



ANTIBIOTIC PROPHYLAXIS IN DENTISTRY: A REVIEW AND PRACTICE RECOMMENDATIONS

DARRYL C. TONG, B.D.S., M.S.D.; BRUCE R. ROTHWELL, D.M.D., M.S.D.

ABSTRACT

Background. The American Heart Association, or AHA, and the American Dental Association recently changed their recommended protocols for antibiotic prophylaxis against bacterial endocarditis. A new recommendation also has been issued by the ADA and the American Academy of Orthopaedic Surgeons, or AAOS, against routine antibiotic prophylaxis in patients with prosthetic joint replacements. These changes reflect increasing scientific evidence and professional experience in opposition to widespread use of antibiotic prophylaxis in these specific situations and others faced in dentistry.

Methods. The authors reviewed the medical and dental literature for scientific evidence regarding the use of antibiotics to prevent local and systemic infections associated with dental treatment. Situations commonly considered by dentists for potential use of prophylactic antibiotics were reviewed to determine current evidence with regard to use of antimicrobial agents. This included prevention of distant spread of oral organisms to susceptible sites elsewhere in the body and the reduction of local infections associated with oral procedures.

Results. There are relatively few situations in which antibiotic prophylaxis is indicated. Aside from the clearly defined instances of endocarditis and late prosthetic joint infections, there is no consensus among experts on the need for prophylaxis. There is wide variation in recommended protocols, but little scientific basis for the recommendations. The emerging trend seems to be to avoid the prophylactic use of antibiotics in conjunction with dental treatment unless there is a clear indication.

Conclusions. Aside from the specific situations described, there is little or no scientific basis for the use of antibiotic prophylaxis in dentistry. The risk of inappropriate use of antibiotics and widespread antibiotic resistance appear to be far more important than any possible perceived benefit.

Clinical Implications. Dentists are wise to use antibiotic prophylaxis in only those specific situations in which there is a valid scientific basis for it. Whenever possible, dentists should follow the standard protocols recommended by the ADA, AHA or AAOS.

The American Heart Association, or AHA, and the American Dental Association recently changed their recommended protocols for antibiotic prophylaxis against bacterial endocarditis. In addition, the ADA and the American Academy of Orthopaedic Surgeons, or AAOS, also issued a new recommendation against routine use of antibiotic prophylaxis in patients with prosthetic joint replacements. These changes reflect changing attitudes toward the use of antibiotics in patients at risk of developing bacteremias from dental proce-

dures. There is often confusion and misinformation concerning the indications and scientific basis for the use of antibiotics in conjunction with dental procedures. In this review article, we highlight specific situations that warrant the use of antibiotic prophylaxis in the dental setting and briefly discuss the rationale behind current recommendations.

The empiric use of antibiotic prophylaxis for dental procedures, especially those that cause bleeding in the mouth, has become a reasonably

well-established practice among dental professionals. However, many dentists are confused by the indications for, and the nature of, antibiotic prophylaxis. They often rely on recommendations from practitioners who quote anecdotal evidence or decide that, when in doubt, the wise and conservative course is to use antibiotic prophylaxis. Furthermore, dentists may consult with a patient's physician and receive a recommendation for the use of antibiotics in widely varying protocols and combinations. This presents a dilemma for the dentist because he or she may feel obligated to use antibiotic prophylaxis in inappropriate or unnecessary scenarios.

There is a long-held belief in the theory of focal infection such that subclinical infectious foci in the oral region, particularly endodontically treated teeth, result in systemic illness or cause disease processes in distant locations.¹ Although generally regarded as not having scientific merit, this concept often drives recommendations for the use of antibiotic prophylaxis. As a result, dentists and physicians tend to use antibiotics in situations in which there are no clear scientific bases.

The correlation between bacterial infection and endocarditis was described before the turn of the 20th century.² It was not until the 1920s, however, that the causal relationship between bacteremia, surgical procedures and infective endocarditis, or IE, was proposed.³ Lewis and Grant³ hypothesized that surgical procedures provided microorganisms with access to the systemic circulation, which ultimately would result in endocarditis. The specific pathophys-

iology of IE was not yet identified. Researchers subsequently showed that IE arises from the colonization of a preexisting lesion, usually composed of fibrin and platelets, which develops from the disruption of the endothelial lining via abnormal development, disease or presence of foreign bodies and turbulent blood flow.^{2,4}

Since the 1930s and 1940s, when studies indicated a significant correlation among dental procedures that cause bleeding, bacteremia and the development of IE, the use of antibiotics has been standard practice for patients identified as being at risk of developing endocarditis. This practice has expanded to

Although the use of prophylactic antibiotics in dentistry is not a major contributing factor to the problem of overuse, the current situation clearly requires judicious and prudent consideration before antibiotic therapy is administered.

include patients at risk of developing infections around prosthetic joints and those with depressed immune systems.⁵ In addition, many medical and dental practitioners use antibiotics in conjunction with surgical procedures for otherwise healthy patients in the belief that such therapy will reduce the incidence of perioperative infections.

Clinicians and researchers are increasingly concerned about the overuse of antibiotics and the resulting development of resistant strains of microorganisms.⁶ Although the use of prophylactic antibiotics in dentistry is not a major contributing factor to the problem of overuse, the current situation clearly requires judicious and prudent consideration before antibiotic therapy is administered.⁷ In this article, we review the literature regarding the scientific rationale for antibiotic prophylaxis and develop a series of practice guidelines to use in making clinical decisions.

CLINICAL SITUATIONS CONSIDERED FOR ANTIBIOTIC PROPHYLAXIS

Infective endocarditis. IE, also known as acute or subacute bacterial endocarditis, is defined as an exudative and proliferative inflammatory alteration of the endocardium; it is characterized by vegetations on the surface or within the endocardium that are caused by an infection with microorganisms. A heart valve is commonly involved and proliferation also may occur in the inner lining of the cardiac chambers.^{8,9} It is well-recognized that IE arises from the colonization of a preexisting lesion, usually composed of fibrin and platelets, that develops from the disruption of the endothelial lining via abnormal development, disease or presence of foreign bodies and turbulent blood flow. This accumulation of fibrin, blood products and platelets, known as nonbacterial thrombotic endocarditis, or NBTE, adheres to the damaged endothelium. The endothelium is later colo-

nized by bacteria, which, in turn, stimulates further platelet aggregation and the bacteria become incorporated into the vegetations of the lesion.

Congenital or acquired cardiac defects and abnormalities may predispose the heart to endothelial damage and formation of NBTE.⁴ Researchers have suggested that these conditions may alter the hemodynamics of the heart, causing turbulence, which, in some way, increases the exposure of pre-disposed cardiac endothelium to bacterial infection (usually streptococcal).

The current AHA recommendations for the prevention of IE are significantly changed in respect to patients with various cardiac conditions (Box, "Cardiac Conditions Considered for Prophylaxis").¹⁰ In general, the trend has been to more specifically describe those conditions that pose significant risk for patients and to delineate low- or negligible-risk situations. As a result, antibiotic prophylaxis is now recommended for fewer conditions. These changes also reflect improvements in the understanding of these disease processes and changing attitudes toward the use of antibiotics. The most notable among these changes include reducing the oral dose of amoxicillin from 3 grams to 2 g, recommending that a follow-up dose of antibiotic be discontinued, and replacing erythromycin with other antibiotics as alternatives to the penicillins.^{10,11} Dajani and colleagues¹² have reported that 2 g of amoxicillin provides several hours of antibiotic coverage. Table 1 shows the new recommendations for prophylactic coverage for certain dental procedures.

Patients with mitral valve prolapse, or MVP, may be at risk of developing tachycardia, syncope, congestive heart failure and endocarditis.¹³ The risk of infection, however, is variable and depends on age and severity of the MVP.¹¹ The decision whether to administer antibiotic prophylaxis is based on the results of echocardiographic tests for regurgitation. The AHA recommends that patients diagnosed as having MVP with regurgitation receive antibiotic prophylaxis before undergoing dental procedures, but patients with MVP alone (without regurgitation) do not require antibiotic coverage. The risk of developing IE remains

The current American Heart Association recommendations for the prevention of infective endocarditis are significantly changed in respect to patients with various cardiac conditions.

greater in patients with prosthetic heart valves and/or a history of endocarditis than in patients with MVP.¹⁴

Patients often indicate on a health history form the existence of a heart murmur at some time without having any further knowledge of the nature or extent of the cardiac defect. Because of concerns about the overuse of antibiotics, it is prudent for the dentist to ask for medical evaluation before continuing dental care, rather than to simply prescribe antibiotic prophylaxis when in doubt.

Similarly, if a dentist is treating a patient with MVP, it may be reasonable to contact the patient's physician to determine the specific cardiac anomaly before making a decision about antibiotic prophylaxis.

Patients with prosthetic joints. Prosthetic joint replacement is becoming increasingly common, especially in developed countries with an aging population. It has been estimated that more than 120,000 hips and knees were replaced in 1990 in the United States.¹⁵ In 1997, approximately 450,000 joints of all types were replaced, reflecting an increasing annual trend.¹⁶ Infections of the prosthetic joints may be classified as early- and late-onset.⁹

Early prosthetic joint infection is presumed to occur after microbial contamination of the surgical site during placement of the prosthesis. Late prosthetic joint infection, or LPJI, typically occurs three or more months after surgery and may involve delayed infection from microorganisms introduced at the time of surgery or via hematogenous spread from a distant site, such as the mouth. With devastating morbidity and a mortality rate of 18 percent, orthopedic surgeons are justified in their concerns about LPJI.¹⁷ The incidence of LPJI associated with dental procedures is extremely low. In a review of 2,693 patient records, Jacobson and Matthews¹⁸ found only one instance (0.04 percent) of LPJI that could be even temporally related to dental treatment.

Routine antibiotic prophylaxis for all patients with prosthetic joints is very expensive (\$480,000 to prevent one case of LPJI in 1990).¹⁵ Studies of rela-

CARDIAC CONDITIONS CONSIDERED FOR PROPHYLAXIS.*

HIGH-RISK CATEGORY	MODERATE-RISK CATEGORY	NEGLIGIBLE RISK: NO ANTIBIOTIC PROPHYLAXIS RECOMMENDED
<ul style="list-style-type: none"> ■ Prosthetic cardiac valves ■ Previous bacterial endocarditis ■ Complex, cyanotic congenital heart disease ■ Surgically constructed systemic pulmonary shunts 	<ul style="list-style-type: none"> ■ Most other congenital cardiac malformations not otherwise indicated ■ Acquired valvular dysfunction ■ Hypertrophic cardiomyopathy ■ Mitral valve prolapse with regurgitation and/or thickened valve leaflets 	<ul style="list-style-type: none"> ■ Isolated secundum atrial septal defect ■ Surgical repair of atrial septal defect, ventricular septal defect or patent ductus arteriosus of more than six months' duration ■ Previous coronary artery bypass graft surgery ■ Physiological or functional heart murmur ■ Previous Kawasaki disease without valvular dysfunction ■ Previous rheumatic fever without valvular dysfunction ■ Cardiac pacemakers ■ Implanted defibrillators

* Adapted with permission of the Journal of the American Medical Association from Dajani and colleagues.¹⁰

tive risks show that the risk of death caused by anaphylaxis, especially from the penicillins, far outweighed the risks of developing LPJI. These factors have moved the current consensus toward discontinuing routine use of antibiotic prophylaxis. In their advisory statement, the AAOS and the ADA have recommended the use of prophylactic antibiotics only for patients with total joint replacements (not for patients with only pins, screws and/or plates) and compromised immune systems, Type 1 diabetes mellitus, recent (within two years) joint replacement, previous prosthetic joint infections, malnourishment or hemophilia.¹⁶

Dentists still may be faced with the situation in which a physician has recommended antibiotic prophylaxis for a patient that the dentist feels is inappropriate. In such cases, the dentist may choose to con-

sult with the patient's physician in an attempt to alter that recommendation. In any case, the dental practitioner is responsible for assessing each patient's situation and deciding whether antibiotic coverage would benefit the patient.

In-dwelling catheters, neurosurgical shunts and other implants. In-dwelling catheters generally do not warrant antibiotic prophylaxis unless the catheter is near the right side of the heart.¹⁹ In cardiac patients with newly placed stents, the initial two weeks after placement is the time of highest risk of infection of the stent. Once an epithelial layer develops, the risks of infection are minimal. For patients in whom catheters are placed to facilitate the administration of systemic medications such as antiviral or chemotherapeutic agents for extended periods, the antibiotic prophylaxis is admin-

istered because of the suppressed immune system rather than the catheter itself.

Patients with renal disease who are undergoing hemodialysis constitute another group that warrants some form of antibiotic coverage for dental procedures because of the presence of an arteriovenous shunt for dialysis.²⁰ These shunts may be made from native (autogenous) tissue or from a silastic tube that is implanted. Regardless of type, the shunts are particularly vulnerable to infection, which could be devastating for the patient receiving hemodialysis. Patients receiving continuous peritoneal dialysis, however, do not require antibiotic prophylaxis.

The patient with hydrocephaly poses a different problem because of the placement of shunts.²¹ Patients with hydrocephaly receive shunts to aid in the drainage of cerebro-

TABLE 1

ANTIBIOTIC PROPHYLACTIC REGIMENS FOR CERTAIN DENTAL PROCEDURES.*

SITUATION	ANTIBIOTIC†	REGIMEN‡
Standard Prophylaxis	Amoxicillin	Adults, 2.0 grams; children, 50 milligrams/kilogram orally one hour before procedure
Cannot Use Oral Medications	Ampicillin	Adults, 2.0 g IM§ or IV§; children, 50 mg/kg IM or IV within 30 minutes before procedure
Allergic to Penicillin	Clindamycin	Adults, 600 mg; children, 20 mg/kg orally one hour before procedure
	Cephalexin or cefadroxil	Adults, 2.0 g; children, 50 mg/kg orally one hour before procedure
	Azithromycin or clarithromycin	Adults, 500 mg; children, 15 mg/kg orally one hour before procedure
Allergic to Penicillin and Unable to Take Oral Medications	Clindamycin	Adults, 600 mg; children, 15 mg/kg IV one hour before procedure
	Cefazolin	Adults, 1.0 g; children, 25 mg/kg IM or IV within 30 minutes before procedure

* Reprinted with permission of the Journal of the American Medical Association from Dajani and colleagues.¹⁰
 † Cephalosporins should not be used in patients with immediate-type hypersensitivity reaction (urticaria, angioedema or anaphylaxis) to penicillins.
 ‡ Total children's dose should not exceed adult dose.
 § IM: Intramuscular; IV: Intravenous.

spinal fluid, or CSF. Two types of shunts are used: the ventriculoatrial, or VA, shunt and the ventriculoperitoneal, or VP, shunt. The VA shunt allows drainage of CSF from the lateral ventricles to the venous circulation, whereas VP shunts drain CSF directly into the abdominal cavity.

VP shunts are currently more common than VA shunts. The overall infection rate ranges from 5 to 30 percent, with a mortality rate of up to 40 percent.^{22,23} Shunt infections usually will present in the initial two-week postoperative period. The literature suggests that VP shunts carry no higher risk of infection after dental treatment than that before dental treat-

ment, whereas VA shunts are more prone to infection. Therefore, patients with VA shunts should be considered for antibiotic prophylaxis.²³

For other types of implants and devices, such as penile implants, implanted defibrillators and cardiac pacemakers, there is no evidence supporting the routine use of antibiotic coverage for dental procedures.²⁴

PREVENTION OF LOCAL INFECTION IN SURGICAL OR OPERATIVE SITES IN THE MOUTH

Surgical procedures in the mouth generally fall into the clean-contaminated category of surgical classification (that is, native organisms are present); this includes routine exodon-

tics, third-molar surgery and orthognathic surgery.²⁵ The incidence of infection after den-toalveolar surgery is very low; for third-molar surgery performed by oral and maxillofacial surgeons, the infection rate is approximately 1 percent.²⁵ Unless the immune system is compromised, antibiotics are not indicated in these cases. For periodontal surgery in which the surgical site is often highly contaminated with microorganisms, antibiotics are usually indicated for most patients with compromised immune systems, for patients at risk of developing IE and for patients with prosthetic joints, especially in the presence of obvious periodontal infections.²⁶

The periodontal literature suggests that localized juvenile periodontitis and other forms of early-onset periodontitis may warrant antibiotic coverage, but there is little evidence to support this view. The American Academy of Periodontology recommends that patients with medical conditions that predispose them to periodontal disease also be considered for antibiotic coverage.²⁷ The use of antibiotic prophylaxis during placement of dental implants is controversial. Preoperative antibiotics appear to decrease the rate of implant failure, but studies have emphasized the prevention of implant failure rather than prevention of the infection itself.²⁸

PREVENTION OF GENERALIZED SPREAD OF INFECTIONS IN PATIENTS WITH COMPROMISED IMMUNE SYSTEMS

Patients with compromised immune systems represent a special category for dentists. Because of their illness and/or the treatment rendered for their specific condition, these patients are at higher risk of developing bacteremias, which, in the absence of an adequate host immune system, may rapidly progress to an overwhelming septicemia.^{4,29}

Patients undergoing chemotherapy are particularly susceptible to systemic infections because their immunosuppressed state is caused by their medications. Not only are these patients at higher risk of developing an infection, but the spread and severity of the infection can potentially be rapid and life-threatening. For these patients, we do not recommend antibiotic coverage for routine

DENTAL PROCEDURES CONSIDERED FOR ANTIBIOTIC PROPHYLAXIS IN SUSCEPTIBLE PATIENTS.*

HIGH-RISK CATEGORY

- Dental extractions
- Periodontal procedures including surgery, scaling, root planing and probing
- Dental implant placement, reimplantation of teeth
- Endodontic instrumentation or surgery beyond the tooth apex
- Subgingival placement of antibiotic fibers or strips
- Initial placement of orthodontic bands but not brackets
- Intraligamentary local anesthetic injections
- Prophylactic cleaning of teeth or implants with anticipated bleeding

PROCEDURES NOT RECOMMENDED FOR PROPHYLAXIS

- Restorative dental procedures with or without retraction cord
- Local anesthetic injections (except for intraligamentary)
- Intra canal endodontic procedures, post placement and buildup
- Placement of rubber dams
- Postoperative suture removal
- Placement of removable orthodontic or prosthodontic appliances
- Taking oral impressions
- Fluoride treatments
- Taking oral radiographs
- Orthodontic appliance adjustment
- Shedding of primary teeth

* Adapted with permission of the Journal of the American Medical Association from Dajani and colleagues.¹⁰

dental procedures, but it should be considered for invasive procedures such as dental extractions, deep periodontal scaling and other procedures that cause significant bleeding and seeding of bacteria into the systemic circulation.

Patients with human immunodeficiency virus and AIDS, in the absence of bacte-

rial infection, do not generally require antibiotic prophylaxis.¹⁹ However, a clinical judgment should be made when a bacteremia is likely to occur, such as in cases of extraction of teeth with abscesses. Practitioners should consider the use of antibiotics in these patients because of the higher risk of overwhelming systemic infec-

TABLE 2

SUMMARY RECOMMENDATIONS FOR ANTIBIOTIC PROPHYLAXIS.		
MEDICAL CONDITION	PROPHYLAXIS RECOMMENDED?	ANTIBIOTIC REGIMEN
Valvular Heart Disease, Previous Endocarditis, Surgical Pulmonary Shunts, Hypertrophic Cardiomyopathy	Yes	AHA protocol**†
Mitral Valve Prolapse With Regurgitation	Yes	AHA protocol
Prosthetic Heart Valves	Yes	AHA protocol
Orthopedic Prostheses More Than Two Years in Place	No, except in exceptional cases of immune compromise	
Implanted Pacemaker or Defibrillator	No	
Vascular Grafts	No, if in place more than six months	AHA protocol if less than six months
Previous Coronary Bypass Graft Surgery	No	
Renal Hemodialysis With AV* Shunts	Yes, although definite evidence is lacking	AHA protocol
VA* Shunts for Hydrocephalus	Yes	AHA protocol
VP* Shunts for Hydrocephalus	No	
Patients With Compromised Immune Systems	No for most dental procedures; may consider for invasive procedures or specific situations	No specific antibiotic regimen recommended
Prevention of Local Infection in Surgical Sites	No, although treatment of coexistent infection is recommended before surgical procedures	No specific antibiotic regimen recommended

* AHA: American Heart Association; AV: Arteriovenous; VA: Ventrículoatrial; VP: Ventrículo-peritoneal.
 † See Table 1 for protocol.

tion and an inability to defend against microbial insult because of a depressed immune system.

The final group in this category of patients with compromised immune systems is the population with diabetes. Diabetics, especially those who are insulin-dependent, have a higher rate of systemic disease and often exhibit some degree of

leukocyte dysfunction, which may contribute to higher incidences of infection.³⁰ Insulin-dependent diabetic patients, particularly those with poorly controlled disease, are vulnerable to infections. Therefore, antibiotic coverage for invasive dental procedures is recommended in patients with poorly controlled or uncontrolled dia-

betes, but is generally not required for those in whom the disease is well-controlled or for those who are not dependent on insulin therapy.³¹

There is some ongoing debate among clinicians and authors over the use of antibiotic coverage for chronic intravenous drug abusers and for patients who have undergone splenec-

tomy.^{32,33} The incidence of IE among chronic intravenous drug abusers is several times higher than that seen in the healthy population. Although there is no clear-cut evidence that antibiotics are effective in cases of native valve endocarditis, antibiotic coverage may be warranted until new evidence suggests otherwise.³³ There is also no evidence that patients who have undergone splenectomy are at higher risk of developing infection from dental procedures than is the general population. These patients are, however, more susceptible to infections from encapsulated organisms such as *Pneumococcus* and *Hemophilus* type B species; physicians often recommend the use of antibiotic prophylaxis for invasive dental procedures in such cases.^{32,34}

DENTAL PROCEDURES AND ANTIBIOTIC PROPHYLAXIS

The link between dental procedures and IE remains a controversial subject. In 1984, Guntheroth³⁵ reported a low incidence of bacteremia associated with dental procedures and suggested that meticulous oral hygiene was more important in the prevention of IE than any antibiotic regimen. In a population-based control study involving 273 patients with cardiac lesions, Strom and colleagues³⁶ found that dental procedures were not a risk factor for IE, even in patients with valvular abnormalities. Furthermore, even when the recommended antibiotic regimen was administered, it was not 100 percent effective in preventing IE.^{36,37}

The evidence is now clear that not all dental procedures

warrant the use of antibiotic prophylaxis. It is safe to perform dental procedures (such as restorative and prosthetic treatment) in which the potential for bleeding is minimal in at-risk patients without the use of antibiotic prophylaxis. Invasive treatment in which bacteremia is more likely to occur (such as periodontal scaling, periodontal surgery and dental extractions) warrant the use of antibiotic coverage in patients with specific conditions, such as prosthetic heart valves and a history of endocarditis.¹⁴ The box ("Dental Procedures Considered for Antibiotic Prophylaxis in Susceptible Patients"; see page 371) is a proposed guideline for clinical situations in which antibiotic prophylaxis is recommended for invasive dental procedures. Table 2 (see page 372) summarizes our recommendations for administering antibiotic prophylaxis.

SUMMARY

As a result of greater understanding of disease processes, an enhanced awareness of cost-effectiveness and risk-benefit



Dr. Rothwell is an associate professor and chairman, Department of Restorative Dentistry, and an adjunct associate professor, Oral and Maxillofacial Surgery, University of Washington, Seattle. Address reprint requests to Dr. Rothwell, Department of Restorative Dentistry, Mail Stop 357456, University of Washington, Seattle, Wash. 98195.

correlations, and better communication between medical and dental practitioners, the guidelines for antibiotic prophylaxis have been significantly altered.^{10,16} Although the major impetus for this change was related to prevention of IE, situations

involving prosthetic joints and patients with compromised immune systems also have been reconsidered. In addition, the specific nature of dental procedures and the risk of patients' developing bacteremias from them have been reconsidered, and many common procedures have been excluded from the list of those that require prophylaxis. It is clear that the trend is toward covering fewer and more specific medical conditions for a limited number of invasive dental procedures. Although some situations are well-delineated, controversy and concern over others continue. Further investigation and research are needed to clarify these issues.

In this article, we have delineated some of the indications for antibiotic prophylaxis in dentistry. Our recommendations can serve as the basis for guidelines for the practicing dentist, with the caveat, however, that guidelines are no substitute for sound clinical judgment. ■

Dr. Tong is a lecturer, Department of Stomatology, University of Otago, Dunedin, New Zealand.

1. Glassman G. Root canal cover up exposed: the resurgence of the refuted focal infection theory. *Oral Health* 1998;88(12):3.
2. Cowper T. Pharmacologic management of the patient with disorders of the cardiovascular system: infective endocarditis. *Dent Clin North Am* 1996;40:611-47.
3. Lewis T, Grant RT. Observations relating to subacute infective endocarditis. *Heart* 1923;10:21-77.
4. Harris R, Kelly MA. Antibiotic prophylaxis of the dental patient. *Gen Dent* 1990;38:212-5.
5. Asikainen S, Alaluusua S. Bacteriology of dental infections. *Eur Heart J* 1993;14 (suppl K):43-50.
6. Barker KF. Antibiotic resistance: a current perspective. *Br J Clin Pharmacol* 1999;48:109-24.
7. Smith A, Bagg J. An update on antimicrobial chemotherapy. 3: antimicrobial resistance and the oral cavity. *Dental Update* 1998;25:230-4.
8. Taylor E, ed. *Dorland's illustrated medical dictionary*. 27th ed. Philadelphia: Saunders; 1988:552.
9. Yagiela J. Prophylactic antibiotics: cardiac and prosthetic considerations. *J Calif Dent Assoc* 1995;23:29-40.

10. Dajani AS, Taubert KA, Wilson W, et al. Prevention of bacterial endocarditis: recommendations by the American Heart Association. *JAMA* 1997;277(22):1794-1801.
11. Wynn R, Meiller TF, Crossley HL. New guidelines for the prevention of bacterial endocarditis: American Heart Association. *Gen Dent* 1997;45:426-34.
12. Dajani A, Bawdon RE, Berry MC. Oral amoxicillin as a prophylaxis for endocarditis: what is the optimal dose? *Clin Infect Dis* 1994;18:157-60.
13. Hope R, Longmore JM, McManus JK, et al. Oxford handbook of clinical medicine. 4th ed. Oxford, England: Oxford University Press; 1998:306.
14. Durack DT. Antibiotics for prevention of endocarditis during dentistry: time to scale back? *Ann Intern Med* 1998;129:829-31.
15. Jacobson JJ, Schweitzer S, DePorter DJ, Lee JJ. Antibiotic prophylaxis for dental patients with joint prostheses? A decision analysis. *Int J Technol Assess Health Care* 1990;6:569-87.
16. American Dental Association/American Academy of Orthopaedic Surgeons. Advisory statement: antibiotic prophylaxis for dental patients with total joint replacements. *JADA* 1997;128:1004-8.
17. ShROUT M, Scarborough F, Powell BJ. Dental care and the prosthetic joint patient: a survey of orthopedic surgeons and general dentists. *JADA* 1994;125:429-36.
18. Jacobson JJ, Matthews LS. Bacteria isolated from late prosthetic joint infections: dental treatment and chemoprophylaxis. *Oral Surg Oral Med Oral Pathol* 1987;63(1):122-6.
19. Pallasch T. Antibiotic prophylaxis: the clinical significance of its recent evolution. *J Calif Dent Assoc* 1997;25:619-32.
20. DeRossi S, Glick M. Dental considerations for the patient with renal disease receiving hemodialysis. *JADA* 1996;127:211-9.
21. Acs G, Cozzi E. Antibiotic prophylaxis for patients with hydrocephalus shunts: a survey of pediatric dentistry and neurosurgery program directors. *Pediatr Dent* 1992;14:246-50.
22. Holloway KL, Smith KW, Wilberger JE Jr, Jemsek JG, Giguere GC, Collins JJ. Antibiotic prophylaxis during clean neurosurgery: a large, multicenter study using cefuroxime. *Clin Ther* 1996;18:84-94.
23. Dempsey R, Rapp RP, Young B, et al. Prophylactic parenteral antibiotics in clean neurosurgical procedures: a review. *J Neurosurg* 1988;69:52-7.
24. Little J, Rhodus NL. The need for antibiotic prophylaxis of patients with penile implants during invasive dental procedures: a national survey of urologists. *J Urol* 1992;148:1801-4.
25. Peterson L. Antibiotic prophylaxis against wound infections in oral and maxillofacial surgery. *J Oral Maxillofac Surg* 1990;48:617-20.
26. Pallasch T, Slots J. Antibiotic prophylaxis for medical risk patients. *J Periodontol* 1991;62:227-31.
27. American Academy of Periodontology. Systemic antibiotics in periodontology. *J Periodontol* 1996;67:831-8.
28. Dent CD, Olson JW, Farish SE, et al. The influence of preoperative antibiotics on success of endosseous implants up to and including stage II surgery: a study of 2,641 implants. *J Oral Maxillofac Surg* 1997;55(suppl 5):19-24.
29. Chiodo G, Tolle SW, Bartley M. Antibiotic prophylaxis for dental treatment: review and update. *Ill Dent J* 1990;59:599-602.
30. Shetty V, Bertolami C. The physiology of wound healing. In: Peterson LJ, ed. Principles of oral and maxillofacial surgery. Philadelphia: Lippincott; 1992:3-18.
31. Hupp J. Medical management of the surgical patient. In: Peterson LJ, ed. Principles of oral and maxillofacial surgery. Philadelphia: Lippincott; 1992:19-48.
32. Glick M. Intravenous drug users: a consideration for infective endocarditis in dentistry? *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1995;80:211-9.
33. White KS, Covington D, Churchill P, Maxwell JG, Normal KS, Clancy TV. Patient awareness of health precautions after splenectomy. *Am J Infect Control* 1991;19:36-41.
34. Westerman E. Postsplenectomy sepsis and antibiotic prophylaxis before dental work. *Am J Infect Control* 1991;19:254-5.
35. Guntheroth WG. How important are dental procedures as a cause of infective endocarditis? *Am J Cardiol* 1984;54:797-801.
36. Strom BL, Abrutyn E, Berlin JA, et al. Dental and cardiac risk factors for infective endocarditis: a population-based, case-control study. *Ann Intern Med* 1998;129:761-9.
37. Durack DT, Kaplan EL, Bisno AL. Apparent failures of endocarditis prophylaxis. *JAMA* 1983;250:2318-22.