Antibacterial Agents in Dental Hygiene Care

A Peer-Reviewed Publication
Written by Dr. Howard M. Notgarnie, RDH, EdD

Abstract
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Educational Objectives
At the end of this self-instructional education activity the participant will be able to:
1. Explain antibiotic effectiveness as a function of selective toxicity
2. Associate antibacterial agents with their antimicrobial mechanisms
3. Describe how bacteria acquire and exercise antibiotic resistance
4. Describe mechanisms of targeted antimicrobial therapy
5. Choose antimicrobial agents appropriate to periodontal conditions
6. Identify conditions at risk of hemogenous infection
7. Choose agents appropriate for antibiotic prophylaxis
8. Discuss the research pertaining to antimicrobials as adjunctive and prophylactic care

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Publication date: July 2013
Expiration date: June 2016
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Dental hygiene care incorporates antimicrobial agents as adjunct services with nonsurgical periodontal therapy, and as a measure to reduce the risk of hematogenous infection subsequent to oral tissue manipulation. Knowledge of antimicrobial properties provides practitioners the ability to make sound decisions when diagnosing conditions treated by dental hygiene intervention and choosing antibiotics dentists prescribe for administration. Antimicrobial agents inhibit structural or metabolic functions of microorganisms, but also render adverse effects to patients. Bacterial mutation and acquisition of genetic material enables development of strains resistant to antibiotics. Understanding the interplay of host, microorganism, and antimicrobials fosters advances in therapeutic choices and delivery systems when treating periodontal disease, as well as when responding to the risk of hematogenous infection of endocardium or prosthetic joints.

Antimicrobial Agents in Dental Hygiene Care
Understanding antimicrobial agents is crucial to modern dental hygiene practice. The properties of these agents influence the effectiveness of medications prescribed by dentists or administered to patients. Dental practitioners use a variety of antimicrobials as adjuncts to traditional mechanical dental hygiene procedures. Although the effectiveness of antibiotic prophylaxis has been questioned, dental professionals have a history of attending to patients who might be at risk of hematogenous infections are protected using antibiotics. This article will address properties of antimicrobials with their use in dental hygiene therapy.

Properties of Antimicrobial Agents
Antimicrobials are chemicals that kill or suppress multiplication of microorganisms. Antibiotics are a subset of antimicrobials that have those antimicrobial effects on bacteria. Clinical practitioners tend to use antibiotic and antimicrobial synonymously. When using antimicrobials, health-care professionals exploit their effects as anti-infective agents.

Antibiotic effectiveness is a result of its selective toxicity: the metabolism of prokaryotic cells makes bacteria susceptible to the toxic effects of antibiotics at far lower concentrations than the concentrations that would adversely affect people, whose cells are eukaryotic. An important factor in antibiotic effectiveness is related to the cell wall structure. Gram-negative bacteria have cell walls with less peptidoglycan than gram-positive bacteria have. Instead, gram-negative bacteria have an extra layer of lipids that protect them from many antibiotics.¹

For most infections, the effectiveness of antibiotics does not depend on whether the antibiotic is bactericidal or bacteriostatic. However, endocarditis or meningitis caused by bacterial infection and infections in some immunocompromised patients require bactericidal antibiotics. An antibiotic’s spectrum refers to the number of bacterial species the antibiotic inhibits or kills. There is no clear definition of broad- and narrow-spectrum, but antibiotics clinically effective against both gram-negative and gram-positive bacteria are generally considered broad-spectrum.¹

Antimicrobial Mechanisms
Antimicrobial agents have a variety of mechanisms of action. Each mechanism inhibits a key structural or metabolic function. Dental practitioners employ antiseptics such as chlorhexidine (CHX) as antimicrobial agents. CHX exhibits its effects on cell surfaces. The cationic nature of CHX gives it several valuable properties: it sticks to anionic oral surfaces, it attaches to the anionic surfaces of bacteria targeted for treatment, and it does not easily pass through skin and mucous membranes.²

Penicillins and cephalosporins, which contain the β-lactam ring, inhibit synthesis of bacterial cell walls. Human cells do not have these cell walls or the peptidoglycan of which cell walls are composed. These drugs are bactericidal because they bind to enzymes involved in formation of cell walls. With poorly formed cell walls, the bacteria are susceptible to swelling and bursting. As a class, these β-lactam antibiotics are effective against a broad spectrum of bacteria because of the variety of synthetic forms available.¹

Quinolones (ciprofloxacin), rifamycins (rifampin), nitroimidazoles (metronidazole), and nitrofurans (nitrofuranantoin) are bactericidal because they inhibit nucleic acid production. Inhibition of DNA production prevents reproduction, and inhibition of messenger RNA production prevents cells from making proteins necessary for metabolism. Metronidazole provides a good example of the reason some antibiotic spectra are narrow. Metronidazole inhibits DNA synthesis only in the absence of oxygen; thus only anaerobic bacteria are sensitive to metronidazole.¹

An additional antibiotic mechanism is inhibition of ribosomes synthesizing proteins. Tetracyclines inhibit the function of transfer RNA, which carries amino acids to a ribosome building a protein. Aminoglycosides (streptomycin) cause errors in the translation of messenger RNA into protein, thereby causing the resultant
Antibiotics can target bacteria metabolically. Metabolically targeted antibiotic therapy involves laboratory testing of bacteria for sensitivity to antibiotics, thereby allowing clinicians to prescribe or administer antibiotics that will most effectively kill or inhibit the particular species present in the patient’s infection. Testing of oral flora and choosing an antibiotic regimen based on the patient’s plaque composition is a promising method for metabolically targeted antibiotic therapy.

The other mechanism of targeted antibiotic application is by site specificity. Effective administration requires materials holding the antimicrobial agent to withstand moisture, heat, and motions of the mouth. Furthermore, a substrate that remains in place for an extended time must be less than 1mm thick, soft, and flexible so as not to irritate the patient. In a systematic review, CHX used as a mouth rinse reduced plaque and gingivitis scores compared with placebo but caused an increase in staining. CHX in a sustained delivery system improved ease of compliance. Reduced risk of adverse effects, and continuous administration balanced the lack of uniformity in dosage associated with the slow release of the drug. This sustained delivery of CHX reduced the load of bacterial plaque and adhesion of the fungus Candida albicans while improving patient experience associated with the taste and staining of CHX mouth rinses.

A widely studied targeted delivery system for nonsurgical periodontal treatment is the subgingival application of minocycline. In a systematic review, pocket depth and attachment of the periodontium improved more with minocycline or doxycycline than with placebo. This improvement occurred despite no significant difference in plaque index or bleeding on probing. Thus, the authors supported targeted subgingival antibiotic therapy as an adjunct to mechanical removal of deposits. Liu and Yang emphasized the direct antimicrobial effects on periodontal pathogens Porphyromonas gingivalis, Porphyromonas intermedia, Eikenella corroden, and Fusobacterium nucleatum. An additional benefit of targeted delivery of these tetracycline derivatives is the reduction in the destructive effects of the immune response. These medications modulate several immune responses, including macrophage activity that produces tumor necrosis factor-α. Such modulation improves indications of periodontal health.

### Systemic Therapy
Bowen recommended including amoxicillin and metronidazole as a bivalent prescription at the initial phase of nonsurgical periodontal treatment of generalized aggressive periodontitis (GAP). Patients with GAP exhibit rapid destruction of periodontal tissues despite being generally healthy systemically. Their neutrophils and serum antibodies function abnormally. Differential diagnosis of GAP includes loss of attachment and bone around first molars, mandibular incisors, and at least three other teeth; deposits that do not benefit the periodontal destruction; and a family history suggesting susceptibility to GAP. GAP often begins under the age of 30. For GAP patients with pockets up to 6mm, the outcomes of bivalent antibiotic treatment during initial nonsurgical periodontal therapy are better than deciding on systemic antibiotic treatment during...
Table 1. Antibiotic Regimens for Infective Endocarditis Prophylaxis

<table>
<thead>
<tr>
<th>Administration</th>
<th>By Mouth</th>
<th>Unable to Take by Mouth</th>
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<tbody>
<tr>
<td></td>
<td>Adult</td>
<td>Child</td>
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<tr>
<td>Standard—Penicillins</td>
<td>2g amoxicillin</td>
<td>50mg/kg amoxicillin</td>
</tr>
<tr>
<td>Penicillin Allergy—Cephalosporins*</td>
<td>2g cephalaxin</td>
<td>50mg/kg cephalaxin</td>
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<tr>
<td>Penicillin Allergy—Clindamycin or Macrolides</td>
<td>600mg clindamycin</td>
<td>20mg/kg clindamycin</td>
</tr>
<tr>
<td>Penicillin Allergy—Macrolides</td>
<td>500mg azithromycin or clarithromycin</td>
<td>15mg/kg azithromycin or clarithromycin</td>
</tr>
</tbody>
</table>

*Not for those with immediate-type penicillin allergic reaction

the maintenance phase. Cases beyond that severity usually require surgical intervention to control periodontitis. Limitations of this bivalent antibiotic regimen are clinical significance of improved pockets, adverse reactions to medications, and bacterial resistance. In addition, differentiating GAP from chronic periodontitis is important because systemic antibiotics are not warranted for initial therapy of chronic periodontitis. The recommended protocol is amoxicillin and metronidazole, each 500 mg three times per day for 7 to 10 days.10

Antibiotic Prophylaxis to Avert Sequelae of Bacteremia

Frequently, patients have used antibiotics to reduce the risk of hematogenous infection. Bod et al. explained the purpose of antibiotic prophylaxis is to reduce the number of bacteria at the treatment site and to reduce the ability of bacteria to colonize. When using antibiotic prophylaxis, the practitioner should ensure an effective concentration of antibiotic from the beginning of treatment to the end of bacteremia, effectiveness of the antibiotic for the bacteria likely to enter the bloodstream, avoiding multiple doses that might lead to resistant bacterial strains, and the patient’s potential for adverse reactions.11 Nevertheless, researchers widely question the value of antibiotic prophylaxis. For example, case reports have inferred prosthetic joint infection of oral origin, yet no known studies have shown a genetic match. Maintaining good oral health reduces risks associated with bacteremia.12

Infective Endocarditis

Common signs and symptoms of infective endocarditis (IE) are fever, heart murmur, chills, weakness, and difficult breathing. Treatment of IE depends upon identifying the pathogen and that pathogen’s antimicrobial susceptibility profile. Surgical intervention is often necessary as well. Although *Staphylococcus aureus* and *Streptococcus* species are predominant pathogens, other bacterial species, parasites, and autoimmune processes may also cause endocarditis. Changes in recommendations for antibiotic prophylaxis reflect a change in epidemiology of IE. Antibiotic overuse has led to bacterial resistance in strains endemic to human environments. Incidence of IE has been very low—less than 10/100,000 in patients under 70 and 14.5/100,000 in patients 70 to 80 years of age. Prosthetic heart valves and degenerative heart disease have supplanted rheumatic heart disease as underlying risk factors for IE. New risk factors for IE include use of intravenous drugs and catheters. Moreover, antibiotic prophylaxis does not seem to be cost-effective. Consequently, only people with a high risk for IE undergoing high risk procedures should have antibiotic prophylaxis. These high risk situations include manipulation of gingival tissues on patients with prosthetic heart valves, a history of IE, cyanotic heart disease that has not been repaired or that has been repaired with a prosthesis less than six months ago, or heart disease repaired with a prosthesis near which a defect remains.13

The American Heart Association explained that except in cardiac patients with the highest risk, the relative risks and effectiveness of antibiotic prophylaxis make routine use of those antibiotics difficult to justify. Infectious endocarditis involves interplay of clotting and immune factors with bacteria in the bloodstream. Bacteria attach to thrombi on cardiac endothelium and reproduce in a vegetation at the attachment site. Turbulence initiates those thrombi.14 Correcting dental problems before prosthetic heart valve replacement, maintaining good oral health, and avoiding procedures that result in bacteremia help avoid IE.15

Windle and Kulkarni (2012) noted antibiotic prophylaxis for IE aims at the most common pathogen for that sequel, *Streptococcus viridans*. The antibiotic is indicated 30 to 60 minutes prior to beginning care. Table 1 displays antibiotic choices.15

Prosthetic Joint Replacement

Benoit and Pickett showed the evolution of antibiotic prophylaxis recommendations over the past two decades to demonstrate lack of a clear rationale for antibiotic prophylaxis:

- In 1985, a survey reflected that most orthopaedic surgeons did not believe there was a significant relationship between oral procedures and infection of prosthetic joint replacements, yet they recommended antibiotic prophylaxis.12 The most common recommendation was a cephalosporin.16 However, concerns over bacterial resistance to antibiotics led many health professionals to question this practice of antibiotic prophylaxis.
• In 1997, the American Dental Association (ADA) and American Academy of Orthopaedic Surgeons (AAOS) jointly issued a statement recommending selective antibiotic prophylaxis, which they later updated, in 2003. The guidelines for antibiotic prophylaxis addressed time since placement of the prosthesis, systemic health problems, medications, history of complications with the prosthesis, and comorbidities.
• In 2009, the AAOS recommended antibiotic prophylaxis of all patients with a total joint replacement for any oral procedures. AAOS did not consult with ADA for this recommendation.
• In 2011 the American and Canadian Dental Associations recommended no antibiotic prophylaxis if joint replacement is more than two years old unless the patient has a history of infection in a prosthetic joint or the patient has a compromised immune system. However, AAOS did not rescind its 2009 recommendations.¹²

Most recently, the AAOS and ADA issued three recommendations based on a systematic review of extant research regarding risk of infection to joint implants. These recommendations are 1) consider discontinuing routine antibiotic prophylaxis; 2) they are “unable to recommend for or against” rinsing with an antimicrobial agent before dental care; and 3) maintenance of oral health is suitable to patients with prosthetic joints. Several peer organizations, including the American Dental Hygienists’ Association, reviewed the recommendations. Studies in the systematic review, informing the first two recommendations, did not show an association between bacteremia and implant infection. In fact, although implant infections are mostly Staphylococcus species, bacteremias associated with dental procedures are mostly Streptococcus species. The third recommendation was a consensus statement based on the benefit of current practices toward good oral health and on evidence that a healthy oral condition reduces bacteremia.¹³

Similarly, in 2008 British health officials recommended against antibiotic prophylaxis for patients with a risk of IE because there is no evidence of efficacy. There is no evidence that antibiotic prophylaxis reduces infections of prosthetic joints, yet bacteremia after brushing teeth and eating is comparable to that of dental care.¹³ Berbari et al. showed that dental procedures were not risk factors for prosthetic hip or knee infections.¹⁴ Thus the low, 2% prevalence of prosthetic joint space infection is inconsistent with the theory that those infections originate from oral procedures. Furthermore, antibiotic prophylaxis does not prevent bacteremia.¹²

With the mounting evidence against effectiveness of antibiotic prophylaxis, Olsen, Snorrason, and Lingaa (2010) advised against antibiotic premedication for dental procedures on patients with joint replacements except in those patients with a high risk for infection. When practitioners prescribe antibiotic prophylaxis for prosthetic joints, Olsen et al. recommended a regimen consistent with that in Table 1.¹⁹

Bod et al. recommend antibiotic prophylaxis for dental procedures when the prosthetic joint is less than two years old, the patient has a compromised immune system, or the patient has a history of prosthetic joint infection. Vancomycin is indicated only when there is a recognizable risk of infection with methicillin-resistant Staphylococcus aureus.¹¹

It is valuable to note that patients with prosthetic joints or a high risk of IE are trying to reduce the risk of an infection subsequent to manipulation of oral tissues. The presumed critical event is bacteremia, which is not associated with the misperception of hierarchy. Thus it would be prudent to question a physician’s rationale when prescribing antibiotic prophylaxis “for fillings but not for cleansings.”

Conclusion
Dental practitioners and their patients benefit when practitioners understand the pharmacology of antimicrobial agents. Dental hygienists have a history of administering antimicrobials upon the prescription of dentists as an adjunct to nonsurgical periodontal care. Furthermore, dentists have a history of prescribing antibiotics as a risk-reduction measure for hematogenous infection. Awareness of modern principles gives dental practitioners the opportunity to offer state-of-the-art care to clientele by choosing effective medications and avoiding those with risks outweighing the benefits.

References

Author Profiles
Dr. Howard M. Notgarnie has been practicing clinical dental hygiene for 20 years, currently in Colorado. He has eight years experience in professional association leadership and five years teaching experience. He can be contacted at howardrdhedd@gmail.com.

Author Disclosure
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Questions

1. Antibiotic resistance is not related to:
   a. Bacterial mutations
   b. Plasmid incorporation
   c. Rate of bacterial reproduction
   d. Human drug tolerance

2. Sulfonamides’ antibiotic effects are inhibiting synthesis of:
   a. DNA
   b. Protein
   c. Folate
   d. Cell walls

3. Implant infections are mostly of what genus?
   a. Staphylococcus
   b. Candida
   c. Porphyromonas
   d. Streptococcus

4. The defining difference between antimicrobials and antibiotics is:
   a. Antibiotics are a subset of antimicrobials
   b. One type affects eukaryotic cells, and the other affects prokaryotic cells
   c. They affect different types of cell walls
   d. One type is bacteriostatic, and the other is bactericidal

5. Antibiotic prophylaxis for dental care is intended to avoid:
   a. Bleeding during dental procedures
   b. Hematogenous infection of prosthetic joints and endocardium
   c. Bacteremia associated with brushing teeth and eating
   d. Poor oral health

6. A 7 to 10 day regimen of amoxicillin and metronidazole has been found most effective for which of the following:
   a. Initial treatment of chronic periodontitis
   b. Treatment of generalized aggressive periodontitis during maintenance phase
   c. Initial treatment of generalized aggressive periodontitis
   d. Treatment when pockets are ≥7mm in depth

7. Which of these statements about chlorhexidine is true?
   a. It is an anionic compound
   b. Its effects are on cell surfaces
   c. It does not interact with oral surfaces
   d. It easily passes through mucous membranes

8. Bacteremia associated with dental procedures is mostly of what genus?
   a. Staphylococcus
   b. Candida
   c. Porphyromonas
   d. Streptococcus

9. Antibiotics with a β-lactam ring act by binding to:
   a. Peptidoglycan
   b. Anionic surfaces
   c. Messenger RNA
   d. Enzymes

10. A substrate for sustained, site-specific antibacterials are more effective if they are:
    a. Rigid
    b. Thicker than 1mm
    c. Kept dry
    d. Heat tolerant

11. Each of the following directly affects protein synthesis except:
    a. Rifampin
    b. Tetracycline
    c. Streptomycin
    d. Erythromycin

12. Bacteria may resist antibiotics by all of the following except:
    a. Preventing the antibiotic from entering the cell
    b. Destroying the antibiotic
    c. Pumping out the antibiotic
    d. Influencing the antibiotic’s toxicity to the host

13. Metabolic antibiotic targeting involves all of the following except:
    a. Bacterial sensitivity testing
    b. Plaque composition
    c. Human sensitivity testing
    d. Oral flora testing

14. Baluta et al. recommended infective endocarditis prophylaxis if the patient has any of the following conditions except:
    a. Prosthetic heart valve
    b. History of infective endocarditis
    c. Prosthetic repair of heart disease with a remaining defect
    d. Cyanotic heart disease that was successfully repaired >6 months ago

15. Targeted subgingival delivery of minocycline does not affect:
    a. Bleeding on probing
    b. Human immune response
    c. Pocket depth
    d. Attachment of the periodontium

16. Typical presentation of a person with generalized aggressive periodontitis is:
    a. Normal immune function
    b. Under age 30
    c. Systemic illnesses are apparent
    d. Periodontal destruction consistent with deposits

17. Changes in antibiotic prophylaxis for infective endocarditis involve all the following epidemiological changes except:
    a. Rheumatic heart disease has become an increasing concern
    b. Incidence of infective endocarditis is very low
    c. Antibiotic prophylaxis is not cost-effective
    d. Antibiotic-resistant strains of bacteria are endemic to human populations

18. Windle and Kulkarni named which microorganism the most common pathogen for infective endocarditis?
    a. Streptococcus mutans
    b. Staphylococcus aureus
    c. Streptococcus viridans
    d. Eikenella corrodens

19. Which of the following inhibits nucleic acid production?
    a. Penicillin
    b. Ciprofloxacin
    c. Sulfonamide
    d. Tetracycline

20. Bod et al. recommended antibiotic prophylaxis for a prosthetic joint if the patient has any of the following conditions except:
    a. Prosthetic joint <2 years old
    b. Pins or screws in a bone
    c. History of infection in the prosthetic joint
    d. Compromised immune system

21. Which of the following inhibits nucleic acid production?
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6. Identify conditions at risk of hemotogenous infection.
7. Choose antimicrobial agents appropriate for antibiotic prophylaxis.
8. Discuss the research pertaining to antibiotics as adjunctive and prophylactic care.

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1. Were the individual course objectives met?  
   - Objective #1: Yes  
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2. To what extent were the course objectives accomplished overall?  
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13. Was there any subject matter you found confusing?  
    - Please describe.
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