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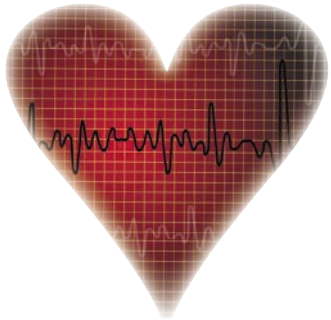

Perspectives on the 2007 AHA Endocarditis Prevention Guidelines

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ABSTRACT From 2005 to 2007, the American Heart Association convened a consensus panel of experts to revisit the guidelines for the premedication of patients with cardiac defects prior to dental treatment. Presented in this article is a summary of the guidelines as well as commentary on the process.

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DISCLOSURE

The author was a member of the Writing Group for the 2007 Prevention of Infective Endocarditis Guidelines from the American Heart Association. The opinions stated herein are not necessarily those of the American Heart Association Perspectives on the 2007 AHA Endocarditis Prevention Guidelines.

This year is the 98th anniversary of the contention that "previously sclerosed endocarditis" was, in most cases, due to mouth microorganisms.[1] It also is approximately 80 years since dental treatment procedures were considered a primary cause of infective endocarditis, even as data increasingly accumulated that random bacteremias associated with daily living activities (brushing, flossing, mastication) were similar in magnitude and incidence to those associated with dental treatment. Most failed to realize that dental treatment occurred only a few times a year, while the bacteremias associated with daily living were more or less continuous.[2]

These early conclusions were severely biased as they occurred during the heyday of the Focal Theory of Infection, which attributed essentially every disease that was untreatable or of unknown etiology (most of them), including arthritis to gastrointestinal upset and stupidity to bacteria originating in the oral cavity or the tonsils.[3,4] Curiously, virtually all foci of infection were surgically accessible. This era is presently being revisited, but more about that later. The Focal Infection Theory clearly brought to light the apparent necessity of medicine to find a reason for everything, including blaming dentistry and the oral flora for endocarditis and just about everything else. Some find it very difficult to say, "I don't know."

Beginning around the early 1980s, a few bold individuals began to contest this conventional wisdom and suggest that dental treatment was not responsible for many, or even any, of these infective endocarditis (IE) cases.[5-27] Some became weary of being accused of seriously injuring or even killing dental patients by physicians who blithely ignored their own record of hundreds of thousands of nosocomial (hospital-acquired) deaths per year due to mistakes and multiple antibiotic resistant microorganisms.

Little attention was paid to the incuba-

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TABLE 1

Recommendations of the 2007 AHA Endocarditis Prevention Guidelines[27]

Dental Procedures for Which Endocarditis Prophylaxis is Recommended
All dental procedures that involve manipulation of gingival tissue or the periapical region of the teeth or perforation of the oral mucosa

Cardiac Conditions Associated With the Highest Risk of Adverse Outcomes From Endocarditis for Which Prophylaxis With Dental Procedures Is Recommended:

- Prosthetic heart valve
- Previous endocarditis
- Cardiac transplant recipients who develop cardiac valvulopathy
- Congenital heart disease (only for conditions listed below and no other CHD)
- Unrepaired cyanotic congenital heart disease (CHD), including palliative stents and conduits
- Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first six 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)

Oral Prophylaxis Regimens Prior to a Dental Procedure in the Above Situations
Single dose 30 minutes to 60 minutes before procedure

Situation	Agent	Adults	Children
Oral	amoxicillin	2 grams	50 mg/kg
Allergic to penicillins	clindamycin or cephalexin[1] or azithromycin or clarithromycin	600 mg 2 grams 500 mg	20 mg/kg 50 mg/kg 15 mg/kg

* Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillins.

tion period (the time from the onset of the bacteremia to the first signs and symptoms) of viridans group streptococcal (VGS) endocarditis (usually seven to 14 days), or that the alleged causative bacteremia could more easily have come from daily living activities before or after the dental treatment. It was impossible to tell which it was, but that was considered irrelevant. The author has been involved for more than 35 years in malpractice litigation involving endocarditis causation (more than 300 cases) with only three occurring within this incubation period (1 percent). It was similarly impossible in these few situations to determine causality from dental treatment or daily living bacteremias.

In all these cases, without exception, the question was asked in the hospital usually of a relative: When was their last dental treatment? A positive response of "yesterday" up to "nine months ago" was inevitably followed by: "That did it!" Two hundred and seventy days between dental treatment and the onset of symptoms may be the world record. Recently, a cardiologist stated he could think of nothing else in the six months after the dental treatment that could have caused the VGS endocarditis.

With the advent of the 2007 American Heart Association Prevention of Infective Endocarditis guidelines, it is hoped that much or all of this thinking will change.[27] However one must recall the observation of a noted scientist that a new idea is accepted only when all its critics are dead. Unfortunately, the proponents of the idea will also likely have passed on. In the words of Schopenhauer, "All truth passes through three stages. First it is ridiculed. Second it is violently opposed. Third it is accepted as being self-evident."

The major changes in the prevention of endocarditis in the 2007 AHA guidelines are: 1) only an extremely small number of cases of IE might be prevented by antibiotic prophylaxis for dental procedures, even if such prophylaxis were 100 percent effective; 2) IE prophylaxis for dental procedures should be recommended only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from IE; 3) for patients with these underlying conditions, prophylaxis is recommended for all dental procedures that involve manipulation of the gingival tissue or the periapical region of the teeth or perforation of the oral mucosa; and 4) prophylaxis is not recommended based solely on an increased lifetime risk of acquisition of infective endocarditis.[27] TABLE 1 places these indications and antibiotic doses in a single chart.

The most fundamental conceptual change since the 1997 guidelines is that the 2007 recommendations are based not solely on the lifetime risk of acquisition of IE but rather on the highest risk of adverse outcomes from IE. It is not the risk of contracting IE, but rather the seriousness of outcome of the disease.

The AHA 2007 guidelines also list the primary reasons for this revision of IE prophylaxis guidelines: 1) IE is much more likely to result from frequent exposure to random bacteremias associated with daily activities than from bacteremia caused by a dental, GI tract, or GU tract procedure; 2) prophylaxis may prevent an exceedingly small number of cases of IE, if any, in individuals who undergo a dental, GI tract, or GU tract procedure; 3) the risk of antibiotic-associated adverse events exceeds the benefit, if any, from prophylactic antibiotic therapy; and 4) maintenance of optimal oral health and hygiene may reduce the incidence of bacteremia from daily living activities and is more important than prophylactic antibiotics for a dental procedure to reduce the risk of IE.[27]

Supporting Evidence

The evidence supporting these conclusions is formidable. Two observational studies found no association between dental treatment and endocarditis.[28,29] None have ever shown any association. These and other studies have concluded that only a very low number of IE cases could ever be prevented with antibiotic prophylaxis prior to dental treatment even if such prophylaxis were 100 percent effective.[30,31] The risks of bacteremia associated with daily living far surpasses any associated with dental treatment: the risk of tooth brushing twice a day for one year has more than 150,000 times greater risk for exposure to bacteremia that a single tooth extraction.[22] The cumulative daily exposure for one year of daily living activities may pose a 5.6 million times greater bacteremic risk than a single tooth extraction.[22]

Possibly the most devastating argument against antibiotic prophylaxis for prevention of dental treatment-induced endocarditis is the absolute risk rate estimation of IE causation. If 250 million people visit the dentist on average of 1.6 times per year (400 million visits per year) and the incidence of infective endocarditis is 11,200 cases annually in the United States with a population of 280 million with a risk rate of 4.0/100,000 population and 25 percent caused by VGS, then the absolute risk rate is 1/142,000 persons for VGS endocarditis if all are caused by dental treatment.[2]

ONLY AN EXTREMELY small number of cases of IE might be prevented by antibiotic prophylaxis for dental procedures.

If it is further assumed that 1 percent of all VGS cases annually in the United States (112 cases) are caused by dental treatment, then the absolute risk rate rises to 1/14,000,000 in the general population with no known cardiac risk factors.[2] The worst-case absolute risk for endocarditis from a single dental treatment procedure rises substantially in persons with known cardiac risk factors: previous endocarditis (1/95,000); cardiac valve prosthesis (1/114,000); rheumatic heart disease (1/142,000); congenital heart disease (1/475,000); and mitral valve prolapse (1/1.1 million).[2,32] Therefore, the number of cases of IE arising from dental treatment is exceedingly small as would be any benefit from antibiotic prophylaxis.[27] It is quite possible the risk of death from penicillin-induced anaphylaxis is greater than any proposed benefit in this scenario.[11,14]

There is no data that bleeding during dental procedures is a realistic predictor of bacteremia.[27] It has always been assumed that if antibiotic prophylaxis reduces the incidence or magnitude of bacteremias, then this is a good surrogate marker for prevention of IE. There is no evidence that this assumption is true.[27]

The absence of evidence is also evidence. There are no consistent data to support the idea that the greater the magnitude of the bacteremia, the greater the risk of IE.[27] The infective dose (inoculum size) of bacteria needed to cause endocarditis is unknown as is the duration of the bacteremia.[27]

Whether a "clean" mouth is more preventive of IE than a "dirty" mouth is contentious since there is only equivocal data to support this assertion.[27] Less than 120 cases of endocarditis due to periodontopathic microorganisms have been reported in the literature with most of these due to *Actinobacillus actinomycetemcommitans*.[2] Viridans group streptococci dominate in a clean, healthy mouth.[27] There are no clinical studies to document that a reduction bacteremias allegedly seen with a healthy mouth reduces the incidence of IE. Practitioners must be careful of surrogate markers and theory falsely rising to the level of fact.

The Role of Microbial Resistance

The world is in the grip of an epidemic of multiple antibiotic resistant microbial

pathogens resulting in more than 18 million deaths annually, not counting AIDS.[33] It is often heard regarding antibiotic prophylaxis that "It's only a single dose!" However, this therapeutic strategy denies the fact that antibiotics are "societal drugs" that affect those nearby (family members) and others globally by fostering the creation of resistant microbes and the transfer their genes.[33,34] The prescriber of antibiotic prophylaxis (or therapy) assumes this is the only time the antibiotic is being used (health care professionals tend to think very locally rather than globally) when it is actually being employed in a similar fashion millions of times per day.

The Lawyers

One of the major factors in the overuse of antibiotics is that they are "drugs of fear" commonly employed to prevent negligence allegations and to assert that "all was done" to treat the patient.[35] This is true with antibiotic prophylaxis probably more than any other application of the drugs. This gross overuse of antibiotics has led to the declining efficacy of the penicillins particularly against oral microorganisms due to microbial resistance, making it even less likely that prophylaxis will be successful.[2,27,33]

Other Observations

A recent feature of endocarditis litigation is the appearance of lawsuits against dentists who followed the 1997 AHA guidelines to perfection; also the inability of medicine to commonly employ the Duke Criteria in the diagnosis of IE.[36,37] Often the disease is "diagnosed" on the basis of a patient-reported fever, one or two positive blood cultures (commonly taken a few minutes apart) and a cardiac murmur with or without a confirmatory echocardiogram for a flail vegetation. This likely leads to a substantial overestimation of the incidence of IE and places at serious risk any attempt by a national registry to document the effect of these new guidelines on endocarditis incidence. If a strict case definition of endocarditis is not employed (unlikely without access to patient records to verify the diagnosis by the Duke Criteria) then the results of such a registry will be very misleading.

Litigation is likely to continue with lawyers attempting to "test the waters" with "experts" who disagree with the preponderance of evidence in the 2007 AHA guidelines. One means of combating these allegations of negligence is to carefully record in the dental records that "in my best clinical judgment" this was the proper treatment of the patient. This need not be restricted to the question of endocarditis prophylaxis but any dental procedure that could be judged improper with the faultless wisdom of hindsight.

EQUALLY REMARKABLE is the ability of the lungs, spleen, liver, and reticuloendothelial system to clear the blood of bacteria.

Dentistry is in danger of creating a similar situation but in reverse. Some are attempting to employ the long-discredited Focal Infection Theory to "prove" the oral cavity, particularly periodontal disease has "systemic ramifications." The current research is limited at best, and, at worst, faulty in its conclusions. It is unlikely that weak odds ratios and wide confidence intervals are going to convince a skeptical scientific community. Claiming that periodontal pathogens are uniquely involved in the infection/inflammation observed in convoluted, sticky atherosclerotic plaque endlessly buffeted by bacteremias is fanciful in the light of the detection of over 50 different microbial species in coronary artery plaque.[38] If the data in the AHA guidelines tell us anything, it is that bacterial assault on the human is unremitting and our welfare utterly dependent on our innate and acquired immune systems along with other factors subsequently discussed, which, from time to time, fail.

Since the incidence and prevalence of IE has not changed with the advent of antibiotic therapy, in spite of all our efforts to reverse this state of affairs, it is likely that other factors are primarily involved.[13] Persons with predisposing factors for endocarditis acquisition are subjected to an endless assault of bacteremias, yet only a few ever develop IE. Certainly the ability of the microorganism to adhere to the valvular vegetation is very important as is the possibility of the organism gaining virulence genes for IE from bacteriophages, plasmids, and transposons.[27,33] The ability of microorganisms to transfer genetic information among themselves is nothing short of remarkable and staphylococci and streptococci are very adept at sticking to surfaces.[33] Equally remarkable is the ability of the lungs, spleen, liver, and reticuloendothelial system to clear the blood of bacteria.

One of the more intriguing aspects of endocarditis is that it may be a platelet disease rather than primarily an infectious one. Platelets are at the very center of IE as they, along with fibrin, form the vegetation that extends from the cardiac valve surface and becomes infected by bacteria. Secondly, the platelets have very significant antibacterial activity both in the blood and at the interface with microorganisms at the surface of the vegeta-

tion. Thirdly, once the vegetation becomes fully established, the antibacterial platelet activity and host defenses may be insufficient to overcome the rapidly multiplying bacteria.[39] Thus, the loss of platelet antimicrobial activity, a deficient innate and acquired immune response, failure to clear the blood of microorganisms, bacterial adhesion factors, and microbial virulence may be at the heart of IE (no pun intended) rather than the bacteremia per se, since it occurs endlessly and rarely produces a problem. As with most calamities, it takes a confluence of deleterious events to create the misfortune rather than a single untoward mishap.

Another interesting aspect of antibiotic prophylaxis is the scant attention paid to the millions who receive the antibiotics but will never benefit from them since the disease to be "prevented" is so rare. Antibiotic prophylaxis in a large population is a poor public health measure since, unlike fluoridation and immunization, where almost all benefit and the risk-benefit ratio is very favorable, antibiotic prophylaxis is rarely, if ever, successful except in hospital situations for surgical infection prevention, and then only under a strict protocol. The principles of antibiotic prophylaxis are well established but rather poorly followed.[2]

Other Antibiotic Prophylaxis Situations

Questions naturally arise as to whether the AHA guidelines apply to other medical conditions that have been proposed for antibiotic prophylaxis. The answer is generally "no." However, the lessons learned can be applied to prophylaxis for dental patients with prosthetic orthopedic joints with even less risk of infection, if any at all, from dental treatment-induced bacteremias. There still is no documented case of a prosthetic joint infection from a dental treatment-induced bacteremia and the risk-benefit ratio is even less than IE.[2]

The subject of other cardiovascular infections due to transient bacteremias has been addressed by another AHA publication with no prophylaxis prior to dental treatment for pacemakers and implantable cardioverter-defibrillators, peripheral vascular stents, prosthetic vascular grafts, coronary artery stents, and left ventricular assist devices.[40] There is no data to support prophylaxis in these situations and the risk from bactermias is very low, if at all. A recent comprehensive study by Lockhart et al. has methodically explored the scientific evidence for antibiotic prophylaxis prior to dental treatment in patients with cardiac-native heart valve disease; prosthetic heart valves and pacemakers; hip, knee, and shoulder prosthetic joints; renal dialysis shunts; vascular grafts; immunosuppression secondary to cancer and cancer chemotherapy; systemic lupus erythematosus; and insulin-dependent (Type I) diabetes mellitus.[41]

The authors found little or no evidence to support antibiotic prophylaxis in these patients or that it prevents distant site infections for any of these eight groups of patients.[41] Other situations for which there is no documented benefit of antibiotic prophylaxis include breast and penile implants and asplenia[42] (TABLE 2).

How Did This All Happen?

The propensity for blaming dental treatment procedures for IE arose from several observations and events: 1) the advent and then demise of the Focal Theory of Infection; 2) the discovery that dental procedures induce bacteremias particularly with VGS; 3) that VGS are a common cause of IE; 4) the failure to appreciate random spontaneous bacteremias; 5) inattention to the incubation period of IE; 6) the necessity to find a culprit for the IE, hopefully, a dentist; and that 7), temporal associations are the weakest of all epidemiologic correlations.[26]

Certainly the tendency of the health sciences to concentrate only on the situation at hand (a patient) to the exclusion of any other more global considerations is very common. That antibiotic prophylaxis and antibiotics in general are drugs that affect the entire world population is of little importance. All that counts is this patient in front of me. All must be done to save this one patient to the exclusion of any deleterious effects on others in the population. Even the best of intentions are no substitute for logic and the scientific method.

TABLE 2

Medical conditions for which no antibiotic prophylaxis is recommended before dental treatment.[40-42]

- Arterial grafts
- Asplenia
- Breast and penile implants
- Cardiac pacemakers and implanted defibrillators
- Cerebrospinal fluid shunts
- Dacron carotid patches
- Diabetes mellitus
- HIV/AIDS
- Immunosuppression secondary to cancer/cancer chemotherapy
- Left ventricular assist devices
- Orthopedic pins and screws
- Orthopedic prosthetic joints
- Peripheral and coronary artery stents
- Renal dialysis shunts
- Solid organ transplants without cardiac valvulopathy
- Systemic lupus erythematosus

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Dentistry in its passivity basically sat on its hands for more than 50 years and allowed medicine to avoid the necessity to say "I don't know" by blaming us for endocarditis. One wonders what they say when there is no one to blame it on. A corollary is that putting the blame on dentists avoids involvement in litigation.

Lessons Learned

Be wary of the tendency as described by Einstein for "the theory to determine what we observe." Often, scientists find what they want to find, not what they should find. There is an incredible amount of "reverse investigation" going on where the final result is predetermined and only data that supports this conclusion is accepted. Be suspicious when the theory has not passed the test of biologic plausibility (biologic sense).

Does it make sense to give antibiotic prophylaxis to 100,000 to a million individuals to try to save one from IE? What does one do about the 99,999 to 999,999 who will not benefit and will possibly suffer harm? Does it make sense to blame the dentist when it is impossible to determine which bacteremia caused the IE? Does it make sense to say oral bacteria causes cardiovascular disease when this disorder is one of the complicated known to science with up to 200 real or potential markers or risk factors?

An important statistical device that is rarely employed today in clinical studies since it would seriously undermine most health-associated therapies is the concept of the "numbers needed to treat (NNT)" or conversely the "numbers needed to harm (NNH)." This is particularly true for chronic diseases that require long-term longitudinal studies that, unfortunately, are rarely done. It is often assumed that every person who receives periodontal therapy benefits from it. All who receive a statin will likely cheat death from coronary artery disease. The reality is that probably for only a limited number of persons is this true.[43,44]

A NNT analysis will determine the actual number of persons in a given population who will benefit from the drug or procedure, and the NNH the number harmed by the therapy.[43,44]

BE WARY OF
the tendency as described by Einstein for "the theory to determine what we observe."

How many patients will it take to prevent one acute myocardial infarction by "dental treatment"? Is it 1/10, 1/100, 1/1000, 1/10,000 (assuming it has any benefit at all), or in the case of endocarditis prevention approaching infinity? What will the cost be to "save" this one person: $1000, $10,000, $1 million?[45] We simply don't know. Yet our patients have a right to know this.

The cost to "save" one person from an endocarditis death using the 1990 AHA guidelines was estimated to be $3 million per life saved and $300,000 for each case prevented (VGS-associated IE is about 10 percent or less fatal).[42] A numbers needed to treat analysis of all proposed clinical therapies should be mandatory in this day and age of unbridled "scientific" hype, particularly when "published by press release."

What to Do With the Patient and Physician

The most obvious questions about the new AHA endocarditis guidelines is what to say to the patient who has taken antibiotic prophylaxis previously before dental treatment, or their physician who refuses to abide by these guidelines. The guidelines list several talking points as listed previously regarding the much greater risk from random daily bacteremias, the limited efficacy of antibiotic prophylaxis, its potential harm, and the potential benefits of good oral health. This will certainly help to explain the changes and may be all that is necessary. However, these do not address the recalcitrant patient or physician.

Toward this end, the following statement may be appropriate, "These new 2007 American Heart Association (AHA) guidelines for the prevention of infective endocarditis may be confusing to patients who have taken antibiotic prophylaxis in the past prior to dental treatment and are now advised that it is unnecessary. These new recommendations are based upon the best current scientific evidence regarding risk, benefit and efficacy of antibiotic prophylaxis to prevent infective (bacterial) endocarditis. If the physician and/or patient chooses not to follow these recommendations, they do so on their own authority. If the advice of the dentist and AHA are in conflict with that of the physician, then the physician can prescribe the antibiotic prophylaxis on their own authority."

With any dental treatment or decision that may be subjected to the infallible hindsight judgment of a plaintiff attorney or a critical "expert," it would again be wise to place in the dental records the statement that this was determined "by my best clinical judgment." This demonstrates particular attention to a potentially controversial judgment decision. It will be tempting to just go along with the

ill-advised advice of the physician, but two wrongs do not make a right . A primer by Brown et al. addresses the proper format for the dentist-physician consultation.[46]

Clinical Caveats

If the antibiotic dosage is *inadvertently* not administered before the procedure, the drug may be administered up to two hours after the procedure.[27] There is no data to support the concept that preprocedural oral antibacterial rinses prevent IE and are not recommended.[27] Routine dental procedures should be scheduled, if possible, at least 10 days apart if the same prophylactic antibiotic is employed. Alternately, for shorter intervals another approved antibiotic (e.g., clindamycin) can be employed.[27]

Conclusions

The 2007 AHA endocarditis prevention guidelines are a meticulous and expert presentation of the scientific data regarding the prevention of endocarditis by antibiotic prophylaxis. It also establishes, finally, that dental treatment is very rarely, if at all, a cause of IE, and that antibiotic prophylaxis is not established as preventive and should only be employed in the very highest risk patients for the sequellae to IE. The guidelines are strictly evidence-based. Assurances are given that sound new data will be reviewed and incorporated in future guidelines when appropriate as science is a long evolutionary process of discovery. The American Heart Association has done well in following the data. Its critics should do the same. ■■■■

REFERENCES

1. Ashrafian H, Bogle RG, Antimicrobial prophylaxis for endocarditis: Emotion or science? *Heart* 93:5-6, 2007.
2. Pallasch TJ, Antibiotic prophylaxis: Problems in paradise. *Dent Clin North Am* 47:665-79, 2003.
3. Pallasch TJ, Wahl M, The focal infection theory: Appraisal and reappraisal. *J Calif Dent Assoc* 28:194-200, 2000.
4. Pallasch TJ, Wahl M, Focal infection: New age or ancient history? *Endodontic Topics* 4:32-45, 2003.
5. Podgrell MA, Welsby PD, The dentist and prevention of infective endocarditis. *Br Dent J* 139:12-6, 1975.
6. Everett ED, Hirschman JV, Transient bacteremia and endocarditis prophylaxis: A review. Medicine (Baltimore) 56:61-7, 1977.
7. Oakley C, Somerville W, Prevention of infective endocarditis. *Br Heart J* 45(3):233-5, 1981.
8. Guntheroth WG, How important are dental procedures as a cause of infective endocarditis? *Amer J Cardiol* 54:797-801, 1984.
9. Kaye D, Prophylaxis for endocarditis: An update. *Ann Int Med* 104:419-23, 1986.
10. Pallasch TJ, A critique of antibiotic prophylaxis. *J Calif Dent Assoc* 14:28-36, 1986.
11. Tzukert AA, Leviner E, Banoliel R, et al, Analysis of the American Heart Association's recommendations for prevention of infective endocarditis. *Oral Surg Oral Med Oral Path* 62:276-9, 1986.
12. Oakley CM, Controversies in the prophylaxis of infective endocarditis. *J Antimicrob Chemother* 20(Suppl A):99-104, 1987.
13. Young SEJ, Aetiology and epidemiology of infective endocarditis. *J Antimicrob Chemother* 20 (Suppl A):7-14, 1987.
14. Pallasch TJ, A critical appraisal of antibiotic prophylaxis. *Int Dent J* 39:183-96, 1989.
15. McGowan DA, Dentists and endocarditis. *Br Dent J* 169:69, 1990.
16. Pallasch TJ, Slots J, Antibiotic prophylaxis for medical-risk patients. *J Periodontol* 62:227-31, 1991.
17. Simmons NA, Ball AP, et al, Antibiotic prophylaxis and infective endocarditis. *Lancet* 339:1292-3, 1992.
18. Wahl MJ, Myths of dental-induced endocarditis. *Ann Int Med* 154:137-44, 1994.
19. Pallasch TJ, Slots J, Antibiotic prophylaxis and the medically compromised patient. *Periodontol 2000* 10:107-38, 1996.
20. Pallasch TJ, Antibiotic prophylaxis: The clinical significance of its recent evolution. *J Calif Dent Assoc* 25:619-32, 1997.
21. Durack DT, Antibiotics for prevention of endocarditis during dental treatment: Time to scale back. *Ann Int Med* 129:829-31, 1998.
22. Roberts GJ, Dentists are innocent! "Everyday" bacteremia is the real culprit: A review and assessment of the evidence that dental surgical procedures are a principal cause of bacterial endocarditis in children. *Pediat Cardiol* 20:317-25, 1999.
23. Lockhart PB, Durack DT, Oral microflora as a cause of endocarditis and other distant site infections. *Infect Dis Clin North Am* 13(4):833-50, 1999.
24. Lockhart PB, The risk of endocarditis in dental practice. *Periodontol 2000* 23:127-35, 2000.
25. Pallasch TJ, Antibiotic prophylaxis. *Endodontic Topics* 4:46-59, 2003.
26. Wahl MJ, Pallasch TJ, Dentistry and endocarditis. *Curr Infect Dis Reports* 7:251-6, 2005.
27. Wilson W, Taubert KA, et al, Prevention of infective endocarditis. Guidelines from the American Heart Association. A guideline from the American Heart Association rheumatic fever, endocarditis and Kawasaki disease committee, council on cardiovascular disease in the young, and the council on clinical cardiology, council on cardiovascular surgery and anesthesia, and the quality of care outcomes research interdisciplinary working group. *Circulation 2007* Single reprint, (800) 242-8721.
28. Strom BL, Abrutyn E, et al, Dental and cardiac risk factors for infective endocarditis: A population-based, case-control study. *Ann Int Med* 129:761-9, 1998.
29. Lacassin F, Hoen B, et al, Procedures associated with infective endocarditis in adults: A case control study. *Europ Heart J* 16:1968-74, 1995.
30. van der Meer JT, Van Wijk W, et al, Efficacy of antibiotic prophylaxis for prevention of native-valve endocarditis. *Lancet* 339:135-9, 1992.
31. Duval X, Alla F, et al, Estimated risk of endocarditis in adults with predisposing cardiac conditions undergoing dental procedures with or without antibiotic prophylaxis. *Clin Infect Dis* 42:e102-7, 2006.
32. Steckelberg JM, Wilson WR. Risk factors for infective endocarditis. *Infect Dis Clin North Am* 7:9-19, 1993.
33. Pallasch TJ, Antibiotic resistance. *Dent Clin North Am* 47:665-79, 2003.
34. Levy SB, The antibiotic paradox. 2nd ed., Plenum Publishing, Cambridge, Mass., 2002
35. Kunin CM, Editorial response: Antibiotic armageddon. *Clin Infect Dis* 25:240-1, 1997.
36. Durack DT, Lukes AS, Bright DK, Duke Endocarditis Service. New criteria for diagnosis of infective endocarditis: Utilization of specific endocardiographic findings. *Amer J Med* 96:200-29, 1994.
37. Li JS, Sexton DJ, et al, Proposed modification to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 30:633-8, 2000.
38. Ott SJ, El Mokhtari NE, et al, Detection of diverse bacterial signatures in atherosclerotic lesions of patients with coronary heart disease. *Circulation* 113:929-37, 2006.
39. Fitzgerald JR, Foster TJ, Cox D, The interaction of bacterial pathogens with platelets. *Nature Rev Microbiol* 4:445-57, 2006.
40. Baddour LM, Bettmann MA, et al, Nonvalvular cardiovascular device-related infections. *Circulation* 108:2015-31, 2003.
41. Lockhart PB, Loven B, et al, The evidence base for the efficacy of antibiotic prophylaxis in dental practice. *J Amer Dent Assoc* 138:458-74, 2007.
42. Pallasch TJ, Antibiotic prophylaxis. In: Pharmacology and therapeutics for dentistry (Yagiela JA, Dowd FL, Neidle EA, eds.) 5th ed., Elsevier Mosby, St. Louis, 2004.
43. Ebrahim S, The use of numbers needed to treat derived from systematic reviews and meta-analysis: Caveats and pitfalls. *Eval Health Professions* 24:152-64, 2001.
44. Barratt A, Wyer PC, et al, Tips for learners of evidence-based medicine: 1. Relative risk reduction, absolute risk reduction and number needed to treat. *Canad Med Assoc J* 171:353-8, 2004.
45. Hamilton J, The link between periodontal disease and systemic diseases: State of the evidence. *J Calif Dent Assoc* 33:29-38, 2005.
46. Brown RS, Farquharson AA, Pallasch TJ, Medical consultations for medically complex dental patients. *J Calif Dent Assoc* 35:343-9, 2007.

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