Antibiotic Prophylaxis for Preventing Endocarditis and Infection in Joint Prosthesis after Dental Treatment: A Review of New Trends and Recommendations in the Literature

SADJ September 2008, Vol 63 no 8 p440 - p444

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There are many controversies in the literature, whether the use of prophylactic antibiotics for the prevention of endocarditis or infection in patients with joint prosthesis is still necessary. Antibiotics are prescribed in dentistry for two main reasons: to treat infections and to prevent infections. It is the latter that can be regarded as prophylactic use of this drugs.[1]

For the purpose of this article, the main indications and controversies relating to prophylactic use of antibiotics in dentistry will be reviewed, notably the prevention of infective endocarditis and infections in patients with joint prosthesis.

All surface coverings of the body are colonized by a unique microflora. Any bacteremia may be caused by separation of the mucosa or skin, gastroenteral mucosa, airway mucosa, genito-urinary mucosa or oral mucosa. Bacteria from these sources frequently enter the blood on a physiologic basis as a transient bacteremia and are dealt with by the host defences.[2]

Oral bacteria do enter the bloodstream during chewing, teeth clenching and tooth brushing although the amounts are small and transient.[3] Transient bacteremias that follow normal activities such as chewing are usually cleared by the host defences within 10 minutes.[4] Generally, the probability of this causing Infective endocarditis (IE) is very low, but is greater in a patient with pre-existing valve damage, in particular a prosthetic valve.[2]

Oral manipulations including dental treatment will produce a greater bacteraemia than physiological function, but is of a low grade and duration. A routine dental extraction in a patient with chronic periodontitis will result in a greater bacterial load than in a patient with optimal oral hygiene.[5]
IE is a microbial infection colonising the epithelium of the cardiac valves.[6,7]

Two possible mechanisms promotes bacterial adherence after ulceration on the valvular endothelium: [6]

- direct contact between the blood and subendotheluim results in production of a coagulum. Pathogens associated with IE in the bloodstream as a result of a bacteremia bind to the coagulum and in turn attract and activate monocytes to produce cytokines. This causes progressive enlargement of an infected vegetation.
- local inflammation promotes cells to express transmembrane proteins that bind fibronectin. Pathogens such as Staphylococcus aureus carry fibronectin binding proteins on the surface. Staphylococcal endocarditis is often seen in patients with normal valves, and micro ulcerations are thought to be responsible for endocarditis by this mechanism

The investigation and management of IE in the developed world have changed radically over the past 30 years.[2] Non-invasive imaging, molecular science, diagnostic protocols and curative surgery have all become commonplace, yet the incidence remains unchanged and annual mortality is around 40%.[8]

The lack of impact of modern medicine reflects important changes in the causes of the disease. In Western populations in particular, chronic rheumatic heart disease is now an uncommon antecedent, whereas degenerative valve disease in elderly people, intravenous drug misuse, preceding valve replacement, or vascular instrumentation have become increasingly frequent, coinciding with staphylococcal infections and those due to fastidious organisms. Furthermore, previously undetected pathogens are now being identified with the disease, and multidrug resistant bacteria is a challenge to conventional treatment regimens.[9]

Meanwhile rheumatic valve disease remains endemic in the developing world, where modern investigations and management are the privilege of the few who live in large urban areas.[10-12]

Infective endocarditis in the Western Cape of South Africa is a disease of younger adults, with a male predominance. Rheumatic heart disease is the major predisposing factor. Degenerative heart disease and intravenous drug abuse are not

imported risk factors, so is HIV infection not an independent risk factor for IE.[13]

From small beginnings with hip replacements in the early 1950s, joint prosthesis surgery has greatly expanded to include the knee, ankle, shoulder, elbow and finger joints. Generally these joint replacements are successful with an over 90% success rate over a 10-year period.[14] In the United States in 1995, 243 919 total knee replacements were performed[15] and in 2003, approximately 450 000 total joint arthroplasties were performed.[16] In Australia in the financial year 2002-2003 a total of 55 836 total hip and knee replacements were performed.[17] In Norway 73 000 arthroplasties were done between 1994 – 1999.[18] Currently no register exists in South Africa on the total of any athroplasties performed locally. The provision of joint prosthesis is thus a common orthopaedic procedure.

In the late 1950s and early 1960s, there was a high prevalence (15-25%) of postoperative infections associated with such surgery.1 Infections that occurred within three months of surgery were categorized as early and were related to the surgical procedure either sourced from the patient or the surgical staff. The incidence of this is low and of the order of 0.97%.[18] Infections after 3 months of surgery were considered as late and were believed to be caused by haematogenous spread of bacteria from another site of infection elsewhere in the body.[1] The incidence is low and in the order of 0.97%.[19] Historically we believe one of the key sources of focal infection was the teeth and widespread dental extraction.[20] The basis of this theory was by the process of anachoresis which is the preferential deposit of bacteria which have localized out of the bloodstream into areas of inflammation.[21] The prevalent bacteria causing the late infection are *Staphylococcus aureus* (35%) and *Staphylococcus epidermis* (15%). These are from skin origin. Group A Streptococci, which are mainly from oropharyngeal origin, occurred in about 8%of cases. Thus bacteremic-related joint infections may occur but generally at a low incidence. Skin organisms are the predominant group. The risk of oral-related infections is very low (0.04-0.07%).[22,23] Antibiotic prophylaxis at the time of surgery reduced the prevalence of postoperative infection to approximately 1%.[1]

Can orthopaedic implants be infected by blood-borne bacteria? There is extensive soundly-based scientific literature on this.[14,17,24-26] It is important that all papers which set out to document joint infections have meticulous methodology as it is easy for the source of the infection to be based on anecdote. Ideally, to confirm that a joint prosthesis has been infected from an oral treatment, one requires a coincidence history and an accurate and simultaneous typing of the oral flora bacteremia and joint organisms.[24] These steps have not usually been taken in most investigations in the literature and some papers are based solely on history.[20] There is little firm evidence to suggest that dental-induced bacteremia can cause haematogenous infection around a prosthetic joint.[25] By contrast, there are several studies that shows the opposite.[27-30]

The frequency of bacteremia associated with various dental procedures and oral activity is presented in Table 1[1]

According to the prevalence of bacteremia in various types of dental procedures and oral activity detailed in Table 1, higher and lower risk procedures in dentistry can be identified (Table 2).[15,31]

Traditionally, the criterion that 'significant bleeding' associates with a dental procedure has being equated with a significant bacteremia. A recent study which involved both pre- and post-procedure bacteremia estimations showed that bleeding is a poor predictor of odontogenic bacteremia above usual physiological levels.[15] It may well transpire that random or spontaneous bacteremia may be more causative in IE (or infection in joint prosthesis) than dental surgeons carrying out treatment.[1]

Table 1: Prevalence of bacteraemia arising after various types of dental procedures and oral activity.[1]

Procedure	Prevalence of bacteraemia
Extractions (single)	51%
Extractions (multiple)	68-100%
Endodontics (intra canal instrumentation)	0-31%
Endodontics (extra canal instrumentation)	0-54%
Periodontal surgery (flap procedure	36-88%
Periodontal surgery (gingivectomy)	83%
Scaling and root planning	8-80%
Periodontal prophylaxis	0-40%
Tooth brushing	0-26%
Dental flossing	20-58%
Interproximal cleaning with toothpicks	20-40%
Irrigation devices	7-50%
Chewing	17-51%

Further evidence to support this hypothesis comes from an analysis of cases of IE in which dental treatment has been implicated as the cause. Oral Streptococci cause approximately 50% of all IE cases.[32] Similarly, only 15% of patients in whom IE has been diagnosed reported dental or medical treatment within the previous 3 months.[33] It has been estimated that 4% or less of all IE cases are related to dental-induced bacteremia.[34,35] Whether such bacteremias arise from dental treatment or were spontaneous is not discernible. It is suggested that if spontaneous bacteremia cause 96% of all cases of IE, then these bacteremias as opposed to those arising from dental treatment also may have caused the remaining 4%.[36] In the study of Strom *et al*,[37] the authors concluded that the lack of a link between dental treatment and IE, together with the rare occurrence of this disease, does not justify the routine use of antibiotic prophylaxis.

No literature could be found on the effect of dental-induced bacteremia on specific the temporomandibular-joint prosthesis. The temporomandibular joint is regarded as a heavy load joint and therefore the same principles should be applied as to all the other joint prosthesis.

Previous guidelines categorized underlying cardiac conditions associated with the risk of IE as those with high risk, moderate

Table 2:[15,31] Incidence stratification of bacteremic dental procedures

Incidence	Dental Procedure
Higher incidence†	• Dental extractions • Periodontal procedures, including surgery, subgingival placement of antibiotic fibres/ strips, scaling and rootplaning, probing, recall maintenance • Dental implant placement and replantation of avulsed teeth Endodontic instrumentation or surgery only beyond the apex • Initial placement of orthodontic bands but not brackets • Intraligementary and intraosseous local anaesthetic injections • Prophylactic cleaning of teeth or implants where bleeding is anticipated
Lower incidence‡§	• Restorative dentistry¶ (operative and prosthodontic) with/without retraction cord • Local anaesthetic injections • Intracanal endodontic treatment, post placement and build-up • Placement of rubberdam • Postoperative suture removal • Placement of removable prosthodontic/orthodontic appliances • Taking of oral impressions • Fluoride treatments • Taking of oral radiographs • Orthodontic appliance adjustment

† Prophylaxis should be considered for patients with total joint replacement who meet the criteria in Table V. No other patients with orthopaedic implants should be considered for antibiotic prophylaxis prior to dental treatment / procedures.
‡ Prophylaxis not indicated.
§ Clinical judgement may indicate antibiotic use in selected circumstances that may create significant bleeding
¶ Includes restoration of carious (decayed) or missing teeth.

risk, and negligible risk and recommended prophylaxis for patients in the high- and moderate-risk categories.[31]

For the present guidelines on prevention of IE, three distinct issues were considered by the American Heart Association:[38]

1. What underlying cardiac conditions over a life time have the highest predisposition to the acquisition of endocarditis?
2. What underlying cardiac conditions are associated with the highest risk of adverse outcome from endocarditis?
3. Should recommendations for IE prophylaxis be based on either or both of these 2 conditions?

Cardiac conditions with a higher risk of IE that need prophylaxis are presented in Table 3[38].

The rationale for the use of antibiotic prophylaxis for surgical, including dental, manipulations is that the procedure causes bacteremia and the bacteremia may cause endocarditis or infection in joint prosthesis. As a result, the antibiotics should be given to susceptible patients before the bacteremia is generated.[1,2]
Where antibiotic prophylaxis is indicated, a single oral dose will achieve adequate serum levels. There may be occasions where it is logistically easier to administer the antibiotic via the intravenous (IV) route.[39]

Antibiotics may prevent endocarditis or infection in joint prosthesis either by killing bacteria or by damaging them to an extent that the host defences can then destroy them. Therefore the antimicrobal medication may work before the bacteria enter the bloodstream, or after they enter the bloodstream or on colonies of bacteria.[1,2]

Table 3:[38] Cardiac conditions associated with the highest risk of adverse outcome from endocarditis for which prophylaxis with dental procedures is recommended

Prosthetic cardiac valve
Previous IE
Congenital heart disease (CHD)*
Unrepaired cyanotic CHD, including palliative shunts and conduits
Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure†
Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)
Cardiac transplantation recipients who develop cardiac valvulopathy

GUIDELINE RECOMMENDATIONS

On review of the international guidelines it is clear that there are many points of agreement. All agree that there is a high-risk cardiac group where the risk of endocarditis exceeds the risk of antibiotic prophylaxis from dental at-risk procedures, thus warranting antibiotic prophylaxis. All agree that there is a large group of patients with a cardiac history who are at no greater risk of endocarditis than the general population. In these patients the risk of anaphylaxis and similar adverse events from the antibiotic prophylaxis is demonstrably greater than the risk of endocarditis. Thus, in these circumstances, antibiotic prophylaxis is not warranted for any type of dental treatment.[2]

Table 4:[15] Patients at potential increased risk of experiencing hematogenous total joint infection

Patient type	Condition placing patient at risk
All patients during first two years following joint replacement	N/A†
Immunocompromised/suppressed patients	• Inflammatory arthropathies such as rheumatoid arthritis, systemic lupus erythematosus • Drug- or radiation-induced immunosupression • Previous prosthetic joint infections
Patients with comorbidities, ‡	• Malnourishment • Hemophilia • HIV infection • Insulin-dependant (type 1) diabetes • Malignancy

† N/A: Not applicable
‡ Conditions shown for patients in this category are examples only; there may be additional conditions that place such patients at risk of experiencing hematogenous total joint infection.

Bacteremias can cause haematogenous seeding of total joint prosthesis, both in the early postoperative period and

Table 5:[38] Regimens for a Dental Procedure			
		Regimen: Single Dose 30 to 60 min	
		Before procedure	
Situation	**Agent**	**Adults**	**Children**
Oral	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin	2 g IM or IV	50 mg/kg IM or IV
	or		
	Cefazolin or Ceftriaxone	1 g IM or IV	50 mg/kg IM or IV
Allergic to penicillins or ampicillin—oral	Cephalexin*†	2 g	50 mg/kg
	or		
	Clindamycin	600 mg	20 mg/kg
	or		
	Azithromycin or Clarithromycin	500 mg	15 mg/kg
Allergic to penicillins or ampicillin and unable to take oral medication	Cefazolin or Ceftriaxone†	1g IM or IV	50 mg/kg IM or IV
	or		
	Clindamycin	600 mg IM or IV	20 mg/kg IM or IV
IM indicates intramuscular; IV, intravenous			

for many years following implantation.[40] It appears that the most critical period is up to two years after implantation.[41] Presently, no scientific evidence supports the position that antibiotic prophylaxis to prevent haematogenous infections is required prior to dental treatment in patients with total joint prosthesis[42] as presented in Table 4.

Antibiotic prophylaxis is not indicated for dental patients with pins, plates and screws, nor is it routinely indicated for most dental patients with total joint replacements[15]

When antibiotics are given prophylacticly to prevent endocarditis or infection in joint prosthesis, the dental surgeon needs to consider the risk of such treatment, especially when penicillin is the first choice of drugs. One to 10% of patients report a penicillin allergy,[43] although many of these are not confirmed if subjected to the appropriate test. More importantly, the change of an allergic reaction following the administration of the drug is in the range of 0.7-5%,[44] with the intramuscular route 5% prevalence and the oral route 0.3% prevalence respectively. High doses of oral penicillin can cause an allergic reaction rate similar to that of intramuscular penicillin.[45] Patients receiving penicillin prophylaxis to prevent endocarditis or infection in joint prosthesis are five times more likely to die from an anaphylactic reaction to the drug than to die from contracting endocarditis or infection in joint prosthesis.[1,46] It would thus seem from these statistics that the risk providing antibiotic coverage to prevent IE or infection in joint prosthesis is far greater than not providing coverage.[1]

At present, recommendations of choice antimicrobial agents for particular forms of dental infections are based on published data. Agents in the penicillin group traditionally have been regarded as the antimicrobials of choice, while erythromycin traditionally has being used as an alternative agents for patients with hypersensitivity to penicilins.[47,48] However, resistance to these antimicrobials has been demonstrated within the oral flora and this observation must be taken into consideration when prescribing these drugs.[49] Other antimicrobial agents have been suggested including clindamycin.[50,51] Clindamycin is a unique antimicrobial that achieves high tissue (including bone) concentrations, penetrates intracellularly, increases phagocytosis, inhibits toxin production and has a post-antibiotic effect. A review of the microbiologic and clinical literature relating to maxillofacial infections has revealed this antimicrobial to be a highly effective agent in the field of dentistry. Brook *et al*[47] suggest on this basis, clindamycin should be considered as a first-line antimicrobial for all dental infections. In addition, where practicable, a pre-operative mouthwash of chlorhexidene gluconate (0,2%) should be administered and held in the mouth for one minute.[39]

The overall prevalence of IE is approximately 15 per one million patients per year. This figure has not changed with the advent of antibiotic prophylaxis and it could thus be inferred that the provision of such prophylaxis has had little impact on the occurrence of the disease, questioning the value of providing such antibiotic coverage.[1]

Good oral hygiene is probably the most important factor in reducing the risk of endocarditis or infection in joint prosthesis in susceptible patients, and access to high-quality dental care should thus be facilitated. Once a patient is found to have a cardiac anomaly, cardiac or joint replacement surgery, putting him or her at risk of endocarditis or infection, the patient should be referred to have their dental hygiene optimized. Interventions ideally should be performed at least 14 days prior to surgery to allow mucosal healing. Those patients who undergo emergency or urgent surgery should have a dental assessment performed as soon as practicable after surgery, and a risk assessment performed to determine the most appropriate plan for any remedial dental treatment. All elective dental procedures should ideally be delayed for at least 3 months post surgery.

Patients who already have had surgery (cardiac or joint), should perform effective daily oral hygiene procedures to re-

move plaque and to establish and maintain good oral health.[13] The risk of bacteremia is far more substantial in a mouth with ongoing inflammation than in one that is healthy.[42]

This position agrees with that taken by the ADA Council on Dental Therapeutics[52] and the American Academy of Oral Medicine[53] and is similar to that taken by the British Society for Antimicrobial Chemotherapy.[54]

The recommended regimens for the prevention of a bacteremia that can cause infective endocarditis or infection in joint prosthesis is similar and is presented in Table 5.

For patients who require sequential dental procedures, these should ideally be performed at intervals of at least 14 days to allow healing of oral mucosa surfaces. If further dental procedures cannot be delayed, alternating amoxicillin and clindamycin should take place. If there is in this scenario a penicillin allergy, seek expert advice.[39]

Patients who are about to have a total joint arthroplasty should be in good dental health prior to surgery and should be encouraged to seek professional dental care if necessary.

DISCUSSION

In South Africa there are presently no national guidelines or protocol available on the use of antibiotics for the prevention of infective endocarditis in patients, nor for the prevention of infection in patients with prosthetic joints. We have to rely on guidelines from other countries, usually from developed countries. On the contrary, South Africa should be regarded as a developing country (economically), with probably different dental treatment profiles as in developed countries. One can assume that more extractions per capita are done in South Africa than in the developed countries. Extractions were regarded as a high risk procedure as in Table 2 for the developing of a bacteraemia that can cause IE or secondary infection in patients with joint replacements.

Medically compromised patients are also at higher risk to get a bacteremia. There is also controversy on the HIV-status in South Africa. The dentist usually does not know what the HIV-status is of the patient he/she is treating and can therefore not decide to do a lower risk dental procedure on a medically compromised patient that might benefit from antibiotic prophylaxis.

There are two topics on antibiotic prophylaxis for the prevention of infective endocarditis and the prevention of secondary infection in patients with prosthetic joints that are causing quite a lot of controversy. What is the risk for the patient receiving antibiotics and is it really effective? A third aspect that must always be borne in mind, is the medico-legal aspect of the prescribing or not prescribing of antimicrobials to prevent infection.

Taken all into account, the responsibility for the treatment the patient receives is that of the person who performed it. Therefore it is very important to make the correct decision for the specific treatment and to have informed consent from your patient.

Declaration: No conflict of interest was declared

REFERENCES

1. Seymour Robin A, Withworth John M. Antibiotic prophylaxis for endocarditis, prosthetic joints, and surgery. *Dent Clin N Am* 2002;**46**:635-31.
2. Prendergast BD. The changing face of infective endocarditis. *Heart* 2006;**92**:879-85.
3. Singh J, I Straznicky, M Avent, AN Goss. Antibiotic prophylaxis for endocarditis: time to reconsider. *Aust Dent J* 2005;**50** Suppl 2:60-68.
4. Guntheroth WG. How important are dental procedures as a cause of endocarditis. *Am J Cardiol* 1984;**54**:797-801.
5. Malinverni R, Overholser CD, Bille J, Glauser MP. Antibiotic prophylaxis of experimental endocarditis after dental extractions. *Circulation* 1988;**129**:761-769.
6. Mylonakis E, Calderwood SB. Infective endocarditis in adults. *N Eng J Med* 2001;**345**:1318-1330.
7. Moreillon P, Que YA, Bayer AS. Pathogenesis of streptococcal and staphylococcal endocarditis. *Infect Dis Clin North Am* 2002;**16**:297-318.
8. Cabell CH, Jollis JG, Peterson GE, Corey GR, Anderson DJ, Sexton DJ, *et al*. Changing patient characteristics and the effect on mortality in endocarditis. *Arch Intern Med* 2002;**162**:90-4.
9. Moreillon P, Que YA. Infective endocarditis. *Lancet* 2004:**363**:139-49.
10. Durack DT. Prevention of infective endocarditis. *N Engl J Med*. 1995;**332**:38–44.
11. S Garg N, Kandpal B, Garg N, Tewari S, Kapoor A, Goel P, et al. Characteristics of infective endocarditis in a developing country-clinical profile and outcome in 192 Indian patients:1992-2001. *Int J Cardiol* 2005;**98**:253-60.
12. Beynon RP, Bahl VK, Prendergast BD. Infective endocarditis: Clinical Review. *Br Med J* 2006;**333**:334-339.
13. Koegelenberg CFN, Doubell AF, Orth H, Reuter H. Infective endocarditis in the Western Cape Province of South Africa: a three year prospective study. *QJM: An Int J of Med* 2003;**96**(3):217-225.
14. American Academy of Orthopaedic Surgeons: National Centre of Health Statistics Rosemont. Illinois. American Academy of Orthopaedic Surgeons 14.1999.
15. Advisory statement: Antibiotic prophylaxis for dental patients with total joint replacements. American Dental Association: American academy of Orthopaedic Surgeons. *J Am Dent Assoc* 2003;**134**:895-8.
16. Australian Orthopaedic Association National Joint Replacement Registry Annual Report. Adelaide: AOA 2004; ISSN:1455-366. http://www.dmac.adelaide.edu.au/aoanjrr/aoanjrr.jsp. Accessed November 2005
17. Peersman G, Laskin R, Davis J, Peterson M. Infection in total knee replacements: a retrospective view of 6489 total knee replacements. *Clin Orthop Relate Res* 2001;**329**:15-23.
18. Havelin LI, Engesæter, Espehaug B, Furnes O, Lie SA, Vollset SE. The Norwegian Arthroplasty Register: 11 years and 73000 arthroplastys. Acta Orthop Scand 2000 ;71(4) :337-53.
19. Saleh KJ, Macaulay A, Radosevich DM, et al. The Knee Society Index of Severity for failed total knee arthroplasty: Development and validation. *Clin Orthop Relat Res* 2001;**392**:153-165.
20. Scott JF, Morgan D, Avent M, Graves S Goss AN. Patients with artificial joints: do they need antibiotic cover for dental treatment? *Aust Dent J* 2005;**50** Suppl 2:45-53.
21. Chronic oral sepsis and its relation to systemic disease. Focal infection. In: Stones HH, ed. Oral and dental diseases. 4th edn. Edinburgh & London: E&S Livingstone, 1962:679-690.
22. Little JW. Dental treatment in patients with joint replacements. *Oral Surgery* 1983;**55**:20-23.
23. Maderazo EG, Judson S, Pasternak H. Late infections of total joint prostheses. A review and recommendations for prevention. *Clin Orthop Relat Res* 1988;**229**:131-142.
24. Sandhu SS, Lowry JC, Reuben SF, Morton ME. Who decides on the need for antibiotic prophylaxis in patients with major arthroplasties requiring dental treatment: Is it a joint responsibility? *Ann R Coll Surg Engl* 1997;**79**:143-147.
25. McPherson EJ, Woodson C, Holtom P, Roidis N, Schufelt C, Patzakis M. Perioprosthetic total hip infection. *Clin Orthop Relat Res* 2002;403:8-15.
26. Rhinelander FW. Physiologic responses of bone implants. In: Biocompatibility of orthopaedic implants. Boca Raton:CRC Press. 1982:51-74.
27. Thyne GM, Ferguson JW. Antibiotic prophylaxis during dental treatment in patients with prosthetic joints. *Br J Bone Joint Surg* 1991;**73**(B):191-4.

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