

Quality Resource Guide

Antibiotic Use in Dentistry

Author Acknowledgement

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Educational Objectives

Following this unit of instruction, the practitioner should be able to:

1. Understand the principles of prescribing antibiotics in dentistry.
2. Be able to describe the actions, rationale for selection and common adult dosage regimens for the antibiotics discussed in this Quality Resource Guide.
3. Be able to describe the major contraindications and warnings associated with antibiotics prescribed in dentistry and discussed in this Quality Resource Guide.
4. Be able to describe the major adverse drug reactions and drug-drug interactions associated with antibiotics prescribed in dentistry and discussed in this Quality Resource Guide.
5. Understand the role of antibiotic prophylaxis and the current recommendations for the use of antibacterial prophylaxis in dentistry.

MetLife designates this activity for **1.0 continuing education credits** for the review of this Quality Resource Guide and successful completion of the post test.

The following commentary highlights fundamental and commonly accepted practices on the subject matter. The information is intended as a general overview and is for educational purposes only. This information does not constitute legal advice, which can only be provided by an attorney.

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Introduction and Principles

Antibiotics play an important role in the management of odontogenic infections (primarily as adjuncts to surgical procedures) and for prevention of systemic infections arising from bacteremias associated with dental procedures in patients at risk for serious systemic infective complications (e.g., infective endocarditis). However, dental professionals must be vigilant in the use of these drugs to avoid their overuse and help address the serious issue of increasing antibiotic resistance.^{1,2} Because common odontogenic infections involve predominantly anaerobic organisms with some facultative ones (e.g., *Streptococci*), appropriate antibiotics are generally limited to narrow-spectrum agents. Therefore, only a few selected classes of antibiotics are indicated for the management of oral infections, including penicillins, cephalosporins, lincosamides and macrolides.³⁻⁵ Tetracyclines and metronidazole may be used in the management of periodontitis, particularly refractory cases, where sub-antimicrobial doses of tetracyclines appear to be beneficial.⁶ This Quality Resource Guide will focus on commonly used oral antibiotics, with an emphasis on high-level scientific evidence. The reader is referred to other sources for information on antiviral and antifungal agents.

There are several important principles that must be understood prior to prescribing an antibiotic for a dental patient:

1. Antibiotics are adjuncts to debridement and/or surgical interventions (tooth extraction, pulpectomy, incision-and-drainage) and should not be used in place of these procedures in the management of infections.
2. Antibiotics are not effective against viruses or fungal organisms. Their successful use depends on an accurate diagnosis, which should confirm a bacterial etiology.
3. An antibiotic regimen should be based upon the signs and symptoms of the bacterial disease. The patient's responses to an antibiotic should be monitored using defined clinical endpoints

(reduction of swelling, reduction of body temperature).

4. Prophylactic use of antibiotics in dentistry is limited (see Prescribing Considerations). The practitioner must be familiar with the current scientific evidence for this use, as well as current guidelines established by dental and medical professional organizations.
5. Some antibiotics may carry a high risk of allergic and other serious reactions and should be used only after careful consideration of the patient's medical and dental history.⁷
6. There are relatively few randomized, controlled clinical trials of antibiotics in dentistry and, therefore, relatively few systematic reviews and meta-analyses on which to base therapeutic decisions.

Antibiotics Commonly Used in Dentistry⁸

Penicillins

There are many forms of penicillin, the most commonly prescribed being amoxicillin, an aminopenicillin. Aminopenicillins have an extended spectrum, which includes some gram-negative organisms that are not typically involved in odontogenic infections. Because penicillins act by inhibition of bacterial cell wall synthesis, they have little systemic toxicity in mammals (mammalian cells lack a "cell wall"). However, penicillins carry a relatively high risk of allergy. Amoxicillin is recommended as the antibiotic of first choice for routine dental infections, due to more favorable pharmacokinetics (a longer dosage interval of eight hours) and the best safety profile among dental antibiotics.⁷

Cephalosporins

Since the development of cephalexin, considered a first-generation agent in the United States, there are now four generations of cephalosporins. Each later generation was synthesized to provide a broader spectrum of activity. While cephalosporins are indicated for antibiotic prophylaxis in selected patients, they are generally not preferred as routine agents in cases of odontogenic infections. They

are included among alternative agents for antibiotic prophylaxis because of their effectiveness against gram-positive *cocci*. For patients with allergy to penicillin, first-generation cephalosporins (cephalexin [Keflex®]) carry a relatively low rate of cross-sensitivity (approximately 1%), but this can vary considerably for other generations of these agents.⁹

Lincosamides

Clindamycin is a lincosamide that is very effective against anaerobic and mixed aerobic-anaerobic infections. It possesses favorable pharmacokinetics and has become a widely used alternative for dental infections in cases of penicillin allergy. However, lincosamides are implicated as a major causative agents for pseudomembranous colitis. Caution is required when prescribing clindamycin because of its relatively high risk for adverse reactions, including skin reactions.⁷ Because of this relatively greater risk of adverse reactions, the American Heart Association's list of recommended antibiotics for the prevention of *S. viridans* infective endocarditis no longer includes clindamycin (see section below, "Antibiotic Prophylaxis").

Macrolides

Erythromycin, clarithromycin and azithromycin are members of this group. Macrolides possess less favorable characteristics for use in dentistry than the other antibiotic classes. Macrolides bind to cytochrome P450 hepatic enzymes and can result in numerous seriously toxic drug interactions. Macrolides (azithromycin) are associated with cardiac arrhythmias, and erythromycin may also stimulate uncomfortable contractions of GI smooth muscle because of its similarity to a locally released GI pro-motility hormone, motilin. Except for use as alternatives for infective endocarditis prophylaxis, they are not preferred as first-choice drugs for routine odontogenic infections. At this time, the safety profile of azithromycin makes it the preferred member of this group for dental patients.⁷

Nitroimidazoles

Metronidazole was originally marketed for use in the treatment of protozoan infections that also has proven bactericidal activity against anaerobes. Because many oral infections (acute periodontal infections) are predominantly anaerobic in nature, metronidazole may be useful alone or in combination with amoxicillin. It has proven to be very effective when tested *in vitro* against periodontal pathogenic organisms.

Tetracyclines

Tetracyclines, including doxycycline, are broad-spectrum, bacteriostatic agents. They chelate calcium ions and thus have a propensity to cause fluorescent tooth staining through incorporation into the enamel of developing teeth, and even into remineralizing enamel of teeth that have already erupted.¹⁰ While not typically indicated for routine odontogenic infections, tetracyclines at sub-antimicrobial doses modulate metalloproteinases (collagenase) involved in the breakdown of

extracellular structures and inflammation. They are used in selected cases of periodontitis refractory to conventional therapy procedures. Some patients may develop photosensitivity to these drugs, which can be severe.⁸ It should be noted that a tetracycline has now replaced clindamycin as an alternative antibacterial agent to prevent *S. viridans* infective endocarditis (see section below, "Antibiotic Prophylaxis").⁸

The specific names and other characteristics of dentally useful antibiotics are shown in **Table 1**.⁸

Prescribing Considerations

1. Following diagnosis of a bacterial infection and removal of the infected tissue, the dental provider can begin antibiotic therapy with a standard dose of an orally administered first-choice agent (such as amoxicillin 500 mg) or an alternative agent. It is appropriate to initiate antibiotic therapy on an empirical basis (without obtaining culture and sensitivity testing). Culture and sensitivity testing require

additional time and may or may not identify specific etiologic pathogens. Culture and sensitivity testing should be considered if initial therapy is not effective.

2. The typical course of antibiotic therapy for dental infections should be 5 to 7 days, unless symptoms persist. The patient should be monitored closely at the beginning of antibiotic therapy. Noticeable improvement should be expected within 24 to 48 hours.
3. Because of reduced absorption in the presence of food, penicillin V should be prescribed one hour before meals or two hours after meals and to be taken every 4 hours to ensure a bactericidal effect.
4. Penicillins do not appear to be effective for the management of symptomatic irreversible pulpitis.¹¹ Guidelines for the selection and use of antibiotics in adults for endodontic infections have been published by the American Association of Endodontists.³

Table 1 - Classification and characteristics of common dental antibiotics for oral administration

Antibiotic	Class	Mechanism of Action	Common Adult Oral Dosage*	Special Considerations
Penicillin VK	Beta lactam penicillin	Bactericidal	500 mg q 4h	Absorption impaired by food, higher risk of adverse reactions than with amoxicillin
Amoxicillin	Aminopenicillin	Bactericidal	500 mg q 8h	Absorption not impaired by food, available with beta lactamase inhibitor
Cephalexin	Cephalosporin	Bactericidal	2 g 30 min-1 h before procedure	Risk of cross-allergy with penicillins is low; alternative agent for prophylaxis
Clindamycin	Lincosamide	Bactericidal	300 mg q 6h	Excellent alternative in cases of penicillin allergy
Azithromycin	Macrolide	Bacteriostatic	500 mg day 1, then 250 mg 1 q d	Once daily dosing; alternative agent for prophylaxis
Clarithromycin	Macrolide	Bacteriostatic	500 mg q 12h	Alternative agent for prophylaxis
Metronidazole	Nitroimidazole	Bactericidal	500 mg q 8h	Disulfiram-like reactions with alcohol; effective against anaerobes only
Doxycycline	Tetracycline	Bacteriostatic	20 mg q 12h prior to meals	Adjunct for periodontal therapy; available in local delivery forms

* See reference 4 for information regarding pediatric dosages

5. The American Academy of Pediatric Dentists has promulgated guidelines for antibiotic use in children.⁴ Note that antibiotic dosages must be adjusted for the child's body weight.
6. Warnings with antibiotic therapy should be issued verbally, and in writing on the prescription. They should include the possible development of allergic reactions, and diarrhea and other GI disturbances.

Antibiotic Prophylaxis

While there is little scientific evidence to support the use of prophylactic antibiotics to prevent postoperative complications, guidance from professional resources suggests its continued use in patients at highest risk of developing complications from infective endocarditis. The most recent publication from The American Heart Association indicates that the guidelines for the prevention of viridans-group infective endocarditis published in 2007 remain unchanged, emphasizing prophylaxis for high-risk individuals. However, these guidelines have now replaced clindamycin with doxycycline 100 mg as an alternative antibiotic in cases of penicillin allergy.¹²

Most regimens involve a single, preoperative dose of a bactericidal agent with activity against *Streptococcus viridans*. There is no documentation showing that a second dose will enhance outcomes.¹³ There is also limited evidence that antibiotic prophylaxis reduces complications following implant placement and no evidence supporting use to prevent complications of third-molar surgery.^{14,15} Antibiotic prophylaxis prior to dental treatment in patients with total joint arthroplasty (artificial joint) is controversial, and professional guidance now emphasizes good oral hygiene to prevent infective complications in these patients. At this time, there is insufficient scientific evidence on which to base the practice.¹⁶ However, when in doubt, the dentist is obligated to consult with the patient's physician(s) to determine the need for antibiotic prophylaxis and the appropriateness of the recommended regimen.

Recent evidence from large-scale observational studies suggests that the risk stratification for patients with conditions that predispose to infective endocarditis needs to be re-evaluated.¹⁷

At this time, dentists should now:

- Make specific patient groups aware of their increased risk of infective endocarditis (including patients with a history of intravenous drug abuse);
- Discuss the advantages and potential drawbacks of antibiotic prophylaxis with their patients;
- Consult with the patient's cardiologists as appropriate; and
- Allow the patient to make the ultimate decision whether or not antibiotic prophylaxis will be used.¹⁷

Adverse Effects

Antibiotics, as prescribed in dentistry, are generally well tolerated. With the exception of allergy, most adverse effects from antibiotics are related to their effects on the gastrointestinal tract. They may irritate the stomach or stimulate contractions of gastrointestinal smooth muscle, resulting in nausea, vomiting and cramping. They may also disrupt the normal flora, resulting in diarrhea or lead to antibiotic-associated colitis, and a potentially life-threatening overgrowth of *C. difficile*.

Symptoms with most cases of antibiotic-associated diarrhea dissipate when the antibiotic is discontinued. It is imperative that patients be cautioned against the use of antidiarrheal drugs and/or probiotics in place of medical diagnosis and management of this rare, but serious, complication.¹ The development of any sign or symptom of an allergic reaction (rash, itching and/or hives) requires that the antibiotic agent be discontinued immediately, and the patient be evaluated medically.

Drug-Drug Interactions

Antibiotics are capable of adversely interacting with other dental and medical drugs, both through pharmacodynamic and pharmacokinetic mechanisms. The most significant adverse pharmacodynamic interaction for commonly prescribed antibiotics is the mutual antagonism that occurs when a bactericidal agent (penicillins, cephalosporins) is co-administered with a bacteriostatic agent (tetracycline). The recent scientific evidence does not support an adverse interaction between oral contraceptives and antibiotics used in dentistry.¹⁸

Conversely, if drugs with similar mechanisms of action are administered together, a beneficial synergism may result. Combinations of antibiotics are not generally recommended in dentistry. However, the addition of metronidazole to a penicillin regimen may improve outcomes because of the selective action of metronidazole on strictly anaerobic organisms. Among the antibiotics discussed here, macrolides are the most likely to produce pharmacokinetic drug interactions. Serious adverse interactions of the various classes of dental antibiotics are listed in **Table 2**.¹⁹

Summary

Antibiotics continue to play an important, albeit adjunctive, role in the management of routine odontogenic infections. They are safe and effective when prescribed at recommended doses and based on the patient's presenting signs, symptoms and coexisting medical conditions. The number of patients who are candidates for antibiotic prophylaxis is relatively small, and prophylactic use should be guided by the current recommendations of professional organizations, as based on scientific review. Dentists should continue to consider emerging evidence for the use of low-dose antibiotics in cases of refractory periodontitis and other inflammatory diseases.

Table 2 - Clinically significant drug interactions involving antibiotics used in dentistry (modified from reference 18)

Primary Drug	Action	Interaction (and Effect)
Alcohol	...metabolism decreased by...	Metronidazole (severe nausea, vomiting)
Benzodiazepines	...enhanced by...	Erythromycin, clarithromycin (increased CNS depression)
Carbamazepine	...enhanced by...	Erythromycin, clarithromycin (increase carbamazepine toxicity)
Coumarins (including warfarin)	...enhanced by...	Erythromycin, clarithromycin, metronidazole, penicillins, tetracyclines (increased risk of bleeding)
Digoxin	...enhanced by...	Erythromycin, clarithromycin (increased toxicity of digoxin, including cardiac arrhythmias)
Lidocaine	...enhanced by...	Erythromycin, clarithromycin (increased toxicity of lidocaine, CNS depression)
Penicillins	...antagonized by...	Coumarin, phenytoin, griseofulvin (reduced efficacy against infection)
Statins	...enhanced by...	Erythromycin, clarithromycin (increased statin toxicity, <i>e.g.</i> , rhabdomyolysis)
Tetracyclines	...antagonized by...	Antacids, iron (reduced absorption of tetracyclines)
Tetracyclines	...antagonizes...	Penicillin (reduced efficacy against infection)
Theophylline	...potentiated by...	Erythromycin, clarithromycin (increase toxicity of theophylline, possible cardiac arrhythmias)

Less significant drug interactions are also possible - the clinician is urged to consult the complete prescribing information for all drugs prescribed.
For medically compromised patients with systemic disease that could impact drug metabolism and/or excretion, consultation with the patient's physician is recommended.

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POST-TEST

Internet Users: This page is intended to assist you in fast and accurate testing when completing the “Online Exam.” We suggest reviewing the questions and then circling your answers on this page prior to completing the online exam.

(1.0 CE Credit Contact Hour) Please circle the correct answer. There is only one correct answer for each question. 70% equals passing grade.

1. Which of the following best characterizes the antibiotics used for odontogenic infections?
 - a. Broad-spectrum
 - b. Narrow-spectrum
 - c. Effective only against anaerobic organisms
 - d. Effective only against facultative organisms
2. Each of the following antibiotics is bactericidal **EXCEPT**:
 - a. penicillin.
 - b. clarithromycin.
 - c. amoxicillin.
 - d. metronidazole.
3. Which of the following antibiotics produces serious systemic toxicity when taken with alcohol?
 - a. amoxicillin
 - b. metronidazole
 - c. cephalexin
 - d. azithromycin
4. Adverse pharmacokinetic drug-drug interactions would be most likely to occur when administering:
 - a. cephalexin.
 - b. clindamycin.
 - c. clarithromycin.
 - d. metronidazole.
5. All of the following are **TRUE** regarding antibiotic-associated colitis **EXCEPT**:
 - a. Best managed with antidiarrheal agents.
 - b. May progress to life-threatening condition.
 - c. May be caused by multiple antibiotics.
 - d. Caused by disruption of GI flora.
6. Antibiotics are **not** indicated for:
 - a. pain of irreversible pulpitis.
 - b. refractory periodontitis.
 - c. odontogenic infections.
 - d. prophylaxis for infective endocarditis.
7. Which of the following agents interacts adversely with benzodiazepines?
 - a. amoxicillin
 - b. penicillin V
 - c. clindamycin
 - d. clarithromycin
8. Which of the following reduces the effectiveness of penicillin V?
 - a. metronidazole
 - b. grapefruit juice
 - c. food
 - d. ibuprofen
9. Which of the following antibiotics is **NOT** indicated for the prevention of viridans group infective endocarditis?
 - a. amoxicillin
 - b. cephalexin
 - c. lincosamides clindamycin
 - d. azithromycin
10. In dentistry, cephalexin is most commonly used for:
 - a. antibiotic prophylaxis.
 - b. prevention of dry socket.
 - c. treating periodontitis.
 - d. management of apical periodontitis.

