Use and abuse of antibiotics

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For the past 90 years, antibiotic therapy has played an essential role in the treatment of bacterial infectious diseases. Since the discovery of penicillin in 1928 by Fleming and sulfanilamide in 1934 by Domagk, the entire world has benefitted from the most potent weapon against disease. 

Yet, the impressive success of antibiotics is now being offset by the alarming rate at which bacteria develop resistance to antibiotics. This development of resistance has contributed significantly to the morbidity and mortality of infections, especially nosocomial infections. 

The selection of dominance of the antibiotic-resistant organisms is a significant contributor to the emergence of more resistant organisms. Patients with infections caused by antimicrobially resistant organisms are then a source of infection for hospitalized staff and other hospitalized patients. These drug-resistant infections may subsequently result in the spread of multidrug-resistant strains. Many worldwide strains of Staphylococcus aureus exhibit resistance to all medically important antibiotic drugs, including penicillin, cephalosporins, and methicillin-resistant S. aureus has become one of the most frequent nosocomial, or hospital-acquired, pathogens. The rate at which bacteria develop resistance to antibiotics is alarming, demonstrating resistance soon after new drugs have been introduced. This rapid development of resistance suggests that bacterial resistance to antibiotics is increasing at an alarming rate. The major cause for this alarming rate is the inappropriate use of antibiotics for treatment or prevention of infections. 

Antibiotics are subsequently being used as prophylaxis in dentistry. 

The American Dental Association reported the results of a survey of antibiotic use in dentistry in the November 2000 Journal of the American Dental Association. The authors surveyed all licensed dentists practicing in Canada and found that confusion about prescribing antibiotics and inappropriate prescribing practices were evident, and that inappropriate antibiotic use, such as improper dosing, duration of therapy and prophylaxis are all factors that may affect development of antibiotic-resistant microorganisms. 

There is a glimmer of hope. A report from Aker University in Oslo, Norway, strongly suggests that bacterial resistance to antibacterial agents can be reversed. While dangerous and contagious staph infections kill thousands of patients in the most sophisticated hospitals in Europe, North America and Asia, there is virtually no sign of this “killer superbug” in Norway. The reason? Norway stopped using so many antibiotics. 

We don’t throw antibiotics at every person with a fever. We tell them to hang on, wait and see, and we give them a tylenol to feel better,” said Dr. John Haug, infectious disease specialist at Aker University Hospital in Norway. 

The review concluded that appropriate antibiotic drug prescribing by dental practitioners is a significant contributing factor in the selection of drug-resistant bacterial strains. The American Dental Association reported the results of a survey of antibiotic use in dentistry in the November 2000 Journal of the American Dental Association. The authors surveyed all licensed dentists practicing in Canada and found that confusion about prescribing antibiotics and inappropriate prescribing practices were evident, and that inappropriate antibiotic use, such as improper dosing, duration of therapy and prophylaxis are all factors that may affect development of antibiotic-resistant microorganisms. 

The Council’s position statement further identified that Antibiotics are properly employed only for the management of active infectious disease or the prevention of metastatic infection, such as infective endocarditis, in medically high-risk patients. 

One method of education is to teach from errors rather than principles. Psychologists from the University of Exeter have identified an “early warning signal” in the brain that helps us avoid repeating previous mistakes. Published in the Journal of Cognitive Neuroscience, their research identifies for the first time, a mechanism in the brain that reacts, in just one-tenth of a second, to things that have tailored us making errors in the past. Evaluating the following eight misconceptions or “myths” may help to establish general guidelines to aid us in making clinical decisions regarding the use of antibiotic therapy, thereby leading to optimum use and therapeutic success. 

Myth No. 1: Antibiotics cure patients. Except in patients with a compromised immune system, antibiotics are not curative, but instead function to assist in the re-establishment of the proper balance between the host’s defenses (immune and inflammatory) and the invasive agent(s). Antibiotics do not cure patients; patients cure themselves. 

Myth No. 2: Antibiotics are substitutes for surgical intervention. Very seldom are antibiotics an appropriate substitute for removal of the source of the infection (extraction, endodontic treatment, incisions and drainage, periodontal scaling and root planing). Occasionally, when the infection is too diffuse or disseminated to identify a nidus for incision, or the clinical situation does not allow for immediate curative treatment, the prudent dentist will choose to place the patient on appropriate antibacterial therapy until such time as curative treatment can be implemented. It is imperative to remove the cause of the infection prior to, or concomitantly with, antibiotic therapy, when the cause is readily identifiable. 

Whenver antibiotic therapy is used, the risk of bacterial selection for antibiotic resistance is present. 

Myth No. 3: The most important decision which antibiotic to use. To avoid the deleterious effects of needless antibiotics on patients and the environment, the most important initial decision is not which antibiotic to prescribe but whether to use one at all. It has been estimated that up to 60 percent of human infections resolve by host defenses alone following removal of the nidus, and that the use of antibiotics without antibiotic intervention. Endodontic disease is infectious. Microorganisms cause virtually all pathologies of the pulp and peripical tissues. There is ample evidence to support that opportunistic normal oral microbiota colonize in a symbiotic manner, without benefit, resulting in endodontic infections. The majority of endodontic disease is cured by systemic antibiotic therapy when the cause of the infection is

Primary Reasons for Revision of Infective Endocarditis Guidelines

1. IE is much more likely to result from frequent exposure to random bacteremias associated with daily activities than from bacteremias caused by a dental, GI tract or GU tract procedure.

2. Prophylaxis may prevent an exceedingly small number of cases of IE, if any, in individuals who undergo a dental, GI tract or GU tract procedure.

3. The risk of antibiotic-associated adverse events exceeds the benefit, if any, from prophylactic antibiotic therapy.

4. Maintenance of optimal oral health and hygiene may reduce the incidence of bacteremia from daily activities and is more important than prophylactic antibiotics for a dental procedure to reduce the risk of IE.

Table 1. (Tables Provided by American Association of Endodontists)
Fig. 4. Acute apical abscess with extraoral diffuse facial cellulitis.

Table 2. (Table Provided by: American Association of Endodontists)

<table>
<thead>
<tr>
<th>Special situations and circumstances:</th>
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<td>Patients already receiving antibiotics—Occasionally, a patient may be taking an antibiotic when coming for a dental appointment. If the patient is taking an antibiotic normally used for endodontics prophylaxis, it is prudent to select a drug from a different class rather that increase the dose of the current antibiotic. If possible, you should delay the dental procedure until at least 10 days after completion of the antibiotic. This will allow for the usual oral flora to be re-established. If an individual receiving long-term parenteral antibiotic therapy for IE requires dental treatment, the treatment should be timed to occur 30 to 60 minutes after the parenteral antibiotic therapy has been delivered.</td>
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<tr>
<td>Failure to administer pretreatment antibiotic dose—If the dosage of an antibiotic is inadvertently not administered before the procedure, the dosage may be administered up to two hours after the procedure. However, administration of the dosage after the procedure should be considered only when the patient did not receive the prophylactic dose.</td>
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<tr>
<td>Individuals with kidney dialysis shunts—Individuals with permanent kidney dialysis shunts should be placed on prophylactic antibiotics using the same protocol as for IE.</td>
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has been properly managed (complete debridement of the pulp space and proper obturation and sealing of the pulp space from the oral environment).

Apical periodontitis lesions of pulpal origin are generated by the immune system and are the result of intraradicular infections (Fig. 1). In most situations, this inflammatory process successfully eliminates the bacteria emerging from the apical foramen and prevents their spread to the periapical tissues. This process is primarily facilitated by the polymorphonuclear leukocytes that eventually phagocytize and kill the bacteria. Asymptomatic apical periodontitis of pulpal origin does not routinely require systemic antibiotic therapy for satisfactory resolution and healing. Endodontic therapy alone is usually sufficient.

When the intraradicular infection is able to overwhelm the host’s immune response, viable bacteria are able to gain access to the periapical tissues and colonize, forming an active infection. This results in the formation of an apical abscess. A chronic apical abscess usually presents with gradual onset, no to mild symptoms and the presence of a sinus tract or punched out (Fig. 2). The majority of chronic apical abscesses of endodontic origin do not require systemic antibiotic therapy for satisfactory resolution and healing.

An acute apical abscess usually presents with rapid onset, spontaneous pain and swelling, both localized and intraoral, sometimes with exudate present, or with diffuse facial cellulitis. When the abscess is intraoral and localized (Fig. 5), debridement of the pulp space and placement of calcium hydroxide and surgical incision for drainage is usually sufficient to resolve the problem. Systemic antibiotic therapy is not routinely indicated, depending on the patient’s general medical status. However, when the patient presents with diffuse facial swelling (cellulitis) resulting from an acute apical abscess or an infection with systemic involvement (fever or malaise) (Fig. 4), debridement of the pulp space with placement of calcium hydroxide, surgical incision for drainage, and an appropriate regimen of systemic antibiotics (oral or IV) are the treatments of choice.

Understanding the enemy is an important factor in winning any battle. The rational choice and use of antimicrobial agents begins with the knowledge of the microorganisms most likely responsible for common dental infections of pulpal origin. The bacterial flora found in endodontic infections is indigenous, mixed (Gram-positive and Gram-negative) and predomi-

antly anaerobic. Several species of bacteria have been associated with acute apical abscesses. These species include dark-pigmented bacteria (Prevotella and Porphyromonas), eubacteria, fusobacteria and actinomyces.

Baurgatner and Xia published a report of the susceptibility of bacteria recovered from acute apical abscesses to five commonly used antibiotics in dentistry, antibiotic susceptibility data from 98 species of bacteria recovered from 12 acute apical abscesses led to the following conclusions:

1. Pen-V-K is the antibiotic of choice for endodontic infections due to its effectiveness in polymicrobial infections, its relative narrow spectrum of activity against bacteria most commonly found in endodontic infections, its low toxicity and low cost.
2. Clindamycin is the antibiotic of choice for patients allergic to penicillins.
3. While amoxicillin and augmentin (amoxicillin plus clavulanate) demonstrated a higher antibacterial effectiveness than Pen-V-K, due to the broader anti-bacterial spectrum of amoxicillin and the increased cost of augmentin, the authors rec-
bined antibiotic therapy results in a greater selective pressure on the microbial population to develop resistance. The greater the antibiotic spectrum of the antimicrobials used, the greater the diversity and resistance microorganisms that develop, and the more difficult it is to treat a resulting sepsis or infection. The primary clinical indication for combined antibiotic therapy is a severe infection in which the offending organism(s) is unknown and multiple agents may enure if antibiotic therapy is not instituted immediately before culture and sensitivity tests are available.1

Myth No. 6: Bactericidal agents are always superior to bacteriostatic agents. Bacteriostatic agents are required for patients with impaired host defenses.1 However, bacteriostatic agents are usually satisfactory when the host’s defenses against infections are unimpaired. Posttreatment persistence of a persistent suppression of bacterial growth after previous exposure is more persistent and reliable with bacteriostatic agents (erythromycin) than with bactericidal agents (beta-lactamase) because the clinical effects of bacteriostatic agents are less dose-dependent.

Myth No. 7: Antibiotic dosages, dosing intervals and duration of therapy are established for most infections. After more than 90 years of antibiotic usage, the proper dosages, dosing intervals and duration of therapy are essentially unknown for most specific infections.1,15 Infectious diseases are associated with a high number of variables that affect treatment outcome (microbial characteristics and drug sensitivity, diverse resistance mechanisms, tissue barriers to antibiotic diffusion, and the integrity and activity of the host’s defense mechanisms). However, basic principles are available to guide the dental health care provider in establishing proper dosages, dosing intervals and duration of therapy once the microbial pathogen(s) is identified or suspected and a rational choice of antimicrobial agent is made.

The following principles of antimicrobial dosage are adapted from Dr. Thomas J. Pallansch.1

1. The current recommendation is to employ an antimicrobial on the basis of the infectious process with vitamin dosage for as short a period of time as the clinical situation permits. The major factor in the clinical success of most antimicrobial agents is the height of the serum concentration of the drug and the resulting amount in the infected tissue(s). Also important to the host to the antimicrobial agent for as short a duration of therapy as possible to support the bacterial colonization and reduce the risk to the patient for the development of antibiotic-induced toxicity and/or allergy, and a reduced risk of developing resistant microorganisms.2

2. The goal of antibiotic dosing is to achieve drug levels in the infected tissue equal to or exceeding the minimal inhibitory concentration of the target organism. Serum levels of antibiotics do not necessarily reflect those in tissues. Blood concentrations of the antibiotic should exceed the MIC by a factor of two to eight times in order to offset the tissue barriers that restrict access of the drug to the infected site.

3. It is advisable to initiate antimicrobial therapy with a loading dose (an initial dose higher than the maintenance dose). An antibiotic loading dose should be used whenever the half-life of the drug is longer than three hours or whenever a delay of 12 hours or longer to achieve a therapeutic blood level is expected. Most antibiotics used in the treatment of oral infections have a half-life shorter than three hours, but, due to their acute nature, most oral infections require therapeutic drug blood levels sooner than 12 hours. Steady-state blood levels of any drug are usually achieved in a time equal to three to five times the drug’s half-life. Amoxicillin has a half-life of one to one-and-a-half hours. A steady-state blood level would then be achieved in three to seven-and-a-half hours, thereby leading to a substantial period of time in which the serum concentration is therapeutic antibiotic blood levels. A loading dose of two times the maintenance dose is recommended for acute oral infections, which better achieves the goal of rapid, high blood levels rather than initiating therapy with the maintenance dose. Persist for two to three times the MIC to this disorder are not susceptible to bactericidal antibiotics (beta-lactamase) because the clinical effects of bactericidal agents are less dose-dependent.

Dental patients presenting for treatment with impaired host defenses (chemotherapy, or conditions that impair the activity and demonstrate very little PDE. Beta-lactam microbial killing requires microorganisms that may be less than optimal (steady-state blood levels) because bacteria divide at different rates.

Myth No. 8: Bacterial infections require a “complete course” of antibiotic therapy. There is no such thing as a “complete course” of antibiotic therapy. The only guide for determining the effectiveness of antibiotic therapy is whether the duration of treatment, is the clinical improvement of the patient. A common treatment assertion is that prolonged (after clinical remission of the disease) antibiotic therapy is necessary to prevent “rebound” infections from occurring. Ongoing bacterial infections do not persist for seven to 21 days, and often less. Patients placed on antibiotic therapy for an oral infection should be clini- cally evaluated on a daily basis. When there is sufficient clinical evidence that infection of the patient’s host defenses have regained control of the infection and that the infection is no longer present, the antibiotic therapy should be terminated.

Antibiotic prophylaxis for prevention of infective endocar- diitis

The American Heart Association (AHA) has been the leader in the use of antibiotic prophylaxis for the prevention of IE in medically-at-risk patients for more than 50 years. The most recent guidelines, published in April 2007, represent a significa- nt change from previous guidelines.17 One of the stated indications for antibiotic prophylaxis is the prevention of infective endocarditis. The 2007 AHA report regarding IE in humans is unknown, the number of microorganisms present in the blood following a dental procedure is low. It has long been assumed that dental procedures may cause IE in patients under- lying cardiac risk factors and that antibiotic prophylaxis is effective. However, recent evidence is lacking support this assumption. Cases of IE caused by oral bacteria probably result from routine daily activities (brushing and flossing) and not from a dental procedure.18

The 2007 AHA report regarding antibiotic prophylaxis is effective, such therapy should be restricted to those patients with the highest
risk of adverse outcomes from IE, and who would derive the greatest benefit from prevention of infection. Individual patient risk in the form of cardiac conditions associated with the highest risk of adverse outcomes from IE is largely unknown, and therefore, for some dental procedures is reasonable, even though we acknowledge that it is effectively unknown.”

Therefore, the 2007 AHA guideline for antibiotic prophylaxis should be considered for patients presenting for dental procedures meeting the conditions identified in Table 2, and who are undergoing any dental procedures that could compromise the gingival tissues or periapical region of a tooth and for that reason be a portal of entry for the oral mucosa. This would include procedures such as biopsies, suture removal, placement of orthodontic bands, and intra- and extraoral local anesthetic injections, but it does not include routine local anesthetic injections through noninfected tissue (Table 5).

Antibiotic prophylaxis for prevention of prosthetic joint infection

In 1997, the ADA and the American Academy of Orthopedic Surgeons convened an expert panel of dentists, orthopedic surgeons, and oral bacteria specialists and published an Advisory Statement on Antibiotic Prophylaxis for Patients with Prosthetic Joints.

A 2003 advisory statement included some modifications of the classification of patients at potential risk and the stratification of hazards associated with antibiotic prophylaxis (Table 4), but no changes in terms of suggested antibiotics or antibiotic regimens. Antibiotic prophylaxis is not indicated for most dental patients with total joint replacements or for those who perform effective daily oral hygiene procedures. However, it is advised to consider antibiotic prophylaxis for active dental procedures applicable to the patient, who may be at potential increased risk of experiencing hematogenous total joint infections (Table 5).

While bacteremias can cause hematogenous seeding of total joint implants, it is likely that more such cases are spontaneously induced by routine daily times than are dental treatments. Patients who have undergone total joint arthroplasty should be encouraged to perform effective daily oral hygiene procedures in order to maintain total oral health. The risk of infection is much higher in a patient with chronic inflammation than in one that is healthy and well maintained.

Occasionally, a patient with a total joint prosthesis may present for dental treatment with a history of infection in the joint. This is a physician's decision regarding antibiotic prophylaxis for the patient. After this consultation, the dental practitioner must either rely on the physician's recommendation or, if he or her professional judgment is not supported, perform the dental treatment under antibiotic prophylaxis. The dentist is ultimately responsible for making treatment decisions for his or her patient based on the dentist's professional judgment.

In February 2000, the AAO published an information statement in which it recommended “that clinicians consider antibiotic prophylaxis after orthopedic operations, in particular hip and knee replacements, as prophylaxis for patients prior to any invasive procedure that may cause bacteremia.” In response to this statement, the American Academy of Oral Medicine published a position statement in June 2010 edition of the Journal of the American Dental Association.

The authors of the AAO position statement reviewed the available literature on the subject as it relates to the AAO 2000 information statement and concluded: “The risk of patients experiencing drug reactions and the cost of antibiotic medications alone do not justify the widespread use of antibiotic prophylaxis (in all patients with prosthetic joints).”

The authors concluded that “multidisciplinary, systematic review of the literature relating to antibiotic prophylaxis has identified patients with prosthetic joints. In the meantime, the joint consensus statement should not be replaced by the 2003 joint consensus statement.”

In December 2012, a panel of experts representing the American Academy of Orthopedic Surgeons and the American Academy of Oral Medicine convened to create a systematic review and clinical practice guideline, titled “Prevention of Orthopedic Implant Infection in Patients Undergoing Dental Procedures: Evidence-based Guideline and Evidence Report.” This report contained the following three recommendations:

1. Antibiotic prophylaxis should be considered for patients presenting for dental procedures meeting the conditions identified in Table 2, and who are undergoing any dental procedures that could compromise the gingival tissues or periapical region of a tooth and for that reason be a portal of entry for the oral mucosa. This would include procedures such as biopsies, suture removal, placement of orthodontic bands, and intra- and extraoral local anesthetic injections through noninfected tissue (Table 5).


