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Should patients with hip joint prosthesis receive antibiotic prophylaxis before dental treatment?

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The safety committee of the American Academy of Orthopedic Surgeons (AAOS) recommended in 2009 that clinicians should consider antibiotic prophylaxis for all patients with total joint replacement before any invasive procedure that may cause bacteremia. This has aroused confusion and anger among dentists asking for the evidence. The present review deals with different aspects of the rationale for this recommendation giving attention to views both in favor of and against it.

Keywords: *hip joint prosthesis*; *oral bacteria*; *antibiotics*; *antibiotic prophylaxis*; *dental treatment*

It has been estimated that by 2030 almost four million primary total hip arthroplasty and total knee arthroplasty procedures will be carried out annually in the USA (1). Prosthetic joint infection is a rare, but well-recognized complication of these procedures, causing significant morbidity and mortality (2, 3). Deep infection has the potential to become the most frequent failure mode for total hip arthroplasty and total knee arthroplasty in the USA within the next two or three decades (4). The financial cost of each infection episode is 3–4 times the cost of a primary joint arthroplasty, usually exceeding US$50,000 (5). Whether dental procedures increase the risk for infection of joint prostheses through bacteremia has been debated for almost 30 years (6), the controversy has never been solved (7). The American Academy of Orthopedic Surgeons (AAOS) and the American Dental Association (ADA) recognized the confusion around this problem and established expert panels in 1997 and 2003. The panels recommended that routine antibiotic prophylaxis for dental procedures in patients with a prosthetic joint should not be administered, and that it should be considered only in selected patients with total joint arthroplasty who undergo high-risk dental procedures (8, 9). Recently, however, the safety committee of the AAOS gave new information on its web site, recommending that clinicians should consider antibiotic prophylaxis for all patients with total joint replacement before any invasive procedure that may cause bacteremia (10). This recommendation has aroused

confusion and anger among dentists asking for the evidence (11), and it has been characterized as irresponsible and indefensible (12). Uçkay et al. (13) reviewing the literature, found that the requirement for antimicrobial prophylaxis before dental treatment in patients with artificial joints lacks evidence-based information and cannot be universally recommended. The present review will deal with different aspects of the rationale for this recommendation, trying to give attention to views both in favor of and against it. Data were collected from a PubMed research focusing on the most recent publications in the field using different key words.

Stages of infected implants

Orthopedic implant infections are generally classified as early, delayed or late (14). The micro-organisms associated with these different stages are given in Table 1. Early infections are mainly presumed to be the result of intraoperative contamination of the surgical site and are frequently caused by higher grade pathogens such as *Staphylococcus aureus* including methicillin-resistant strains. Beta-hemolytic streptococci and anaerobic Gram-negative rods can also be detected. Delayed infections, however, are more often caused by coagulase-negative staphylococci (CNS) and other skin commensals. These infections can also be caused by intraoperative contamination or by hematogenous spread. Clinical symptoms here are pain and swelling. Late infections appear more than 12 months postoperatively and are

Table 1. Different stages of infected implants with corresponding bacteria[a]

Early infection (up to 3 months)	Staphylococcus aureus
	Coagulase-negative staphylococci
	Aerobic Gram-negative rods
	Beta-hemolytic streptococci
Delayed infection (4–12 months)	Coagulase-negative staphylococci
	Other skin commensals
	S. aureus
Late infection (including hematogenous seeding)	Coagulase-negative staphylococci
	Other skin commensals
	S. aureus
	Aerobic Gram-negative rods
	Anaerobes
	Mycobacterium tuberculosis

[a]Adopted from Ref. (14).

mostly caused by Gram-positive skin commensals that have chronically infected the prosthesis since implantation. Importantly, they also include cases of hematogenous seeding with organisms causing bacteremia.

Oral species most frequently associated with hip joint infection

The most frequently detected organisms in joint infections as such are staphylococci. According to Geipel (15), S. aureus dominates in acute purulent arthritis while CNS are found mainly in periprosthetic infections and after diagnostic arthroscopies. Antibiotic-resistant staphylococci may occasionally compromise the treatment outcome of prosthetic joint infections (16). Most authors think that staphylococci are not common parts of the oral microbiota and that the oral cavity therefore plays no major role in total hip joint infections. However, according to Smith et al. (17), making a comprehensive review, staphylococci can frequently be found in the oral cavity, and this site may serve as a potential reservoir for transmission to other body sites (18). According to these authors, oral species such as staphylococci and streptococci are most frequently associated with prosthetic hip or knee joint infection. In a recent study from the Mayo Clinic (6), beta-hemolytic streptococci, Peptostreptococcus species, Actinomyces species, viridans group streptococci, Abiotrophia/Granulicatella species and Gemella species from 339 cases with prosthetic hip or knee joint infection isolated in 2001–2006 were considered as potential oral or dental organisms for such infection. They constituted 35 (10.3%) of the prosthetic hip or knee infections. However, S. aureus and CNS, that comprised 58% of the isolates, were not listed as potential oral pathogens. LaPorte et al. (19) reviewed the records of 2,973 patients with total hip arthroplasty. Of the late infections in 52 patients, three (6%) were strongly associated with dental procedures. 'Streptococcus viridans' was recovered from two patients and Peptostreptococcus from one. The authors suggested that infection of a total hip arthroplasty after dental procedures is more common than previously thought and that patients with systemic disease, or who are undergoing extensive dental procedures, should be considered for antibiotic treatment. Maderazo et al. (20), reviewing 67 infections developing more than 1 year after arthroplasty, found that the most common site of origin for the infectious agents was the skin and soft tissues (46%), followed by the mouth (15%) and the urinary tract (13%). The most common pathogens responsible for late prosthetic joint infections were staphylococci (54%), both S. aureus and Staphylococcus epidermidis, even when the infection was of dental origin. Generally, anaerobes such as Bacteroides fragilis are rarely found and usually as parts of a polymicrobial infection (15). The importance of oral anaerobes in prosthetic joint infections is therefore unclear.

To what extent do we find staphylococci in the oral cavity?

There is considerable controversy as to whether Staphylococcus species play a role in the ecology of the normal oral flora, and there is surprisingly little knowledge on the role of staphylococci in oral health and disease. It has been claimed that S. aureus and S. epidermidis constitute only 0.005% of the oral microbiota (21). However, a growing body of evidence suggests that staphylococci can be isolated more frequently from the oral cavity of some patient groups such as children (22), elderly (23), terminally ill patients (24), rheumatoid arthritis patients (25), and patients with hematological malignancies (26). Therefore, the oral cavity may represent a hitherto poorly recognized reservoir of staphylococci, which under the right conditions may cause local or systemic infection (17).

Contributing to additional insight into the oral cavity as a reservoir for staphylococci, a Japanese study among 56 systemically and periodontally healthy adults 22–43 years of age, recovered nine different Staphylococcus species (27); 334 isolates were found in saliva and supragingival plaque. Staphylococci have also been reported from periodontitis (28–30). Murdoch et al. (31) isolated staphylococci from 54% of diseased subgingival and 43% of healthy subgingival sites in over 50% of periodontitis patients ($n = 28$) and from 29% of healthy subgingival sites in 54% controls ($n = 28$). Rams et al. (32) found subgingival staphylococci in approximately 50% of gingivitis and periodontitis patients. After systemic doxycycline therapy of 21 adult periodontitis patients, more than a 10-fold increase was observed in subgingival numbers of Enterobacter aerogenes (two patients),

Escherichia coli (one patient), *Candida albicans* (82 patients), and staphylococci (11 patients) (33).

Significantly higher proportions of staphylococci were recovered from periimplantitis lesions (15.1%) compared to gingivitis (0.06%) and periodontitis (1.2%), and it was suggested that staphylococci may play a role in some failing osseointegrated dental implants (32). Another study with 37 patients with failing implants detected staphylococci, organisms associated with the gut (*Enterococcus faecalis, E. aerogenes, Klebsiella* species, *E. coli*) and *Candida* species in 55% of peri-implant lesions and almost as frequently as periodontopathogens (34). Implants surrounded by healthy periodontium ($n = 51$) had a microflora compatible with microbial health.

Increased carriage rates of *S. aureus*/staphylococci have been demonstrated in denture-wearing patients, and denture-induced stomatitis was associated with increased amounts of staphylococci in the saliva and the oral mucosa (35–37). From angular cheilitis of 64 patients, *S. aureus* was isolated at a rate of 62.5% (38). Daniluk et al. (39) detected *Staphylococcus* species far more frequently in denture plaque from diabetics compared to non-diabetics ($p < 0.05$), and they were isolated more often from denture plaque, palate, and tongue dorsum in patients with cancer compared to those without ($p < 0.05$).

Staphylococci have also been isolated from periodontitis in diabetic patients (29) and from acute periodontal abscesses in immunocompromised patients (40). Also, patients with rheumatoid arthritis and xerostomia receiving long-term immunosuppressive treatment had large amounts of *S. aureus* on tongue and in oropharynx (25, 41).

Staphylococci have been reported as the sole isolate from aseptically opened infected root canals (42). The authors argued that the possibility of oral staphylococci causing acute exacerbations of root canal infections or bacteremias should not be overlooked. In support of this statement, staphylococci were recovered from intraoral acute infections (18, 43, 44). They were amongst the most common bacteria isolated from head and neck space infections of odontogenic origin (45). In addition, patients with odontogenic infections resulting in swelling of the face/throat demanding extraoral drainage, yielded *S. aureus* and CNS in a polymicrobial environment (46).

S. aureus has further been recovered from jaw cysts (47) and oral mucosal lesions (34).

Elderly healthy persons (≥ 70 years) had a higher frequency of staphylococci in saliva than younger persons (48). This suggested age-related changes in the oral microflora particularly after the age of 70. Elderly persons in institutions also had significantly more oral staphylococci than persons of the same age living in their own homes (49).

In addition, staphylococci/micrococci were present in the dental operation area constituting 15.7% of the total bacterial isolates (50). Staphylococci together with streptococci were the most common organisms in rooms with restorative dentistry (51).

From a regional diagnostic oral microbiologic laboratory, a hand search of laboratory records from 5,005 specimens during 1998–2000 revealed *S. aureus* in 1,017 specimens, of which 5% contained isolates resistant to methicillin (18).

In contrast to the reports above, there is a general view that staphylococci, particularly CNS are not usually found in the oral cavity (Morris and Howie (12), Blomgren et al. (52, 53)).

What *Staphylococcus* species are most frequently reported from the oral cavity?

S. epidermidis and *S. aureus* are most frequently reported in oral samples. In addition, *Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus warneri, Staphylococcus capitis, Staphylococcus saprophyticus, Staphylococcus xylosus*, and *Staphylococcus simulans* have been isolated (28, 32).

Interpretation problems

Most studies used selective agar to culture *S. aureus* from clinical specimens. Very few authors reported the actual numbers (cfu/ml) of staphylococci isolated and few longitudinal studies have been performed. This often makes it difficult to determine whether the staphylococci isolated have a role in the disease or belong to the transient microflora (17). The high virulence of *S. aureus* may involve a low threshold for causing disease, particularly in compromised patients. An oral disease where *S. aureus* clearly has been incriminated is a severe form of mucositis in patients with orofacial granulomatosis and Crohn's disease (54) and in elderly dehydrated patients (23) where treatment with anti-staphylococcal agents led to a marked clinical improvement.

Can staphylococci and other oral bacteria reach hip joints?

The frequency of bacteremia after dental procedures is high (55). Guntheroth (56) found that transient bacteremia also occurs in up to 51% of individuals following routine daily activities such as chewing and in up to 50% after tooth brushing or oral irrigation. Dental flossing can cause bacteremia in periodontally healthy and periodontally diseased persons at a rate comparable with that caused by some dental treatments for which antibiotic prophylaxis is given to prevent infectious endocarditis (57). A number of different bacterial species from the mouth have been detected in bacteremias after a single tooth extraction (58) and transient bacteremia after dental procedures has been suggested to be the

source of infection in total joint arthroplasties. Uçkay et al. (13) conducted a PubMed search of the literature to identify articles in the English, French, and German language before 1 July 2007. They retrieved 144 articles and found that many cases had been suggested where infection of a joint replacement had an oral origin, but efforts to record genetically identical strains in the mouth and joints had not been made. LaPorte et al. (19) reported that a review of the literature had identified more than 30 cases of late infection in arthroplasties in which bacteria might have originated from the oral cavity, although in many cases there was no clear proof for this. Interestingly, Bartzokas et al. (59) found that *Streptococcus sanguinis* strains from the mouth were indistinguishable from those on infected prostheses in four patients assessed by antibiograms and cell wall polypeptides. Jacobsen and Murray (60) reviewed 33 cases of infected hips out of 1,855 hip prosthesis replacements and found that the risk of infection associated with dental procedures was extremely low (0.05%). *S. aureus* was the most frequently isolated organism from infected hips and its incidence was twice as high in the late (>6 months after replacement) as in the early (<6 months after replacements) infections. In a literature review of 23 cases of late prosthetic joint infection where the source of infection was suggested to be the oral cavity due to treatment or infection, 10 cases (43%) were caused by *Staphylococcus* species, the most common being *S. aureus* (eight cases) (61). According to Deacon et al. (62), *S. epidermidis* has been implicated in 7% of infections related to a dental procedure, but the evidence linking late infections around a prosthetic joint to a specific dental procedure is ambiguous at best. Berbari et al. (6) argued that reported prosthetic joint infections are more likely to be caused by bacteremia related to routine daily activities than to bacteremia caused by dental procedures. This emphasizes the importance of maintaining good oral hygiene and eradication of oral disease to prevent bacteremia. Bacteremias probably have greater clinical significance in the immunocompromised patient than in the healthy subject (17). It is well known that anti-cancer drugs are cytotoxic and may cause ulceration of the oral mucosa as a side effect. This ulceration may be an entrance point for oral bacteria so that they can reach the blood circulation. In a 15-year old bone marrow transplant patient, *S. epidermidis* and *Streptococcus oralis* were cultured from the blood stream (63). Pulsed field gel electrophoresis of *Sma*I chromosomal DNA digests indicated that the mouth was the source of both isolates while the site of venous access was negative, but it was responsible for subsequent episodes of staphylococcal bacteremia.

After insertion of a hip joint prosthesis, part of the synovial membrane may be retained. Interestingly, synovial inflammation in active rheumatoid arthritis and psoriatic arthritis was suggested to facilitate trapping of a variety of DNAs from oral bacteria (64, 65). Although staphylococci were not examined, these studies suggested that DNA from oral bacteria can reach joints and that there can be a perpetuating effect of oral pathogens in joint disease. In a report by Fe Marqués et al. (66), septic arthritis of the knee occurred due to *Prevotella loeschei* 48 h after tooth extraction. Presence of an active antibody response in synovial tissue also illustrated a potential connection between periodontal and joint diseases (67). Individuals with rheumatoid arthritis had a higher prevalence of *S. aureus* in the oral cavity compared to gender-matched controls (25). A significantly higher portion (56%) of patients with rheumatoid arthritis carried oral *S. aureus* than controls (24%) ($p < 0.05$) (17). Many rheumatoid arthritis patients have dry mouth resulting in a significant change in the oral microflora as seen in Sjögren's syndrome (68), and are often subjected to immunosuppressive or cytotoxic treatment. Over the last decade, a number of publications have demonstrated that throat carriage of *S. aureus* is quite common. A significant number of persons carrying *S. aureus* in the nose are also throat carriers. In fact, some papers report throat carriage to be more frequent than nasal carriage (69–71).

Can methicillin-resistant *Staphylococcus aureus* (MRSA) occur in the oral cavity?

According to Small et al. (72), the oral cavity can be an overlooked site for methicillin-resistant *Staphylococcus aureus* (MRSA). This may have implications for how to treat an orally induced joint infection. Among children (0–5 years) attending a pediatric department, 84% carried *Staphylococcus* species; 6% of *S. aureus* were MRSA (22). Acute parotitis caused by MRSA has been reported in elderly patients (73, 74). Dentures may carry MRSA (37, 75–78). Staphylococci colonizing the oral cavity may serve as a potential reservoir for transmission of MRSA to other body sites, possibly hip joints, or cause cross-infection in other patients or health care workers.

Recommending antimicrobial prophylaxis

Of total knee joint replacements in 3,490 patients treated between 1982 and 1993, 0.2% resulted in infection that was considered strongly associated with dental procedures (79). Five of the nine patients with infections related to dental procedures had systemic risk factors that predisposed to infection. The authors held that patients with a total knee arthroplasty, undergoing extensive dental procedures, who have systemic disease that compromises host defense, should receive a prophylactic antibiotic. According to Geipel (15), antibiotic prophylaxis during dental procedures are useful in order to prevent late-onset prosthetic infection. LaPorte et al. (19) suggested that infection of a total hip arthroplasty

after dental procedures is more common than previously suspected and that patients with systemic disease, or who are undergoing extensive dental procedures, should be considered for antibiotic treatment. Jaspers and Little (80) recommended that dental practitioners who treat patients with arthroplasty should consult with and follow the recommendations of the orthopedic surgeon regarding antibiotic prophylaxis. As mentioned previously, the AAOS 2009 statement (10) recommends antibiotic prophylaxis before any invasive procedure that may produce bacteremia regardless of the length of time after the total joint replacement surgery. The ADA/AAOS recommendation from 2003 (9) concluded that antibiotic prophylaxis is neither indicated for dental patients with pins, plates or screws, nor that it is routinely indicated for most dental patients with total joint replacements. Prophylaxis should only be considered in the small number of patients who may be at potential increased risk of hematogenous total joint infection. Friedlander (81) emphasized that the oral microbiota is more diverse than previously thought and that it is altered by age and related changes in immune competence, gender, underlying illness, medication, salivary flow, and wearing of dental prostheses. It therefore logically follows that invasive dental procedures may cause both *Staphylococcus* and *Streptococcus* bacteremias which have been implicated in late joint infections. According to this author the claim that *S. aureus* and *S. epidermidis* make up only 0.005% of the oral flora is an underestimation of staphylococci in the oral cavity of individuals without and with dental infection, and it also underestimates the significant role of streptococci in late infections of total joint prosthesis. Also, Wijngaarden and Kruize (82) recommended antibiotic prophylaxis, particularly for patients with risk factors such as rheumatoid arthritis and hemophilia. The reported incidence of late infections after dental procedures may be underestimated by the high rate of antibiotic prescription in the past and the difficulty in establishing the origin of late infection. Podbielski et al. (83) found that the causality of professional dental procedures for prosthesis infections has never been conclusively demonstrated, e.g. by molecular methods. However, the association remains plausible and the consequences for the patients are severe. Patients with systemic disease or those undergoing intensive procedures should be considered for antibiotic prophylaxis (19). According to these authors, infection of a total hip arthroplasty after dental procedures is more common than previously suggested. Interestingly, a healthy man having undergone revision hip arthroplasty 11 months previously developed acute signs of infection of the hip prosthesis with an oral organism 30 h after non-invasive supragingival dental cleaning performed without antibiotic (84). Antibiotic prophylaxis during dental procedures or genitourinary tract and gastrointestinal tract interventions are useful to prevent late-onset prosthetic infection (85). Norden (86) advocated that for routine dental work on most patients with total joint replacement there is insufficient evidence to support antibiotic prophylaxis. However, for individuals with periodontal disease or potential dental infection, antimicrobial prophylaxis seems indicated. Maderazo et al. (20) argued that mortality and cost calculations indicate that chemoprophylaxis is justified for dental procedures and probably also for other surgical procedures in organs containing microflora. Tomás et al. (87) recommended routine use of an 0.2% chlorhexidine mouthwash before dental extractions to reduce the risk of postextraction bacteremia. Also, oral health care may have beneficial effects on the oropharyngeal microflora. Thus, the total levels of oropharyngeal organisms such as streptococci, staphylococci, *Candia*, *Pseudomonas*, and black-pigmented *Bacteroides* decreased or disappeared after weekly professional oral health care (88).

Rejecting antibiotic prophylaxis

There are more authors rejecting antibiotic prophylaxis before dental treatment of patients with hip prosthesis than those recommending it. A recent note by Morris and Howie (12) called recommendations for antibiotics in patients with joint prosthesis irresponsible and indefensible. They claimed that the organisms most responsible for both early and late prosthetic joint infection are *S. aureus* and CNS, both uncommonly found in the oral cavity. Since only 0.05–0.2% of late prosthetic joint infections are related to dental procedures, dentists by prescribing antibiotics may confer more harm than benefit to their patients (13). In an editorial, Assael (89) held that only a small proportion of bacteremias from an oral source are associated with dental treatment and that it would not be reasonable to recommend that millions of patients be medicated at enormous costs depending upon a few case reports. van der Bruggen and Mudrikova (90) argued against antibiotic prophylaxis because randomized placebo-controlled trials supporting this is lacking, and Bauer et al. (91) maintained that antibiotic therapy is not indicated for routine dental care in the majority of patients but is recommended whenever there is a high risk of arthroplasty contamination. They also claimed that the most important objective is to obtain and maintain a good state of oral hygiene to prevent bacteremia. Lockhart et al. (21) selected eight groups of patients with specific medical conditions and devices who often are given antibiotic prophylaxis before undergoing dental procedures: natural heart valves, prosthetic heart valves, pacemakers, renal dialysis and cerebrospinal fluid shunts, and hip, knee, and shoulder prosthetic joints. They searched the literature from 1966 through 2005 and found little or no evidence for the use of antibiotics

before dental procedures for these eight groups of patients. In an invited commentary for *Special Care Dentistry*, Marek and Ernst (11) argued against the recent recommendation of AAOS that healthcare providers should consider antibiotic prophylaxis prior to any invasive procedure performed on all patients with total knee or hip replacements, regardless of the age of the joint arthroplasty or the patient's medical history, asking for the evidence. Napeñas et al. (92) pointed out that the new statement by AAOS from 2009 has not been developed collaboratively with the ADA, as was the case in the previous statement of 1997 and revision in 2003. The 2003 statement limited the use of prophylaxis to the first 2 years following joint replacement surgery and patients with comorbidities that might involve increased risk of bacteremia, e.g. immunocompromised patients, for more than 2 years after surgery (Table 2). The reason for the 2009 recommendation was potential adverse outcomes and cost of treating an infected joint replacement. Jenny (93) found it questionable if prophylactic antibiotic treatment can be advocated based only on a high incidence of late infections in total hip arthroplasty associated with dental procedures since the frequency among all infected total hip arthroplasties varies in the literature from 0.04% to 6%. One reason for this variation could be differences in dental status. In an editorial, Sandhu et al. (94) maintained that prophylactic antibiotics should not be administered because there is no scientific evidence supporting their use. According to Abraham-Inpijn (95), the risk associated with antibiotic prophylaxis is greater than the risk of having a joint infection. There is no evidence that links prosthetic joint infections to dental procedures and none to prove that antibiotic prophylaxis is effective (96). Seymour et al. (97) thought that the case for providing antibiotic prophylaxis prior to dental treatment of patients with a joint prosthesis is weak or virtually non-existing. They also held that the risk associated with prophylaxis is greater than the risk of joint infection. Pallasch and Slots (7) citing McGowan and Hendrey (98), expressed that the fear of a tragic complication following a proportionately trivial procedure is not in itself a justification for irrational and excessive prophylactic therapy. They also advocated that linking a prosthetic joint infection to a single event such as dental treatment occurring amid months of random cases of bacteremia and invasive events associated with daily living remains impossible. Several studies have indicated that prosthetic joint infections of oral microbial origin have a possible prevalence rate of 0.03–0.04% (7), yet not a single reliable case-control, cohort, retrospective or prospective study has documented such a relationship and no studies have ever been performed to test the proper drug, dose, and dosing interval (7).

What antibiotic prophylaxis should be chosen to prevent staphylococcal joint infection?

According to Geipel (15), perioperative antibiotic prophylaxis clearly demonstrates reduction of the infection rate after joint surgery. Important is the application time before operation, about 30–60 min before incision. Cefalosporins of the first or second generation are most widely used in orthopedic surgery. Alternatives in patients with beta-lactam allergy are clindamycin or vancomycin. In hospitals with high prevalence of MRSA, vancomycin is preferred. As staphylococci sometimes are resistant to beta-lactam antibiotics, Friedlander (81) recommended 2 g of amoxicillin clavulanate or 600 mg of clindamycin by mouth 1 h before dental treatment. This is quite consistent with the German Society for Orthopedics and Traumatology Prophylaxis recommendations (83). The antibiotic prophylactic regimen suggested by ADA/AAOS (9) is given in Table 3. For intravenous use, Friedlander (95) recommended clindamycin 600 mg usually 30 min before the procedure. According to Mechan et al. (99), the cefalosporins (cefazolin and cefuroxime) have been the preferred antimicrobials with proven success for prophylaxis in hip and knee arthroplasty. However, the rate of *S. aureus* resistance to cefazolin was 50% and the rate of *S. epidermidis* resistance to cefazolin was 70% for all sources of infection at their working place. The authors therefore added preoperative vancomycin along with cefazolin as prophylaxis against these resistant organisms and the other common bacterial causes of infection in joint replacement.

How effective is antibiotic prophylaxis related to dental procedures to prevent prosthetic hip infections?

Data (1987–2001) from the Norwegian Arthroplasty Register on the effects of antibiotic prophylaxis systemically and in bone cement, on the revision rate of 22,170 primary hip replacements, showed that the best results were achieved when antibiotic prophylaxis was given both systemically and in the bone cement, and if the systemic antibiotic was given four times on the day of surgery (100). However, according to Berbari et al. (6) there have been no well-designed, case-control or cohort studies linking definitely any type of dental procedure with an increased risk of prosthetic joint infection. In an attempt to define the actual risk of prosthetic joint infection and the role of antibiotic prophylaxis, these authors carried out a single-center, case-control study on 339 case patients and 339 control subjects for the period 2001–2006. There was no increased risk of prosthetic hip or knee infection in patients undergoing high-risk or low-risk dental procedures who were not given antibiotic prophylaxis compared to the risk for patients not undergoing a dental procedure. Antibiotic prophylaxis

Table 2. Summary of some national guidelines/recommendations concerning antibiotic prophylaxis before invasive dental procedures in patients with joint replacements[a]

References	Association	Prophylaxis	Indications
Scott et al. (105)	Australian Orthopaedics	Yes	High-risk dental procedures in immunocompromised patients
ADA/AAOS (9)	ADA/AAOS 2003	Yes	For the first 2 years after joint replacement: all patients for all high-risk dental procedures. After 2 years: previous infection of artificial joint, inflammatory arthritis, type-1 diabetes, hemophilia, immunosuppression, history of prior or present malignancy, dental extractions, periodontal procedures, dental implantation, root canal work cleaning if bleeding is anticipated, specialized local anesthetic injections, placement of orthodontic bands
AAOS (10)	AAOS 2009	Yes	All patients with total knee or hip arthroplasties are at sufficient risk from bacteremias by dental procedures to require antibiotics considered prior to invasive dental procedures
Simmons et al. (106)	Working Party of British Society for Antimicrobial Chemotherapy	No	No specific mention of higher-risk groups. Prophylaxis not recommended
Seymour et al. (97)	British Orthopaedic Association/ British Dental Association	Yes	Prophylaxis may be considered in patients with diabetes mellitus, rheumatoid arthritis, hemophilia, malignancy, overt oral sepsis, or when dental treatment is invasive, complex and of long duration (>45 min)
Rossi et al. (107)	Sweizerische Gesellschaft für Infektiologie	Yes	Implantation of prosthesis last 12 months. No general recommendation even for immunocompromised
Blomgren et al. (52, 53)	Svenska Infektionsläkar-föreningen Revision 2008	No	Antibiotic prophylaxis for dental treatment is not recommended in healthy patients with joint prosthesis

[a]Partly modified from Ref. (13).

in high-risk or low-risk dental procedures did not decrease the risk of subsequent total hip or knee infection. The authors admitted that a small increase in prosthetic joint infection following dental procedures might have been undetected because the number of patients and control subjects needed to reveal this would have to be extremely high and not feasible in a single-center study. Deacon et al. (62) reported five cases of late prosthetic joint infection associated with dental treatment despite antibiotic prophylaxis. A similar find-

Table 3. Suggested antibiotic prophylactic regimen for patients undergoing dental procedures with a higher bacteremic risk[a]

Patient	Drug	Regimen[b]
Patients not allergic to penicillin	Cefalexin, cefradin or amoxicillin	2 g orally 1 h prior to dental procedure
Patient not allergic to penicillin and unable to take oral medication	Cefazolin or ampicillin	Cefazolin 1 g or ampicillin and unable to take oral medication 2 g intramuscularly or intravenously 1 h prior to dental procedure
Patient allergic to penicillin	Clindamycin	600 mg orally 1 h prior to dental procedure
Patient allergic to penicillin and unable to take oral medication	Clindamycin	600 mg intravenously 1 h and unable to take oral prior to the dental medications procedure

[a]Adopted from Ref. (9).
[b]No second dose recommended for any of the dosing regimens.

ing was reported by Skiest and Coykendall (101) using erythromycin in a patient treated with corticosteroids for systemic lupus erythematosus. This demonstrated that antibiotic prophylaxis is not always effective. Accordingly, antibiotic prophylaxis for high-risk patients has been recommended by several authors but this contention has not been substantiated by clinical evidence (7).

Side effects of antibiotic prophylaxis

It has been estimated that routine prophylaxis with oral penicillin in one million hypothetical patients with total joint arthroplasty undergoing dental treatment would result in 400 cases of anaphylaxis (102). This suggests that the risk-benefit ratio for beta-lactam prophylactic antibiotics may not be favorable (7). Antibiotic use may also be associated with risks such as toxicity, superinfection, selection of antibiotic resistance, pseudomembranous colitis, cross-reactions with other drugs and death (103, 104).

Concluding remarks

Most authors hold that staphylococci, particularly CNS do not usually occur in the oral cavity and accordingly, the organisms dominating in infections of joint prostheses are not of oral origin. Other authors think that staphylococci are more prevalent in the oral cavity than previously believed and there are many reports supporting this. These organisms may colonize the oral cavity both in healthy and diseased sites. Particularly elderly with underlying systemic disease seem to be susceptible. Also, MRSA occasionally occur in the oral cavity. Knowledge of the real prevalence and ecology of staphylococci in the oral microbiota is hampered by the fact that samples, which usually have been recovered from the saliva or mucosa, have been cultivated on selective media making it difficult to determine their real part of the total microflora. Furthermore, proof of the source of infection would require the organism to be cultured from the mouth, blood, and infected joint simultaneously and analyzed by molecular microbiological methods for comparison. There is a possibility that oral staphylococci can reach the blood stream, causing infection in distant sites, but the evidence that this should be a frequent event is not available. This does not exclude that such spread may occur, and the consequences could be dramatic for the patient with joint prosthesis. A number of DNAs from oral bacteria have been detected in joints of rheumatoid and psoriatic patients possibly trapped there by synovial inflammation. Therefore, the importance in joint infection of oral organisms other than staphylococci should not be overlooked. Daily procedures such as tooth brushing or chewing can cause bacteremia. This could be more important to the health of implanted joints than dental procedures. An optimal dental hygiene and regular dental visits are more important than antibiotic prophylaxis in maintaining joint health. This is important to realize because the efficiency of antibiotic prophylaxis against joint infection has not been convincingly proved. Under any circumstance the rare occurrence of late joint infections would not justify antibiotic prophylaxis on a regular basis. Unfortunately, the AAOS recommendation from 2009 has created much confusion on this point among dentists. Many think that the previous ADA/AAOS recommendation stating that it is advisable to consider premedication for only a small number of patients who may be at potential risk for experiencing hematogenous total joint infection is more acceptable. Others totally reject antibiotic prophylaxis in otherwise healthy patients with joint prosthesis. Disregarding the last recommendation from AAOS, which many dentists feel is not at all based on scientific evidence, may bring them into a medical–legal problem if joint infection occurs. It would appear that the ADA should give some help here by guiding dentists in relation to the latest AAOS recommendation. However, as long as ADA has not given any comments related to this, it would appear reasonable for dentists to follow the guidelines for the use of hip joint prophylaxis as given in 2003 in the joint ADA/AAOS recommendation.

Conflict of interest and funding

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