunosuppression
- Patients with the following comorbidities:
  - History of previous prosthetic joint infection
  - Malnourishment
  - Hemophilia
  - Human immunodeficiency virus infection
  - Insulin-dependent diabetes (Type I)
  - Malignancy

undergoing total joint replacement experience a late infection requiring treatment; by contrast, if all 100,000 patients were prescribed prophylactic antibiotics, 40 cases of anaphylaxis and 4 deaths would be incurred.[52]

In spite of such statistical observations, the American Dental Association (ADA) and the American Academy of Orthopedic Surgeons (AAOS) have published antibiotic prophylaxis guidelines.[48] Furthermore, the AAOS and the American Urological Association (AUA) performed a thorough review of all available data to determine the need for antibiotic prophylaxis to prevent hematogenous prosthetic joint infections in urological patients who have undergone total joint arthroplasties. Similar to the advisory statement issued jointly by the AAOS and ADA, the AAOS and AUA issued an advisory statement[49] that has been adopted by both organizations. The guidelines do not recommend the routine use of antibiotic prophylaxis for most dental patients with total joint arthroplasty. Instead, antibiotic prophylaxis is considered for selected at-risk patients (Table 1).[48] In making the decision to provide antibiotic prophylaxis prior to dental treatment in patients with an existing joint prosthesis, the clinician must accurately assess the level of oral disease, type of treatment required (See Table 2 entitled *Stratified Risk for Bacteremia, by Dental Procedure,*[48] which may be accessed and downloaded from the *Clinical Decision-Making Tools* section at www.thesystemiclink.com), risk of bacteremia, potential risk of prosthesis-related infection, associated secondary risk factors (e.g., diabetes, immunocompromised status, obesity, and smoking),[36] type of antibiotic indicated (See Table 3 entitled *Suggested Antibiotic Prophylaxis Regimens,*[48] which may be accessed and downloaded from the *Clinical Decision-Making Tools* section at www.thesystemiclink.com) and its spectrum of action, and the potential for adverse side effects. Applications of these guidelines are not part of the orthopedic surgeon's skill set. Orthopedic surgeons must rely on dental assessment and application of these guidelines to prevent total joint infections from oral bacteremia.

In addition, the clinician must be aware of the potential for bacteremia resulting from untreated oral disease. Ching and colleagues[56] have reported 4 cases of late infection of joint prostheses with *Streptococcus viridans* in patients with poor oral health. An additional 4 cases, reported by Bartzokas and colleagues,[57] involved *S. sanguis*-mediated late joint infections in patients with documented oral sepsis and poor oral hygiene. The evident implication of this small series of case reports is that prevention and/or treatment of oral disease and good oral hygiene are a requisite of good orthopedic surgery and dental practice. Performing total joint arthroplasty only in patients without chronic dental bacteremia is good practice, as is preventing dental procedure-related bacteremia in patients with existing total joint prostheses.

Conclusion

The current literature in both dentistry and orthopedic surgery indicates a need for better collaboration between dental and medical professionals concerning the management of patients with orthopedic joint replacements. Although rare, joint prosthesis infections that emanate from oral bacteremias are potentially devastating to patients and can result in failure of the prosthesis and the need for revision surgery. Antibiotic prophylaxis of patients at high risk for systemic complications from oral bacteremia has become the standard of care for dentistry and appears to be a satisfactory approach to management of such patients; however, routine antibiotic prophylaxis is not recommended for patients who are not at risk. Given the virulent nature of the microbes associated with inflammatory periodontal disease and the potential for bacteremia, it is recommended that patients be evaluated by a dental professional prior to any elective joint replacement surgery. The collaborative effort between the dental professional and the orthopedic surgeon should continue subsequent to joint replacement surgery, as an ongoing measure to promote proper healing. Further research is needed to verify the severity and frequency of joint replacement infections caused by oral bacteremias, and to determine the degree of protective benefit derived from antibiotic prophylaxis.

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