



## Review

# Antibiotic Prophylaxis During Dental Procedures in Patients with Prosthetic Joints

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## Abstract

In patients with artificial joints, the need for antimicrobial prophylaxis during dental procedures is often raised. The present document describes the pathogenic mechanisms and epidemiological data on the subject of periprosthetic joint infections (PJI) after dental procedures. The document reflects the opinion and recommendations of the expert group 'Infection' of Swiss Orthopaedics. Microorganisms belonging to oral flora can seed haematogenously to an artificial joint. The proof of a causative relation with dental procedures is not possible, because the responsible bacteraemia can originate from the oral cavity at any time, irrespective of when the dental procedure occurs. Good oral hygiene is associated with a lower risk for PJI. Transient bacteraemia occurs during daily oral hygiene activity (e.g., tooth brushing) and thus the cumulative risk for a haematogenous PJI from tooth brushing is higher than that from a dental procedure. PJI after a dental procedure are rarely reported. On the basis of an epidemiological model, several thousand patients with artificial joints must receive antimicrobial prophylaxis to prevent a single PJI. Considering this ratio, the number of adverse events due to the antimicrobial compound exceeds the benefit of administering it by a large magnitude. Therefore, as a rule for the vast majority of cases, antimicrobial prophylaxis during dental procedures is not recommended. It is important that a patient has a good oral health status before joint implantation and that good oral hygiene is continuously maintained in patients with artificial joints.

Key words: periprosthetic joint infections, antimicrobial prophylaxis, dental procedure.

## Introduction

Dentists and general practitioners often ask orthopaedic surgeons and infectious diseases specialists whether or not a patient with arthroplasty should have antimicrobial prophylaxis during dental procedures, dental interventions or dental hygiene

treatment. In 2008, Uçkay et al. [1] summarized the evidence in answer to this question. Numerous recommendations have been published from various professional societies in different countries (supplementary material: **Table S1**). However,

observations from clinical practice and surveillance studies [2] demonstrate a divergence between these recommendations and their translation into patient management [3, 4]. On the one hand, a statement by one working group [5] may be followed by a contradictory statement by another group [6], leading to confusion [7]. On the other, professional societies sometimes use wording in their recommendations that is correct from a legal perspective (i.e., ‘not attackable’), but which may nonetheless be unhelpful in clinical practice (supplementary material: **Table S1**). Moreover, as the number of patients with multiple comorbidities grows, so too does a frail population with increased risk for complications during anaesthesia and orthopaedic surgery. Understandably, responsible dentists and physicians have an interest in avoiding infection, in particular in this group of patients. This document reviews the pathogenic mechanisms and epidemiological reasoning behind haematogenous seeding of artificial joints from oral flora, and it provides Swiss recommendations for antimicrobial prophylaxis during dental procedures for patients with artificial joints.

### Dental examination prior to implantation of a prosthetic joint

A dental examination *prior to* implantation of an arthroplasty is recommended. The extent and details of such an examination cannot uniformly be defined, because they depend on the patient’s oral health status and his oral hygiene practices. Nevertheless, the goal of such an examination includes the detection and treatment of potential infection sources prior to implantation of foreign body material. In addition, a patient’s oral health status can be judged and the importance of continuous maintenance of good oral hygiene emphasized (**Table 1**).

It is important to note that this recommendation should be interpreted with a justifiable view of differentiation. Patients with an already existing good

oral health status and regular dental visits may not benefit from an additional examination shortly prior to implantation of an arthroplasty. The awareness of the importance, and hence, the average level of the oral health status in a population may differ between countries. Similarly, cost coverage of dental examinations and interventions vary between different health care systems. To the best of our knowledge, there are no cost-effectiveness studies examining the role of dental examinations in reducing the incidence of periprosthetic joint infections (PJIs). Nonetheless, we are convinced that patients with poor oral health status and remote infection foci in the oral cavity may benefit from this recommendation.

### Antimicrobial treatment of an apical periodontitis or an abscess

It is important to differentiate whether the dental procedure is being performed in a patient because of an infection in the oral cavity (e.g., an apical periodontitis or an abscess) or in a patient without an infection. For the former case, we discuss ‘antimicrobial treatment’ (see next paragraph). For the latter case, we evaluate the necessity of ‘antimicrobial prophylaxis’ (subject of this document).

In patients *without* an arthroplasty, in the case of apical periodontitis or abscess, the benefit of systemic antibiotics after a dental procedure is unclear [8]. Such cases may be treated without antibiotics. Therefore, we recommend differentiating between patients with and without arthroplasties. In patients *with* artificial joints, treatment of infections is recommended with systemic antibiotics (amoxicillin/clavulanate 1 g or – in patients with known allergy to penicillin – clindamycin 600 mg three times per day for 3 to 5 days; then evaluation of the disease course and decision to stop or continue treatment). This recommendation is not based on existing evidence, but on reasoning regarding the pathogenic mechanism. In the case of an abscess, the bacterial load is hypothesized to be high. In the same line of

**Table 1.** Recommendation of antibiotic use during dental procedure prior to and after implantation of an arthroplasty.

Dental procedure	
<b>Prior to implantation of an arthroplasty</b>	<b>Systemic antimicrobial prophylaxis</b>
Dental examination (including panoramic radiograph)	No
All dental diseases should be treated prior to implantation of an arthroplasty	
Coordinate dental examinations on a regular basis for the time after implantation of an arthroplasty	
<b>After implantation of an arthroplasty without an infection in the oral cavity</b>	<b>Systemic antimicrobial prophylaxis</b>
Good oral hygiene, regular dental examinations in reasonable time intervals	No
All dental procedures/interventions (including tooth extraction, dental root canal treatment) without multiple risk factors (Table 2): mouth rinse with 0.2% chlorhexidine	No
<b>After implantation of an arthroplasty with an infection in the oral cavity (e.g., apical periodontitis or abscess)</b>	<b>Antimicrobial treatment</b>
Rapid dental/oral surgical treatment	Amoxicillin/clavulanate 1 g three times daily OR Clindamycin 600 mg three times daily for 3 to 5 days*

\*After 3 to 5 days of antimicrobial treatment, clinical re-evaluation and decision making regarding continuing or stopping antimicrobial treatment. Recommended dose for normal body weight with adequate liver and renal function.

reasoning, the dental procedure for an abscess is assumed to trigger bacteraemia, and the bacterial load within this kind of bacteraemia is thought to be higher than can be expected during a dental procedure for non-infectious causes. On the basis of these arguments, the risk for haematogenous seeding to an artificial joint would be higher. In an animal foreign-body infection model, a bacterial load of 100 to 1000 colony forming units of *Staphylococcus aureus* per milliliter of blood caused a haematogenous infection of an extravascular implant [9]. Such a bacterial load with this bacterial species is not expected during a routine dental procedure, although it is conceivable that the bacterial load is higher in the case of an abscess in the oral cavity.

### Theoretic relationship between dental procedures and PJI

Asymptomatic bacteraemia can occur shortly after dental root treatment (31%-54% of patients in [10]). Consequently, the potential exists for haematogenous seeding to an artificial joint. Case reports have demonstrated identical clones of microorganisms isolated from samples in synovial fluid and dental plaques [11]. From this pathogenesis, these reports suggest a relationship between dental procedures and PJI. The microorganisms in these cases belong to those commonly found in the oral flora [1, 12-16]. Although these arguments strongly point to the source of haematogenous seeding, they cannot ascertain 'when' the responsible bacteraemia occurred: it may have occurred without a dental procedure [16]. Asymptomatic transient bacteremia can occur after tooth brushing, chewing gum, the use of dental floss or spontaneously [17-19]. Moreover, many of the microorganisms that are present in the oral flora can also be found in the microbiome of the upper intestinal tract, making it difficult to identify the source. Case reports use the timely association between dental procedures and the occurrence of PJI as an argument in favour of a causal relationship. These arguments are convincing in cases of a virulent organism [20]. However, many bacteria of the oral flora are considered to have low virulence and hence, would cause so-called low-grade PJIs.

From these results taken together, it can be stated that microorganisms of the oral flora can seed to an artificial joint, but it is not possible to identify a causal relationship with a defined dental procedure performed at a specific time. The temporal association is a convincing argument in rare cases, but it is not proof, as the responsible bacteraemia can occur prior to or after the dental procedure. Nonetheless, good oral hygiene is associated with a lower risk of PJI [21]. Therefore, it is recommended that patients with

artificial joints maintain good oral hygiene (Table 1).

### Epidemiological considerations

In their effort to answer an unresolved question, doctors frequently raise the need for prospective randomized controlled trials. In the case of the current question ('Is antimicrobial prophylaxis needed during dental procedures in patients with artificial joints?'), however, such a study is not feasible. The trial would require several hundred thousand persons with artificial joints, comparable numbers and types of dental procedures, and follow-up investigations of  $\geq 2$  years [22]. Therefore, recommendations are based on retrospective analyses (summarized in [1] and supplementary material: Table S1) and case-control studies [21, 23, 24].

PJI after dental procedures are - in consideration of the number of patients with artificial joints - extremely rare, and hence, not quantifiable. In the next sections, we review two epidemiological considerations that may offer some answers to the present question.

First, the incidence of hip or knee PJI ranges from 0.7% [25] to 1.4% [26]. The reported incidence varies, however, depending on the observation period, the study design and the country in which the study was performed. The potential proportion of PJI caused by microorganisms belonging to the oral flora is frequently less than 4%; few studies report a proportion of up to 8% (i.e., absolute incidence of <0.028% or <0.1%, respectively) [27-29]. In other words, 3 to 10 of 10,000 individuals with an artificial joint have a PJI with a microorganism belonging to the oral flora. These figures are comparable to those from retrospective studies (0.04% in [30], 0.05% in [31]) [1]. However, the number of these patients in which PJI occurs, irrespective of a dental procedure, remains unknown. Thus, antimicrobial prophylaxis would be beneficial in only some of these patients because haematogenous seeding can occur at any time, even without a dental procedure. Even if 80% [32] of the above-mentioned 3 to 10 PJI could be prevented with antimicrobial prophylaxis, mathematically, this means that 1,250 to 4,167 individuals with artificial joints must be treated to prevent a single PJI.

In a second epidemiological consideration, the risk of PJI after bacteraemia can be reviewed, given the postulated pathogenic mechanism of infection. In the case of *S. aureus* (typically not belonging to the oral flora), the risk is high (30%-40%) [33], whereas in the case of other microorganisms, the risk is estimated to be low (ca. 0.1%) [34]. The potential of haematogenous seeding and that of infectivity is also estimated to be low for many bacteria belonging to the oral microbiome (e.g., *Peptostreptococcus* spp.,

anaerobes). These arguments are relevant because a study analysing microorganisms in patients with an infected dental root showed that 70% of the 224 isolates were strict anaerobes or microaerophilic bacteria [35]. Ainscow and Denham prospectively followed 1,000 individuals after arthroplasty implantation for a mean duration of 6 years [36]; 128 of them had at least one dental intervention during the observation period, and none of them developed a PJI.

From these epidemiological considerations, as well as from the high frequency of asymptomatic transient bacteraemia after daily oral hygiene procedures (e.g., tooth brushing, see also below "*What is the evidence to recommend antimicrobial prophylaxis in so-called risk groups?, Type of Dental Procedure*") and hence the cumulative haematogenous risk [17, 32], we postulate that the risk of PJI after dental procedures is markedly low at less than 0.1%. It is possible that other reported incidences (calculated retrospectively) of 0.1% [37] and 0.2% [38] overestimate the true risk. Even with these numbers, and in analogy to the mathematical calculation stated earlier, 1,250 or 625 patients with artificial joints must receive antimicrobial prophylaxis to prevent a single PJI [22].

### Potential adverse events

Earlier we calculated how many patients had to be treated to prevent a single PJI. Consequently, the potential of adverse events must be reviewed when the same number of patients are treated with antibiotics.

Every antimicrobial therapy is associated with collateral damage to the human microbiome. Therefore, the use of antimicrobial prophylaxis can have an influence on the penicillin susceptibility of selected oral streptococci [5, 39-41].

The number of known adverse events (allergies with various clinical manifestations, nausea, diarrhoea, etc.) is clearly higher than the number of prevented PJI per 1,000 prescriptions for antimicrobial prophylaxis. These side effects occur more frequently in elderly individuals [42], namely in the population that typically requires an arthroplasty. The same argument is valid for *Clostridium difficile* infections. They rarely occur when a single antimicrobial prophylaxis is administered, but the risk can increase if several dental visits are scheduled within a short time [5, 43].

Considering the numbers needed to treat, it is not surprising that antimicrobial prophylaxis during dental procedures is not cost-efficient, as demonstrated in a recent study with a mathematical model (Markov decision modelling) [44]. According to an estimation performed in the United States, the

yearly cost for antimicrobial prophylaxis during dental procedures in patients with arthroplasty is 50 000 000 dollars [5, 45].

### General consensus

The overall low incidence of PJIs, the low proportion of microorganisms belonging to oral flora found in PJI, the low risk of haematogenous seeding, and the low virulence of these bacteria are arguments in favour of *not* recommending antimicrobial prophylaxis during dental procedures in patients with artificial joints. Several thousand prescriptions of antimicrobial prophylaxis would be required to prevent a single PJI. These numbers are clearly higher than the numbers known to cause adverse events.

### What is the evidence to recommend antimicrobial prophylaxis in so-called risk groups?

Four parameters are frequently cited when evaluating variables associated with a higher risk of haematogenous PJI after dental procedures: (1) the time interval between joint arthroplasty and the dental procedure, (2) the immunosuppression/comorbidity of the patient, (3) the type of dental procedure, and (4) the duration of the dental procedure. Insufficient data (if at all) are available to scientifically estimate the risk of PJI on the basis of these four parameters. The reasons for nonetheless prescribing antimicrobial prophylaxis are, therefore, not evidence-based, but frequently based on an analogy to other circumstances, hypothetical pathogenic mechanisms, or fear of causing an infection.

#### (1) Time interval between joint arthroplasty and the dental procedure

In the postoperative period of a newly implanted arthroplasty, the tissue has been injured from the surgery. Hence, the anatomic barriers have not yet been completely restored. From a pathogenic point of view, the migration of bacteria into the joint during bacteraemia is facilitated (i.e., locus minoris resistentiae). In parallel to this view, frequency graphs have indicated that not only exogenous but also haematogenous infections occur more often in the first year after implantation than is observed in later stages [46]. For these reasons, previous recommendations categorized the first 12 [1, 47] to 24 months [48] after implantation of an arthroplasty as a risk period for infection. Counter arguments include the fact that large cohort studies have shown a PJI incidence of less than 1% in the first year after implantation [26] and that of these, among haematogenous infections, the proportion of those

due to viridans streptococci or anaerobes is approximately 4% or less (i.e., absolute  $\leq 0.04\%$ ) [49]. The time that is required for tissue healing is often misinterpreted as the time for achieving good joint function. The time required for the latter is estimated to be 1 year. It is conceivable that – provided there is no reason for impaired tissue healing – the anatomic barriers are restored at a much earlier point (e.g., after 4 to 6 weeks). Because there are no substantial scientific grounds to suggest a risk period, we categorize – as do our colleagues from Australia (supplementary material: **Table S1** [50]) – the first 3 postoperative months to be the risk period (**Table 2**). In future recommendations, when more data become available, the duration of this period may be shortened.

**(2) Immunosuppression/comorbidity of the patient**

Patients treated with immunosuppressive drugs, as well as those with diabetes mellitus, rheumatoid arthritis, severe liver cirrhosis, haemophilia or other diseases associated with severe immunosuppression, have an increased risk of infection. An important aspect concerning these patients is that the risk is increased because of the nature of the disease or function of the medication, independent of a dental procedure. In reviewing the absolute number of individuals with artificial joints, it is not surprising

that more cases of PJI after dental procedures are reported in patients without immunosuppression than in immunocompromised hosts [1]. The low number of these case reports makes a risk analysis impossible. Moreover, many of these comorbidities have different stages of severity and other factors influencing the risk of infection (doses and type of immunosuppression, blood sugar control, duration of disease, etc.). Consequently, no recommendation for antimicrobial prophylaxis can be made. In the vast majority of cases, antimicrobial prophylaxis is not justified [51]. We recommend – prior to a dental procedure – a discussion of the severity of the disease or immunosuppression with the physician managing the patient’s comorbidity or immunosuppressive drugs. In Switzerland, this is commonly a specialist (e.g., oncologist, rheumatologist) and rarely a general practitioner. In our view, specialized knowledge is required to estimate which disease in what extent impairs the host’s immune status. This argument may help to judge whether or not elimination of transient bacteraemia via the reticulo-endothelial system without antimicrobial chemotherapy can be expected. In the case of a severe immunosuppressive state (e.g., neutropenia due to a haematological malignancy) plus other risk factors (**Table 2**), we recommend consultation with a specialist centre prior to the dental procedure (**Table 3**).

**Table 2.** Postulated variables reflecting an increased risk for bacterial haematogenous seeding from the oral cavity to an artificial joint. Recommendations in patients without an established infection in the oral cavity.

	Condition/Recommendation	2 <sup>nd</sup> Condition	Recommendation prior to dental procedure
<b>1. Time interval between joint arthroplasty and the dental procedure</b>			
≤ 3 months after implantation	Delay dental procedure (if possible) to >3 months after implantation		
	Dental procedure cannot be delayed	Time interval is the only risk factor	Mouth rinse with 0.2% chlorhexidine
	Dental procedure cannot be delayed	Multiple risk factors	Table 3
<b>2. Immunosuppression/comorbidity of the patient</b>			
Dependent on the severity of the disease or level of immunosuppression, respectively	A discussion of the severity of the disease or immunosuppression with the physician managing the patient’s comorbidity or immunosuppressive drugs (e.g., oncologist, rheumatologist)	For many comorbidities, systemic antimicrobial prophylaxis is not recommended (e.g., diabetes mellitus, low-dose treatment with corticosteroids)	Mouth rinse with 0.2% chlorhexidine
		Severe immunosuppression (e.g., neutropenia due to a haematological malignancy, immunosuppressive drugs because of solid organ transplantation)	Table 3
<b>3. Type and duration of dental procedure</b>			
Complex and long dental procedures	Type and duration is the only risk factor		Mouth rinse with 0.2% chlorhexidine
As an experience-based opinion, we define the term ‘long intervention’ as a dental procedure that takes more than 60 minutes (no evidence)	Multiple risk factors		Table 3

**Table 3.** Recommendations if multiple risk factors (Table 2) are present.

Systemic antimicrobial prophylaxis – in addition to mouth rinsing with 0.2% chlorhexidine – should be considered.
Cases with multiple risk factors are rare (including those in which the dental procedures cannot be delayed). We do not think it is meaningful to publish generalizable recommendations on antimicrobial substances for such a minority of patients.
Multidisciplinary case discussion (including the physician managing the patient's comorbidity or immunosuppressive drugs, infectious diseases specialist, orthopaedic surgeon).
Consideration of performing the dental procedure at a centre where a corresponding specialist is available.

### (3) Type of dental procedure

As mentioned earlier, bacteraemia frequently occurs after a dental procedure [10]. After tooth extraction, studies have shown a cumulative bacteraemia incidence of approximately 60% (33% even with antimicrobial prophylaxis). The duration of bacteremia is 15 to 20 minutes (in a few patients up to 60 minutes) [32, 52, 53]. Bacteraemia incidence after tooth brushing was 23% [32, 53]. These studies allow the following conclusions: Antimicrobial prophylaxis may reduce a proportion of bacteraemia but does not completely prevent its occurrence. The host's immune status can eliminate this transient bacteraemia via the reticulo-endothelial system without antimicrobial chemotherapy. Tooth brushing performed multiple times a day has a higher cumulative incidence of bacteraemia than a single tooth extraction. These arguments lead us to question the benefit of systemic antimicrobial prophylaxis. A complex dental intervention may have a higher risk of bacteraemia, although, in the same line of reasoning, a complex intervention alone does not justify systemic antimicrobial prophylaxis.

Studies have shown that the bacteraemia incidence after tooth extraction can be reduced via pre-interventional mouth rinsing with 0.2% chlorhexidine in comparison to placebo (after 15 to 20 minutes, 23% versus 4%,  $p = 0.005$  in [52]; 64% versus 30%,  $p < 0.001$  in [54]). This magnitude of risk reduction is comparable to that when systemic antimicrobial prophylaxis is administered [1, 32]. Therefore, we recommend pre-interventional mouth rinsing with 0.2% chlorhexidine, including when tooth extraction or complex dental interventions is planned (Table 2).

### (4) Duration of dental procedure

In analogy to all surgical interventions, it seems logical that the longer the duration of the intervention, the higher the risk of infection. However, for dental procedures, there is no cut-off time that is associated with a higher risk of infection, and the time term 'long' is not defined. One series described three patients with PJI after a dental procedure, all of whom had a dental intervention of  $\geq 45$  minutes [37]. In another case series consisting of nine patients with PJI after a dental procedure, the intervention time ranged

from 75 to 205 minutes [38]. On the basis of these experiences, in previous recommendations, a dental intervention that took more than 45 minutes was classified as an intervention with a higher risk of infection. A statistically significant association is not possible with these small numbers. An argument against such fixed time cut-offs for risk classification is the observation of a study in which a small proportion of volunteers (<5%) still had bacteraemia even 60 minutes after tooth brushing [32].

Although it is arbitrary and without evidence, as an experience-based opinion, we define the term 'long intervention' as a dental procedure that takes more than 60 minutes. This recommendation has no scientific background. However, a routine dental procedure rarely takes longer than 60 minutes.

### Consensus statement regarding antimicrobial prophylaxis in so-called risk groups

In our view, none of these conditions previously classified as risk factors justifies as a single parameter the use of systemic antimicrobial prophylaxis for dental procedures. In rare cases, a patient may have multiple risk factors (e.g., triple immunosuppression because of a lung transplant plus hip arthroplasty 3 months ago plus a complex dental procedure that takes more than 60 minutes). Although some experts would consider the use of antimicrobial prophylaxis in these rare cases, we do not think it is meaningful to publish generalizable recommendations on antimicrobial substances for such a minority of patients. We recommend discussing these cases with a specialist centre and consideration of performing the dental procedure at a centre where a corresponding specialist is available (Table 3).

### Supplementary Material

Supplementary table S1.

<http://www.jbji.net/v01p0042s1.pdf>

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## Competing Interests

The authors have declared that no competing interest exists.

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