

Antibiotic Prophylaxis for Dental Patients at Risk for Infection

Latest Revision

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Abstract

This best practice offers recommendations regarding antibiotic prophylaxis to minimize or eliminate transient bacteremia in at-risk dental patients undergoing invasive dental procedures. Evidence supporting the efficacy and use of antibiotic prophylaxis is limited among children. Considering the potential to contribute to antibiotic-resistant microorganisms and possible risk of adverse events, prudence is needed when determining whether prophylaxis is necessary. Antibiotic prophylaxis is warranted for some patients with cardiac conditions and compromised immunity when undergoing dental procedures that involve the manipulation of gingival tissue or the periapical region of teeth or perforation of oral mucosa. While recommendations for certain conditions are discussed within the document, consultation with the patient's physician is recommended for management of other patients potentially at risk due to immune compromise, indwelling vascular catheters or shunts, or implanted devices. Dentists should be familiar with current evidence-based antibiotic prophylaxis recommendations, and specific antibiotic regimens aimed at the microorganisms mainly implicated in infective endocarditis are included.

This document was developed through a collaborative effort of the American Academy of Pediatric Dentistry Councils on Clinical Affairs and Scientific Affairs to offer updated information and guidance on antibiotic prophylaxis for dental patients at risk for infection.

KEYWORDS: PREMEDICATIONS, ANTIBIOTICS; ANTIBIOTIC PROPHYLAXIS; ENDOCARDITIS; ANTIMICROBIAL RESISTANCE

ABBREVIATIONS

AAPD: American Academy of Pediatric Dentistry. **ADA:** American Dental Association. **AHA:** American Heart Association. **CIED:** Cardiovascular implantable electronic device. **GI:** Gastrointestinal. **GU:** Genitourinary. **IE:** Infective endocarditis. **VGS:** Viridans group Streptococcal

Purpose

The American Academy of Pediatric Dentistry (**AAPD**) recognizes that numerous medical conditions predispose patients to bacteremia-induced infections. Prophylactic antibiotics are recommended when patients with a high risk of adverse outcomes from bacteremia and infection undergo invasive oral/dental procedures. These recommendations are intended to help practitioners make decisions regarding antibiotic prophylaxis for dental patients at risk.

Methods

Recommendations on antibiotic prophylaxis for dental patients at risk for infection were developed by the Clinical Affairs Committee, adopted in 1990¹, and last revised in 2019². This revision is based on a review of *Prevention of Infective Endocarditis: Guidelines from the American Heart Association*³, *Infective Endocarditis in Childhood: 2015 Update: A Scientific Statement From the American Heart Association*⁴, the American Dental Association (**ADA**) report *The Use of Prophylactic Antibiotics Prior to Dental Procedures in Patients with Prosthetic Joints*⁵, and the 2021 guideline on *Prevention of Viridans Group Streptococcal Infective Endocarditis: A Scientific Statement From the American Heart Association*⁶. It also included PubMed®/MEDLINE database searches using key terms: infective endocarditis (**IE**), bacteremia, antibiotic prophylaxis, and dental infection. Articles were evaluated by title and/or abstract and relevance to dental care for children, adolescents, and those with special health care needs. Two hundred forty-three articles met these criteria. When data did not appear sufficient or were inconclusive, recommendations were based upon expert and/or consensus opinion by experienced researchers and clinicians.

Background

Bacteremia (bacteria in the bloodstream) is anticipated following invasive dental procedures and can lead to complications in an immunodeficient patient.^{7,8} High risk cardiac disease, immune-suppression, and immunodeficiencies may compromise one's ability to fight simple infection. The rationale for antibiotic prophylaxis is to reduce or eliminate transient bacteremia caused by invasive dental procedures.^{9,10}

Antibiotic usage may result in the development of resistant organisms.¹¹ Utilization of antibiotic prophylaxis for patients at risk does not provide absolute prevention of infection. Post-procedural symptoms of acute infection (e.g., fever, malaise, weakness, lethargy) may indicate antibiotic failure and need for further medical evaluation.

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The decision to use antibiotic prophylaxis should be made on an individual basis. Some medical conditions that may predispose patients to post-procedural infections¹² are discussed below. This list is not intended to be exhaustive; rather, the categorization should help practitioners identify children who may be at increased risk. If a patient reports a syndrome or medical condition with which the practitioner is not familiar, it is appropriate to discuss the risk and susceptibility to bacteremia-induced infection with the child's physician prior to any invasive dental procedures.

To date, randomized controlled clinical trials supporting the efficacy and use of antibiotic prophylaxis are limited, especially in the pediatric population. Many recommendations are based on expert consensus.^{4,6,10,13-16} A study found 80 percent of pre-procedural antibiotic prescriptions unnecessary as risk-factors were not present, highlighting a concern regarding the appropriateness of prescribed prophylaxis.¹⁷ Conservative use of antibiotics helps minimize the risk of developing resistance to current antibiotic regimens.^{3,18-20} Given the increasing number of organisms that have developed resistance to antibiotic regimens, as well as the potential for an adverse anaphylactic reaction to the drug administered²¹, antibiotic/antimicrobial stewardship and the judicious use of antibiotics for the prevention of IE or other distant-site infections are critical for safe and effective care.^{6,11,17,18} While use of antibiotic prophylaxis is indicated for certain patients undergoing invasive dental procedures, the prevention of oral disease by maintenance of good home care habits and regular dental care is considered more important.^{6,22} This may prevent the frequent need for the use of antibiotic therapy and, thus, decrease the risks of resistance and adverse events related to use of antibiotics.^{9,16,23}

Recommendations

Antibiotic prophylaxis for patients at the highest risk of adverse outcomes from bacteremia-induced infections is recommended with certain dental procedures^{3,4,6,7,9,16,24} and should be directed against the most likely infecting organism. Antibiotic stewardship and judicious use are integral to preventing adverse reactions and resistance. Table 1 shows the recommended antibiotic regimen for at-risk patients undergoing invasive procedures, with amoxicillin as the first choice.^{6,10} Recent changes to the American Heart Association (AHA) guidelines have removed the use of clindamycin due to frequent and severe reactions.⁶ Clindamycin has been associated with significant adverse drug reactions related to community-acquired *Clostridium difficile* infections.²¹ Doxycycline is recommended as an alternative for patients unable to tolerate a penicillin, cephalosporin, or macrolide (Table 1).⁶ Short-term use (less than 21 days) of doxycycline had not been associated with tooth discoloration in children under eight years of age.²⁵⁻²⁷ Antibiotic prophylaxis should be given 30-60 minutes prior to the procedure; however, it can be given up to two hours after a dental procedure.⁶ A different class of antibiotics is indicated if the patient is already on oral antibiotic therapy or has an allergy or

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anaphylactic reaction.⁶ If unsure of a reported history of an allergic reaction, consultation with an allergy specialist and skin testing can help determine severity of allergic reactions and course of antibiotic regimen.⁶ If the patient is receiving parenteral antimicrobial therapy for IE or other infections, the same antibiotic can be continued for the dental procedure.⁶ If possible, elective procedures should be delayed 10 days after completion of short course antibiotic therapy.⁶ When procedures involve infected tissues or are performed on a patient with a compromised host response, additional doses or a prescribed pre- and post-operative course of antibiotics may be necessary.

Situation	Agent	Adults	Children
Oral	Amoxicillin	2g	50 mg/kg
Unable to take oral medication	Ampicillin OR Cefazolin or ceftriaxone	2 g IM or IV 1 g IM or IV	50 mg/kg IM or IV 50 mg/kg IM or IV
Allergic to penicillin or ampicillin —oral	Cephalexin* OR Azithromycin or clarithromycin OR Doxycycline	2 g 500 mg 100 mg	50 mg/kg 15 mg/kg <45 kg, 2.2 mg/kg >45 kg, 100 mg
Allergic to penicillin or ampicillin and unable to take oral medication	Cefazolin or ceftriaxone†	1 g IM or IV	50 mg/kg IM or IV

Clindamycin is no longer recommended for antibiotic prophylaxis for a dental procedure.

IM indicates intramuscular; and IV, intravenous.

* Or other first- or second-generation oral cephalosporin in equivalent adult or pediatric dosing.

† Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillin or ampicillin.

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Patients with cardiac conditions

The AHA has published guidelines for the prevention of IE and reducing the risk of producing resistant strains of bacteria.^{3,6} IE is an example of an uncommon but life-threatening complication resulting from bacteremia. The incidence of pediatric admissions due to IE was between 0.05 and 0.12 cases per 1000 admissions in a multicenter study of U.S. children's hospitals from 2003-2010.⁴ Although there is no high-quality data showing mortality from or frequency of viridans group streptococcal (VGS) infective endocarditis in children, there also has been no convincing evidence of an increase in these cases among high-risk patients since the publication of the 2007 AHA guidelines.^{6,10,28}

Only a limited number of bacterial species have been implicated in resultant postoperative infections; Viridans group streptococci, *Staphylococcus aureus* and *Enterococcus* species are the main microorganisms implicated in IE.^{3,4,29} Enterococcal and other organisms such as *Haemophilus*

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species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species are less common.⁴ Routine daily activities such as toothbrushing, flossing, and chewing contribute more to the incidence of bacteremia when compared to dental procedures.⁴ Thus, focus for preventing IE has shifted from antibiotic prophylaxis to an emphasis on oral hygiene and the prevention of oral diseases with regular dental care.^{4,6,9,14-16,24}

A summary of key findings and suggestions by the AHA 2021 scientific statement writing group are outlined in Table 2.

TABLE 2. SUMMARY OF FINDINGS AND SUGGESTIONS
Key findings
VGS IE is much more likely to develop as a result of transient VGS bacteremia attributable to routine daily activities such as chewing food and toothbrushing than from a dental procedure.
An exceedingly small number of cases of VGS IE could be prevented by AP for a dental procedure, even if prophylaxis is 100% effective.
If AP for a dental procedure is effective in preventing a very small number of cases of VGS IE, it should be suggested only for those patients with the highest risk of adverse outcome from VGS IE.
There is no convincing evidence of an increased frequency of or morbidity or mortality from VGS IE in patients at low, moderate, or high risk of adverse outcome since publication of the 2007 document.
AP for a dental procedure is not suggested solely on the basis of an increased lifetime risk of acquisition of VGS IE
Suggestions
AP for a dental procedure that involves manipulation of gingival tissues, periapical region of teeth, or perforation of the oral mucosa is suggested only for patients with the highest risk of adverse outcome from VGS IE.
Maintenance of good oral health and regular access to dental care are considered more important to prevent VGS IE than AP for a dental procedure. We suggest that patients have biannual dental examinations when such care is available.
Shared decision making is important between patients and health care providers. There may be instances when a health care provider and a patient disagree with the suggestions in the 2021 scientific statement. In these cases, the health care provider should be familiar with and understand the 2021 suggestions to adequately inform patients of the risks and benefits of AP for a dental procedure so that an informed decision may be made.

The AHA guidelines recommend antibiotic prophylaxis prior to certain dental procedures (see Table 3) for patients with the highest risk of adverse outcomes from VGS IE (see Table 4).^{6,20} Comorbidities such as obesity, diabetes, cardiopulmonary disease, vascular disease, hemodialysis, lack of access to tertiary hospitals or immunosuppression affect the morbidity and mortality of patients with IE.^{7,20} Global consensus with regards to the benefit of antibiotic prophylaxis for prevention of IE is lacking.^{6,9,16,24,28}

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TABLE 3. DENTAL PROCEDURES AND AP	
AP suggested	
	All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa
AP not suggested	
	Anesthetic injections through noninfected tissue, taking dental radiographs, placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of primary teeth, and bleeding from trauma to the lips or oral mucosa

The antibiotic regimens suggested for prophylaxis for a dental procedure in patients at a high risk of adverse outcome from viridans group streptococcal infective endocarditis are shown in Table 1.

AP indicates antibiotic prophylaxis.

Table 4. AP FOR A DENTAL PROCEDURE: UNDERLYING CONDITIONS FOR WHICH AP IS SUGGESTED*	
Prosthetic cardiac valve or material	
	<ul style="list-style-type: none"> Presence of cardiac prosthetic valve Transcatheter implantation of prosthetic valves Cardiac valve repair with devices, including annuloplasty, rings, or clips Left ventricular assist devices or implantable heart
Previous, relapse, or recurrent IE	
CHD	
	<ul style="list-style-type: none"> Unrepaired cyanotic congenital CHD, including palliative shunts and conduits. Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by transcatheter during the first 6 mo after the procedure. Repaired CHD with residual defects at the site of or adjacent to the site of a prosthetic patch or prosthetic device. Surgical or transcatheter pulmonary artery valve or conduit placement such as Melody valve and Contegra conduit.
Cardiac transplant recipients who develop cardiac valvulopathy	
AP for a dental procedure not suggested	
	<ul style="list-style-type: none"> Implantable electronic devices such as a pacemaker or similar devices Septal defect closure devices when complete closure is achieved Peripheral vascular grafts and patches, including those used for hemodialysis Coronary artery stents or other vascular stents CNS ventriculoatrial shunts Vena cava filters Pledgets

* AP indicates antibiotic prophylaxis; CHD, congenital heart disease; CNS, central nervous system; and IE, infective endocarditis.

Children with cyanosis with specific periodontal concerns may have an increased risk of IE.^{3,4,6} At-risk patients with poor oral hygiene and gingival bleeding after routine activities (e.g., toothbrushing) have shown an increased incidence of bacteremia as a measure for risk of IE.^{3,29} These patients and their parents need to be educated and motivated to maintain personal oral hygiene, including flossing and regular professional preventive dental care, and to be discouraged from getting tattoos or piercings.^{3,6,14-16,23,24} Professional prevention strategies should be based upon the individual's assessed risk for caries and periodontal disease.³⁰

In addition to those diagnoses listed in the AHA guidelines, patients with a reported history of injection drug use may be considered at risk for developing IE.²⁰ Consultation with the patient's physician may be necessary to determine susceptibility to bacteremia-induced infections.

Antibiotics are recommended for all dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa for cardiac patients with the highest risk for adverse outcomes from IE^{3,6} (see Tables 3 and 4). Specific antibiotic regimens can be found in Table 3. Practitioners and patients/ parents can review the entire AHA guidelines in the AHA Circulation archives⁶ (available at “<https://www.ahajournals.org/doi/10.1161/CIR.0000000000000969>”) for additional background information as well as discussion of special circumstances (e.g., patients already receiving antibiotic therapy, patients on anticoagulant therapy).

Patients with shunts, indwelling vascular catheters, or medical devices

The AHA found no convincing evidence that microorganisms associated with dental procedures cause infection of cardiovascular implantable electronic devices (CIED) and nonvalvular devices at any time after implantation.^{6,29,31} The infections occurring after device implantation most often are caused by *Staphylococcus aureus* and coagulase-negative staphylococci or other microorganisms that are non-oral in origin but are associated with surgical implantation or other active infections.^{29,32} The AHA does not recommend antibiotic prophylaxis for prosthetic cardiovascular devices such as CIED, septal defect closure devices, peripheral vascular grafts and patches, central nervous system ventriculoatrial shunts, vena cava filters and pledgets. (see Table 4) Consultation with the child’s physician is recommended for management of patients with nonvalvular devices.

Ventriculoatrial (VA), ventriculocardiac (VC), or ventriculovenous (VV) shunts for hydrocephalus were considered at risk of bacteremia-induced infections due to their vascular access.^{31,33} while ventriculoperitoneal (VP) shunts were not deemed vulnerable.^{31,33} Antibiotic prophylaxis is no longer recommended for patients with VA and VP shunts.^{6,33} If concerned, consultation with the child’s physician is recommended for management of patients with vascular shunts.

Patients with compromised immunity

Non-cardiac patients with a compromised immune system may be at risk for complications of bacteremia and distant site infection following invasive dental procedures. Existing evidence does not support the extensive use of antibiotic prophylaxis; prophylaxis should be limited to immunocompromised patients and those at high risk for adverse outcomes from distant site infection.²³ Consultation with the patient’s physician is recommended for management of patients with a compromised immune system. High-risk patients who should be considered for use of prophylaxis includes, but is not limited to, those with^{6,14,15,22,31}:

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1. Immunosuppression* secondary to:^{22,34}
 - a. human immunodeficiency virus (HIV);
 - b. severe combined immunodeficiency (SCIDS) and other primary immunodeficiency diseases;
 - c. neutropenia and other neutrophil related disorders (e.g., severe congenital neutropenia, leukocyte adhesion deficiency, Chediak-Higashi syndrome);
 - d. cancer chemotherapy, immunosuppressive therapy and/or radiation therapy; or
 - e. hematopoietic stem cell or solid organ transplantation.
2. History of head and neck radiotherapy.^{22,34}
3. Autoimmune disease (e.g., juvenile arthritis, systemic lupus erythematosus).
4. Sickle cell anemia.^{35,36}
5. Asplensism, status post splenectomy, or complement deficiencies.²²
6. Chronic high dose steroid usage.
7. Uncontrolled diabetes mellitus.
8. Medication-related osteonecrosis of the jaw (MRONJ).^{37,38}
9. Hemodialysis.

Patients with prosthetic joints

Given the lack of evidence and recognizing the increase in antibiotic resistance and adverse drug reactions, antibiotic prophylaxis prior to dental procedures is no longer recommended for patients with a history of total joint arthroplasty or prosthetic joint infections^{5,17,39} (see Table 5) If unsure of medical history or risk, consultation with the child's physician is recommended for invasive dental management.^{5,31,39,40}

Table 5. MANAGEMENT OF PATIENTS WITH PROSTHETIC JOINTS UNDERGOING DENTAL PROCEDURES(Sollecito et al. 2015)

Clinical Recommendation:

In general, for patients with prosthetic joint implants, prophylactic antibiotics are *not* recommended prior to dental procedures to prevent prosthetic joint infection.

For patients with a history of complications associated with their joint replacement surgery who are undergoing dental procedures that include gingival manipulation or mucosal incision, prophylactic antibiotics should only be considered after consultation with the patient and orthopedic surgeon.* To assess a patient's medical status, a complete health history is always recommended when making final decisions regarding the need for antibiotic prophylaxis.

Clinical Reasoning for the Recommendation:

- There is evidence that dental procedures are not associated with prosthetic joint implant infections.
- There is evidence that antibiotics provided before oral care do not prevent prosthetic joint implant infections.
- There are potential harms of antibiotics including risk for anaphylaxis, antibiotic resistance, and opportunistic infections like *Clostridium difficile*.
- The benefits of antibiotic prophylaxis may not exceed the harms for most patients.
- The individual patient's circumstances and preferences should be considered when deciding whether to prescribe prophylactic antibiotics prior to dental procedures.

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* In cases where antibiotics are deemed necessary, it is most appropriate that the orthopedic surgeon recommend the appropriate antibiotic regimen and when reasonable write the prescription.
Sollecito T, Abt E, Lockhart P, et al. The use of prophylactic antibiotics prior to dental procedures in patients with prosthetic joints. Evidence-based clinical practice guideline for dental practitioners — a report of The American Dental Association Council on Scientific Affairs. JADA. 2015;146(1):11-16.

References

1. American Academy of Pediatric Dentistry. Antibiotic chemoprophylaxis for pediatric dental patients. Boston, Mass.: American Academy of Pediatric Dentistry; 1990.
2. American Academy of Pediatric Dentistry. Antibiotic prophylaxis for dental patients at risk for infection. The Reference Manual of Pediatric Dentistry. Chicago, Ill: American Academy of Pediatric Dentistry; 2019:416-21.
3. Wilson W, Taubert KA, Gevitz M, 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 and Outcomes Research Interdisciplinary Working Group. *Circulation* 2007;116(15): 1736-54. E-published April 19, 2007. Available at: “<https://www.ahajournals.org/doi/full/10.1161/circulationaha.106.183095>”. Accessed January 16, 2022. Erratum in *Circulation* 2007;116 (15):e376-e7.
4. Baltimore RS, Gweitz M, Baddour LM, et al. Infective endocarditis in childhood: 2015 update: A scientific statement from the American Heart Association. *Circulation* 2015;132(15):1487-515.

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5. Sollecito TP, Abt E, Lockhart PB, et al. The use of prophylactic antibiotics prior to dental procedures in patients with prosthetic joints: Evidence-based clinical practice guideline for dental practitioners—A report of the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc* 2015;146(1):11-6.
6. Wilson WR, Gweitz M, Lockhart PB, et al. Prevention of viridans group streptococcal infective endocarditis: A scientific statement from the American Heart Association. *Circulation* 2021;143(20):e963-e978. Available at: "<https://www.ahajournals.org/doi/pdf/10.1161/CIR.0000000000000969>". Accessed March 26, 2022. Erratum in: *Circulation* 2021;144(9):e192.
7. Lockhart PB, Brennan MT, Kent ML, Norton JH, Weinrib DA. Impact of amoxicillin prophylaxis on the incidence, nature, and duration of bacteremia in children after intubation and dental procedures. *Circulation* 2004;109 (23):2878-84.
8. Roberts GJ, Jaffrey EC, Spract DA, Petrie A, Greville C, Wilson M. Duration, prevalence and intensity of bacteremia after dental extractions in children. *Heart* 2006;92(9):1274-7.
9. Daly CG. Antibiotic prophylaxis for dental procedures. *Aust Prescr* 2017;40(5):184-8.
10. Lauffaurie GI, Noriega LA, Torres CC, et al. Impact of antibiotic prophylaxis on the incidence, nature, magnitude, and duration of bacteremia associated with dental procedures: A systematic review. *J Am Dent Assoc* 2019;150(11):948-59.
11. Centers for Disease Control and Prevention. Antibiotic/Antimicrobial resistance. About antimicrobial resistance: A brief overview. Available at: "<https://www.cdc.gov/drugresistance/about.html>". Accessed January 24, 2022.
12. Buonavoglia A, Leone P, Solimando AG, et al. Antibiotics or no antibiotics, that is the question: An update on efficient and effective use of antibiotics in dental practice. *Antibiotics (Basel)* 2021;10(5):550.
13. Glenny AM, Oliver R, Roberts GJ, Hooper L, Worthington HV. Antibiotics for the prophylaxis of bacterial endocarditis in dentistry. *Cochrane Database System Rev* 2013;4 (10):CD003813. Available at: "<https://doi.org/10.1002/14651858.CD003813.pub4>". Accessed March 8, 2022.
14. Cahill TJ, Dayer M, Prendergast B, Thornhill M. Do patients at risk of infective endocarditis need antibiotics before dental procedures? *BMJ* 2017;358:j3942.
15. Cahill TJ, Harrison JL, Jewell P, et al. Antibiotic prophylaxis for infective endocarditis: A systematic review and meta-analysis. *Heart* 2017;103(12):937-44. Wilson et 2021
16. National Institute for Health and Care Excellence. Prophylaxis against infective endocarditis: Antimicrobial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures. 2008. Updated July 8, 2016. London: NICE. Available at: "<https://www.nice.org.uk/guidance/cg64>". Accessed January 24, 2022.

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17. Suda KJ, Calip GS, Zhou J, et al. of the appropriateness of Assessment antibiotic prescriptions for infection prophylaxis before dental procedures. *JAMA Netw Open* 2019;2(5):e193909.
18. Fluent MT, Jacobsen PL, Hicks LA. Considerations for responsible antibiotic use in dentistry. *J Am Dent Assoc* 2016;147(8):683-6.
19. Watters W, Rethman MP, Hanson NB, et al. Prevention of orthopaedic implant infection in patients undergoing dental procedures. *J Am Acad Orthop Surg* 2013;21(3): 180-9.
20. Baddour LM, Shafiyi A, Lahr BD, et al. A contemporary population-based profile of infective endocarditis using the expanded Rochester Epidemiology Project. *Mayo Clin Proc* 2021; 96(6):1438-45.
21. Thornhill MH, Dayer MJ, Prendergast B, Baddour LM, Jones S, Lockhart PB. Incidence and nature of adverse reactions to antibiotics used as endocarditis prophylaxis. *J Antimicrob Chemother* 2015;70(8):2382-8.
22. Squire JD, Gardner PJ, Moutsopoulos NM, Leiding JW. Antibiotic prophylaxis for dental treatment in patients with immunodeficiency. *J Allergy Clin Immunol Pract* 2019;7(3):819-23.
23. Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): The Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). *Eur Heart J* 2009;30(9):2369-413.
24. National Heart Foundation of New Zealand Advisory Group. Guideline for the prevention of infective endocarditis associated with dental and other medical interventions. Auckland: National Heart Foundation of New Zealand. December, 2008. Available at: "<http://www.ttophs.govt.nz/vdb/document/312>". Accessed March 8, 2022.
25. Todd SR, Dahlgren FS, Traeger MS, et al. No visible dental staining in children treated with doxycycline for suspected Rocky Mountain Spotted Fever. *J Pediatr* 2015;166(5):1246-51.
26. American Academy of Pediatrics. Tetracyclines. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2021-2024 Report of the Committee on Infectious Diseases*, 32nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2021: 978-1-61002-578-2.
27. Stultz JS, Eiland LS. Doxycycline and tooth discoloration in children: Changing of recommendations based on evidence of safety. *Ann Pharmacother* 2019;53(11):1162-6
28. Dayer MJ, Jones S, Prendergast B, Baddour LM, Lockhart PB, Thornhill MH. Incidence of infective endocarditis in England, 2000-13: A secular trend, interrupted time-series analysis. *Lancet*. 2015; 385(9974):1219-28.
29. Baddour LM, Epstein AE, Erickson CC, et al. Update on cardiovascular implantable electronic device infections and their management. *Circulation* 2010;121(3):458-77.

Official but Unformatted

30. American Academy of Pediatric Dentistry. Periodicity of examination, preventive dental services, anticipatory guidance/counseling, and oral treatment for infants, children, and adolescents. The Reference Manual of Pediatric Dentistry. Chicago, Ill: American Academy of Pediatric Dentistry; PENDING.
31. Lockhart PB, Loven B, Brennan MT, Fox PC. The evidence base for the efficiency of antibiotic prophylaxis in dental practice. *J Am Dent Assoc* 2007;138(4):458-74.
32. Hong CHL, Allred R, Napenas JJ, Brennan MT, Baddour LM, Lockhart PB. Antibiotic prophylaxis for dental procedures to prevent indwelling venous catheter-related infections. *Am J Med* 2010;123(12):1128-33. Baddour et 2003
33. Baddour LM, Bettman MA, Bolger AF, Bolger A, Ferrieri P. Nonvalvular cardiovascular device-related infections. *Circulation* 2003;108(16):2015-31.
34. American Academy of Pediatric Dentistry. Dental management of pediatric patients receiving immunosuppressive therapy and/or radiation therapy. The Reference Manual of Pediatric Dentistry. Chicago, Ill.:American Academy of Pediatric Dentistry; PENDING.
35. Tate AR, Norris CK, Minniti CP. Antibiotic prophylaxis for children with sickle cell disease: A survey of pediatric dentistry residency program directors and pediatric hematologists. *Pediatr Dent* 2006;28(3):332-5.
36. Hsu LL, Fan-Hsu J. Evidence-based dental management in the new era of sickle cell disease: A scoping review. *J Am Dent Assoc* 2020;151(9):668-77.e9.
37. Montefusco V, Gay F, Spina F, et al. Antibiotic prophylaxis before dental procedures may reduce the incidence of osteonecrosis of the jaw in patients with multiple myeloma treated with bisphosphonates. *Leuk Lymphoma* 2008;49(11):2156-62
38. Yarom N, Shapiro CL, Peterson dE, et al. Medication-related osteonecrosis of the jaw: MASCC/ISOO/ASCO Clinical Practice Guideline. *J Clin Oncol* 2019;37(25):2270-90.
39. Rethman MP, Watters W 3rd, Abt E, et al. The American Academy of Orthopedic Surgeons and the American Dental Association clinical practice guideline on the prevention of orthopaedic implant infection in patients undergoing dental procedures. *J Bone Joint Surg* 2013;95(8):745-7.
40. Berbari EF, Osmon DR, Carr A, et al. Dental procedures as risk factors for prosthetic hip or knee infection: A hospital-based prospective case-control study. *Clin Infect Dis* 2010;50(1): 8-16. Erratum in *Clin Infect Dis* 2010;50(6):944.