

IN BRIEF

- This paper provides an up-to-date review of the dilemma facing dentists over chemoprophylaxis for patients with joint prostheses undergoing dental treatment.
- The authors' views are based on a literature study – the evidence suggests that dental treatment without antibiotic prophylaxis does not render patients susceptible to joint infections.
- Current proposed guidelines from the Orthopaedic Association are considered and the dilemma that dentists find themselves in when challenged by the orthopaedic surgeon to provide antibiotic prophylaxis are discussed.

Antibiotic prophylaxis for patients with joint prostheses – still a dilemma for dental practitioners

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Objectives: To provide a critical review of the current evidence that implicates dental-induced bacteraemia as a risk for joint infections in patients fitted with joint prostheses and appraise the need for antibiotic prophylaxis.

Design: Retrospective analysis.

Setting: Mainly hospital-based patients or subjects.

Outcome measures: The relationship between joint infections and dental treatment is equivocal at the best and there is no evidence that antibiotic prophylaxis provides such patients with any protection.

Results: Microbiological evidence linking dental treatment-induced bacteraemia to joint infections is weak and if an oral commensal is implicated, it is more likely to have arisen either from a spontaneous bacteraemia or from a dental infection. As a consequence of the latter, we recommended the institution of good dental health prior to joint replacement. There may be a case for providing prophylaxis to the immuno-compromised patient, but only if the immuno-suppression is associated with a neutropenia. In such circumstances, only emergency treatment should be considered until the neutropenia is resolved. Antibiotic regimens that are recommended by orthopaedic surgeons have not been evaluated in a randomised placebo-controlled study and many of the drugs are not licensed for this purpose. The evidence on cost-risk benefit seems to demonstrate that antibiotic prophylaxis with either amoxicillin or penicillin is not cost effective when compared with no prophylaxis.

Conclusion: The case for providing antibiotic prophylaxis prior to dental treatment in patients fitted with a joint prosthesis is weak or virtually non-existent. Furthermore, the risk from providing prophylaxis is greater than the risk of a joint infection.

Antibiotic prophylaxis for patients with prosthetic joints remains a contentious issue. The dilemma persists despite reports and guidelines from the British Society for Antimicrobial Chemotherapy (BSAC),¹ the American Dental Association,² the American Academy of Orthopedic Surgeons,³ the

British Orthopaedic Association and the British Dental Association (personal communication). The main area of concern to the dental practitioner is that many orthopaedic surgeons are still insisting that antibiotic prophylaxis is required prior to dental treatment that may produce a bacteraemia.

In this paper, we consider the evidence on the whole issue of antibiotic prophylaxis for patients with joint prostheses. The following issues will be addressed:

1. Do dental-induced bacteraemias cause haematogenous infections in patients with joint prostheses?
2. Does antibiotic prophylaxis prevent such infections?
3. What is the cost-risk benefit of providing such prophylaxis?

The evidence arising from these three points will then be considered against the proposed BOA/BDA guidelines (Table 1).

DO DENTAL-INDUCED BACTERAEMIAS CAUSE HAEMATOGENOUS INFECTIONS IN PATIENTS WITH JOINT PROSTHESES?

In the late 50s and early 60s, there was a high prevalence (15–25%) of post-operative infections associated with prosthetic joint surgery. These were classified as early and late infections. Early infections occurred within 2 months of surgery and were related to wound infection, whereas late infections (> 2 months) were thought to be caused by haematogenous spread of bacteria from another site of infection elsewhere in the body.⁴ To reduce these high rates of infection, it was deemed appropriate to give antibiotic prophylaxis prior to

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Table 1 Proposed British Orthopaedic Association and British Dental Association guide to practice on joint replacement, dental treatment and antibiotic

Indications for antibiotic prophylaxis	
1.	Intuitively, good oral hygiene and regular dental advice are imperative for patients with large joint replacements or those anticipating such operations. Dental advice should be sought where there is doubt about oral sepsis.
2.	Routine antibiotic prophylaxis should <u>not</u> be offered to all patients undergoing dental treatment.
3.	Antibiotic prophylaxis is advised in patients with systemic immuno-suppressive disease eg diabetes (type I and II), rheumatoid arthritis, haemophilia or malignancy (either from the immuno-suppressive effects of the malignancy or those of treatment).
4.	Prophylaxis is clearly indicated where there is overt oral sepsis, eg any kind of pre-existing oral infection which could lead to metastatic spread.
5.	Prophylaxis should be considered where dental treatment is invasive, complex and of long duration.
Suggested antibiotic prophylaxis	
Under local or no anaesthetic:	
Patients not allergic to penicillin:	Amoxicillin 3g orally, 1 hour prior to dental procedure
Patients allergic to penicillin:	Clindamycin 600mg orally, 1 hour prior to dental procedure
Under general anaesthetic	
Patients not allergic to penicillin:	Amoxicillin 1g IV at induction followed by amoxicillin 500mg orally 6 hours later
Patients allergic to penicillin:	Clindamycin 300mg IV at induction over 1 hour

joint surgery. This use of antibiotics reduced the prevalence of post-operative infection to about 1%.⁵ These findings suggested that most of the late infections were due to wound contamination and not from haematogenous spread. Despite such evidence, many orthopaedic surgeons still insist that their patients receive antibiotic prophylaxis prior to those dental procedures that can induce bacteraemia.

To establish whether a dental-induced bacteraemia has caused a joint infection, it is necessary to confirm the following criteria: a) the same organism must be isolated from the oral site and infected joint; b) the presence of the organism should be confirmed, whenever possible, with a positive blood culture; c) the timing of the dental event and the procedure carried out must relate to the onset of the joint infection. For both (a) and (b) traditional colony-shape and fermentation-pattern identification is inadequate. DNA fingerprinting techniques have to be used to confirm that isolates from infected joints are the same as those found in the mouth.⁶

A synopsis of the evidence relating possible dental causes to hip and joint infections is shown in Table 2.

In a review of 21 joint infections reported, it was suggested that 5 could be caused by dental treatment. However, only one case out of the 21 could be considered to fulfil some of the criteria listed above.⁷ The case in question had a joint infection that was caused by a β-haemolytic streptococcus and the same organism was cultured from the mouth and blood. No further identification techniques were completed on the isolates and it would be difficult to establish whether the bacteraemia was

induced by the dental treatment or arose spontaneously as a consequence of the patient cleaning their teeth or from a source of infection elsewhere. In a prospective 6-year study on 1,000 patients, only 3 developed joint infections.⁸ Of those 1,000 patients, 224 had undergone an invasive dental procedure and again there was no episode of late joint infection. Two further reviews of patients with joint infections^{9,10} implicated skin and soft tissue infections as being the most likely primary cause. Four out of 110 cases were attributable to *Viridans streptococci*.¹⁰ It is interesting to note that all four patients had recent experience of an acute dental infection. This does emphasise the need for good oral health before patients are fitted with a prosthetic joint.

An analysis of 2,693 patients, in whom total prosthetic joints had been placed, showed an incidence of late joint infections of approximately 1%.¹¹ In only one of these patients the infection was temporally asso-

ciated with previous dental treatment. As with so many cases, the imprecise microbiological data was unable to confirm whether the infection arose from an oral source. The authors concluded that the data did not support the practice of prescribing prophylactic antibiotic prophylaxis for patients with prosthetic joints prior to dental treatment.

Although the evidence linking dental treatment-induced bacteraemia to prosthetic joint infections is tenuous, such infections are serious. Most of the infections are caused by Staphylococci (> 66%) and only 4.9% to streptococci of possible oral origin. Again, it was not determined whether the oral streptococci entered the circulation spontaneously or from dental treatment. It should be emphasised that *Viridans streptococci* can come from non-oral sources such as the colon. Thus from an analysis of the microbiology of joint infections, it is difficult to justify antibiotic prophylaxis prior to dental treatment.

DOES ANTIBIOTIC PROPHYLAXIS PREVENT JOINT INFECTION?

The efficacy of antibiotic prophylaxis prior to dental treatment in preventing prosthetic joint infection has not been evaluated in a randomised placebo control study. It is highly unlikely that such a study will be completed because of the large number of patients required. This relates to the overall low prevalence of prosthetic joint infections (around 1%) and the even lower incidence of such infections arising from an oral source.

Animal studies have been used to support the need for prophylactic use of antibiotic, but the findings are difficult to interpret in relation to dental practice. Two studies^{12,13} have both used the rabbit model and a large inoculation of *Staphylococcus aureus* to demonstrate the risk of prosthetic joint infection. The inoculations used in these experiments contained 20–23,000 times more *Staph. aureus* than found in 1 ml of human mixed saliva.

Table 2 Synopsis of the evidence relating possible dental causes to hip and joint infections

Study	Number of patients	Findings
Ainscow and Denham, 1984 ⁸	1000 fitted with joint prostheses	3 patients developed joint infections, but the incident was not related to any dental interventions.
Jacobson <i>et al</i> , 1986 ¹¹	2693 fitted with joint prostheses	1% incidence of late joint infections. Only 1 patient (0.04% of sample) showing an association with dental treatment.
Ching <i>et al</i> , 1989 ¹⁰	110 with joint infections	4 episodes attributable to <i>Viridans streptococci</i> but in all 4 cases there was a recent history of an acute dental infection.
Thyne and Ferguson, 1991 ⁷	21 with joint infections	5 of the 21 could have been caused by dental treatment, but in only 1 case was the same bacteria isolated from the blood and infected joint

Furthermore, the relevance of the rabbit model fitted with a prosthetic joint bears no relationship to a clinical situation.

It is difficult to evaluate whether antibiotic prophylaxis prior to dental treatment prevents prosthetic joint infections. Further support to this argument comes from an analysis of 180 late joint infections.⁹ Of these 180 cases, an invasive procedure was suspected as the cause in only 34. Five of these patients (all dental) had received antibiotic prophylaxis prior to their dental treatment. Thus if the dental procedure-induced bacteraemia was implicated as the cause of the joint infection, then providing prophylaxis failed to prevent this. It can be concluded that even if antibiotics are administered prophylactically, they cannot be guaranteed to provide protection.

The most commonly prescribed regimen for antibiotic prophylaxis is 3g amoxicillin. There is no evidence that this antibiotic has any prophylactic effect in joints of any kind. Amoxicillin is also not licensed for use in joints either prophylactically or therapeutically. However, many antibiotics are used for purposes which are not included in the granting of the original licence. This does not prevent their usage in clinical practice, and it is up to the clinician who is responsible for the patient's care to decide on the most appropriate drug. Clindamycin does penetrate bone and does get into joints, but again there is no evidence either from experimental animals or clinically that it is effective for prophylaxis. Clindamycin is also not licensed for prophylaxis for total joint replacements. The cephalosporins, cephalexin and cefradine do penetrate bone effectively and have been used prophylactically to prevent early post-operative infections in total joint replacements. There is however no evidence that they work prophylactically with dentally-induced bacteraemia in total joint replacements. There is thus no evidence to support any of the usual antibiotics mentioned above to be used prophylactically for total joint replacements or any indications as to the dosages to be used.

There are possible further medico-legal complications to using antibiotics prophylactically for patients with total joint replacements. If a patient developed a severe antibiotic-induced reaction who would be sued? It would be the person who prescribed the antibiotic on the grounds that the antibiotic was unnecessary. We believe that the court would look at the evidence for the efficacy of the antibiotic and undoubtedly conclude that the dentist was culpable. If the dentist prescribed the antibiotic on the advice of an orthopaedic surgeon could the latter be also guilty of negligence? It is unlikely because ultimately the decision to prescribe the antibiotic

was the responsibility of the dentist who should have made an informed risk assessment. The answer therefore to orthopaedic surgeons who wrongly insist that antibiotics are prescribed for dental treatment is to ask that they prescribe themselves for the patient and take the consequent risks.

RISK-BENEFIT OF PROVIDING ANTIBIOTIC PROPHYLAXIS

If antibiotics are justified to prevent haematogenous infections then benefits have to outweigh the risks that are associated with these drugs.

It has been estimated that around 70,000 hip and knee replacements are performed in the UK every year and this number is likely to increase. As patients are living longer and keeping their teeth into old age, there will be a significant number of patients with joint prostheses presenting for dental treatment. The risks of providing antibiotic prophylaxis to patients with prosthetic joints needs to be evaluated against the possible risks of a joint infection when no prophylaxis is provided. Such information has been subjected to a decision utility analysis¹⁴ and the results are shown in Table 3. A safer option (but more costly) appears to be provided by cephalexin, but the reduced prevalence of joint infections needs to be balanced against the risk of anaphylactic reaction to the drug.

Other cost-effectiveness studies have been carried out in which the cost of treating a joint infection, should it arise from dental treatment, was compared with the cost of providing antibiotic prophylaxis for such dental treatment.¹⁵ The calculated risk of an infection from dental treatment in these patients is 0.03 per 100,000 patients with hip replacements. Treating such infections (which also includes joint replacements) is approximately £15,000 per patient (total cost of £450,000). Providing these patients with antibiotic prophylaxis will cost just under £1 million. If penicillin or amoxicillin is the drug of choice, then in this cohort of patients there is likely to be 5,000 possible adverse reactions to penicillin and 40 cases of anaphylaxis would be

expected to occur.¹⁴ The evidence on cost-risk benefit seems to demonstrate the antibiotic prophylaxis with either amoxicillin or penicillin is not cost effective when compared with no prophylaxis. On purely financial terms, it is cheaper to provide no prophylaxis and treat joint infections as and when they arise as opposed to providing antibiotic prophylaxis. Factors that need to be entered into the equation include litigation costs of the joint infection and replacement. However, this needs to be considered against the background of the cost associated with the life threatening condition of anaphylaxis, the development of resistant strains arising from antibiotic misuse and the increased risk of super infection in an ageing population.

COMMENTARY ON THE BOA/BDA RECOMMENDATIONS

1. Intuitively, good oral hygiene and regular dental advice are imperative for patients with large joint replacements or those anticipating such operations. Dental advice should be sought where there is doubt about oral sepsis.

Basically this is good advice but should apply to all patients, not just those anticipating or fitted with joint prostheses. There is evidence that residual or untreated sources of oral infection are more likely to cause haematogenous joint infections than a dental procedure-induced bacteraemia.^{10,16} Thus there is justification for patients to be screened and rendered dentally fit prior to their hip or joint replacement. This now becomes an issue of responsibility. It has to be the dentist's role to check for and treat any potential sources of oral infection. Likewise, we would consider it the responsibility of the orthopaedic surgeon to ensure that patients are dentally fit before joint replacement surgery. Whilst such a paradigm is fine in theory, the reality is that in our experience very few orthopaedic surgeons request dental advice before joint replacement. By contrast, many insist upon antibiotic prophylaxis before dental treatment. We feel that patients would be

Table 3 Costs and risks associated with various treatment options (ie different types of antibiotic prophylaxis or no prophylaxis) for 1 million hypothetical patients with prosthetic joints who require dental treatment. After Jacobson *et al.* 1991

Option	Deaths arising from joint infection	Number of amputations	Other outcomes	Costs
No antibiotic prophylaxis	1.93	2.93	—	£1.52 million
Prophylaxis with penicillin or amoxicillin	2.31	2.14	400 cases of anaphylaxis	£4.26 million
Prophylaxis with cephalexin	0.75	0.46	200 cases of anaphylaxis	£8.86 million

better served all round, and hence at a lesser risk of joint infection, if they attended to their oral health before surgery, as opposed to relying upon the questionable practice of antibiotic prophylaxis.

2. Routine antibiotic prophylaxis should not be offered to all patients undergoing dental treatment.

We presume that this statement must apply to all types of dental treatment irrespective of the potential bacteraemia that the procedure will produce (see note 4). If this is the case then why do some orthopaedic surgeons continue to disregard the guidelines issued by their own professional boards, and insist on prophylaxis being provided?

3. Antibiotic prophylaxis is advised in patients with systemic immuno-suppressive disease, eg diabetes (types I and II), rheumatoid arthritis, haemophilia or malignancy (either from the immuno-suppressive effects of the malignancy or those of treatment).

The BSAC has commented that there is little evidence that dental treatment (the bacteraemia arising from such treatment) carries any significant problem in patients who are immuno-suppressed¹⁷. They concluded that antibiotic prophylaxis is not required for such patients. A review of the literature suggests that patients whose joints have been replaced as a consequence of rheumatoid arthritis are more susceptible to haematogenous infections.^{9,18}

Those with prosthetic knee joints are more at risk than those who have had a total hip replacement. It is difficult to establish from the data what role dental-induced bacteraemia may play in haematogenous infection in these patients. If an oral commensal is identified in such an infected joint then the same argument must apply – did the bacteraemia arise from dental treatment or did it occur spontaneously?

The arguments for diabetic patients, haemophiliacs, patients on long-term corticosteroid therapy and those who suffer from malignant disease are far less convincing. Most of the data has come from small studies, and in many instances there is a combination of immuno-suppressive factors (ie steroid treatment for patients with rheumatoid arthritis) operating in the same patient concomitantly.

There may be a case for providing antibiotic prophylaxis for patients with artificial knees – and a history of rheumatoid arthritis. If this is the case, then the mechanism will need elucidating and the risk related to the degree of activity of the underlying rheumatoid arthritis.

Despite the evidence, we believe that the patient's underlying medical problem, which may lead to immuno-suppression, needs to be put into context. It is the authors' view that a medically compromised patient at risk from dental-induced bacteraemia is one who exhibits a *proven* impairment of their host responses. This occurs primarily when there is a defect in white blood cell (WBC) numbers or function. In such instances, it is more appropriate to correct, wherever possible, the WBC defect. If this cannot be achieved, then antibiotic prophylaxis should be provided.

4. Prophylaxis is clearly indicated where there is overt oral sepsis, ie any kind of pre-existing oral infection which could lead to metastatic spread.

This guideline is likely to cause confusion since it is unclear what is meant by pre-existing oral infection, how is it quantified and how will dental practitioners recognise that their management of such infection is going to cause metastatic spread. A particular problem area would relate to the endodontic management of apical periodontitis and the management of periodontitis. Both conditions could be considered from a microbial perspective as examples of oral sepsis, the treatment of which may cause a bacteraemia. If such infections are going to be quantified, then presumably their management must be treated similarly. For example, should we be applying restrictions on the numbers of periodontal pockets that are treated on any one occasion, or the number of periapical areas that should be considered for endodontics. It is well recognised that patients with moderate to advanced periodontitis can generate significant bacteraemias from toothbrushing and using floss.¹⁹ If patients fitted with joint prostheses are equally at risk from such bacteraemias as those generated by the dentist, should they be on long-term antibiotic prophylaxis? An easier solution is to render the patient dentally fit prior to joint surgery, thus reducing oral sepsis without compromising the patient.

5. Prophylaxis should be considered where dental treatment is invasive, complex and of long duration.

This is probably the most contentious of the guidelines, it does not appear to be evidence based and requires to be quantified. In their preamble, the guidelines state that where treatment lasts 45 minutes or longer, antibiotic prophylaxis should be provided. The nature of the treatment is not specified. Furthermore, can dentists always predict the duration of treatment to the nearest minute? Invasive

treatment probably implies treatment of a surgical nature. Bacteraemia arising from a dental surgical procedure is more pronounced in the early stages than the latter stages.²⁰ Is there something significant at 45 minutes that changes a patient's susceptibility to dental-induced bacteraemia and, if so, what is it? The AHA is very prescriptive at what procedures should require prophylaxis. If, and in our opinion it is a very big if, any dental treatment does require prophylaxis to patients with prosthetic joints, then the guidelines should be much more prescriptive and avoid reference to terms such as invasive, complex and long duration.

CONCLUSION

The need for antibiotic prophylaxis prior to dental treatment for patients with prosthetic joints seems to be driven exclusively by our orthopaedic colleagues. The supportive evidence for such an indication appears equivocal at best and does not seem to be based upon a clear understanding of oral bacteraemia arising either spontaneously or from dental treatment.

It has not been established in a randomised, placebo-controlled study whether any of the antibiotic regimens recommended are efficacious. The low prevalence of joint infections and the high occurrence of dental treatment would suggest, as with infective endocarditis, a large number of patients will need to be recruited to come up with meaningful information.

Antibiotics recommended are not without risks and anaphylaxis from amoxicillin is a much more likely event than a joint infection. Even on a cost basis, it is more expensive to provide prophylaxis than to treat joint infections.

Thus the case for antibiotic prophylaxis prior to dental treatment in patients with joint prosthesis is weak or virtually non-existent. If the risk of prophylaxis is greater than the risk of joint infection and is added into the equation then the whole argument falls apart. Litigation and potential conflict with patients and their orthopaedic surgeons does cloud the issue. Certainly when dentists are placed in such a situation they would benefit from National Guidelines from a body such as NICE to fall back upon. If such guidelines showed that antibiotic prophylaxis was not required and certain orthopaedic surgeons still insisted upon prophylaxis, then they would risk facing disciplinary measures from their Medical Director or Chief Executive.

Until such guidelines are issued the dental profession will still receive dictates from certain orthopaedic surgeons to provide antibiotic prophylaxis for their patients. We would offer the following advice.

1. The dental surgeon is responsible for the patient's dental care not the orthopaedic surgeon. The final responsibility for presenting antibiotic prophylaxis resides with the dentist and not the orthopaedic surgeon.²¹ If a conflict still exists, then the orthopaedic surgeon should be referred to the guidelines issued in the BNF.
2. If there is concern about a dental-induced bacteraemia, then chlorhexidine mouthwash 1–2 minutes before the procedure is likely to be more effective than antibiotic prophylaxis.²²
3. It has been recommended elsewhere²³ that if an orthopaedic surgeon still insists upon prophylaxis being provided then ask him to administer the drugs. This would then exonerate the dentist from any unwanted effect arising from such antibiotic usage. While such an approach has its merits, it is likely to cause considerable inconvenience to all parties (especially the patient) and subject them to unnecessary risk.

There is an urgent need for this whole issue to be resolved. In this age of evidence-based medicine and dentistry, there is no place for ambiguous guidelines and a systematic review is required. The dental profession needs to be able to respond to challenges to their clinical practice from elsewhere. Furthermore they need to be comfortable and assured that the treatment

they are providing to their patient is appropriate, carries minimal risk and adheres to evidence-based guidelines.

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