INVITED ARTICLE

USE OF PROPHYLACTIC ANTIBIOTICS IN THE PREVENTION OF INFECTIVE ENDOCARDITIS AND PROSTHESIS INFECTION

M S Lam, S Y Wong

ABSTRACT

In the field of antimicrobial therapy, few areas have created more debate and controversy than the subject of antibiotic prophylaxis for infective endocarditis. Firstly, there still exists considerable controversy about the efficacy of prophylactic antibiotics for prevention of bacterial endocarditis. Secondly, dental surgeons, orthopaedic surgeons, cardiologists and endoscopists have differing opinions regarding indications for pre-procedural prophylactic antibiotics against infective endocarditis. The British have a different set of recommendations from the Americans although the basic tenets on which these recommendations are founded are similar. This article summarises the updated recommendations issued by the American Heart Association (AHA) as well as those from the British Society for Antimicrobial Chemotherapy. A short discussion of the use of prophylactic antibiotics prior to endoscopy and surgery for patients with non-valvular prosthetic devices has been included in this paper. Practitioners should also be reminded that these recommendations are issued as guidelines and clinical judgement must be exercised when dealing with individual patients.

Keywords: *antibiotic prophylaxis, infective endocarditis, prosthesis, endoscopy*

SINGAPORE MED J 1995; Vol 36: 424-427

Introduction

Since Rushton reported a case of infective endocarditis following dental extraction[1] and others have shown that extractions release showers of bacteria into the bloodstream, there has been a heightened awareness of the relationship between dental procedures and infective endocarditis. Although it has been known that bacteraemia causes infective endocarditis, it is not clear exactly how this occurs. *Viridans streptococcus,* a component of endogenous oral flora, are the most common pathogens accounting for almost half the cases of infective endocarditis[2]. Other Gram-positive organisms such as *Enterococci* and *Streptococcus bovis* also have a marked affinity for heart valve tissue. In contrast, *E. coli,* a common organism causing bacteraemia in humans infrequently causes infective endocarditis or prosthetic joint infections. Anaerobic bacteria including *Bacteroides* species, the predominant gut flora in man, are uncommon pathogens in infective endocarditis. Explanation of the disparity in the frequency of endogenous flora causing infective endocarditis is an area of intensive research.

In recent years, owing in part to the rapid advances in diagnostic skills, the experience with new antibiotics and advances in the field of cardiothoracic surgery, several controversial issues concerning infective endocarditis have emerged. These include problems in clinical diagnosis in patients with no classical clinical stigmata of infective endocarditis, diagnosis in patients with *Staphylococcus aureus* bacteraemia, optimal treatment for *Staphylococcus aureus* endocarditis, use of ceftriaxone for *viridans streptococci* endocarditis, role of echocardiography in the diagnosis and management of endocarditis, optimal therapy for prosthetic valve endocarditis due to coagulase-negative Staphylococcus, management of extracardiac complications of endocarditis, especially cerebrovascular mycotic aneurysms and, last but not least, administration of chemoprophylaxis for endocarditis; readers are referred to an excellent review by Bayer[3] on these issues. Durack et al[4] have recently proposed new case definition criteria for the diagnosis of endocarditis, modeled after the Jones criteria for acute rheumatic fever. Both the American and British Heart Association have also revised their latest recommendations for chemoprophylaxis of endocarditis in order to streamline regimens from both sides of the continents[8,9].

Infective endocarditis, in particular prosthetic valve endocarditis, is a disease associated with a high morbidity and mortality. Prophylactic antibiotics are therefore recommended for patients at risk for developing endocarditis who are undergoing procedures likely to produce bacteraemia with organisms that may cause endocarditis. It is extremely difficult to prove that any prophylactic regimen is effective because trials of such nature may face significant ethical issues. Also, the number of patients involved in such a trial in order to attain statistical significance has been estimated to be over 6,000 because the incidence of procedure-related infective endocarditis is small[16]. Hence recommendations have been based on in vitro data, clinical studies of bacteraemias, pharmacokinetic studies, and animal models of infective endocarditis.

The rationale for antibiotic prophylaxis

Medical procedures can result in bacteraemias; some with organisms that are common pathogens which result in

Department of Infectious Disease
Communicable Disease Centre
Tan Tock Seng Hospital
Moulmein Road,
Singapore 1130

M S Lam, MBBS, MMed (Int Med), MRCP, FAMS
Consultant

S Y Wong, MBBS, MMed (Int Med), FAMS
Consultant

Correspondence to: Dr M S Lam

infective endocarditis in susceptible individuals. Many of these bacteria are exquisitely sensitive to commonly used antibiotics like penicillins. Therefore, it is intellectually attractive to give prophylactic antibiotic to patients with predisposing cardiac disorders before procedures that may cause bacteraemia. However, there has been no prospective study to prove the efficacy of prophylactic antibiotic usage.

Important considerations in the use of prophylactic antibiotics for infective endocarditis

Prophylactic antibiotics are believed to act by interruption of one or more of three major mechanisms believed to be important in the pathogenesis of infective endocarditis; viz bacteraemia (by reducing the number of micro-organisms in the blood)[5], adherence (by decreasing the affinity of mirco-organisms for heart valves)[6], and multiplication of micro-organisms on the heart vales (by interfering with the metabolic activity of the micro-organism)[7].

Effective antibiotic prophylaxis must satisfy the following criteria:

1 Its antimicrobial spectrum must include activity against the bacteria most likely to cause the bacteraemia in question.
2. It must be given pre-operatively in doses sufficient to ensure adequate antibiotic levels in the serum during and shortly after the procedure.
   (a) It should be given 1 - 2 hours before the procedure and should not be continued for more than 6 - 8 hours following the procedure without good reasons.
   (b) To reduce the likelihood of antimicrobial resistance, it should be used strictly only during the perioperative period.

The likelihood of acquiring infective endocarditis is determined by:

1. The type of procedure involved. Dental extraction is more likely to cause bacteraemia than bladder catheterisation of uninfected urine than gastrointestinal diagnostic procedure in that order[16].
2. The organism involved in bacteraemia caused by the procedure. As mentioned above, some organisms have a higher predilection for heart valves than others.
3. The focus that is being manipulated. An infected focus is more likely to cause bacteraemia than an uninfected one.
4. The pre-existing cardiac lesion: "high risk versus low risk" lesions. (see below).
5. The immune status of the patient: an immuno-compromised patient is theoretically at a higher risk of being infected than an immunocompetent one. Hence, a lower threshold for using prophylactic antibiotics in this group of patients.
6. A previous episode of infective endocarditis.

Recommendations

A. Endocarditis prophylaxis is recommended for the following dental and surgical procedures:

1. Dental procedures known to produce gingival or mucosal bleeding including extractions, periodontal surgery, subgingival scaling, scaling plus polishing.
2. Tonsillectomy and/or adenoidectomy
3. Surgical operations involving intestinal or respiratory mucosa
4. Rigid bronchoscopy
5. Sclerotherapy for oesophageal varices
6. Oesophageal dilatation
7. Gallbladder surgery
8. Cystoscopy
9. Urethral dilatation
10. Urethral catheterisation if urinary tract infection is present
11. Urinary tract surgery if urinary tract infection is present
12. Prostatic surgery
13. Incision and drainage of infected tissue
14. Vaginal hysterectomy
15. Vaginal delivery in the presence of infection

(Recommendations by the American Heart Association)[8]

B. Endocarditis prophylaxis is recommended when the following cardiac conditions exist:

1. Prosthetic cardiac valves
2. Previous bacterial endocarditis
3. Most congenital cardiac malformations (exceptions listed below)
4. Rheumatic or other acquired valvular dysfunction
5. Hypertrophic cardiomyopathy
6. Mitral valve prolapse with valvular regurgitation (Men > 45 years with mitral valve prolapse with thickening and/or redundancy of the valve leaflets may be at increased risk).

The Committee on Rheumatic Fever and Infective Endocarditis of the American Heart Association (AHA)[8] defines high risk cardiac conditions as:

1. History of previous endocarditis
2. Presence of prosthetic cardiac valves, including bioprosthesis and homografts.
3. Presence of surgically constructed systemic pulmonary shunts or conduits
4. Presence of vascular graft material (in the first year/ subsequently low risk)

In patients with these conditions, the AHA recommends prophylactic antibiotics even for low risk procedures involving the lower respiratory, genitourinary or gastrointestinal tracts eg. flexible bronchoscopy, endoscopy with or without biopsy, urethral catheterisation, dilatation and curettage. For instance, lower gastrointestinal endoscopy is generally a low risk procedure as far as inducing bacteraemia is concerned; but when it is performed on a patient with a "high risk" cardiac condition, the use of prophylactic antibiotics may be justified. The clinician is therefore urged to use his or her clinical judgement in dealing with individual patients; but suffice to say that, as a general rule, it is always prudent to consider using prophylactic antibiotics in "low risk" cardiac conditions when performing "high risk" (of inducing bacteraemia) procedures and in "high risk" cardiac conditions when performing "low risk" procedures.

Endocarditis prophylaxis is not necessary for the following cardiac conditions :

1. Isolated secundum atrial septal defect
2. Surgical repair beyond 6 months of secundum atrial septal defect, ventricular septal defect or patent ductus arteriosus
3. Previous coronary bypass graft surgery
4. Mitral valve prolapse without valvular regurgitation
5. Physiologic, functional or innocent heart murmurs
6. Previous Kawasaki disease without valvular dysfunction
7. Previous rheumatic fever without valvular dysfunction
8. Cardiac pacemakers and implantable defibrillators.

The AHA standard prophylactic regimen is: Amoxicillin 3.0 g orally (paediatric 50 mg/kg) 1 hour before procedure;

then 1.5 g 6 hours after the initial dose.

For the amoxicillin/penicillin allergic patients, erythromycin ethylsuccinate 800 mg or erythromycin stearate 1.0 g orally (paediatric 20 mg/kg) 2 hours before procedure; then half the dose 6 hours after the initial dose. Alternatively, clindamycin 300 mg orally (paediatric 10 mg/kg) 1 hour before procedure and 150 mg 6 hours after the initial dose.

Alternative prophylactic regimens include: Ampicillin 2.0 g parenterally (IV or IM) 30 minutes before procedure; then 1.0 g 6 hours after the initial dose for those unable to take orally. For the penicillin-allergic, clindamycin IV 300mg 30 minutes before procedure and IV 150mg 6 hours after the initial dose is suggested.

For patients considered high risk, IV or IM ampicillin 2.0 g plus gentamicin 1.5 mg/kg 30 minutes before procedure and repeated 8 hours after the initial dose is recommended. For penicillin-allergic high risk patients, vancomycin IV 1.0 g over 1 hour starting 1 hour before procedure should be given. A subsequent dose is unnecessary.

(NB: The parenteral route is recommended for high risk patients.)

For genitourinary and gastrointestinal procedures, the antibiotic regimen should include prophylaxis directed against the enterococci, hence parenteral ampicillin/gentamicin or vancomycin/gentamicin were recommended.

Table I - Summary of antibiotic prophylaxis recommendations from both the American Heart Association and the British Society for Antimicrobial Chemotherapy

AHA Recommendations (1990)	British Society for Antimicrobial Chemotherapy Recommendations (updated May 1992)
Amoxicillin 3g p.o. 1h before and 1.5 g 6 h after	Amoxicillin 3g p.o. 1 h before
If penicillin-allergic:	If penicillin-allergic:
Erythromycin ethylsuccinate 800mg p.o. 2 h before or Erythromycin stearate 1 g orally 2 h before	Teicoplanin 400 mg IV and gentamicin 120 mg IV at the time of induction or 15 mins before dental procedure
Alternatively: Clindamycin 300 mg p.o. 1 h before and 150 mg 6h after	Alternatively: Vancomycin 1 g IV and gentamicin 120 mg just before induction or 15 mins before procedure
For high-risk patients: Ampicillin IV or IM 2 g and gentamicin 1.5 mg/kg 30 mins before and repeat 8 h after initial dose	For high-risk patients: Above regimen plus gentamicin IM 120 mg
If penicillin-allergic: Vancomycin 1 g IV 1 h before procedure. Subsequent dose not necessary	

The recommendations of the Endocarditis Working Party of the British Society for Antimicrobial Chemotherapy for anti-biotic prophylaxis of infective endocarditis, updated May 1992[9] are as follows:

Amoxicillin 3 g orally 1 hour prior to procedure.

For the penicillin-allergic, they recommend oral clindamycin 600 mg as one dose 1 hour before a dental procedure. Children 5 - 10 years old should receive half the adult dose (300 mg) and those under 5 years should get a quarter of the adult dose (150 mg)

For those unable to take orally, IV amoxicillin 1 g just before procedure/induction and 0.5 g orally 6 hours later is recommended. Special risk patients including those with prosthetic valves and those who had a previous history of endocarditis should be given in addition to the above regimen IM gentamicin 120 mg as well.

For adults who are allergic to penicillin or who had penicillin more than once in the previous month, they have recommended teicoplanin 400 mg IV (not available in Singapore) and gentamicin 120 mg IV as the first alternative, to be given at the time of induction or 15 minutes before the dental procedure. A second alternative is IV vancomycin 1 g (slow infusion over 1 hour) plus IV gentamicin 120 mg just before induction or 15 minutes before the surgical procedure.

Although the efficacy of prophylaxis against endocarditis has not been proven by any prospective studies, it is now considered routine practice in modern medicine based on the rationale and the various circumstantial evidence supporting its usefulness. If one considers the mortality and morbidity involved in untreated and even in treated infective endocarditis, then prevention as a cornerstone of good medical care would be appreciated. Readers are however referred to the suggested reading list at the end of this paper for an insight into the arguments against the routine use of antibiotic prophylaxis for the prevention of infective endocarditis.

Antibiotic prophylaxis prior to endoscopy/surgical procedures for non-cardiac prosthetic devices

Having discussed the role of antibiotic prophylaxis in infective endocarditis, we now turn to a less frequent clinical problem; albeit with similar attendant morbidity and mortality, that of non-valvular non-cardiac prosthetic infections. Surgical procedures that are likely to generate bacteraemia can result in seeding of a distant prosthetic device. However, the recommendations for the use of antibiotic prophylaxis to this end is shrouded in even more controversy. Below are a summary of the more commonly adopted standard of practice and recommendations.

The recommendations for antibiotic prophylaxis before dental and surgical procedures for other (non-cardiac) prosthetic devices are as follows:

1. Orthopaedic prostheses: Controversial. The decision to use antibiotic prophylaxis in patients undergoing endoscopy or other surgical procedures with prosthetic joints in place should be made on an individual basis. There has only been rare and anecdotal reports of late prosthetic joint infections by oral bacteria, these numbers seem negligible considering the large numbers of such procedures done. Ultimately, the risks of antibiotic prophylaxis in this group of patients far outweigh the benefits. Segreti and Levin[10] do not recommend prophylaxis in this group of patients unless the surgery involves infected tissue or infection of the prosthetic joint itself. A distant focus of infection should be treated promptly to avoid seeding the prosthesis.
2. Central nervous system devices - not recommended[11]
3. Penile prostheses - Kabalin and Kessler[12] recommended prophylactic antibiotics.
4. Intraocular lens - not being recommended. The majority of intraocular lens infections occur intra-operatively during surgical implantation. The healed lens is almost never infected through haematogenous spread but mainly through contiguous spread of infection. There has been no report of a haematogenous seeding of an intraocular prosthesis[13].
5. Pacemakers - no evidence for use of prophylactic

antibiotics[14] (see AHA recommendations).

6. Reconstruction and local tissue augmentation - not being recommended. This includes breast augmentation/ reconstruction, hernia repair and other synthetic material for wound reconstruction/reinforcement. Like in the case of intraocular implants, infection occurs as a result of contamination at the time of surgery or by direct contiguous spread from an adjacent septic focus; haematogenous spread is virtually unheard of[15].

Concluding Remarks

Finally, it must be emphasised that these guidelines were issued primarily as a guide for practitioners and not as a "standard of care" for all patients. A reasonable standard of care would involve a clinician understanding the relationship between procedure-induced bacteraemia and endocarditis; the ability to elicit a history of and/or clinically detect a predisposing cardiac disorder, to inform the patient of the small risk and to decide on appropriate antibiotic prophylaxis, if necessary. Negligence claims often arise as a result of the failure to carry out one or more of the above practices. As long as the physician uses sound clinical judgement, with the principles of prophylaxis in mind, the patient's interests will be served.

References

1. Rushton MA. Subacute bacterial endocarditis following the extraction of teeth. Guy's Hosp Rep 1930;80:39-44.
2. Lerner PI, Weinstein L. Infective endocarditis in the antibiotic era. N Engl J Med 1966;274:199-206, 323-31, 388-93.
3. Bayer AS. Infective endocarditis. Clin Infect Dis 1993;17:313-22.
4. Lukes A, Bright D, Durack D. New criteria for the diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Am J Med 1994;96:200-9
5. Baltch AL, Pressman HL, Schaffer C, et al. Bacteraemia in patients undergoing oral procedures: study following parenteral antimicrobial prophylaxis as recommended by the American Heart Association, 1977. Arch Intern Med 1988; 148:1084-8.
6. Bernard JP, Francioli P, Glauser MP. Vancomycin prophylaxis of experimental *Streptococcus sanguis:* inhibition of bacterial adherence rather than bacterial killing. J Clin Invest 1981;68:1113-6.
7. Berney P, Francioli P. Successful prophylaxis of experimental streptococcal endocarditis with single-dose amoxicillin administered after bacterial challenge. J Infect Dis 1990;161:281-5.
8. Dajani AS, Bisno AL, Chung KJ, Durack DT, Freed M, Gerber MA, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. JAMA 1990;264(22):2919-22.
9. Simmons NA, Cawson RA, Eykyn SJ, Lambert HP, Littler WA, McGowan WA, et al. Antibiotic prophylaxis of infective endocarditis. Recommendations from the Endocarditis Working Party of the British Society for Antimicrobial Chemotherapy. Lancet 1990;335:88-9.
10. Segreti J, Levin S. The role of prophylactic antibiotics in the prevention of prosthetic device infections. Infect Dis Clin North Am 1989;3:357-70.
11. Bisno AL. Infections of central nervous system shunts. In: Bisno AL, Waldvogel FA, eds. Infections associated with indwelling medical devices. Washington DC: American Society for Microbiology, 1989:93-109.
12. Kabalin JN, Kessler R. Infectious complications of penile prosthesis surgery. J Urol 1988;139:953-5.
13. Baker AS, Schein OD. Ocular infections. In: Bisno AL, Waldvogel FA. eds. Infections associated with indwelling medical devices. Washington DC: American Society for Microbiology, 1989:75-92.
14. Neu HC. Recommendations for antibiotic prophylaxis before endoscopy. Am J Gastrointest 1989;84(12):1488-93.
15. Dougherty SH, Simmons RL. Endogenous factors contributing to prosthetic device infections. Infect Dis Clin North Am 1989;3:199-209.
16. Durack D. Prevention of infective endocarditis. N Engl J Med 1995;332:38-44.

Suggested Reading

1. The American Society of Colon and Rectal Surgeons. Practice parameters for antibiotic prophylaxis to prevent infective endocarditis or infected prosthesis during colon and rectal endoscopy. Dis Colon Rectum 1992;35:277-85.
2. Grant A, Hoddinott C. Joint replacement, dental surgery and antibiotic prophylaxis. Be Med J 1992;304:959.
3. Cawson CA. Antibiotic prophylaxis for dental treatment. Br Med J 1992;304:933-4.
4. Simmons NA, Ball AP, Cawson RA, Eykyn SJ, Littler WA, McGowan DA, et al. Antibiotic prophylaxis and infective endocarditis. Br Med J 1992;339:1292-3.
5. Simmons NA, Ball AP, Cawson RA, Eykyn SJ, Hughes SPF, McGowan D, et al. Case against antibiotic prophylaxis for dental treatment of patients with joint prosthesis. Lancet 1992;339:301.
6. Van der Meer JTN, Van Wijk W, Thomson J, Vandenbroucke JP, Valkenburg HA, Michel MF. Efficacy of antibiotic prophylaxis for prevention of native-valve endocarditis. Lancet 1992;339:135-9.