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ENDODONTICS

COLLEAGUES FOR EXCELLENCE

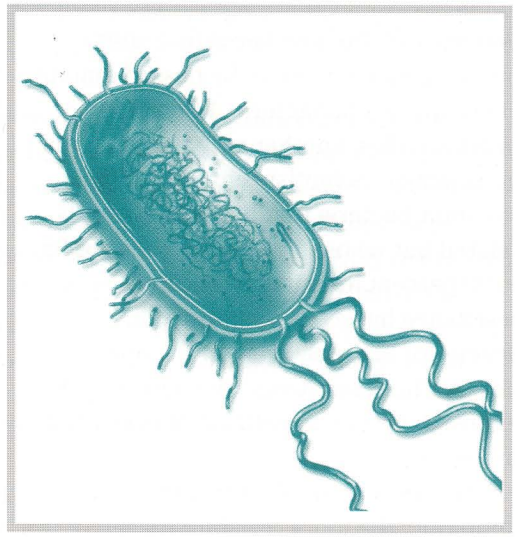
Rx

Prescription for the Future

Responsible use of antibiotics in endodontic therapy

Miracle drugs or superbugs—maintaining the balance of power

"Microbes were the first organisms to evolve on the Earth and were its sole inhabitants for billions of years...only during the last 0.01 percent of Earth history have humans been around...bacteria may still dominate our biosphere today in number of species, number of organisms, or total mass." (Bruce Jackosky, Planetary Review, July/August 1998)



Bacteria are primitive cells, but they are undeniable heavy-weights in the evolutionary process. The discovery of penicillin in 1928 initiated a delicate balance of power between men and microbes. Over time, the "miracle drugs" revolutionized healthcare. Antibiotics cured or controlled tuberculosis, syphilis, pneumonia and other bacterial infections. The Surgeon General of the United States announced to Congress in 1969 that it was time to "close the book on infectious diseases."

The arrival of supermicrobes, such as Vancomycin Intermediate-Resistant *Staphylococcus aureas*, has tempered previous optimism. This virulent strain appeared in a New York hospital in 1998. There are no known antibiotics to control it. Its presence in the environment is evidence that antibiotics have not eliminated bacterial infections. They have established an uneasy détente, at best.

Bacterial resistance to antibiotics raises critical questions and considerations for healthcare providers. Clinicians must understand the impact of antibiotics on patients and on the quality of public health. As specialists in diagnosing orofacial pain, treating infections of the pulp and periradicular tissues and managing emergencies, endodontists can share information that will help all dentists write a safer and more effective prescription for the future.

Act locally, Think globally

"Antibiotics are one of the few kinds of drugs that affect not only a single patient but entire populations of individuals through their collective effects on microbial ecology. Our responsibility lies not only with our own patients but with a world of such patients." Excerpt, American Dental Association statement adopted by the Council on Scientific Affairs at its September 1996 meeting.

Most dentists are aware of the complex consequences of human behavior on the environment. Mankind's effect on microbial ecology is equally complicated. Antibiotic treatment is a double-edged sword that alters the natural balance of organisms. Each time an antibiotic is used to eliminate bacteria, other pathogens gain strength.

All organisms evolve, but bacteria are genetic overachievers. They reproduce exponentially and meet challenging conditions with incredible ease and flexibility. One *Escherichia coli* cell can create 20 generations, more than one million progeny, in about seven hours. To put the microbial population into perspective, consider that more bacteria occupy one foot of human intestine than there are people on the planet.

In the presence of a threat, bacteria either render the attacker harmless or make themselves less vulnerable. Mutation and genetic transfer are the processes that enable cells to adapt or change. Mutations occur spontaneously and alter a gene within the bacterial chromosome. Once a mutation is present, all offspring generally acquire the new trait. Most mutations weaken bacteria, but occasionally a mutation makes microorganisms stronger. For example, some bacteria produce beta-lactamase, an enzyme that neutralizes the effects of penicillin.

The transfer of genetic material among bacteria is a much more effective survival mechanism. Genetic transfer allows families of bacteria to share desirable traits with a wide range of microbial species. The full implications of genetic transfer have only recently been understood. We now know that antibiotic-resistant genes can be passed among every species of bacteria. When one organism dies, another may absorb some of its genes. Scientists have identified resistant bacteria that are only distantly related but whose DNA sequences are 95 to 99 percent identical. Antibiotic resistance has even been found in species of bacteria living in the open ocean. These microbes have never been exposed directly to antibiotics produced by humans.

The longer a population of bacteria is subjected to an antibiotic, the more resistant the survivors become. As vulnerable microorganisms die, the number of surviving microbes increases, making each successive generation better equipped to meet future antibiotic challenges. Beneficial microbes that might have helped curb the growth of the pathogenic microbes are also killed. The selection process accelerates when the drugs are administered in doses small enough to allow stronger bacteria to survive the assault. Eventually, bacterial strains are created that may resist available antibiotic regimens.

Antibiotic resistant bacteria are present throughout the food chain. Animals and plants are exposed to repetitive small doses because antibiotics are used in agricultural feed and fertilizers. This creates ideal conditions for resistant strains to thrive. Milk, eggs and meat can all be contaminated with antibiotic-resistant *Salmonella*.

Antibacterial agents may also stimulate resistance in the microorganisms they do not eliminate. A host of consumer products such as soaps, lotions and dishwashing detergents contain antiseptic substances once used exclusively in hospitals. Household items such as children's toys, mattress pads and cutting boards are also impregnated with antibacterials.

The numbers speak clearly. Only about 158 antibiotics currently are available, and strains of bacteria resistant to each of these antibiotics have been identified. It takes millions of dollars and many years to develop a new antibiotic. Few new drugs are under development because bacteria can render an antibiotic useless with a single shuffle of the genetic deck. The day may be rapidly approaching when even the most powerful antibiotics will be ineffective against pathogens now considered harmless.

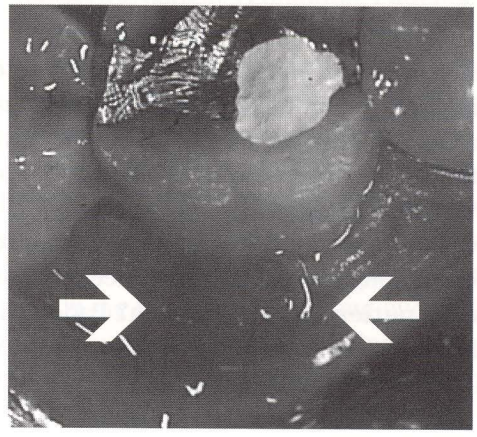
Healthcare providers all over the world unwittingly contribute to this problem. Researchers at the national Centers for Disease Control and Prevention estimate that *approximately one third of all outpatient antibiotic prescriptions are unnecessary*. As clinicians discover the gravity of this situation, they are re-evaluating how and when to prescribe antibiotics. Understanding the microbiology of diseases and recognizing when the immune system requires antibiotic assistance to eliminate an infection can help both dentists and physicians make better treatment decisions.

Just say no! Kill the bugs without the drugs!

Bacteria from the oral cavity may gain access to the root canal system through caries, exposed pulp or dentinal tubules and cracks into dentin. Other avenues include leaking restorations and apical, lateral or furcation canals affected by advancing periodontal disease and its treatment. Bacteria in the root canal system cause inflammation and/or infection. Potential sequelae such as pulpitis, apical periodontitis, draining sinus tract or localized swelling *can usually be treated endodontically without antibiotics.*

The circulation within the pulp is compromised in the presence of inflammation or infection. Because an antibiotic is carried by the vascular system, its ability to reach bacteria in a therapeutic concentration will be limited. This environment diminishes the efficacy of the antibiotic.

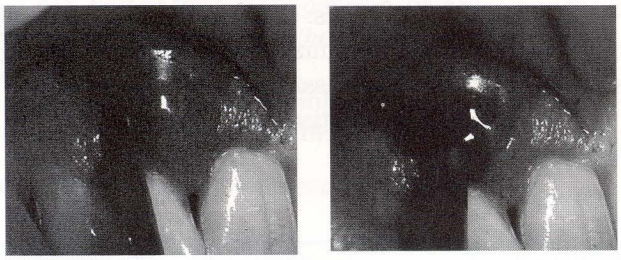
Endodontic treatment — removing the bacteria and their by-products by thoroughly debriding the root canal system — effectively eliminates the infection, curtails the inflammation and promotes healing. If the canal system is not obturated at the initial appointment, a medication such as calcium hydroxide may be placed inside the pulp chamber and root canal system to kill remaining bacteria. The medication should be covered with a sterile cotton pellet and sealed with a temporary restoration at least 3mm in thickness. Successful healing depends on optimal debridement followed by a well-placed permanent root canal filling and final restoration. The patient's condition should improve rapidly once the source of infection is eliminated. If the problems persist, consultation with a specialist may be warranted.



Localized tissue swelling (arrows)— antibiotics are not necessary.

Occasionally, the infectious process will move beyond the tooth and bone into the soft tissue creating an intraoral swelling. Swellings can be drained through the tooth by a soft tissue incision or through a naturally occurring sinus tract. Even if antibiotics are used, the immune system cannot function optimally until the purulence is eliminated. Drainage stimulates healing, relieves pressure, improves circulation and eliminates bacteria.

So—when do you need the drugs to kill the bugs?



Localized swelling—drainage achieved through tissue with incision. No antibiotics are necessary.

An infection must either be persistent or systemic to justify the need for antibiotics. *Pain alone or localized swelling do not require antibiotic treatment.* Most dental pain can be managed using non-narcotic analgesics such as NSAIDs.

Evaluating the following signs and symptoms will assist in determining the status of the infection.

Is the patient in good health? Patients in poor health or who are immunocomprom-ised are more likely to need antibiotics.

How rapidly did the symptoms occur? Swelling or fever that escalates within a 24 to 72 hour period may indicate that an infection is spreading. If the symptoms have developed over a longer time period, antibiotics are probably not necessary.

What is the extent of soft tissue inflammation? If an intraoral swelling is localized, the infection may be managed by surgical drainage. Practitioners should consider consulting a specialist if the swelling spreads into extraoral musculofascial spaces or impedes breathing or swallowing. A large, diffuse swelling may require antibiotics as well as surgical drainage.

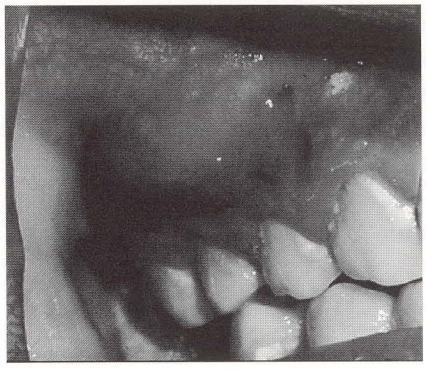
Do the benefits to the patient justify the risk of antibiotic therapy? Approximately three to six percent of patients experience an allergic reaction to penicillin. This can be as minor as a rash or as significant as life-threatening anaphylaxis. Patients may also develop adverse side effects such as gastrointestinal problems and secondary infections. Women of childbearing age should be alerted to the possibility that antibiotics may interfere with the efficacy of birth control pills.

Are there signs of regional or systemic involvement? Patients who have cellulitis or extraoral swelling, lymphadenopathy, elevated body temperature, malaise or unexplained trismus usually require antibiotic therapy and/or surgical drainage. Practitioners should monitor these patients carefully until the infection is under control.

Of microbes and men

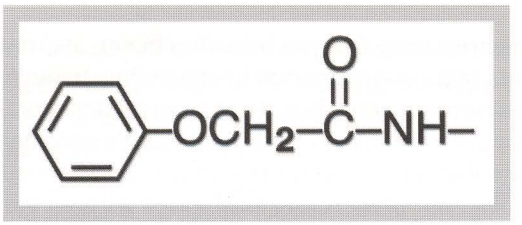
Antibiotics have an impact that extends far beyond the clinician and his or her patients. By stimulating the development of resistant strains of bacteria, these medications permanently alter the microbial environment. In an age when travel to every point on the globe is possible in less than 24 hours, drug resistant pathogens are easily transmitted. Dentists, physicians and patients have a serious responsibility to understand why antibiotics must be administered with caution and to adhere to the principles that govern their appropriate use.

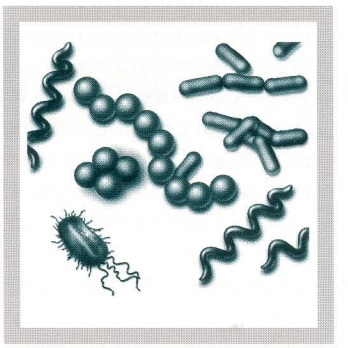
Today, most bacterial infections can be treated successfully. Tomorrow the balance between microbes and men is uncertain.



Large diffuse swelling that will require both drainage and antibiotics.

Killing with Penicillin and its Substitutes





Penicillin VK is effective against most aerobic and anaerobic bacteria that are commonly present in the oral environment. Amoxicillin, a derivative, has a broader spectrum and is a good choice for immunocompromised patients. However, treatment with amoxicillin increases the likelihood of inducing antibiotic resistance. *Penicillin VK is the drug of choice for most oral infections.*

Clindamycin is an appropriate substitute if the patient is allergic to penicillin. It is beta-lactamase-resistant and is highly effective against orofacial infections. Clindamycin has been linked with antibiotic-associated pseudomembranous colitis, but studies show that colitis is a possible side effect of most antibiotics, especially broad-spectrum penicillins and cephalosporins. This condition generally occurs in elderly, debilitated patients who have been recently hospitalized, have had previous abdominal complaints and are receiving high doses of the drug.

Erythromycin, which is commonly prescribed for penicillin-allergic patients, has been shown to be ineffective against most of the anaerobes associated with endodontic infections. Other antibiotics are now preferred.

Clarithromycin is another acceptable penicillin substitute. This drug has a more limited spectrum of activity than clindamycin but has some advantages over erythromycin. Clarithromycin is effective against facultative anaerobes and some of the obligate anaerobic bacteria associated with endodontic infections. It is also less likely than some other antibiotics to cause gastrointestinal problems.

Metronidazole is a synthetic antibiotic that is highly effective against obligate anaerobes but is not effective against facultative anaerobic bacteria. If penicillin is ineffective after 48 to 72 hours, Metronidazole is a valuable antimicrobial agent for combination antibiotic therapy.

Proper dosage and selection of an antibiotic with the right spectrum of activity are equally important. Treatment regimens should be short and aggressive to minimize the development of resistant bacteria and to achieve a therapeutic concentration of the drug. The patient must understand clearly that adherence to the dosing schedule is critical to eliminate the infection. A loading dose of 1000 mg of penicillin VK should be followed by 500 mg every six hours for five to seven days. Consider contacting the patient 24 hours after administration of the antibiotic to assess the patient's condition. Patients taking penicillin or other beta-lactam antibiotics should improve rapidly. If there is no improvement after 48 hours, penicillin can be supplemented with a dosage of metronidazole. The recommended oral dosage of metronidazole is 250 mg (500 mg loading dose) every six hours for seven to ten days.

The usual adult dose of clindamycin begins with a loading dose of 300 mg followed by 150 mg every six hours for seven to ten days. Clarithromycin may be given in a dose of 250-500 mg every 12 hours for seven to ten days.

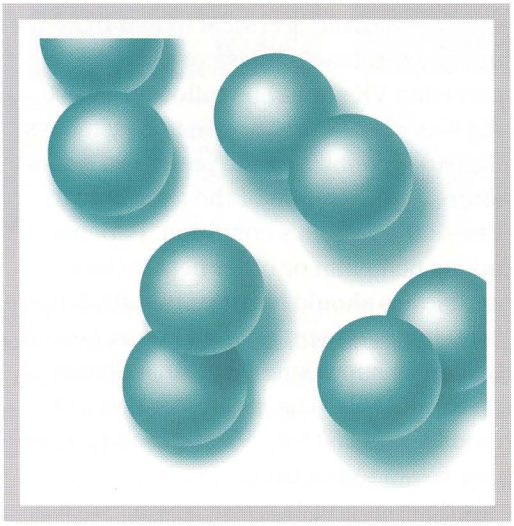
To culture or not to culture

Culturing of the root canal for endodontic infections is rarely recommended. The variety of microorganisms involved makes a positive identification of the main pathogen unlikely. Culturing of the swollen area may be helpful when infection persists or progresses or in the case of the medically compromised patient where extra precaution is necessary to prevent a systemic infection. Antibiotic treatment should begin immediately even when a culture is taken because oral infections progress so rapidly.

When defenses are down, antibiotics are sound.

In 1995, half of the top ten generic drugs prescribed for patients in the United States were antibiotics.

All these prescriptions reinforce the misguided and widespread belief that antibiotics make recovery from an infection faster, less painful and more certain. Patients request medication because they believe it will be beneficial. Sometimes, even when there is no clinical justification, healthcare providers comply to gain the patient's confidence or to supplement or substitute for other treatment. It can be difficult to deny a patient's request, but prescribing antibiotics without carefully evaluating the patient's signs and symptoms feeds the public's misconception that antibiotics are necessary to eliminate infections and contribute to antibiotic resistance.

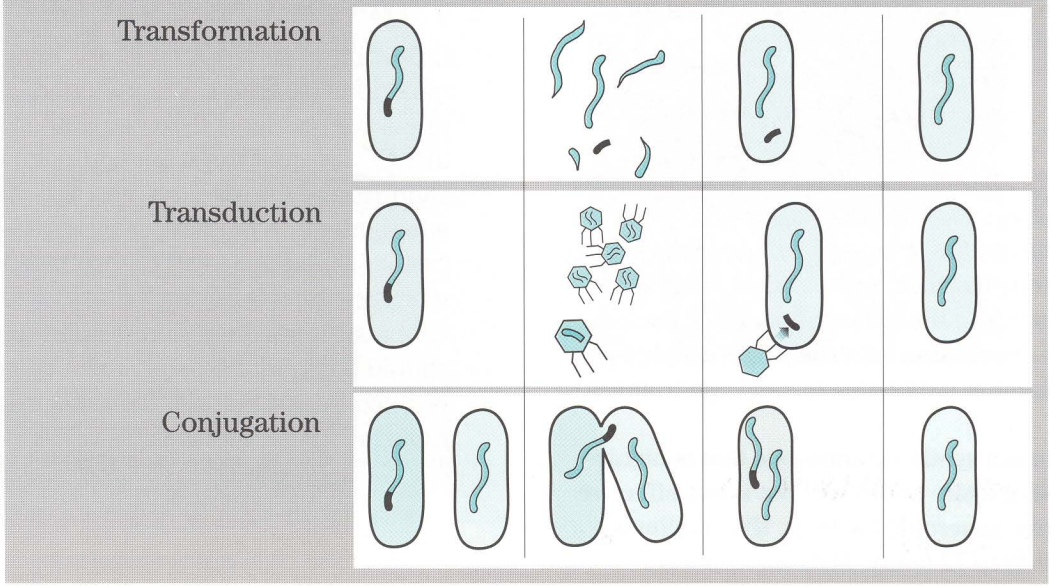


Over 350 distinct species of bacteria coexist in an adult mouth. When the healthy ecology of microorganisms is altered, an infective process may begin. Normally, the immune system defends against the proliferation of harmful bacteria. If bacteria are too virulent or the immune system becomes too weak to control their growth, then antibiotics may be necessary.

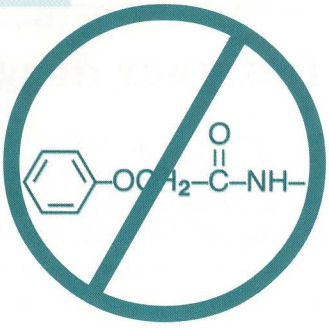
Antibiotics are an adjunct to treatment. The patient's own immune system provides the cure. Without a functional immune defense, antibiotic treatment will eventually fail.

What is genetic transfer?

Bacteria can transfer genetic information via three mechanisms detailed below — transformation, transduction, or conjugation.



Root Canal



Wondering whether to prescribe an antibiotic? In cases like these, the right decision is to "just say no":

Janet

Janet, a 43 year-old patient, is experiencing pain when she bites against her maxillary right first molar. Janet's examination reveals that the tooth, which was heavily restored with amalgam, is sensitive to percussion when compared with adjacent and contralateral teeth. The overlying facial mucosa exhibits a localized, firm swelling. Janet is in good health. Her only known allergy is to aspirin. Janet does not have a fever or any other signs of systemic infection, and she does not need an antibiotic.

After administering a local anesthetic, an incision is made into the area of the swelling and a latex drain is placed. Access into the crown of the tooth is then prepared. The pulp is necrotic, there is no drainage into the canals, and root canal therapy is performed in a single visit. Four separate canals are treated. The access preparation is closed with IRM over sterile cotton pellets. After 24 hours, the drain is removed and Janet is completely asymptomatic after three days. She will be re-examined periodically.

Mike

Mike, who is 47, complains of swelling, pain and limited mouth opening associated with a mandibular right molar. The pain began several days prior to his office visit and is gradually getting worse. He is in good health, and he does not have a fever or known allergies. Over the last nine months, Mike has experienced several less severe episodes of vague pain in this area. These episodes were treated with an antibiotic and were thought to be sinus related. He states that his lower molar had a crown placed within the last five years.

An oral examination reveals that tooth #30, compared to adjacent and contralateral teeth, is not responsive to CO_2 snow. The tooth is highly mobile and tender to percussion. Swelling is present in the mandibular right vestibule that is fluctuant and confined to the molar area. Radiographs reveal thickened PDL spaces at all root apices of this tooth. After administering a local anesthetic, root canal treatment is initiated. The pulp is necrotic, and four canals are cleansed and shaped. Calcium hydroxide is placed into the canals as an inter-appointment medicament, the coronal access is closed with IRM over sterile cotton pellets, and an incision and drainage is performed. Much exudate is suctioned from the incision, and a latex drain is placed. Mike receives a prescription for ibuprofen, but he does not need an antibiotic. At two or three days post op the drain is removed. He no longer has any swelling and the tooth is only moderately tender to biting pressure. After six weeks, Mike is completely free of symptoms and the canals are obturated. The access is sealed with amalgam. At six months follow-up, the periradicular tissues are normal, and the patient is sympton free.

Talking points: antibiotics and endodontics

Clinical trials have demonstrated that administering antibiotics before treatment does not reduce the incidence of flare-ups following treatment. The appropriate uses of antibiotics stated in this newsletter also apply to managing mid-treatment or post-operative flare-ups. To justify the use of an antibiotic in the management of a flare-up, an infection must either be persistent or systemic.

Should antibiotics be used to prevent the consequences of bacteremias that can occur after root canal treatment? Although the incidence of bacteremia is low with root canal procedures, antibiotics may be recommended prophylactically for some medically compromised patients. Check the most recently published American Heart Association guidelines for the prevention of bacterial endocarditis.

On the Horizon

Designer drugs

Microbes have an evolutionary advantage, but advances in science and technology may help to keep the scales balanced.

Researchers believe that studying bacterial function at the molecular level holds the key to rapid new drug development. Future antibiotics may be "customized" to disarm bacteria chemically and prevent the development of resistant strains.

Scientists are using high-tech tools such as super computers and x-ray crystallography to study the enzymes that promote drug resistance. Computer modeling and screening allows researchers to test many different compounds in a short period of time. This process, called "rational or structure-based drug design," has already yielded interesting information. Over 100 naturally occurring antibacterial peptides have been identified. Eventually, peptides may form the basis of a new category of antibiotic that not only kills bacteria, but also neutralizes enzymes that make the bacteria resistant.

Genetics is another promising avenue of exploration. Bacteria that causes diseases such as tetanus, syphilis, botulism and diptheria are harmless until a particular stimulus occurs. Researchers at Brandeis University reported in a 1998 article in *Nature, (Andre White et al: Structure of the metal-ion-activated diphtheria toxin repressor/tox operator complex, Nature* 394, 502-506, 1998) that they have discovered how this genetic trigger works for diphtheria. As long as a complex called DtxR is attached to the bacterial DNA, diphtheria's lethal potential is repressed. An iron deficiency in the host harboring the bacteria causes DtxR to fall off. This activates the genetic signal for the bacteria to attack the host. Theoretically, antibiotics based on a similar concept of preventing virulence could be developed.

Did you enjoy this issue of *ENDODONTICS*? Did the information have a positive impact on your practice? Are there topics you would like *ENDODONTICS* to cover in the future? We want to hear from you! Send your comments, questions, and suggestions to the American Association of Endodontists at the address below.

If you would like more information, call your local endodontist or contact the American Association of Endodontists, 211 E. Chicago Avenue, Ste. 1100, Chicago, Illinois 60611.

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For Further Reading
***ENDODONTICS: Colleagues for Excellence*, Spring/Summer 1999**
"Antibiotics in Endodontics"

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