

Antibiotic Prophylaxis for Dental Treatment in Patients with Immunodeficiency



Jacqueline D. Squire, MD^{a,*}, Pamela J. Gardner, DMD^{b,*}, Niki M. Moutsopoulos, DDS, PhD^b, and Jennifer W. Leiding, MD^a

St Petersburg, Fla; and Bethesda, Md

Routine antibacterial prophylaxis is recommended before dental procedures in select patient populations. Currently, no guidelines are in place for routine prophylaxis before dental procedures in patients with primary immunodeficiency diseases. We review risk factors and provide recommendations on routine dental care and antibacterial prophylaxis in patients with primary immunodeficiency diseases. © 2019 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;7:819-23)

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INTRODUCTION

Dental and oral mucosal infections may pose an increased risk for systemic infection in patients with immune deficiencies. As such, appropriate preventive dental care is necessary in these patients to prevent infection. Questions regarding antibiotic prophylaxis are often raised when immunodeficient patients undergo dental procedures. To date, there is a paucity of studies investigating sequelae of dental disease and/or management in chronically immunocompromised patients. Standard practice is to treat dental infections before immunosuppression for hematopoietic cell transplantation, to avoid any risk of systemic infection, but no official guidelines exist for dental management of immunocompromised patients. Herein, we review current evidence and suggest recommendations for the use of antibiotic prophylaxis.

^aDivision of Allergy and Immunology, Department of Pediatrics, University of South Florida, Johns Hopkins-All Children's Hospital, St Petersburg, Fla

^bNational Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, Md

* Co-first authors.

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Corresponding author: Jennifer W. Leiding, MD, Division of Allergy and Immunology, Department of Pediatrics, University of South Florida, Johns Hopkins-All Children's Hospital, 601-4th St South, CRI 4008, St Petersburg, FL 33701. E-mail: jleiding@health.usf.edu; Or: Niki M. Moutsopoulos, DDS, PhD, National Institute of Dental and Craniofacial Research, National Institutes of Health, 30 Convent Drive, Bethesda, Md. E-mail: nmoutsop@mail.nih.gov.

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PREVENTIVE STRATEGIES

Preventive strategies remain the strongest factors that reduce the risk of oral infections in immunocompetent and immunodeficient patients. These include the following:

Oral hygiene: For immunodeficient patients, standard routine oral hygiene practices apply. Recommended oral hygiene includes the brushing of the teeth and tongue 2 to 3 times per day and flossing once a day. Ultrasonic or rotary toothbrushes can be used if the patient is proficient in their use. If periodontal disease is present, periodontal treatment with regular specialized dental cleanings is recommended.

Diet: A noncariogenic diet is recommended that includes avoidance of foods and drinks containing a high amount of sugar. Liquid nutritional supplements and liquid formulations of medications also have a high sugar content and care must be taken to rinse with water or brush teeth after use. Chewing gum containing high amount of sugar is also not recommended. Sugar-free gum is preferable.

Fluoride: Fluoridated toothpaste should be used. In cases of a high caries risk, prescription-strength fluoride toothpastes and application of fluoride varnish by a dental professional may be recommended.

Regular oral evaluation: Individuals at risk for oral infections should be evaluated by a dentist routinely for early identification and treatment of oral issues and reinforcement of adequate oral hygiene practices. Oral evaluation of patients with primary immunodeficiency diseases (PIDDs) should include examinations of dentition, periodontal tissues, soft tissues (for presence of lesions including aphthous ulcers and candidiasis, which are common in certain PIDDs), hard tissues and bone via radiographs, and tonsils. Oral examination should also include screening for oral cancer. Evaluation every 6 months is sufficient for a healthy mouth; however, for individuals with dental decay, gingivitis, and/or periodontal disease, follow-up evaluation every 3 to 4 months would be appropriate.

DENTAL CARE

Routine dental care usually involves 3 different types of procedures.

1. **Noninvasive procedures:** These include oral examinations, x-rays, dental impressions (negative imprint of teeth and soft tissues of the mouth), small supragingival restorations that do not require anesthetic, fluoride treatment, and placement and tightening of orthodontic brackets.
2. **Minimally invasive procedures:** These include dental cleaning in which calculus (tartar) and dental plaque (soft tooth-adherent bacterial biofilm) are removed from the teeth

Abbreviations used

AAPD- American Academy of Pediatric Dentistry

AHA- American Heart Association

CVID- Common variable immunodeficiency

PID- Primary immunodeficiency disease

above the gums. This group also includes dental restorations that require local anesthetic and the placement of packing cord or matrix band (materials placed below the gingiva).

3. *Invasive procedures:* This group includes any dental procedure that involves a break of mucosal tissues including, but not limited to, deep scaling/root planning, root canal therapy, or surgical procedures including tooth extraction, biopsies, and/or implant placement.

SYSTEMIC DISSEMINATION OF ORAL MICROBES (THE ORAL MICROBIOME)

The oral cavity is a niche for microbial colonization and a potential entry point for infectious agents to the gastrointestinal tract and blood stream. In fact, the oral cavity is one of the main habitats of the human body for commensal microbial colonization¹ and the first site of microbial encounter before entry into the gastrointestinal tract.² The microbiome of the oral cavity is incredibly rich and diverse,³ with more than 700 bacterial species detected to date.⁴ In particular, the microbial communities found on tooth surfaces are particularly complex and form elaborate biofilms.^{5,6} The microbial communities on teeth also have the greatest access to the systemic circulation, because they are adjacent to a very thin-layered epithelium of the gingival crevice (pocket), which often becomes ulcerated during local inflammation in the common oral diseases gingivitis and periodontitis. In fact, this epithelium is routinely breached during physiologic functions such as chewing and brushing, allowing transient microbial translocation.^{7,8} Microbial translocation of oral microbes is reported after chewing and during dental procedures,^{9,10} because of breach of the local epithelial barrier. However, this microbial translocation is transient and not considered to be a risk factor for distal infections in the presence of oral health. Yet, in the presence of ongoing odontogenic infections, microbial translocation from the oral cavity has been considered a risk factor for distal infections, particularly during invasive dental procedures. Invasive dental procedures, primarily tooth extractions, are those that are shown to have the highest incidence of bacteremia (ranging from 13% to 96%); the incidence depends on the timing interval between the procedure and the sample collection.⁸ The incidence and duration of bacteremia have been shown to be influenced by the presence primarily of ongoing odontogenic infections and secondarily of periodontitis/gingivitis, suggesting that an increased bacterial burden as well as an ongoing breach of the oral mucosal barrier will contribute to bacteremia.⁸

Odontogenic infections have been associated most commonly with infectious endocarditis,¹¹ but also with infections in the central nervous system and less commonly with distal skeletal infections.⁸ Cases of infections in the central nervous system have been reported in immunocompromised patients, and in a few cases the organism has been traced from the primary odontogenic

infection.^{12,13} Septicemia from oral infections has also been reported in patients with hematologic malignancies, in multiple cases with the organism *Leptotrichia buccalis*.⁸

DENTAL PROPHYLAXIS—CURRENT GUIDELINES

Recommended guidelines have been established by the American Academy of Pediatrics (AAP), the American Dental Association (ADA), the American Academy of Pediatric Dentistry (AAPD), the Infectious Diseases Society of America (IDSA), and the American Heart Association (AHA) for routine antibiotic prophylaxis in patients undergoing hematopoietic cell transplantation, receiving chronic immunosuppression or radiation, and having HIV or cardiac conditions.

Patients with cardiac conditions

The AHA in collaboration with the ADA, IDSA, and AAP¹¹ has published guidelines on the prevention of infective endocarditis in patients with cardiac conditions after routine dental care. In addition, these guidelines are supported by the AAPD.¹⁴ Recommendations for prophylaxis before dental procedures exist for patients with certain cardiac conditions: prosthetic cardiac valve or prosthetic material used for cardiac valve repair, previous infective endocarditis, certain types of congenital heart disease, and cardiac transplantation recipients who develop cardiac valvulopathy. Dental prophylaxis is considered reasonable for minimally invasive or invasive dental procedures. The recommended regimen for antibiotic prophylaxis includes a single dose 30 to 60 minutes before the procedure (Table I). If the antibiotic cannot be given before the procedure, it should be administered within 2 hours of the procedure.

Patients receiving immunosuppressive therapy and/or radiation

The AAPD has published guidelines¹⁵ regarding the dental management of pediatric patients receiving immunosuppressive therapy and/or radiation therapy. As per their recommendations, it is preferred that all dental care be completed before initiation of immunosuppressive therapy and no elective dental care should be provided during the time the patient is immunosuppressed. If dental care is required, the neutrophil count may help guide the decision to use antibiotic prophylaxis. It has been recommended to consider antibiotics, as per the AHA guidelines (Table I), in patients with absolute neutrophil counts between 1000 and 2000/mm³. If the neutrophil count is less than 1000/mm³, dental care should be deferred or it is recommended to discuss antibiotic coverage with the medical team before proceeding with treatment. It was also noted that thrombocytopenia may be another complication of immunosuppression or cancer treatment and require additional management. The AAPD recommends that if platelets are between 40,000 and 75,000/mm³, a platelet transfusion should be considered before and 24 hours after dental care. If the platelet count is less than 40,000/mm³, it is recommended that dental care be deferred. Brennan et al¹⁶ have offered similar recommendations for the use of antibiotics in patients with cancer who have a central venous catheter, because these patients are at high risk of infection.¹⁷ They also noted that neutropenia is an important risk factor to consider for these patients, although no specific values were recommended at which to consider prophylaxis. Antibiotic prophylaxis as noted by the AHA was recommended.

TABLE I. Regimens for antibiotic prophylaxis before a dental procedure*

Situation	Agent	Adult dose	Children's dose
Oral	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin	2 g IM or IV	50 mg/kg IM or IV
	<i>or</i>		
	Cefazolin or ceftriaxone	1 g IM or IV	50 mg/kg IM or IV
Allergic to penicillins or ampicillin, oral	Cephalexin	2 g	50 mg/kg
	<i>or</i>		
	Clindamycin	600 mg	20 mg/kg
	<i>or</i>		
	Azithromycin or clarithromycin	500 mg	15 mg/kg
Allergic to penicillins or ampicillin and unable to take oral medication	Cefazolin or ceftriaxone	1 g IM or IV	50 mg/kg IM or IV
	<i>or</i>		
	Clindamycin	600 mg IM or IV	20 mg/kg IM or IV

IM, Intramuscular; IV, intravenous.

*Recommended regimen: single dose 30-60 min before procedure.

Patients with HIV

No consensus guidelines are available for the dental treatment of patients with HIV, but Shirlaw et al¹⁸ published recommendations regarding their care. Both the CD4 count and the neutrophil count were recommended values to consider regarding the need for antibiotic prophylaxis. Shirlaw et al¹⁸ recommended that antibiotic prophylaxis be provided for patients with a neutrophil count of less than 500/mm³ before oral surgery or periodontal treatment. The AHA guidelines for prophylaxis regimens should be used (see Table I) for these patients.

Patients with PIDDs

No guidelines currently exist for the use of dental prophylaxis in patients with PIDDs, but these patients do develop many oral manifestations that could potentially place them at higher risk of dental-related infections after a dental procedure. Peacock et al¹⁹ comprehensively reviewed the oral manifestations of PIDDs, which include primarily viral and candidal infections, hypodontia (developmental absence of 1 or more teeth), enamel defects, aphthous stomatitis, lichenoid-like lesions, gingivitis, and periodontitis. Because the tonsils are a lymphoid organ, tonsillar hypertrophy is common in patients with PIDDs. In some cases, such as X-linked agammaglobulinemia, there is an absence of lymph tissue and so tonsils are absent as well. Increased risk of odontogenic infection is not reported with specific PIDDs.¹⁹

ANTIBODY DEFICIENCIES

Both cellular and humoral immunity are important for mucosal immunity.² Patients with hypogammaglobulinemia, specific antibody deficiency, X-linked agammaglobulinemia, and common variable immunodeficiency (CVID) have varying degrees of antibody deficiency. In CVID, patients may also have T- and/or natural killer-cell lymphopenia, which may predispose them to oral infections such as oral herpes simplex virus. Oral manifestations in antibody deficiencies include aphthous stomatitis, lichenoid-like lesions, ulcerations, candidiasis, and gingivitis.^{20,21} Immunoglobulin reaches the oral cavity through saliva and gingival crevicular fluid.²² Secretory IgA, also present in the saliva, is thought to help protect against dental caries.²³ On the basis of these known roles, incidence of dental

infections or oral pathology has been studied in patients with primary antibody deficiency. Oral manifestations in patients with antibody deficiency include recurrent aphthous ulcers, lichenoid-like lesions, and herpetic lesions. Results are conflicting, showing that increased incidence of dental caries in some cases²⁰ but not in others.²⁴ Periodontal manifestations have been studied more extensively in patients with IgA deficiency. One study detected that IgA-deficient patients were not at increased risk of periodontal disease or dental decay.²² There have been very few reports of periodontal infections in patients with antibody deficiency. Dalla Torre et al²⁵ describe an 18-year-old female with severe necrotizing periodontitis that prompted an immune evaluation and led to a diagnosis of CVID.

On the basis of current literature, there does not appear to be an increased risk of odontogenic infections in patients with primary antibody deficiency diseases. As such, no prophylactic antibiotics are recommended before dental procedures. However, it is of importance that patients achieve or maintain therapeutic IgG levels on immunoglobulin replacement therapy before undergoing dental procedures. Our recommendation is that patients with primary antibody disorders with no history of oral infections or periodontal disease, who are generally healthy and have a therapeutic IgG level, do not need to receive antibacterial prophylaxis.

NEUTROPHIL DISORDERS

Neutrophils play an important role in host-microbial symbiosis of the mouth. There is an increased risk of periodontal and gingival disease in quantitative and functional neutrophil defects including leukocyte adhesion deficiency,²⁶⁻³⁰ Chediak-Higashi syndrome,³¹⁻³⁴ severe congenital neutropenias,³⁵⁻³⁷ cyclic neutropenia,^{38,39} and chronic granulomatous disease.⁴⁰ Acute and chronic neutropenia occurs in many PIDDs, often placing patients at increased risk of systemic bacterial infections, but systemic infections from commensal mouth flora have not been reported in relation to a dental procedure in those with neutropenia related to PIDDs. However, because of the predisposition toward periodontal and gingival disease at baseline in patients with phagocyte defects, it is the common practice of the authors and recommendation to provide antibiotic prophylaxis

before moderately invasive and invasive dental procedures according to the AHA-recommended antibiotics.⁴¹

COMPLEMENT DEFICIENCIES

The complement system and a functioning spleen provide important early defense against invading microbes. Complement consists of serum and cell surface proteins that interact with other immune cells leading to the generation of proteins that eliminate microbes. The spleen is the main filter for blood-borne pathogens and antigens. There is no increased risk of periodontal or gingival disease, odontogenic infections, or systemic infections from mouth flora in complement deficiency, asplenia, or functional asplenia. However, the risk of systemic bacterial infections in these patients is high. Antibacterial prophylaxis is the standard of care for the prevention of infections in complement-deficient and asplenic patients and so additional antibacterial prophylaxis should not be necessary for dental procedures. However, if the patient is not stable on prophylactic antibiotics, we recommend that patients receive antibiotic prophylaxis before minimally invasive and invasive dental procedures according to the AHA-recommended antibiotics.

SUMMARY

Most cases of oral microbiota leading to systemic infections in immunocompromised hosts are related to the presence of ongoing odontogenic infections and/or the performance of invasive dental treatments in the presence of an existing dental infection (but not in the presence of oral health). Therefore, for most cases, there is a lack of compelling evidence for antibiotic prophylaxis, particularly for noninvasive dental procedures. Presence of an ongoing dental infection is the strongest risk factor for the development of a systemic infection from a dental procedure in patients with PIDDs. The following recommendations have been developed for patients with PIDDs undergoing dental procedures:

- Patients should use preventive strategies and undergo routine dental cleanings and oral examinations as part of their care.
- For invasive dental procedures, patients with PIDDs should receive antibiotic prophylaxis.
- Antibiotic use is required for patients with PIDDs with odontogenic infections before and during treatment.
- Clinicians should weigh the clinical scenario and risk associated when considering the use of antibiotic prophylaxis before a minimally invasive or invasive dental procedure.

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