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Systemic Disease
Host Modulation
Antimicrobials

NEW APPROACHES TO PERIODONTAL MANAGEMENT

PATIENTS

PATHOGENS

POCKETS

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OF THE CALIFORNIA DENTAL ASSOCIATION
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DEPARTMENTS

FEATURES

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Leadership for the Future

Jack F. Conley, DDS

A number of years ago, when we discussed California Dental Association leadership issues with a dentist colleague, he referred to CDA volunteers such as officers, trustees, and members of committees as "dental politicians." His rather negative view of those who volunteer to serve the profession extended to suggest that decisions were accomplished "in smoke-filled rooms behind closed doors."

Fortunately, this rather view of clandestine workings was not entirely accurate even in the "good old days"! Shortly after I entered the world of service to organized dentistry, the only accurate part of the above definition -- "smoke-filled rooms" -- disappeared because CDA adopted a no-smoking rule for all official association meetings in the mid-1980s. As for the rest of this inaccurate perception, we have found the decision process to be open and fair to the interests of the membership. Only rarely in the past did we observe a personal agenda interfering with development of an objective solution.

While the process has continued to improve as a result of concerned leadership over the span of years we have observed it, organized dentistry still falls short of the expectations placed upon it by many members and potential members. From treatment techniques to ethical considerations, most members of the dental profession set high performance standards and expect that level of performance from colleagues, be it in patient care or service activity.

A few of the critical issues the association must face and resolve if it is to achieve the stature of value expected by the membership base it seeks are the increased ethnic diversity of the profession, educational indebtedness, changing patterns of dental disease, and external access to care issues facing the profession.

However, through a strategic planning activity that has been in place for slightly more than two years, the staff and volunteer leadership of the California Dental Association have become more acutely aware of the expectations of the member at large than any of their predecessors. This is not a criticism of those who have served in the past, but an acknowledgment of the considerable sacrifice and commitment that current leadership has demonstrated in their efforts to become educated in the methodologies necessary to function within a knowledge-based system of governance.

Some notable accomplishments have been achieved in the past 12 months. The strategic plan, which originally featured 19 goals and 77 objectives, has been streamlined into eight goals and 25 objectives structured along the lines of business of the association. Staffing of the association was completely reorganized last year into a divisional structure to address the goals and objectives. Planning activities for the first five years of the plan

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were established, 2002 being the second year of the plan.

In the latter part of 2001, approximately 1,000 members responded to an e-mail survey, and CDA delegates were surveyed during the House of Delegates to identify priority issues for 2002. The top three issues were relationships with third parties, a shortage of dental auxiliaries, and government relations/advocacy. Delegates added recruitment and retention of members to this list slightly ahead of third parties, which then dropped to the fourth most frequently mentioned position on a list of mega issues.

In addition to the changes in structure and the identification of issues to be addressed, renewed efforts to prepare volunteers to successfully engage in the business of the association have been moving forward. In early February, component society volunteer leaders and staff as well as association officers, trustees, council members, and staff participated in a stimulating Leadership Conference that featured noted consultant Bud Crouch. He facilitated a keynote session on creating a knowledge-based association that engaged all participants, enabling them to better understand the roles of the CDA Board of Trustees as well as the role of leadership at the component societies.

At the conclusion of the conference, attendees had a better understanding of facilitative leadership. They learned that:

- They must engage in leading rather than telling or driving;
- Leaders utilize a strategic agenda, rather than personal agendas; and
- Volunteer leaders know that they are accountable to all members in their efforts to leave the association in a better place than where they found it.

The most recent display of progress occurred at the February meeting of the CDA Board of Trustees. At that time, the trustees were exposed to an exercise in knowledge-based strategic governance. In this exercise, the trustees met in breakout groups organized along the lines of business and gained valuable experience in engaging in the elements of this new model of governance. Trustees and council chairs engaged in dialogue that defined some of the issues facing the association. This activity, followed by deliberation, will be continued at all future Board meetings. The ultimate goal is informed strategic decision-making by the Board, a considerable change from the reaction and ratification processes that have traditionally characterized Board activity.

These recent activities showed conclusively the merit of transitioning to the knowledge-based governance strategy, even though the changes have sometimes seemed to occur rather slowly to some in leadership. Continuing improvements in leadership decision-making will bring greater efficiency to the deliberative process. It is hoped that members and nonmembers will see outcomes that they value, which will convince them to support organized dentistry.

We are impressed with the progress to date. As the frequently inaccurate characterizations of volunteer dental leadership of yesteryear fade as a result of current and future achievements, it is hoped that more members will become energized to participate in the process. That will improve the potential for success in achieving membership value from association initiatives. During the next few months, the screening committee of the Board of Trustees is undertaking its annual task of reviewing applicants for association service in 2003.

It is hoped that the changes in association governance described herein will encourage more interest and enthusiasm in serving the profession in California. The future strength of the profession will be dependent upon a dedicated leadership that provides the direction necessary to achieving the value that all colleagues seek from their professional organization. That future is NOW.

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California's Oral Health Grade Remains Mediocre

By Debra Belt

The United States is a little "down in the mouth" according to the newly issued Oral Health Report Card. The nation earned an uninspiring C on the 2001-2002 report, which is intended to provide a snapshot of dental health in America by compiling data from all 50 states and the District of Columbia.

The country's overall grade inched up from the C- received on the 2000 report card. The slightly improved grade reflects increased national awareness of oral health issues, but the coast-to-coast assessment also shows that there is much work to be done.

"The 2001-2002 report signifies hope for the future, but also underscores the widespread unmet needs that have not changed in a year's time," said Elizabeth Rogers, director of communications for Oral Health America, the nonprofit advocacy group that develops the grading project.

In determining the national grade, Oral Health America gathered data from each state and looked at prevention, access to care, oral health leadership, and oral health status. Each state also received an individual grade; and California once again received a C, with low marks in the areas of prevention and oral health leadership dragging down the state's overall grade.

"California's C grade and its poor score in prevention is especially disappointing due to its reputation as a trend-setting state concerned about health, fitness, and well-being," said Robert Klaus, president of Oral Health America.

"We cannot underestimate the importance of prevention and preventive services in maintaining a lifetime of good oral health," Klaus said. "Prevention is the area in which dentistry has distinguished itself, and so much can be done for so little money."

ORAL HEALTH REPORT CARD GRADES

	National	California
Prevention	**C**	**F**
Factors: Fluoridation, sealants		
Access to care	**C-**	**C**
Factors: Availability of dentists, children's Medicaid dental program, visits to dentists, dental insurance status of adults and elderly		
Oral health leadership	**B+**	**D-**
Factors: dental director, oral health coalition		
Oral health status	**C+**	**B-**
Factors: oral health of children, use of spit tobacco, edentulous elderly, oral cancer mortality rates		

However, California received an F in prevention because less than 49 percent of the state's population receives fluoridated water, and the use of dental sealants on children falls between 12 percent and 22 percent

The report also noted that even though California received an F in the fluoridation category, progress has been made; and approximately 30 percent of the population receives fluoridated water.

Klaus also pointed to California's D-grade in oral health leadership.

"Gov. Davis has not included oral health in his priorities," Klaus said. "California does not have a state dental director, leadership in fluoridation efforts are lagging, and a statewide oral health coalition is not visible."

Klaus also pointed out that several states -- including Minnesota, Kentucky, Missouri and Michigan -- have taken "oral health issues to heart" and worked to appoint state dental directors, provide more money to Medicaid, and increase access to care for senior citizens.

The other low point in California's score was a D in access to dental care for low-income individuals. According to Oral Health America, 43 percent to 54 percent of California adults with an annual income of less than $15,000 reported a visit to a dentist or dental clinic in the previous year. California was not alone in receiving low marks in this area: All but nine states earned D's and F's.

On the other hand, California received healthy marks in several categories, including visits to dentists by individuals with an income of more than $15,000. The Golden State also earned an overall B- in oral health status, a category that looks at oral health of children, use of spit tobacco, edentulous elderly, and oral cancer mortality rates.

In addition to California, 19 other states received a C grade, 19 states scored C+'s and eight states received C-'s. Four states -- Connecticut, Hawaii, Iowa, and Utah -- scored the highest grade of B-.

Klaus said the purpose of the report is to drive home the message from the Surgeon General's Report on Oral Health that was released in 2000.

The grades on the Oral Health Report Card reflect statistics brought to light in that report, including:

- More than 108 million U.S. adults and children are without dental insurance.
- Almost 2.5 million days of work are lost each year due to dental problems.
- Tooth decay is the most common chronic childhood disease, affecting 50 percent of first-graders and 80 percent of 17-year-olds.
- The full report available online at www.oralhealthamerica.org.

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Staff Changes Can Garner Publicity

By Dell Richards

Many dentists don't realize that adding new dentists, hygienists, or office managers to a practice can be a source of publicity for a dental office. Sending a simple press release about staff changes to the local business media is all that needs to be done.

Business notices are usually published one day a week in daily newspapers and every issue in weekly business journals. To find out who to send the information to, one need only look at the bottom of the column. If there isn't a name, the title of the column should be used, i.e., "News and Notes."

When one is writing the press release, a few rules apply:

- The obvious should be stated in short sentences: "(Name) was hired or promoted at (practice name)."
- The person's full name, including middle initial, should be given.
- The exact name of the practice, including "Inc." if appropriate, should be used.
- The person's duties should be listed in one sentence. "(Name) will be responsible for (list of duties)."
- The person's previous position and duties should also be given.
- This information should be printed on letterhead with the words "For immediate release" at the top as well as the name and phone number of a contact at the office for questions. Someone specific should be designated to answer calls and track publication by looking at the issues as they come out. The newspaper should not be called to check if the item has been published.
- If an editor phones, the call should be returned immediately. Reporters work on very fast deadlines. If an editor calls in the morning, and the dentist calls back in the afternoon, it may be too late.
- A business portrait should be included, if possible. A photo sometimes increases the chance the notice will be used.
- The office should not expect the photo to be returned, even if a self-addressed, stamped envelope is included. Photos become the newspaper's property.

It usually takes at least a month for such an item to be published. Once the item is published, the dentist should send a thank-you note.

The office should not ask the editor for copies. The newspaper receptionist can be asked if the paper gives free copies to people included in the issue. Papers cost less at the time of publication if they are picked up than they will later if they are ordered and mailed.

Although feature stories have more immediate impact, frequent newsworthy items also keep a dental office's name in the public eye.

Dell Richards is the owner of the Sacramento public relations firm Dell

Orderly Practice Transfer an Ethical Obligation

Among the important details to be addressed before closing a practice transfer is a plan for patient retention, wrote Rise and Martin Mattler in the November 2001 issue of the Bulletin of the Ninth District Dental Society (New York).

Dentists have an ethical obligation to make the transfer to a new dentist as orderly and seamless as possible for both patients and staff, according to the Mattlers.

They said that dentists should meet with their staff immediately after the closing to let them know about the transition. If a dentist has a warm, longstanding relationship with employees, the dentist may elect to tell staff before the closing.

Patients should be notified of the transition immediately after the practice sale closing. The Mattlers said that dentists should tell patients before word gets out that the dentist is leaving. They recommend a three-step practice transfer plan for notifying patients.

First, an introductory letter should be sent to all current patients immediately after the practice transaction closes and ownership has changed. The purpose of the letter is to recommend the new dentist to the patients. The Mattlers recommend that the copy refrain from indicating that the practice has been "sold," since most patients don't like the idea of their dental records being sold to the "highest bidder."

The second step is to call any patients who are scheduled for an appointment before they will receive the introductory letter. The authors add that before calling, the selling dentist should discuss this with the buyer, since some new owners prefer that patients be informed the day of their appointment rather than beforehand.

The last step is geared to the buyer of the practice. The Mattlers said the new owner should send a letter to all patients about a month after taking over the practice. This letter would welcome patients and reiterate professional, personal, and practice-related information of interest to patients.

The Mattlers said many well-intentioned sellers plan to stay longer with the practice than necessary to ease the transition, often creating unintended problems for the new dentist. Two problems that arise are insufficient workload for two dentists and the perception by patients and staff that the incoming dentist is "second string." The Mattlers recommended that a dentist plan to stay up to three months at most to ensure a smooth transition and to protect the cash flow of the practice.

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Richards Publicity, which specializes in health care clients across California.

Free Genetic Disease Information Center Launched

The National Human Genome Research Institute and the National Institutes of Health's Office of Rare Diseases have launched a new information center that delivers free and immediate access to information specialists who can provide accurate, reliable information about genetic and rare diseases to patients and their families.

There are more than 6,000 genetic and rare diseases afflicting more than 25 million Americans, but many of these illnesses affect relatively few individuals. As a result, information about these rare disorders may be limited or difficult to find. The new service, called the Genetic and Rare Diseases Information Center, will help relieve this problem by providing reliable information about individual disorders.

Opened in February 2002, the center provides experienced information specialists to personally answer questions from patients and family members on the phone, as well as by e-mail, fax, and regular mail.

"I am delighted we can provide a resource that should be of great benefit to individuals with genetic and rare diseases, and their families," said Francis Collins, MD, PhD, director of the research institute. "Valid and accessible information about these conditions is hard to find, and having an information center staffed by professionals will fill a critically important need. The National Human Genome Research Institute is delighted to be partnering with the Office of Rare Diseases to establish this center."

"Now people can talk to someone -- personally -- and get information right away," said Henrietta Hyatt-Knorr, the office's acting director. "There will be a quick turn around. If you just received a diagnosis for yourself, your spouse, or your child, now you won't have to wait to find useful information."

The Genetic Alliance, an international coalition of more than 300 lay advocacy organizations and health professionals, staffs the center with information specialists. The center provides callers with authoritative information about specific illnesses from existing public domain sources, including reliable Web sites, brochures, articles, and even chapters from books. Experts at the information center ensure that the information sent out is current and accurate. The center, however, does not provide genetic counseling and does not offer diagnostic testing, referrals, medical treatment, or advice.

Contact information for the center is as follows:

- Telephone, answered Monday through Friday, noon to 6 p.m., Eastern time: voice (888) 205-2311; TTY (888) 205-3223
- E-mail: gardinfo@nih.gov
- Fax: (202) 966-5689
- Mail: Genetic and Rare Disease Information Center, P.O. Box 8126, Gaithersburg, MD 20898-8126.

Top Challenges for the New Dentist

Most young dentists face five common challenges, according to Ted C. Schumann, CPA, in the November/December 2001 issue of the Bulletin of the West Michigan District Dental Society.

Finding and negotiating an associateship

Most new dentists do not buy a practice right out of dental school, Schumann says, so choosing their first professional experience is one of the most important decisions. Young dentists often make the mistake of taking the first job offered them, he said.

According to Schumann, young dentists should consider many questions before taking the first job, including:

- What type of dentistry do they want to do?
- Is this the owner's first associate?
- Will the owner share patients?
- Is the owner financially sound?
- Are there enough patients to support a second dentist?
- How will lab fees be handled?

When and how to become an owner

According to Schumann, the only true way for a young dentist to build wealth is through the ownership of a practice.

He said most young dentists eventually reach a point where they are comfortable owning their own practices. Usually that time comes when the young dentist is comfortable practicing clinically and realizes the owner will never teach much about how to run a practice.

The opportunity to become an owner could come from purchasing a retiring dentist's practice, buying into a practice, or starting from scratch. Schumann said young dentists should spend a lot of time researching which is best for them.

Leadership and management of people

This is the area in which young dentists are least prepared, Schumann wrote. Schumann advises young dentists to seek out training to develop leadership skills. After gaining these skills, the next challenge is to assemble a team that will follow their vision.

Operation of practice

For many dentists, young and old, the greatest challenge is to understand how to run the business side of a practice. Schumann says it's important to know how to read and understand financial statements and to know how to track key numbers in the practice.

Financial aspects to know include accounts receivable and collections, scheduling for productivity, labor costs, occupancy costs, marketing and advertising, lab fees, cost of supplies, equipment expenses (repairs and maintenance and depreciation), costs of continuing education, and administrative expenses.

Investing, retiring debt and living within one's means

Schumann said that in financial planning literature, authors refer to dentists as "celebrity investors." He said this means dentists are the type of investors who want

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to invest in "what's hot."

According to Schumann, the market loses money about one in four years. People who wish to accumulate wealth do so by consistent and systematic investment. He said by using dollar cost averaging and understanding the portfolio allocation process, an investor with a long-term perspective can achieve financial goals.

Most young dentists graduate with considerable debt and within a few years have even more debt for a home and practice. Schumann said much of this debt is necessary and inevitable; but with proper planning, young dentists can look down the road to becoming debt-free.

Dentist Saves the Day in Kindergartner's Winning Story

A Georgia dentist received a happy surprise while reading his morning paper recently when he found that one of his young patients had won an essay contest with a story featuring a dentist as the hero.

Dr. Keith Crummey, a general dentist in Waycross, Ga., discovered the story as he perused the Waycross Journal-Herald. Trey Chafin, a first-grade student, was named a state winner in the 2001 Young Georgia Authors' Writing Competition for his essay "The Crazy Glupaste Day," which he penned as a 5-year-old kindergarten student.

In the story, a little boy named Cococ buys glupaste instead of toothpaste at the store, and glues his teeth together that night. He seeks help from his uncle, a builder, who tries to open his mouth with a hammer; from his mother, who tries a chainsaw; and from his father, who calls 911. But finally, Cococ's dad calls the dentist who used his "speshul drill ... and carefully and gently opened Cococ's mouth."

Crummey said, "People seem to enjoy telling stories of traumatic dental visits. They delight in portraying the dentist as a villain or ogre. Seldom are we cast as the hero. It was refreshing and encouraging to read a story written by a child portraying the dentist as competent and kind."

Third-Party Financing for Cosmetic Dentistry an Effective Tool

Offering third-party financing as an option to potential cosmetic dental patients is a highly effective tool for gaining treatment acceptance, wrote Roger P. Levin, DDS, MBA, in the fall 2001 issue of the Journal of Cosmetic Dentistry.

Levin said that although interest in cosmetic dentistry is increasing somewhat, patients often decline care because they need special financial arrangements. He noted that American consumers spend millions of dollars on discretionary beauty products, but cosmetic dentistry is still not one of those priorities.

If dentists can offer convenient low monthly payment plans, they are sure to increase the number of patients who accept treatment, Levin said.

It is important for dentists to understand the current economy. When economic conditions begin to slide in any way, people cut back in discretionary spending areas, including expensive cosmetic-related items.

Levin says it is important to help patients afford cosmetic care. Although factors such as fear, procrastination, and time may enter into a patient's refusal of treatment, Levin said cost should no longer be a factor when dentists offer third-party financing as an option.

Estrogen Receptor Variations Related to Tooth Loss

Estrogen receptor genotypes may be connected to tooth loss in elderly women, Japanese researchers report in the Nov. 14, 2001 issue of the Journal of the American Medical Association.

Researchers studied the effect of estrogen receptor genotype on tooth loss and alveolar height in 132 Japanese women who visited a clinic from 1996 to 2001. Sixteen subjects had received estrogen replacement therapy for six months or less, and one had received the therapy for four years. None of the patients was taking other medications that affect bone metabolism, and none had a history of tobacco use.

Researchers analyzed the subjects' estrogen receptor genes in blood samples. They found that one gene variant was linked to having fewer teeth. A second gene variant was associated with great alveolar bone loss. They concluded that these genes might not influence alveolar bone loss but rather alveolar bone fragility. The findings did not change after researchers made adjustments for age and time lapsed since menopause and estrogen replacement therapy.

The results, according to researchers, indicate that the type of estrogen receptor a woman carries could signal her risk of experiencing tooth loss.

Universities Collaborate on $5 Million TMD Study

Researchers from the Universities of Buffalo, Minnesota and Washington will collaborate on a $5 million study to establish valid and reliable criteria for the diagnosis and treatment of temporomandibular joint disorder.

The four-year study is being funded by the National Institute of Dental and Craniofacial Research.

"This research study represents the most comprehensive examination of diagnostic methods and concepts yet conducted for any chronic pain disorder," said Dr. Richard Ohrbach of the Center for the Study of Pain at the University at Buffalo School of Dental Medicine. "TMD is difficult to diagnose because there is no single measure that provides objective independent evidence of this disorder."

To establish universal, definitive standards for diagnosing TMD, study investigators will revalidate existing criteria and assess the validity of potential new indicators through blinded clinical examinations, mental status assessments, computer-aided imaging scans, and fluid and tissue analysis.

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Patients, Pockets, Pathogens: New Approaches to Periodontal Management

ROBERT L. MERIN, DDS, MS, AND ALAN R. STEIN, DDS

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CO-CONTRIBUTING EDITOR

Alan R. Stein, DDS, is a clinical assistant professor in the Division of Diagnostic Sciences at the University of Southern California School of Dentistry. He is also the director of continuing education in the Department of Dentistry at Northridge Hospital Medical Center and a past chief of the department. Dr. Stein is also a past president of the San Fernando Valley Dental Society. He maintains a private general dentistry practice in Northridge, Calif.

When we became contributing editors for an issue of the CDA Journal on periodontics, we wanted to include articles dealing with new research and technologies, and we wanted the information to be clinically relevant for the general practitioner. After the articles came back from review, it became clear that two issues of the Journal would be required to publish them all. Although the April and May Journal articles fit together as a package, we tried to place them in the most logical grouping for each issue. The May issue will include articles on the following topics:

1. Demographics affecting periodontal and implant therapy with suggestions on how to position your practice.

2. Therapeutic choices in the molar region. This article gives suggestions on when to perform traditional procedures (such as endodontics, root resection, crown lengthening and periodontal surgery), and when to extract a molar and place an implant.

3. The immediate dental implant. This article gives practical suggestions on this emerging technology.

4. Laser curettage: Where do we stand? The article takes a critical look at the use of the laser for curettage.

These issues on periodontics are about technology. Dentists live in a rapidly evolving world of technological change and must analyze the usefulness of many new technologies. We often hear dentists question whether dental lasers work or site-specific antimicrobials are any good. However, these are the wrong questions. Just as a hammer is a very bad technology for accurately cutting wood, it is extremely effective for driving nails. We should be asking: "Is a specific technology effective in a specific application?" We must not only look at whether a new technology works in a given application, but also whether it is more efficacious than conventional treatment. We must also evaluate the potential for side effects, immediate and remote. To complicate the analysis, a minor change in the technology or a new procedure may

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render a previously useful technology useless; or just the opposite, make a heretofore useless one extremely effective.

In these issues, our authors evaluated specific applications and techniques. We hope you will use them as a starting point for your own analysis. With apologies to the academicians of the world, we assert that all targeted research has a bias, intentional or not. That is human nature. It is your professional obligation to determine what is best for your patients. Analyze a new technology. Does its method of action make sense on a biological basis? What is the potential for harm? Read all the literature you can find and find out who paid for the research and what their bias and motivation is. Look to your peer- reviewed journals, nonprofit testing organizations such as the ADA and CRA, and position papers from the American Academy of Periodontology or the California Society of Periodontists. Ask your colleagues about their experiences, but remember that they too have biases. Finally, when you decide to incorporate a new technology, technique, or material into your practice, chart and track your cases so you can review their effectiveness and safety.

The editors and authors hope you enjoy this issue, and we look forward to any dialogue it may generate. The articles that follow will bring us one step closer to providing the best care for our patients.

Greetings from the California Society of Periodontists

The California Society of Periodontists is proud that its members helped with this issue of the CDA Journal. The CSP is a nonprofit organization of periodontists committed to enhancing and promoting excellence in periodontics in California and protecting the health and safety of the public. CSP has always worked with CDA in attempting to serve the highest and most noble interests of California dentists and periodontists in their service to California citizens. We are committed to continuing this long-standing relationship, just as we are committed to continue to serve our members in their responsibilities to the public.

A listing of periodontist members of CSP can be found in this issue of the Journal.

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Host Modulation: Conceptualization to Clinical Trials and Integration into Clinical Practice

Maria Emanuel Ryan, DDS, PhD

ABSTRACT A better understanding of the pathogenesis of periodontitis has resulted in pharmacotherapeutic advancements, addressing both the microbes and the host response, leading to improved management of this chronic progressive disease by the dental practitioner. The adjunctive use of host-modulatory agents can enhance therapeutic responses, slow the progression of the disease, and allow for more-predictable management of patients. This article will review the pathogenesis and risk factors associated with periodontitis and address in detail the concept and clinical utility of host modulation as a therapeutic strategy.

Author

Maria Emanuel Ryan, DDS, PhD, is an associate professor in the Department of Oral Biology and Pathology at the School of Dental Medicine at Stony Brook, N.Y. She is actively involved in teaching, practice, and research at the school. Her research is funded by the National Institutes of Health and industrial sources. She holds U.S. patents for the prevention of long-term complications of diabetes.

This is truly an exciting time in the field of dentistry because the benefits of the many scientific and technological advances that have occurred during the past 20 years are now entering clinical practice. This is particularly true for the management of periodontitis, the most common dental disorder. These advancements have occurred as researchers better elucidate the causative factors of periodontitis, leading to improved management of this chronic progressive disease. The understanding of the pathogenesis of periodontitis has evolved from purely a plaque-associated disease to the current thinking, which places a renewed emphasis on the host's response to the bacteria.

The first-ever Surgeon General's Report on Oral Health in America[1] has helped to educate not only the general public but also the medical profession on the potential consequences of the periodontitis. In particular, this report recognizes the importance of dental health in the overall general health and well-being of patients. Along with these findings and the emergence of the discipline of periodontal medicine, there have been developments in adjunctive chemotherapeutic approaches to the management of periodontitis. This article will address the concept and

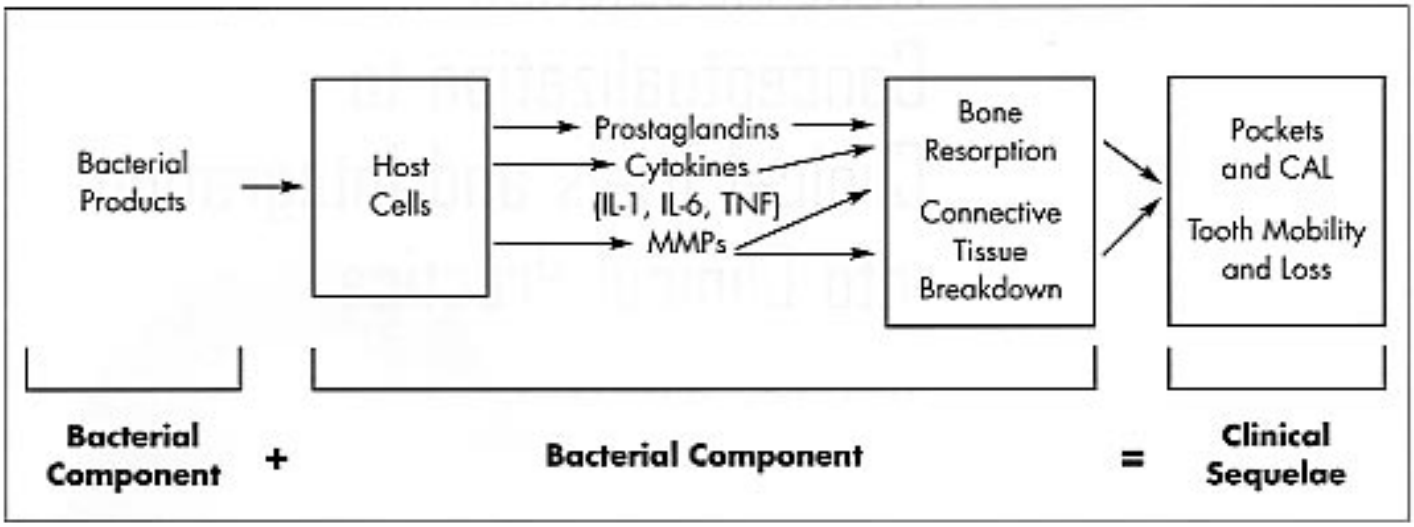

Figure 1. Simplified schematic depicting etiologic factors and cascade of events contributing to periodontitis.

clinical utility of host modulation for the management of periodontal disease. The concept of host modulation is fairly new to the field of dentistry but is a universal concept understood by most physicians and routinely applied in the management of chronic progressive disorders such as arthritis and osteoporosis.

Pathogenesis

Periodontal disease does not appear to behave like a classical infection, but more like an opportunistic infection. There is no way to eliminate bacteria from the oral cavity, so bacteria are always present in the periodontal milieu. When certain more-virulent species exist in an environment that allows for them to be present in greater proportion, there is the opportunity for periodontal destruction to occur. However, while it is apparent that plaque is essential for the development of the disease, the severity and pattern of the disease are not explained solely by the amount of plaque present. In 1985, research began to focus very closely on bacterial-host interactions, leading to the "Host-Bacteria Inter-Relationship Era".2 During this era, it was recognized that although there is evidence that specific bacterial pathogens initiate the pathogenesis of periodontal disease, the host response to these pathogens is equally, if not more, important in mediating connective tissue breakdown, including bone loss. It has become clear that it is the host-derived enzymes known as the matrix metalloproteinases (MMPs), and changes in osteoclast activity driven by cytokines and other inflammatory mediators known as prostanoids that cause the majority of the tissue destruction in the periodontium3 (**Figure 1**). This shift in paradigms to a concentration on the host response has led to the development of host-modulatory therapies to improve therapeutic outcomes, slow the progression of disease, allow for more predictable management of patients, and possibly even work as preventive agents against the development of periodontitis.

Risk

There are a number of environmental and acquired risk factors that increase a patient's susceptibility to periodontitis. The risk factors that can affect onset, rate of progression, and severity of periodontal disease, as well as response to therapy, include:

- Heredity;
- Smoking;
- Hormonal variations such as those seen in pregnancy (where there are increased levels of estradiol and progesterone, which may change the environment and permit the virulent organisms to become more destructive);
- Menopause (in which the reductions in estrogen levels leads to osteoporosis);
- Systemic diseases such as diabetes;
- Immunocompromise, such as with HIV;
- Stress
- Nutrition;
- Medications such as calcium channel blockers;
- Faulty dentistry; and
- A previous history of periodontal disease.4-6

Some of these risk factors can be modified to reduce a patient's susceptibility. Risk management may include smoking cessation, improved control of diabetes, nutritional supplementation, and stress management. The field of "perioceutics", or the use of pharmacological agents specifically developed to better manage periodontitis, is emerging to aid in the management of these susceptible patients who develop periodontal disease. Host modulatory therapy, which can be used to

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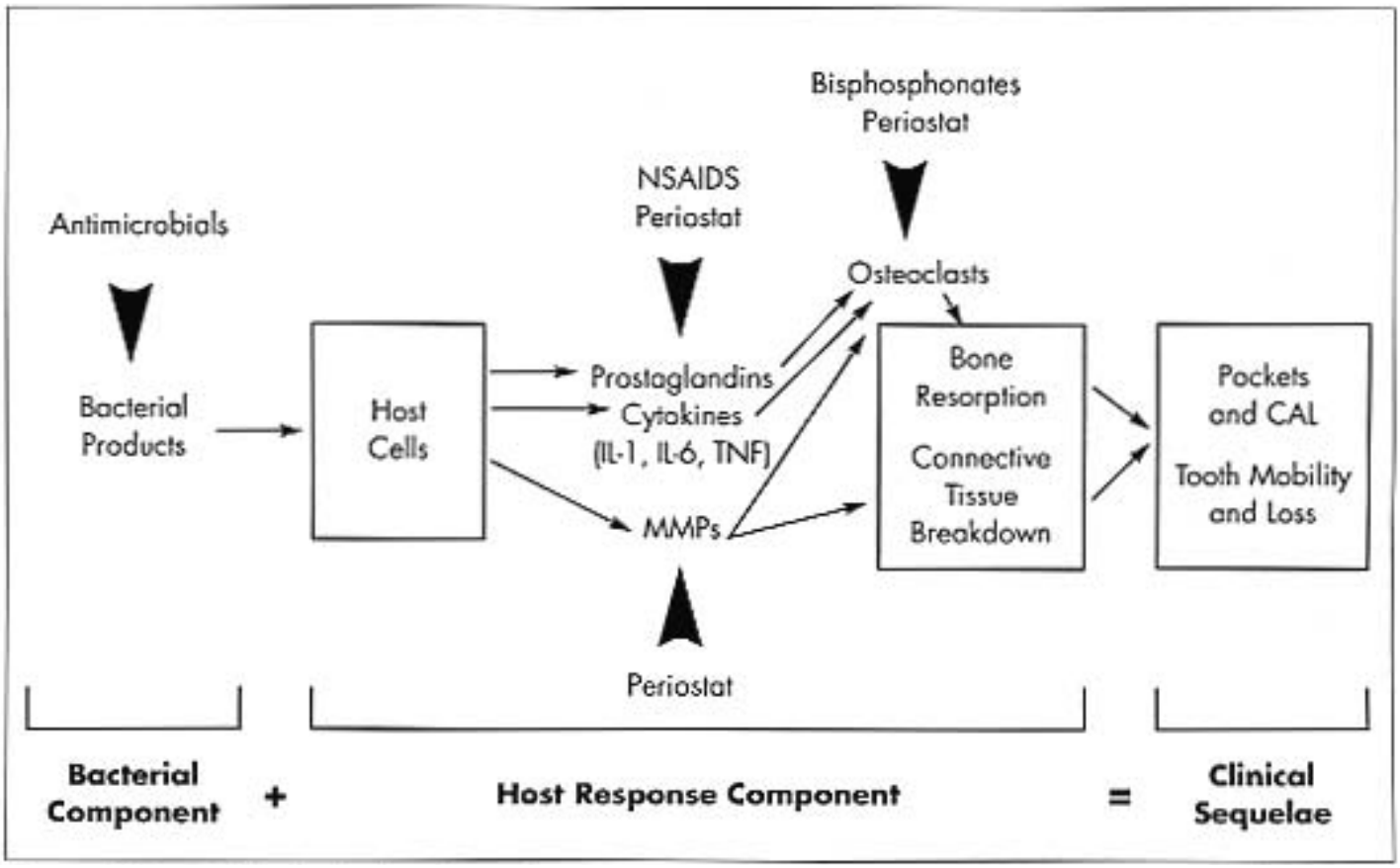

Figure 2. Potential adjunctive therapies and points of intervention in the treatment of periodontitis.

bring down excessive levels of enzymes, cytokines, and prostanoids as well as modulate osteoclast function is the key to addressing many of these risk factors that have adverse effects on the host response.

Host Modulators

A number of host modulatory agents have been investigated in clinical trials for their potential use as adjuncts to mechanical nonsurgical periodontal therapy. These have included the systemic (Flurbiprofen) and topical (Ketoprofen) use of nonsteroidal anti-inflammatory drugs, the systemic use of sub-antimicrobial dose doxycycline (Periostat) and the systemic use of bisphosphonates (Fosomax). The only systemic host modulatory agent approved by the FDA (Food and Drug Administration) for adjunctive use in conjunction with nonsurgical periodontal procedures is Periostat. The points of intervention of these agents in the host response can be seen in **Figure 2**. In addition, a number of local host modulatory agents have been investigated in clinical trials for their potential use as adjuncts to surgical procedures not only to improve upon wound healing but also to stimulate regeneration of lost bone, periodontal ligament, and cementum, restoring the complete periodontal attachment apparatus. These have included enamel matrix proteins (Emdogain), bone morphogenetic proteins (BMP-2 and BMP-7), growth factors (platelet-derived growth factor and insulin-like growth factor), and tetracyclines. The only host modulatory agent currently approved by the FDA for adjunctive use during surgery is Emdogain. The paper will focus on the clinical utility of host modulation for nonsurgical procedures in clinical practice, so it will be limited from here on to the use of sub-antimicrobial dose doxycycline (SDD or Periostat) in clinical practice.

Since Periostat is based upon a sub-antimicrobial dosage of doxycycline, a member of the tetracycline family of compounds, it is important to place the use of tetracyclines for the management of periodontal diseases into perspective. As far as incorporation of a medical pharmacological approach to the management of a disease in the dental practice setting, no class of drugs has made more of an impact on periodontal therapy than the tetracyclines. They have been used in conjunction with scaling

and root planing, the gold standard of nonsurgical therapy, as well as with surgical procedures, both resective and regenerative. The tetracyclines have been used locally and systemically as antimicrobial agents and more recently systemically as a host-modulatory agent. The tetracyclines have been used not only to address chronic adult periodontitis but also for the management of specific, often more aggressive, types of periodontitis. Most recently, the tetracyclines have been advocated for the management of patients with systemic diseases, such as diabetes. The use of tetracyclines has lead not only to improvements in the periodontal health of compromised diabetic patients, but also to improvements in long-term markers of glycemic control such as glycated hemoglobin.7 Clinically, the purpose of using tetracyclines as adjunctive agents has been to kill the pathogens in the tissues and pockets, modulate the host response, and thereby increase the predictability of a variety of periodontal therapies including scaling and root planing. As an adjunct to mechanical therapies, the goal has been to enhance reattachment or even to stimulate new attachment of the supporting apparatus and osseous formation. The literature is replete with references to the use of tetracyclines in the management of periodontal disease, so this paper will concentrate on the use of these pleiotropic or multi-use compounds for modulation of the host response in the treatment of periodontitis.

Clinical Trials on SDD

Tetracyclines work so well as host modulatory agents because of their pleiotropic effects on multiple components of the host response (**Figure 2**). The only enzyme (MMP) inhibitors that have been tested for the treatment of periodontitis are members of the tetracycline family of compounds. In an early study using these different tetracyclines, Golub and colleagues8 reported that the semisynthetic compounds were more effective than tetracycline HCl in reducing excessive collagenase activity in the gingival crevicular fluid (GCF) of adult periodontitis patients. Because doxycycline was found to be a more effective inhibitor of collagenase than either minocycline or tetracycline,9,10 recent clinical trials have focused on this compound. In an effort to eliminate the side effects of long-term tetracyclines therapy, especially the emergence of tetracycline-resistant organisms, sub-antimicrobial-dose doxycycline (SDD) capsules were prepared and tested.11 Each capsule contained 20 mg of doxycycline, compared to the commercially available 50 and 100 mg, antimicrobially effective, capsules. In multiple clinical studies conducted using sub-antimicrobial dose doxycycline, there has not been a difference in the composition or resistance level of the oral flora,12,13 and more recent studies demonstrate no appreciable differences in either fecal or vaginal microflora samples.13 In addition, these studies have also demonstrated no overgrowth of opportunistic pathogens such as Candida in the oral cavity or gastrointestinal or genitourinary systems.

Early studies indicated that SDD reduced the peak blood level of the drug by 92 percent compared with the regular dose doxycycline regimen based on a bio-assay.14,15 Subsequent studies using high performance liquid chromatography (HPLC) analysis of total doxycycline in the serum indicate that blood levels (Cmax) range from 0.5 to 0.7 mg/ml rather than 0.29 mg/ml previously reported by bioassay. The discrepancy in these findings may be due to the fact that much of the doxycycline measured by HPLC in the serum is bound to serum proteins and would not be available and active when measured by bioassay techniques.

With regards to MMP inhibition, Golub and colleagues16 reported that a two-week regimen of SDD reduced collagenase in GCF and in the adjacent gingival tissues surgically excised for therapeutic purposes. Subsequent studies using SDD therapy adjunctive to routine scaling and prophylaxis indicated that after one month of treatment there were continued reductions in the excessive levels of collagenase in the GCF, but that after cessation of SDD administration there was a rapid rebound of collagenase activity to placebo levels, suggesting that a one-month treatment regimen with this host modulatory agent was insufficient to produce a long-term benefit.17 In contrast, during the same study, a three-month regimen produced a prolonged drug effect without rebounding to baseline levels during the no-treatment phase of the study. The mean levels of GCF collagenase were significantly reduced (47.3 percent from baseline levels) in the SDD treated group vs. the placebo group, which received scaling and prophylaxis alone (29.1 percent from baseline levels). Accompanying these reductions in collagenase levels were gains in the relative attachment levels in the SDD treated group,17,18 as seen in **Figure 3**. Continuous drug therapy over a period of several months appears to be necessary for maintaining collagenase levels near normal over prolonged periods. However, it is reasonable to speculate that these MMPs will eventually reappear in the more susceptible patients, and those individuals having the most risk factors and the greatest microbial challenge will require more frequent host modulatory therapy than other patients.

A series of double-blind, placebo-controlled studies of three, six and nine months' duration, all showed clinical efficacy based on the reduction of pocket depth and inhibition of gingival attachment loss as well as biochemical efficacy, based on the inhibition of collagenase activity, and protection of serum a1-antitrypsin (a naturally occurring protective mediator) from collagenase attack, in the periodontal pocket.9,19,20 Golub and colleagues21

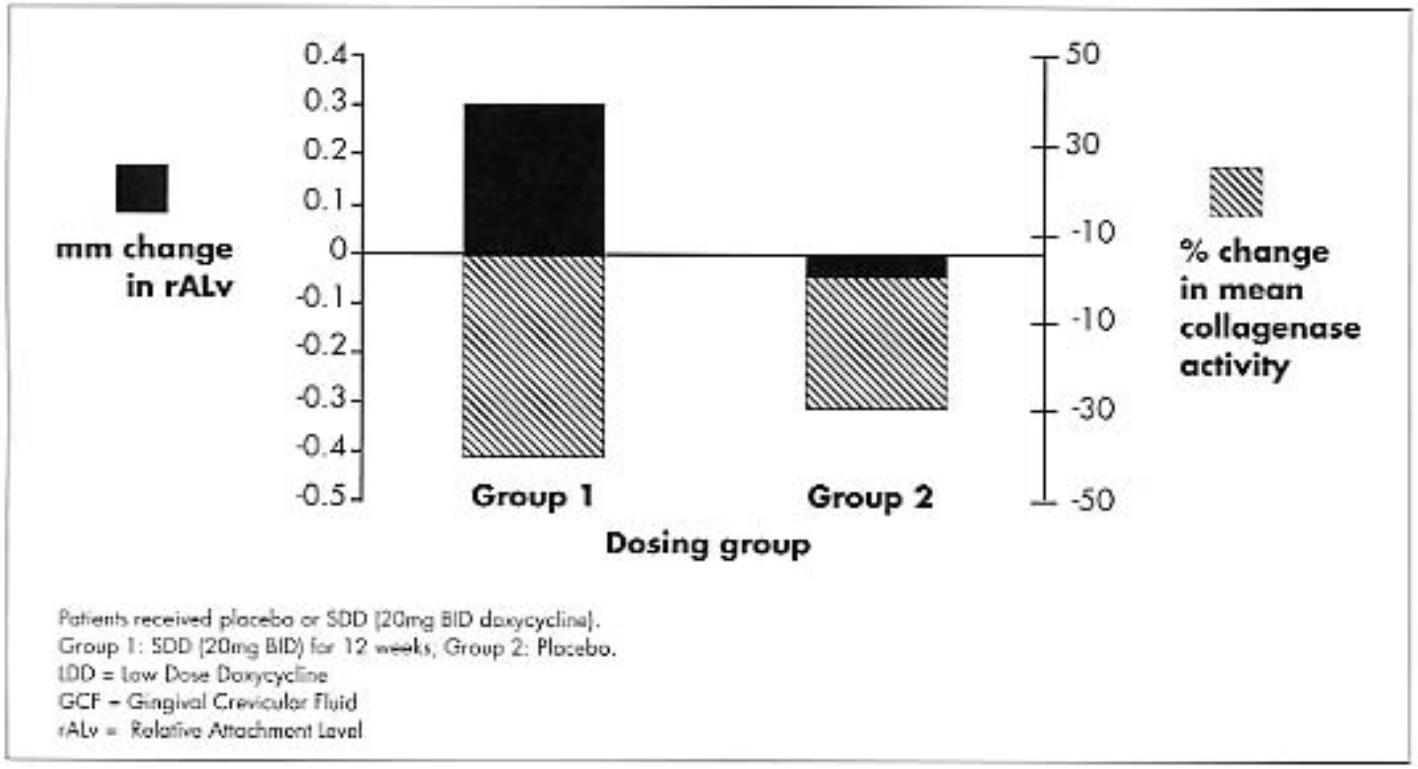

Figure 3. Effect of SDD on GCF collagenase activity and rALv.

showed that a two-month regimen of SDD significantly decreased both the level of bone-type collagen breakdown products (ICTP; a pyridinoline-containing crosslinked peptide of Type I collagen) and MMP-13 enzyme levels (bone-type collagenase) in adult periodontitis subjects providing biochemical evidence of reduction of bone resorption to support computer-assisted subtraction radiography data,22,23 the latter providing evidence of a reduction in the loss of alveolar bone height after 12 months of therapy with SDD.

There is clear evidence that modulation of the host response -- whether it be by effects on MMPs, cytokines, prostanoids, or osteoclast function -- can play a role in slowing periodontal disease progression. In the case of enzyme suppression, SDD has been found to be useful for preventing disease progression as can be seen in **Figure 4**, which shows the percentage of tooth sites that lost 3 mm or more of attachment during the 12 month course of a Phase III clinical trial.22,24 Adjunctive treatment with SDD in conjunction with dental scaling and prophylaxis was shown to reduce disease progression by 85 percent, 73 percent and 36 percent in sites with severe, mild-to-moderate, and essentially no disease, respectively. This demonstrates that host modulatory therapy can aid in the maintenance of normal sites, preventing them from developing disease, as well as in the prevention of further progression of disease in already diseased sites. Only with the systemic administration of a drug would it be possible to see effects on the normal sites that are usually ignored due to inadequate diagnostics that would otherwise alert the practitioner to incipient disease activity at these "normal" sites.

Upon analysis for attachment loss of 3 mm or more during the first six months of this 12-month study, a subset of susceptible patients in each treatment arm became evident. As seen in **Table 1**, there are far fewer sites in the group treated with the host modulatory agent SDD (14 sites) that experienced this rapid loss of attachment compared with the placebo group (52 sites), which corresponds to a 73 percent reduction in the incidence of rapid progression of periodontitis. In addition, when recovery therapy was performed (in this case scaling and root planing with anesthesia) the average attachment gain was significantly greater in the adjunctive SDD group (2.16 mm) than in the adjunctive placebo group (0.78 mm) as measured six months later, 12 months following baseline.17 The adjunctive use of an MMP inhibitor clearly made these most susceptible patients, with active disease sites, more responsive to the more definitive therapy (scaling and root planing), thereby demonstrating almost a

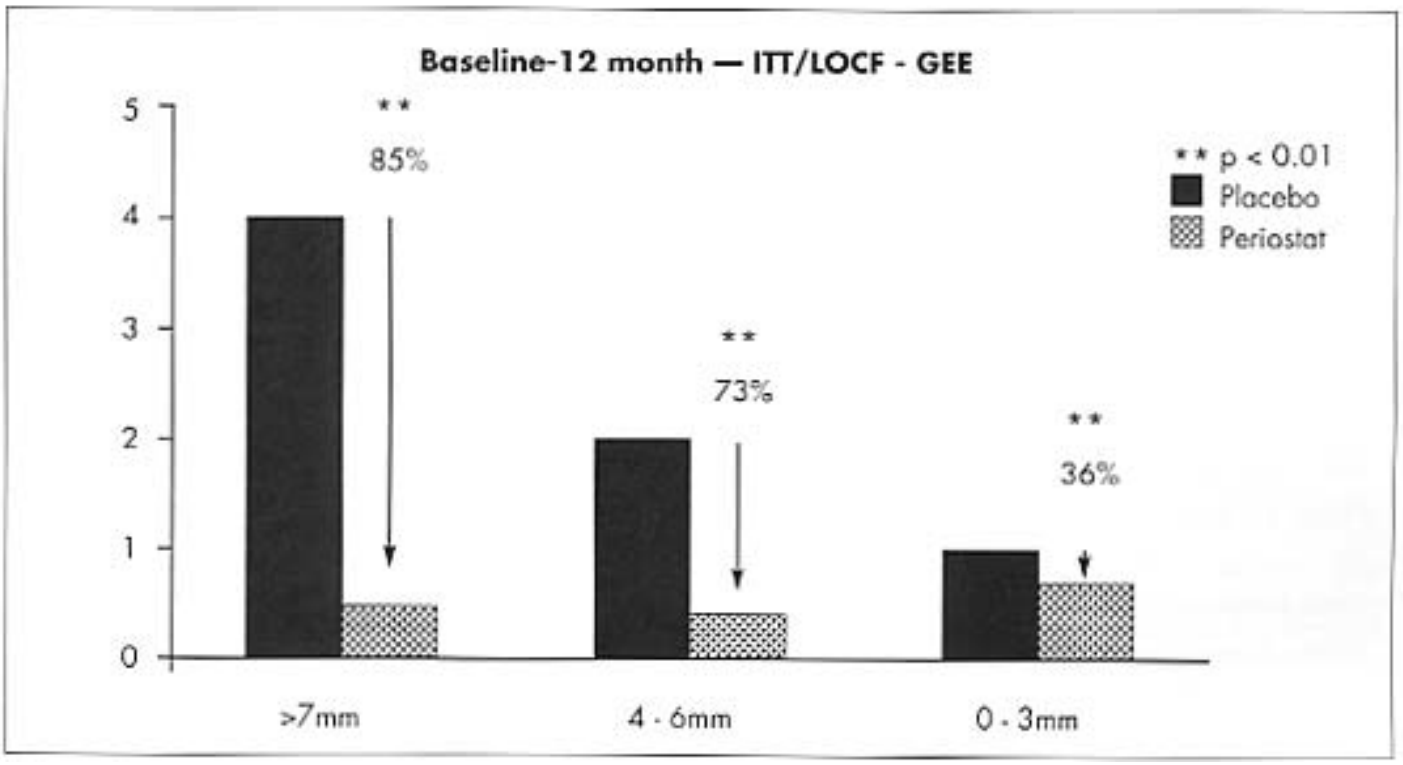

Figure 4. Tooth sites losing >3 mm CAL Periostat phase III scaling trial.

reversal in these rapidly progressive sites in the SDD treated group of patients. It is likely that patients who are susceptible to rapidly progressive periodontitis have dysfunctional host responses that would benefit from host modulatory therapy. The same may be true of tooth sites that are refractory to traditional therapies.

A nine-month randomized, double-blind, placebo-controlled trial, conducted at five dental centers demonstrated clinical efficacy and safety of SDD vs. placebo adjunctive to scaling and root planing. Once again, the benefits of host modulatory therapy in addition to mechanical therapy were seen with statistically significant reductions in probing depths, bleeding on probing, and gains in clinical attachment levels as well as the prevention of disease progression.24,25 A clear effect of SDD therapy can be seen with regard to the need for recovery therapy and tooth extraction as seen in **Table 2**. There are reductions in the numbers of individuals and tooth sites requiring recovery therapy due to rapid attachment loss of 2 mm or more along with less need for extraction in the SDD treated group. In a discontinuation study, where SDD administration was discontinued after nine months of continuous therapy, the incremental improvements demonstrated in the SDD group were maintained for at least three months post-treatment. There was no rebound effect in either the pocket depth reductions or clinical attachment level gains; in fact there appeared to be slight continued improvements in both of these clinical parameters.24,25 The clinical relevance of such findings confirm the utility of an MMP inhibitor in the management of adult periodontitis.

More recent Phase IV clinical studies have revealed success using LDD in very susceptible individuals. One such patient population is one with a specific variation in the genes that regulate the cytokine interleukin-1 (IL-1). Currently there is a PST Genetic Susceptibility Test for Periodontal Disease to determine whether a patient has this susceptible genotype. PST-positive patients have an increased inflammatory response in the presence of bacteria, producing two to four times more IL-1 with microbial challenge.26 Therefore, these patients are at greater risk for developing severe periodontal disease27 and subsequently at greater risk for tooth loss.28 A five-month preliminary investigation by Ryan and colleagues29 was designed to evaluate the impact of treatment on IL-1 and MMP levels of PST-positive patients who presented with elevated levels of these biochemical markers in their GCF. These patients were initially treated with SRP, resulting in no change in the levels of these biochemical markers after one month. Al-Shammari

and colleagues30 reported similar findings with no changes in GCF levels of IL-1b and ICTP before and after scaling and root planing in patients who had not had not been genotyped. When the genotypically positive patients were placed on SDD and these biochemical markers where monitored at two and four months, a significant decrease (50 percent to 61 percent) in the IL-1b and MMP-9 levels was noted after treatment with Periostat. Correspondingly, gains in clinical attachment and reduced probing depths were also observed. The conclusions of the study were that a sub-antimicrobial dose of doxycycline may provide PST-positive patients with a therapeutic strategy that specifically addresses their exaggerated host response. It may be speculated that the subjects of the Al-Shammari and colleagues study may have also benefited from the use of a host modulatory agent. Another recent study was conducted in susceptible patients with severe generalized periodontitis using host modulation as an adjunct to a mechanical therapy known as "repeat sub-gingival debridement."31 Fifty percent of the patients who participated in this nine-month double-blind, placebo-controlled study were smokers. Sub-antimicrobial dose doxycycline as an adjunct to mechanical therapy vs. mechanical therapy alone, respectively, resulted in significant improvements in probing depth reductions, in pockets greater than or equal to 7 mm at baseline, as early as 1 month after therapy (2.52 mm vs. 1.25 mm) which were maintained during the 5.25 months of therapy (2.85 mm vs. 1.48 mm) and even after three months of drug therapy cessation (3.02 mm vs. 1.41 mm), demonstrating that there was no rebound effect. Due to all of these beneficial effects of host modulatory therapy in susceptible patients, multicenter studies are anticipated using SDD in diabetic and osteoporotic patients as well as in institutionalized patients.

Table 1.

Need for Intervention (SRP) During Periostat Phase III Scaling Trial

	Placebo	Periostat	p-value
Number of patients	9	9	—
Number of tooth sites	52	14	—
CAL change (mm) post SRP	0.78	2.16	0.005

Table 2.

Tooth Loss and Need for Recovery Therapy Periostat Phase III SRP Trial

	Placebo	Periostat
Tooth extraction		
Number of teeth	23	5
Number of patients	14	4
Recovery therapy		
Number of tooth sites	59	24
Number of patients	21	11

Clinical Application

Host modulation with a sub-antimicrobial dose of doxycycline has been FDA approved for adjunctive use with scaling and root planing and has recently been granted the ADA Seal of Approval. The duration of use may vary from patient to patient. A risk factor assessment in addition to clinical evaluation of patients can help to guide the practitioner with regard to length of use and need for repeat use. A minimum of three months of host modulatory therapy is suggested. Patients who are allergic to tetracyclines, pregnant, nursing, or younger than 8 should not take this medication.

The author has implemented a two-pronged approach to periodontal therapy into her clinical practice. The initial visit by a patient will include a medical and dental history, a risk assessment profile (**Table 3**), periodontal charting, and radiographic analysis. The patient must be made aware of the fact that periodontal disease is not curable but that it can be well-controlled with constant monitoring by the dentist/hygienist and good patient compliance. The patient must also be informed of the need for periodontal therapy, which is not an option but rather a necessity for good general health, as studies have indicated. Initial therapy consists of oral hygiene instructions, which must be continuously reinforced over the course of therapy; scaling and root planing with anesthesia as needed (both approaches designed to reduce the bacterial load); and host modulation to reduce excessive levels

of enzymes, cytokines and prostanoids. Modification of any risk factors such as smoking, nutrition, stress, contributing medications, faulty restorations, poor oral hygiene, and poor diabetic control can also be addressed at this time. A patient's refusal or an inability to modify contributing risk factors are important considerations for treatment planning and evaluation of therapeutic responses. In the case of host modulation, the more risk factors and the poorer the hygiene, the greater the need for host modulation of longer duration or repeat therapy in the future.

After completion of initial therapy, re-evaluation is most critical. At this point, the decision is made to either continue with active (additional) therapy or to place the patient into the maintenance phase. If all probing depths are less than 5 mm, then the decision is made to place the patient into the maintenance phase of therapy. The author will typically keep the patient on the host modulatory agent through the first maintenance visit. If the treated sites remain stable for this three-month period, the patient will be removed from host modulatory agent and placed into the typical maintenance program until additional active therapy is required. If there are probing depths greater than 5 mm at re-evaluation, then the therapeutic approach may differ depending on the number of sites and radiographic assessment of those sites. Typically for isolated sites, a nonsurgical approach may include rescaling the site and placement of a locally applied antimicrobial with the continued adjunctive use of the host modulatory agent. If this is insufficient to achieve adequate pocket depth reduction or if there are multiple sites in a quadrant, then a surgical approach is used to reduce the probing depths through resective or regenerative techniques. Once all probing depths are less than 5 mm, the patient is placed into the maintenance phase of therapy as described above.

In patients truly refractory to the therapy provided above, systemic antimicrobials or additional host modulatory agents have been used, often in a polypharmacologic approach. Examples of additional host modulatory approaches used include low doses of NSAIDS (flurbiprofen), or the newer Cox-2 inhibitors (Vioxx), or low doses of bisphosphonates. These types of patients who are most susceptible with multiple risk factors or patients presenting with moderate-severe disease requiring comprehensive periodontal treatment planning should be referred to the specialist for care and close monitoring.

With regards to periodontal therapy, better diagnostics would be very useful. Therapeutic technologies have surpassed dentists' ability to adequately diagnose active vs. inactive lesions, to pick up subtle changes in the tissues thereby preventing additional loss of attachment and bone. Studies have shown that scaling and root planing alone may not be sufficient to reduce excessive levels of many of the destructive mediators, particularly in the more susceptible patients. Until such diagnostic techniques are made available, clinicians have no choice but to rely on clinical judgement to determine the most appropriate course of therapy.

Conclusion

Periodontal pathogens and destructive host responses are involved in the initiation and progression of periodontitis. Therefore, the successful long-term management of this disease may require a treatment strategy that integrates therapies that address both etiologic components. It is clear that standard therapy, such as the removal of supra- and subgingival plaque and calculus deposits by scaling and root planing results in more predictable outcomes for mild-moderate periodontitis than for moderate-severe periodontitis. The use of a host modulatory agent, or a combination of host modulatory agents, capable of inhibiting MMPs, cytokines, and other mediators of the disease, can assist in the conventional treatment for periodontitis. When used adjunctively, chemotherapeutics can enhance and make clinical therapeutic responses more predictable in the more susceptible patient.

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The Ins and Outs of Periodontal Antimicrobial Therapy

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ABSTRACT A multifaceted antimicrobial approach is necessary for the successful management of destructive periodontal disease. Effective antimicrobial periodontal therapy aims to overwhelm periodontal pathogens with aggressive initial therapy and prevent previously suppressed pathogens from rising up anew through daily oral hygiene measures and frequent professional cleaning. Current antimicrobial periodontal therapy employs mechanical debridement performed with and without surgery, antibiotics, and antiseptics. Subgingival irrigation with povidone-iodine at the dentist's office and subgingival irrigation with dilute sodium hypochlorite for home-care constitute effective, safe, and affordable periodontal antimicrobial therapy. This article describes theoretical and practical guidelines for implementing rational and cost-effective antimicrobial principles in the management of periodontal disease.

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Periodontal disease is probably the most widespread inflammatory disorder in humans, affecting virtually all adults throughout the world. Severity of periodontal disease ranges from mild gingival inflammation to advanced periodontal attachment loss, sometimes resulting in loss of teeth. Historically, a predominantly mechanical approach to treatment has been employed; and outcomes have often been disappointing, due to clinicians' inability to adequately control periodontal pathogens and patients' inability or unwillingness to comply with measures necessary to prevent recurrence of disease. Use of antimicrobial agents in periodontal treatment has often been somewhat haphazard and empirical; however, there is evidence that the addition of appropriate antimicrobial therapy to traditional periodontal treatment may substantially enhance clinical outcomes and reduce the need for costly surgical procedures. At the University of Southern California School of Dentistry, a comprehensive scientifically based protocol has been developed that emphasizes rational uses of antimicrobial agents in periodontal therapy. It is the aim of this article to

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evaluate current periodontal antimicrobial therapies with respect to efficacy, safety, and affordability. A proficient cost-effective antimicrobial periodontal treatment may offer populations who are currently unable to receive adequate care due to lack of financial resources a practical and valuable means of maintaining a functional periodontium and dentition for a prolonged period.

Periodontal Microbiota

Destructive periodontal disease is an infectious process and, hence, may best be managed by anti-infective intervention. Causes may include nonspecific bacterial plaque, as in gingivitis and mild forms of chronic (adult) periodontitis, or specific bacterial infections, as in aggressive (early onset) periodontitis. Both specific and nonspecific dental plaque microorganisms colonize tooth surfaces as biofilms, a phenomenon that makes treatment of these infections particularly challenging.1 Biofilms are defined as sessile communities of microbial cells that develop on surfaces in aquatic ecosystems. Biofilm microorganisms reside as highly structured populations and assume a phenotype that is clearly different from that of their free-living counterparts. The biofilm concept has several clinical implications and is particularly important in understanding the killing and resistance of oral microorganisms. The biofilm phenotype shows a remarkable resistance to antibiotics, biocides, and components of host defenses that are effective in controlling planktonic cells. To overcome the protective effect of biofilms, it is important to disrupt subgingival plaque at the time of initiation of antimicrobial therapy, either mechanically (scaling and root planing), chemically (dilute sodium hypochlorite irrigation), or by using a combination of these approaches.

Another complicating factor in managing some periodontal diseases is the invasion of gingival tissues by periodontopathic microorganisms.

Table 1. Periodontal putative pathogens in refractory periodontitis [a]

Microorganisms	% infected lesions
Actinobacillus actinomycetemcomitans	30
Porphyromonas gingivalis	15
Prevotella intermedia	40
Bacteroides forsythus	25
Peptostreptococcus micros	30
Campylobacter rectus	25
Staphylococcus epidermidis/Staphylococcus aureus	30
Enteric rods/pseudomonads	10
Candida albicans	15

[a] Approximate values from own unpublished studies

Table 2. Features of systemic antibiotics used in periodontal therapy.

Antibiotics	% absorption after oral administration	Peak serum level in m g/ml	Serum half-life in hours	Approximate wholesale price (generic) for one usual adult dosage
Clindamycin	90	5	2.4	$3.25
Metronidazole	90	20-25	6-14	$0.25
Penicillins (amoxicillin)	75	5-8	1.2	$0.25
Tetracyclines (doxycycline)	93	2-4	18	$0.10
Erythromycins Azithromycin Clarithromycin	18-45 37 50	0.1-2 0.4 2-3	2-4 12 5-7	$0.25 $6.50 (250 mg) $3.50
Fluoroquinolones (ciprofloxacin)	70	1.5	4	$3.75

Actinobacillus actinomycetemcomitans is a tissue-invading organism that cannot always be removed by mechanical debridement, topical antibiotics, or antiseptics, but can be eradicated by a properly selected systemic antibiotic regimen.2 Certain anatomic variations, such as narrow furcations, root concavities, and close root proximity severely limit the effectiveness of mechanical therapy; and in these situations systemic antibiotics arriving via crevicular fluid may be a valuable adjunctive treatment. Periodontitis lesions that are recalcitrant to conventional periodontal therapy often harbor a variety of periodontal pathogens that have escaped the cleaning efforts of the dentist and the patient (**Table 1**). However, refractory periodontitis can often be successfully treated using a combination of systemic antibiotics and locally delivered antiseptics.3

Clearly there are advantages to augmenting traditional mechanical periodontal therapy with properly selected antimicrobial agents. Currently there are a wide variety of systemic and locally delivered products available to the dental practitioner. These will be reviewed and guidelines will be presented to assist clinicians in selecting appropriate treatment strategies for their patients.

Figure 1. Microbiological sampling kit.

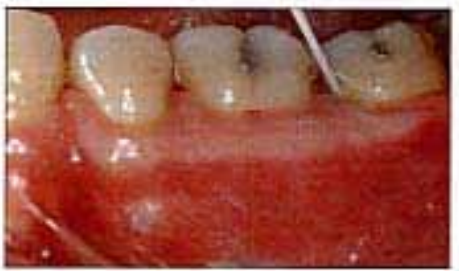


Figure 2. A sterile endodontic paper point is inserted into periodontal pocket, removed after 10 seconds, placed in the vial of transport medium, and delivered to the laboratory. In one to two weeks a report is returned describing the periodontal pathogens present.

Systemic Antibiotics

Routine use of systemic antibiotics in treating chronic (adult) periodontitis is not recommended; it is unnecessary and is likely to increase the development of resistant strains of bacteria.4 Selection of antibiotics in clinical practice is either empirical or based upon the results of microbiological tests. Empirical antibiotic therapy may be used for periodontal diseases with known microbial etiologies, such as acute necrotizing ulcerative gingivitis that is caused by anaerobic organisms that can be cured by metronidazole, and early localized juvenile periodontitis that mostly involves A. actinomycetemcomitans that can be eradicated by systemic amoxicillin-metronidazole combination therapy. However, even the most careful clinical examination cannot delineate the likely microbial pathogens in most types of periodontitis nor determine their susceptibility to various antibiotics. Microbiological analysis of subgingival plaque provides valuable information that will facilitate accurate diagnosis and optimal treatment planning (Figures 1 and 2). Fortunately, therapeutic antibiotic therapy in periodontics can be deferred until the results of culture, nucleic acid-based diagnostic tests, and antimicrobial susceptibility determination are available. Recent articles outline criteria for selection of antibiotics and the value of microbiological testing in periodontal treatment.5,6

Systemic antibiotics may be used singly or in combinations. Single-agent antibiotic therapy in current periodontics includes metronidazole (500 mg/3x daily/for 8 days), clindamycin (300 mg/3x daily/for 8 days) and ciprofloxacin (500 mg/2x daily/for 8 days) (all adult dosages). Common combination therapy in periodontics includes metronidazole and amoxicillin (250 mg each/3x daily/for 8 days), and metronidazole and ciprofloxacin (500 mg each/2x daily/for 8 days). Food does not influence the bioavailability of most oral antimicrobial agents, with the exception of tetracyclines, quinolones, and azithromycin. These three groups of antimicrobial drugs should be given one hour before or two hours after food intake. When a choice must be made between equally effective antibiotics, it is prudent to consider the financial cost of therapy (**Table 2**).

A low dosage of doxycycline (20 mg) taken twice daily has the potential to inhibit mammalian collagenases and has been suggested as an aid in controlling periodontitis.7 However, the postulated absence of antimicrobial activity from this therapeutic approach has been questioned,8,9 and therefore potential problems with antibiotic resistance and development of hypersensitivity may need to be addressed. Compared to placebo medication, low-dosage doxycycline treatment of periodontal sites probing greater than or equal to 7 mm gives rise to only about 0.48 mm additional reduction in probing pocket depth and 0.38 mm additional gain in clinical attachment level.10 Even if low-dose doxycycline might temporarily retard the progression of periodontitis, long-term efficacy and safety of the therapy has not been established. It is troublesome that minimal resolution of gingival bleeding occurs even after nine months of daily doxycycline administration.10 Since repeated gingival bleeding is one of the most useful clinical predictors

of future periodontal breakdown,11 long-term follow-up data are warranted on the periodontal status after the low-dose doxycycline therapy has been discontinued.

Locally Delivered Antibiotics

Controlled-release devices that contain tetracycline-HCl, doxycycline, minocycline, metronidazole, or ofloxacin for direct pocket placement are commercially available in various countries. In controlled-release drug delivery, the antimicrobial agent is released during an extended period of time by zero-order drug-release kinetics.12 The usefulness of topical antibiotic therapy in periodontics is controversial. Most published studies have monitored the effect of controlled drug delivery on clinical variables characteristic of gingivitis and not necessarily of periodontitis, and the adjunctive or alternative role of topical antibiotic therapies in short- and long-term management of periodontal disease has not been defined either.

Table 3 describes clinical outcomes of some commercial controlled-release devices for antimicrobial periodontal therapy. As an adjunct to scaling and root planing, subgingival placement of minocycline-loaded microcapsules has been reported to enhance reduction in bleeding upon probing.13 Topical minocycline, however, is likely to be ineffective in eradicating tissue-invading A. actinomycetemcomitans from periodontal pockets and may even promote subgingival overgrowth of minocycline-resistant yeasts and various enteric rods.14 In patients with moderate to severe chronic periodontitis, application of 2 percent minocycline hydrochloride gel failed to provide any additional probing depth reduction or clinical attachment gain when used as an adjunct to scaling and root planing.15 Locally applied tetracycline fibers have been shown to have some clinical benefits up to six months following therapy when used in conjunction with scaling and root planing;16 however, follow-up evaluation after five years revealed no benefit compared to scaling and root planing alone.17 Considering potential problems with selectivity of antimicrobial action and possibly development of resistant bacteria and adverse host reactions as well as high medication costs, topical antibiotic therapy seems to constitute an inferior choice to topical use of a low-cost, broad-spectrum antiseptic agent with low potential for adverse reactions.

Table 3. Reduction of probing depth in 4-7 mm pockets following periodontal therapy [a]

Treatment	Authors	Average probing depth reduction in mm
Repeated scaling and root planing	Magnusson et al. (1984)[18]	2.3
Repeated scaling and root planing	Listgarten et al. (1978)[19]	2.2
Tetracycline fibers + scaling and root planing	Newman et al. (1994)[16]	1.8
Metronidazole gel + scaling and root planing	Stelzel & Flores-de-Jacoby (1996)[20]	1.3
Minocycline gel + scaling and root planing	Timmerman et al. (1996)[21]	2.3
Minocycline microcapsules + scaling and root planing	Yeom et al. (1997)[13]	1.6
Minocycline ointment + scaling and root planing	Van Steenberghe et al. (1999)[22]	1.9
Minocycline microspheres + scaling and root planing	Williams et al (2001)[23]	1.3
Doxycycline gel (monotherapy)	Garrett et al. (2000)[24]	1.3

[a] Caution must be exercised in comparing treatment studies that are noncalibrated and differ in types of patients and clinical measurement techniques

Locally Delivered Antiseptics

Mechanical root debridement to remove dental calculus is important in periodontal therapy but is frequently inadequate in curing severe periodontal infections.25 To augment mechanical debridement, topical antiseptics may be used to kill periodontal pathogens during initial therapy and to suppress their repopulation during maintenance therapy.25 Antiseptics are chemical agents that have the ability to inactivate the growth of a large range of microorganisms

in or on living tissue. To have therapeutic value, pharmaceuticals must be delivered at an effective concentration and for an adequate length of time. Gingival crevicular fluid flow averages 20m l/ hour and increases with gingival inflammation,26 which is equivalent to a turnover rate of 40 times per hour in a medium-sized periodontal pocket with a volume of 0.5 m l.27

Subgingival antimicrobials can be administered either by noncontrolled delivery for fast-acting pharmaceuticals or by controlled drug-delivery devices for slow-acting agents. Povidone-iodine is able to kill microorganisms rapidly enough to overcome the drug-diluting effect of gingival crevicular fluid and is effective when delivered by subgingival irrigation, provided a contact time of at least five minutes is achieved.28 The American Heart Association suggested that antiseptic mouthrinses such as povidone-iodine applied immediately prior to dental procedures might reduce the incidence or magnitude of bacteremia.29 Blue povidone-iodine stains on starched linen will wash off with soap and water. Other iodophore stains can be readily removed with a 5 percent solution of sodium thiosulfate.

Sodium hypochlorite is a strong oxidizing agent that possesses numerous attractive properties for antiseptic use, including rapid bactericidal action, ease of use, and very low cost. Irrigation with dilute (0.5 percent) sodium hypochlorite solution has been shown to cause significantly greater and longer-lasting reduction in plaque and gingivitis than irrigation with water.30

In contrast, chlorhexidine digluconate mouthrinses at concentrations of 0.1 percent to 0.2 percent, which have a long history of use in controlling supragingival plaque and gingivitis,31 may require controlled-release delivery to exert effective killing of subgingival microorganisms.32 Also, chlorhexidine tends to be more bactericidal for gram-positive organisms populating supragingival plaque than for gram-negative species inhabiting periodontal pockets.33 Recently, a controlled local delivery system containing 2.5 mg of chlorhexidine gluconate incorporated into a biodegradable chip of hydrolyzed gelatin was introduced for subgingival antimicrobial treatment (Periochip, Astra Pharmaceuticals, Westborough, Mass.). Initial studies found that the use of the chlorhexidine chip in conjunction with scaling and root planning had some potential to reduce periodontal probing depth, clinical attachment loss, and bleeding on probing.34,35 However, a recent prospective clinical study that evaluated changes in levels of periodontal pathogens before and after scaling and root planning with and without adjunctive use of the chlorhexidine chip showed no microbiological benefits to placement of the chlorhexidine chip following thorough mechanical debridement.36

Clinical Protocol for Antimicrobial Therapy

Prior to developing a suitable treatment plan, it is essential to establish a complete and accurate assessment of the patient's oral/periodontal and medical conditions. First, it is important to determine the chief complaint or the patient's reasons for seeking treatment. These could include pain, swelling, gingival bleeding, impaired function, unsatisfactory esthetics, or a combination of these reasons. Next, the medical status of the patient must be reviewed and vital signs recorded. This will determine the patient's suitability for dental treatment and identify any special precautions that must be taken, such as premedication for prevention of bacterial endocarditis.29 Medications with the potential to adversely effect gingival health include phenytoin, cyclosporin, and various calcium channel blockers.37 Poorly controlled diabetes and smoking have been reported to predispose patients to periodontal disease and adversely effect response to treatment.38,39 Anticoagulant therapy, including low-dose aspirin, may need to be modified to ensure adequate hemostasis during and after surgical procedures.40,41 Patients having compromised host defense mechanisms may require more frequent and comprehensive antimicrobial periodontal therapy. An appropriate dental examination including periodontal pocket depth measurements will lead to an accurate diagnosis. Periodontal conditions should be classified under one of the following three general categories: gingivitis, chronic periodontitis, or aggressive periodontitis. **Figure 3** describes how each of these disease categories can be effectively treated.

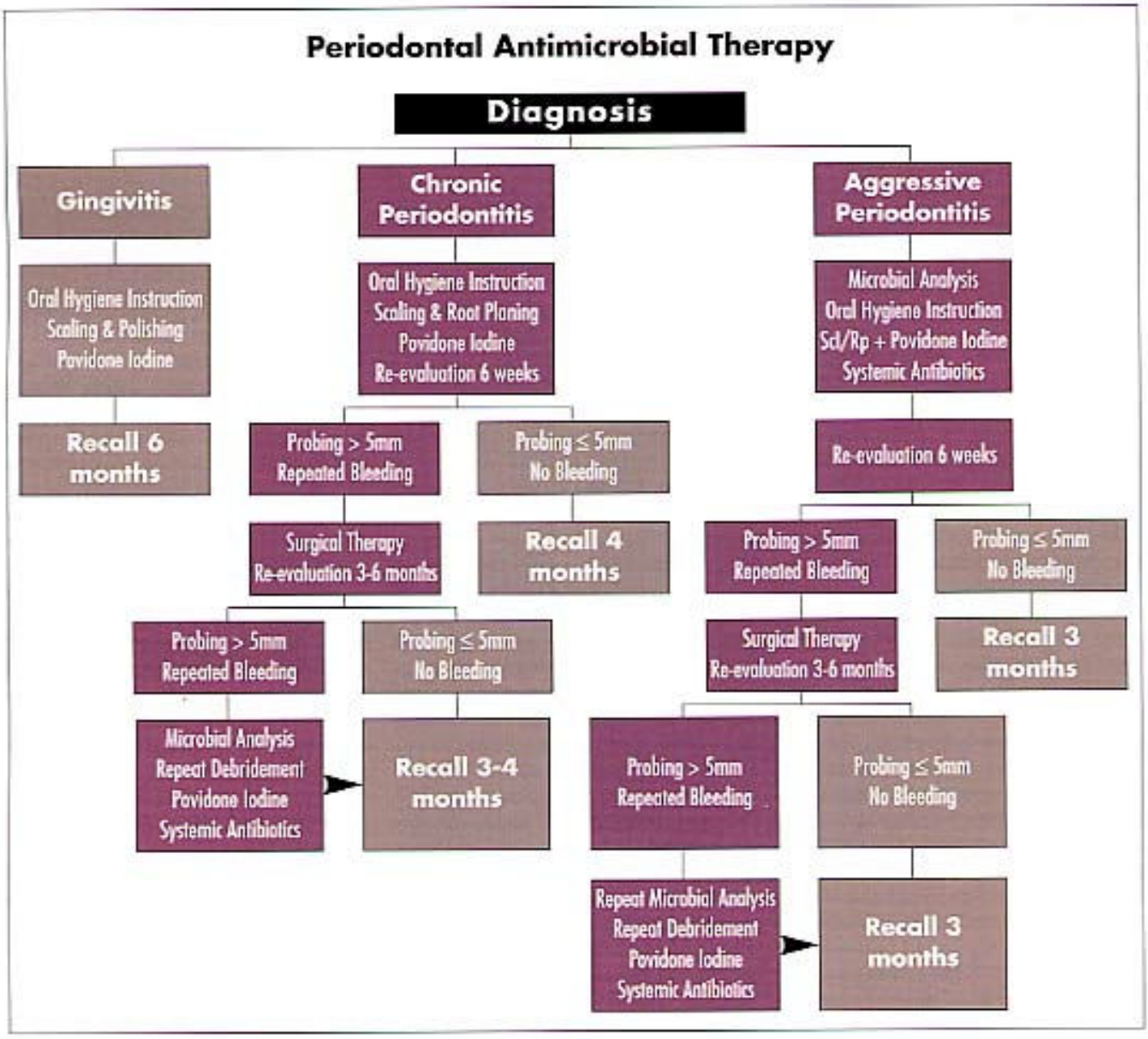
Plaque-Induced Gingivitis

Oral hygiene instruction should educate and motivate the patient to accomplish effective daily plaque removal. Soft and hard deposits and stains are removed by scaling and polishing. Disinfection of subgingival sites is performed by repeated irrigation with 10 percent povidone iodine (Betadine, Perdue Frederick Co., Norwalk, Conn.) with a contact time of at least five minutes. Irrigation is performed using a 3 cc disposable syringe with a 23 gauge blunt-tipped cannula. Iodine should not be used during pregnancy or nursing, nor in patients with thyroid disease or sensitivity to iodine. For patients who should not be treated with iodine, 0.12 percent or higher concentrations of chlorhexidine gluconate may be used as an irrigant, though it is less effective due to protein binding with crevicular fluid and blood. Dilute sodium hypochlorite may also be used as a subgingival antiseptic. For most gingivitis patients, six months is a suitable recall interval; patients who require additional motivation for plaque control may need to be seen more often.

Chronic Periodontitis

In addition to daily plaque removal, patients who have experienced loss of periodontal attachment require

more extensive debridement. This is accomplished initially by scaling, root planing, and subgingival irrigation with 10 percent povidone iodine. Approximately six weeks after initial debridement, periodontal conditions are re-evaluated. If no probing depths are greater than 5 mm, gingival bleeding is not seen, and plaque control is effective, the patient is scheduled for periodontal recall in four months. If probing depths greater than 5 mm or bleeding remain, surgical therapy or referral to a periodontist should be considered. Surgical treatment will provide improved access for debridement and a reduction in probing depths. Additional re-evaluation is performed in three to six months. If at that time, no probing depths are greater than 5 mm, bleeding is not seen, and plaque control is effective, the patient is scheduled for periodontal recall in three to four months. If probing depths greater than 5 mm remain or repeated bleeding is seen, microbial analysis should be performed followed by repeated mechanical debridement, subgingival irrigation



with 10 percent povidone iodine, and prescription of systemic antibiotics guided by the results of microbial analysis. An additional re-evaluation is performed in approximately six weeks. If probing depths are then reduced and bleeding has subsided, the patient is scheduled for recall in three months.

Aggressive Periodontitis

It is especially important to consider microbiological testing and appropriate use of antimicrobial agents when treating patients with aggressive periodontitis. Subgingival sampling should be performed prior to any mechanical debridement. As in cases of gingivitis and chronic periodontitis, oral hygiene instruction should be an integral part of each appointment. Scaling, root planing, and subgingival irrigation with 10 percent povidone iodine is generally performed in several appointments. After completion of the last session of scaling and root planing, systemic antibiotics may be prescribed based on the results of microbial analysis. If microbial analysis is not available, prescribing the combination of amoxicillin and metronidazole, 250 mg each, three times daily for eight days, will be beneficial in approximately 70 percent of cases. Overgrowth of resistant pathogens may occur in some patients, however; and microbial testing is therefore strongly recommended whenever possible. Six weeks after completion of scaling and root planing, re-evaluation is performed. If probing depths are not greater than 5 mm and no bleeding is detected, the patient is scheduled for recall in three months. If probing depths greater than 5 mm remain or repeated bleeding is seen, surgical therapy or referral should be considered. Additional re-evaluation is performed in three to six months. If no probing depths are greater than 5 mm, bleeding is not seen, and plaque control is effective, the patient is scheduled for periodontal recall in three months. If probing depths greater than 5 mm or repeated bleeding are still seen, additional microbial analysis is indicated followed by further mechanical debridement, subgingival irrigation with 10 percent povidone iodine and an additional course of systemic antibiotics. The patient should be seen at least every three months, and may require even more frequent visits. In the majority of aggressive periodontitis cases, expedient, thorough treatment will result in a highly favorable response, including significant osseous repair of periodontal defects.

Antimicrobial Agents Used by the Patient

Chlorhexidine

0.12 percent chlorhexidine gluconate may be prescribed as a mouth rinse, initially used twice daily for two weeks as part of whole mouth disinfection.42 An additional one-week course of rinses may be prescribed at recall appointments. Staining of teeth and tooth-colored restorations frequently occurs, and long-term continuous use of chlorhexidine is not recommended.

Chlorine

The American Dental Association Council on Dental Therapeutics proposed using dilute sodium hypochlorite as a topical antiseptic for irrigation of wounds and as an antiseptic mouthrinse.43 Sodium hypochlorite, 0.05 percent to 0.10 percent, may be used for oral irrigation. Patients should prepare a fresh solution for each use by placing one teaspoon of 5.25 percent sodium hypochlorite (plain household bleach) in the small (300 cc) reservoir of the oral irrigator (Waterpik Technologies, Inc., Fort Collins, Colo.). and then filling it with warm water. Concentration of the sodium hypochlorite solution can be adjusted to suit patients' acceptance of the taste, and some patients may find one of the scented commercial bleaches more agreeable. The authors suggest performing subgingival irrigation with sodium hypochlorite two to three times per week. Subgingival plaque, being a biofilm, is particularly susceptible to sodium hypochlorite.30

Fluoride

Fluorides have some antimicrobial properties, although they are not as effective as chlorhexidine or sodium hypochlorite. Use of fluoride rinses and/or fluoride gels for their anticaries properties is strongly recommended for periodontal patients, since as periodontal pathogens are eliminated or reduced, organisms responsible for root surface caries may proliferate. A 0.4 percent stannous fluoride gel can be applied with a toothbrush or delivered via a custom tray.44

Povidone-iodine is not recommended for home care because of the risk of developing hyperthyroidism after frequent long-term usage.

Periodontal Maintenance

Maintenance care at regular intervals is essential to ensure long-term stability in treated periodontitis patients.45 A recent publication describes current approaches to periodontal maintenance utilizing antimicrobials.25 Briefly, patients are scheduled for maintenance care at intervals determined by clinical history and current conditions. Shallow probing depths (less than 5 mm) are more easily maintained than deeper periodontal pockets.

Stable periodontal conditions are associated with an absence of repeated bleeding upon gentle probing, presence of radiographic lamina dura, and an absence of periodontal pathogens in microbial analysis. Therapy in stable cases includes oral hygiene review, selective scaling, polishing, and irrigation with povidone iodine. It is important to avoid unnecessary instrumentation; root planing should be performed only in areas where deposits are detected, since the trauma inherent in thorough mechanical debridement often results in attachment loss in areas probing less than 3 mm.46

In cases where periodontal disease

activity is suspected, microbial analysis may be considered, more extensive debridement and subgingival povidone iodine irrigation are performed, systemic antibiotics may be prescribed depending upon the results of microbial analysis, and the interval between maintenance visits should be reduced. In patients showing signs of persistent disease activity, it may be necessary to consider retreatment, including surgical intervention to establish shallower, more easily maintainable probing depths.

Conclusion

Periodontal disease is an infectious process ranging in severity from mild gingivitis to advanced loss of connective tissue attachment and supporting bone. Dental plaque is a complex biofilm that forms on tooth surfaces as bacteria colonize. To establish and maintain periodontal health, this biofilm must be eliminated or markedly reduced, either by mechanical debridement, topical antiseptics (dilute sodium hypochlorite) or a combined mechanical and chemical approach.

Gingivitis and most chronic periodontitis involve nonspecific plaque and respond well to local treatment. Locally delivered antiseptics, such as povidone iodine and sodium hypochlorite, have a considerably broader spectrum of activity, exhibit fewer potential adverse effects, and are more effective and much less costly than locally applied antibiotics, especially those administered as controlled drug devices.47

Aggressive periodontitis often involves one or more specific periodontal pathogens that may invade pocket epithelium and connective tissue; control of these infections may require use of systemic antibiotics in addition to topical antimicrobial measures. Microbiological analysis of subgingival plaque can provide information that is valuable in arriving at an accurate diagnosis and in selecting an appropriate antibiotic or combination of antibiotics.

Following successful periodontal treatment, gingival tissue may shrink, exposing root surfaces with little fluoride content. Also, as periodontal infections resolve, a shift toward a more gram-positive streptococcal microbiota may occur, resulting in increased numbers of cariogenic bacteria. Therefore, it is prudent to instruct patients to apply topical fluoride gel, with a toothbrush or via custom trays, on a daily basis.

Monitoring periodontal conditions on a regular basis will enable the clinician to intercept lapses in effective plaque control, perform additional debridement as necessary, and thereby ensure continued periodontal health. Properly managed, the vast majority of periodontitis patients can retain their dentition for a lifetime.

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Periodontal Disease and Systemic Health — What You and Your Patients Need to Know

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ABSTRACT For many years, dentists have recognized the importance of dental health to general health. Recent research findings point to possible associations between chronic oral infections such as periodontitis and systemic health problems. This article will review the evidence for some of these associations and explore factors that may underlie oral-systemic disease connections.

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For many years, most dentists have recognized the importance of dental health to the general health of their patients. Since the surgeon general's report on oral health in America1 was issued by the U.S. Department of Health and Human Services, the medical profession, the news media, and the public have become more aware of this association. Recent research findings point to possible associations between chronic oral infections such as periodontitis and systemic health problems such as diabetes, heart and lung diseases, stroke, and low birth weight premature births. This article will review the evidence for some of these associations and explore factors that may underlie oral-systemic disease connections.

Within the oral cavity dwells a dynamic microbiologic ecosystem of approximately 6 billion microbes living in a delicate balance that can be altered by the health of the host and the integrity of its defenses. The periodontium, as well as other body surfaces, carry an enormous microbial load, yet underlying tissues and blood are relatively sterile. Protective barriers prevent easy penetration of bacteria. Skin and mucous membranes, immunologic defenses, and high oxidation reduction potentials with oxygen levels of host cells provide barriers from bacterial penetration and invasion. If the host is immunosuppressed, immunodeficient, hypoxic, or injured, the potentials for microbial penetration increase.2 In recent years, evidence points to the health of the host as playing an intimate role in the maintenance of periodontal stability. Therefore, both patient and clinician should recognize health status and its influence on periodontal diseases or inversely, periodontal diseases and risk to health.

As a result of exposure of the periodontium to complex dental plaques consisting of more than 400 bacterial species, periodontal disease occurs.3 Periodontitis is generally a chronic infection that results in the inflammatory destruction of the periodontal ligament and alveolar bone. This destruction occurs due to toxic bacterial byproducts (lipopolysaccharides, peptidoglycans, hydrolytic enzymes); a mounted host response (cytokines, interleukins, and prostaglandins); and systemic reaction via serum antibodies.4 It is, therefore, reasonable to hypothesize that periodontal infections may influence overall health and the course of some systemic diseases.5

Cardiovascular Disease

Orally derived bacteremia infecting damaged heart valves is currently the strongest association between dental plaque/periodontal inflammation and systemic disease.6 It is well-accepted that dental and other surgical procedures predispose susceptible patients to infectious endocarditis or infections in the mural endocardium.7 Periodontal bacteria and/or their byproducts may also gain access to the circulation by direct invasion of periodontal tissues.8,9 Bacteremia from oral origin appears to be directly related to the severity of periodontal inflammation.10

There are two forms of infectious endocarditis, acute and subacute. Clinical manifestations and implicated microflora frequently differ. Acute infectious endocarditis presents with abrupt onset of fever, cutaneous and oral petechia, and focal dermal gangrene. The clinical course is rapid, less than six weeks. Intravascular coagulation may occur, which increases the risk for emboli and metastatic infection in any body organ.11 Death occurs unless antibiotic therapy is instituted.

Subacute infectious endocarditis may persist for months. During its chronic course, patients present with low-grade fever, fatigue, myalgias, arthralgias, and anemia. Antimicrobial therapy at early stages will cure the disease, but it is fatal without intervention. Oral streptococci, i.e., Streptococcus viridans and S. sanguis, have been isolated from subacute infectious endocarditis patients. Strains of S. sanguis adhere to thrombotic vegetations on heart valves and may cause in vivo thrombus formation.12

Note that infectious endocarditis can also be caused by other periodontal pathogens: Hemophilu species, Actinobacillus actinomycetemcomitans, Eikenella corrodens, Capnocytophaga species, and Fusobacterium nucleatum. Clinical therapy, therefore, should focus primarily on minimizing gingival inflammation in at-risk patients. The current American Heart Association guidelines recommend antibiotic prophylaxis in procedures that induce bleeding. Frequent periodontal maintenance, preventive home care, and necessary periodontal interventions need to be performed because maintenance of periodontal health is imperative in this patient population.

Patients with heart valvular disease, heart valve replacement, or a history of infectious endocarditis are at high risk for infectious endocarditis, congestive heart failure, or significant arrhythmias. Clinicians treating the periodontium should consult with the patient's cardiologist. It is equally important that the dental team advise the physician regarding the periodontal/dental disease status.

Is there an association between cardiovascular disease, atherosclerosis, and periodontal disease? Several studies indicate possible relationships with chronic periodontal/oral infection and

Table 1. Adjusted Odds Ratios for Cardiovascular Disease (CVD), Fatal CVD, and Stroke for Patients With Periodontal Disease [34]

Total CVD	Fatal CVD/Stroke	Reference
1.67		Joshipura -- 1996[16]
1.5		Beck -- 1996[15]
	2.2	Beck -- 1996[15]
	2.8	Beck -- 1996[15]
	2.6	Grau -- 1997[33]
1.29		DeStefano -- 1993[14]
	1.46	DeStefano -- 1993[14]

atherosclerosis, myocardial infarction, and cerebrovascular disease.13-16 Severe periodontal disease, including advanced alveolar bone loss in multiple sites with edema, suppuration, and/or swelling may be a risk factor for cardiovascular disease (**Figure 1**). Correlations with gingivitis and periodontal disease are not evident. Some researchers, for example, Hujoel and colleagues, could not find convincing evidence of a causal association between periodontal disease and coronary heart disease.17 Further research is needed to evaluate this association.

Periodontal infections may directly effect atheroma formation as seen in Porphyromonas gingivalis studies, which found P. gingivalis in carotid and coronary atheromas,18 invading endothelial cells,19 and inducing platelet aggregation. Another mechanism that may associate periodontal infections and infections in general with atherosclerosis is via indirect or host-mediated responses, i.e. ,production of C-reactive proteins and fibrinogen, which are independent risk factors for coronary disease.20 This inflammatory response characteristic of periodontal disease, marked by high levels of inflammatory mediators, may exacerbate the process of atherogenesis.5

Recent studies indicate a possible association of stroke or cerebrovascular ischemia with dental infection (odds ratio, 2.6).21 Also, the Normative Aging Study and the Dental Longitudinal Study of the Department of Veterans Affairs found that incidence odds ratios for bone loss and total cardiovascular disease, fatal cardiovascular disease, and stroke were 1.5, 2.2, and 2.8 respectively.15

Patients with periodontal disease who are at risk for atherosclerosis should have thorough periodontal examinations and medical review. Comprehensive periodontal therapy should be provided with meticulous preventive care and maintenance therapy. Patients need to be informed about possible periodontal disease relationships to cardiovascular diseases (**Table 1**). Also, patients with pre-existing cardiovascular disease should have open communication with medical care providers for consultation regarding both periodontal/dental and medical concerns.

Respiratory Disease

Chronic obstructive pulmonary disease was the fourth leading cause of death (100,000 lives), and pneumonia/influenza caused 84,000 deaths in the United States in 1996.22 There is increasing evidence that oral bacteria, especially periodontal pathogens, may alter the course of respiratory infections. Also, it is known that the lower airway can be contaminated by microorganisms through aspiration of oropharyngeal contents, inhalation of infectious aerosols, hematogenous spread, or spread from contiguous sites.23 Oral pathogens may serve as a reservoir for these respiratory infections and influence the bacterial flora of the lower bronchi. There are documented studies that show poor oral hygiene in patients hospitalized , institutionalized,24 or admitted to intensive care units.25,26

Potential respiratory pathogens may become established in the oral flora of patients with periodontal disease. Patients treated with antibiotics appear to have greater numbers of potential respiratory pathogens adherent to bacteria in subgingival plaque. High-risk pneumonia patients may be more prone to oral colonization by respiratory pathogens following mucosal modification due to prolonged exposure to dental plaque. Also, many at-risk patients have compromised swallowing reflexes, which leads to easier aspiration.

Bacterial pneumonia, chronic bronchitis, emphysema, and chronic obstructive pulmonary disease may be adversely affected by oral microflora. Antibiotic-resistant strains of bacteria are emerging, and oropharyngeal flora and secretions are directly responsible for potential respiratory infection. Aspiration of oral bacteria may be responsible for exacerbation of chronic obstructive pulmonary disease.27

Recommendations for the dental clinician include:

1. Reducing levels of periodontopathic flora by maintaining good home care and frequent periodontal maintenance.
2. Rinsing with chlorhexidine prior to dental/periodontal therapy
3. Performing required periodontal therapies to stabilize the periodontium
4. Due to xerostomia in this population from mouthbreathing/obstruction and medications, close monitoring of dental caries is recommended, as well as fluoride therapy at home.
5. Consultation with the patient's physician for periodontal/dental or medical concerns.

Adverse Pregnancy Outcomes

Preterm low birth weight is a significant cause of perinatal morbidity and mortality. Despite attempts to reduce recognized risk factors for preterm low birth weight, including low socio-economic status, poor prenatal care, a mother older than 34 or younger than 17, alcohol abuse, smoking, hypertension, genitourinary tract infections, diabetes, multiple pregnancies, and African American ancestry,27 minimal alteration in the number of preterm low-birth-weight infants occurred.

Recent studies suggests that infection may increase the likelihood of preterm low birth weight. Genitourinary or other infections, possibly periodontal, may adversely affect pregnancy outcomes.28,29 Prostaglandin E2, and tumor necrosis factor a are normal biologically active molecules during childbirth. They may be raised to high levels with infection and induce premature labor. In a case-control study, preterm low-birth-weight infants had mothers with significantly more periodontal attachment loss than the control group with normal-weight infants at birth.30

In light of the possible link between

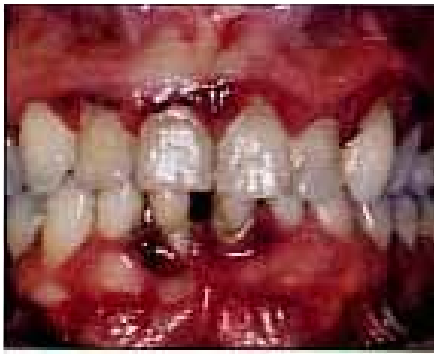

Figure 1. Severe gingival inflammation in a poorly controlled diabetic.

periodontal infection and adverse pregnancy outcomes, the dental/periodontal clinician will need to educate the pregnant patient on the latest research and the implications. The incidence of pregnancy gingivitis (30 percent to 75 percent) is high. This may be due to alterations in the composition of subgingival plaque, altered immunoresponse, and increases in sex hormone concentrations during pregnancy.31 More frequent periodontal maintenance visits in order to maintain periodontal health during pregnancy is paramount.32 The second trimester is the safest time to treat the pregnant patient because most organ systems have been formed. The third trimester is also safe, however, the clinician should be aware of the pressure of the gravid uterus on the inferior vena cava creating a risk for postural hypotension. In light of the new research, however, it is apparent that the patient should have closer monitoring and management of periodontium and oral infections.

Conclusion

In this new millennium, dental practitioners are obligated to care for the patient's total health. They are able to see the links and potential risks of periodontal and other oral infections to systemic health. Future research will help dentistry unravel the complex interactions between host susceptibility, immune response, genetic associations, behavioral components, and disease control. Dentists must not only treat localized oral infections, but manage risk that varies with each individual patient.

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Periodontal Disease and Systemic Health — Diabetes

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ABSTRACT This article discusses the biologic basis of periodontal disease and diabetes mellitus. Following is a consideration of the possibility of a link between diabetes and periodontal disease. Mounting evidence suggests that there is, indeed, a connection between periodontal disease and diabetes.

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The number of patients with diabetes, a potentially devastating group of metabolic disorders, is increasing in the United States due in part to a sedentary lifestyle, obesity, an increasing elderly population, increased longevity of diabetics, and a change in the diagnostic criteria of diabetes.1 The prevalence of diabetes rose from 4.9 percent to 6.5 percent from 1990 to 1998.2 Estimated projections of the total U.S. population with diagnosed and undiagnosed diabetes is 15.6 million.3 Of the 7.8 million diagnosed diabetics, the vast majority -- approximately 90 percent -- have type 2 diabetes (previously called non-insulin-dependent diabetes); and the remaining 5 percent to 10 percent of these have type 1 diabetes (previously insulin-dependent diabetes). It is estimated that there are as many undiagnosed type 2 diabetics as diagnosed, and each year 30,000 Americans develop Type 1.1, 4,5 Rarer types of diabetes include gestational and drug- or chemical-induced. Regardless of diabetic diagnosis, all types have increased serum glucose or hyperglycemia in common.

The onset of type 1 diabetes usually occurs before the age of 20. Pancreatic b cells are destroyed, and blood glucose levels increase rapidly without good control. The process of destroying pancreatic b cells is thought to be of autoimmune origin.6

Though the exact etiology of type 2 diabetes is not known, genetic and environmental factors are strongly implicated. Individuals who are older than 40 and obese seem to be predisposed to develop type 2 diabetes. There is increased production of glucose by the liver in the fasting state. Adequate amounts of insulin are produced; but defects in the insulin molecule, altered cell receptors for insulin, and insulin resistance (unresponsiveness to

insulin's action in target tissues, specifically liver, muscle, and fat) are present.7 This results in an elevation of blood glucose. Other systemic manifestations of type 2 diabetes are elevated triglycerides and decreased HDL production.

The American Diabetic Association has recognized major complications of diabetes, which include retinopathy, neuropathy, cardiopathy, altered wound healing, and nephropathy.8 In 1993, it was suggested that periodontal disease become the sixth complication of diabetes.9 These complications increase the morbidity and mortality of patients with diabetes. The presence of elevated serum glucose levels affects the macro and microvasculature leading to atherosclerosis and the development of cardiovascular, cerebrovascular, visual, and renal complications. Additionally, peripheral nerves are affected.10,11

The pathogenesis of diabetic complications is not fully understood. There are direct and indirect effects of hyperglycemia. A direct effect is the increased production of sorbitol, which may lead to the development of diabetic retinopathy, neuropathy, and nephropathy. Indirect effects may be due to irreversible molecules called advanced glycation end products (AGEs). These are glucose-derived compounds that are formed in direct relationship to blood glucose concentrations. Evidence suggests that AGEs accumulate in the plasma and tissue of diabetics, altering cellular structure and composition resulting in the complications seen in diabetes.12,13

Cells such as endothelial cells, smooth muscle cells, neurons, and monocytes have cell surface binding sites for AGEs called receptor for AGE (RAGE). In diabetes, the number of RAGE is significantly increased.14 Binding of AGEs to endothelial cells results in the development of changes in cellular function. It is likely the alterations in endothelial cells may result in the development of vascular lesions, focal thrombosis, and vasoconstriction in diabetes.15, 16 In addition, AGEs interaction with vascular smooth muscle cells, with possible cellular disturbance, may further injure the vasculature.

AGEs bind to monocytes, resulting in enhanced chemotaxis and activation with the increased release of pro-inflammatory cytokines, tumor necrosis factor alpha (TNF-a), interleukin 1 (IL-1), and insulin-like growth factor. TNF-a has a number of diverse functions including activation of macrophages and osteoclasts. In addition, it has been implicated in the development of insulin resistance in both obesity and type 2 diabetes.17 Oxygen free radicals are also produced, which further destroy tissue.

There is evidence that AGE binds to RAGE on fibroblasts.18 Alterations in fibroblast function due to this binding may contribute to the impaired connective tissue remodeling seen in diabetics. Binding of AGEs to collagen increases the crosslinking between collagen molecules thereby resulting in reduced solubility and decreased turnover rate.19

Conventional wisdom suggests that patients with poor glycemic control are at greater risk for the development of infections than nondiabetic patients, but there is no conclusive evidence to suggest this. However, there is evidence suggesting that specific infections are more common or occur with increased severity in diabetics.20, 21 Diabetics appear to be more prone to infections caused by certain bacteria such as Gram-negative anaerobes.

Poorly controlled diabetics are more prone to specific infections, and the incidence of infection correlates to the level of glycemic control in these patients. The exact mechanism that predisposes these individuals to infections is not known, but several aspects of immunity may play a role. Reduced polymorphonuclear leukocyte (PMN) chemotaxis, phagocytosis, and an impaired antioxidant killing of bacteria have been implicated.22, 23 Thickening of the vascular basement membranes may reduce tissue nutrition and inhibit the migration of PMNs.

Wound healing appears to be compromised in diabetics, and the exact mechanism is not known. Possible mechanisms include altered cellular activities and failure of PMNs to migrate toward the area of wound healing. As previously mentioned, collagen synthesis is decreased in diabetics. Increased crosslinking and glycosylation of collagen renders it less soluble and possibly with an increased remodeling time. Increased collagenase production may degrade newly formed collagen.

Periodontal disease is a group of related, generally chronic inflammatory diseases of the supporting tissues of the teeth that leads to the destruction of the periodontium, which consists of alveolar bone, periodontal ligament, gingiva, and cementum. There is strong evidence that a number of periodontopathic organisms, specifically Gram-negative anaerobes such as Porphymonas gingivalis and Prevotella intermedia, are the suspected etiologic agents of periodontitis.24,25

It has been considered that the subgingval microflora may be altered in diabetic periodontal patients as compared with nondiabetic patients. Laboratory data from in vivo studies suggest that the microflora of type 1 and type 2 diabetics is not specific or unique to these periodontal patients when compared to nondiabetic patients.26,27

Bacterial endotoxin, toxins, and cell membrane products challenge the host, activating an inflammatory cascade with the synthesis and secretion of IL-1b , TNF-a and IL–6, which induce and enhance the production of PGE2 and matrix metalloproteinases. The upregulation of cytokines is a major factor in the connective tissue destruction and alveolar bone resorption seen in periodontal disease.28,29 Cytokine levels are elevated in sites demonstrating periodontal disease. IL-1b , TNF-a and IL–6 levels increase during periods of tissue and bone destruction, while levels decrease after periodontal therapy.30,31

The systemic consequences of

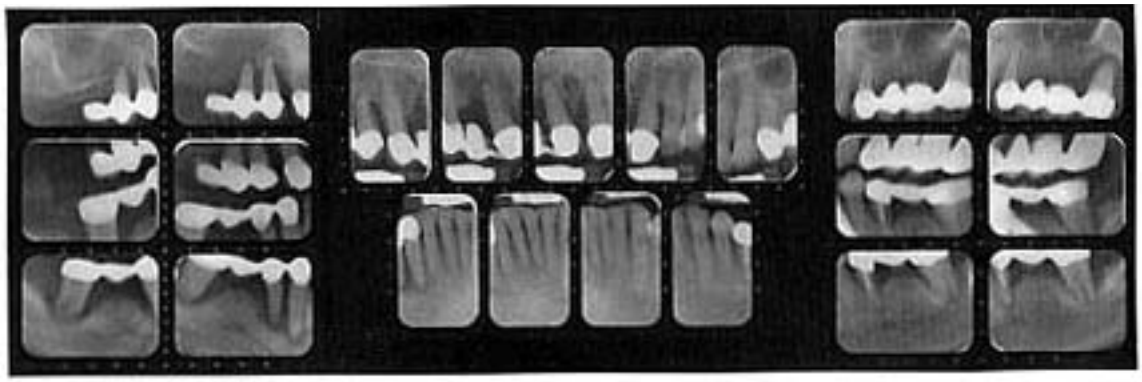

Figure 1. Example of a case with chronic periodontal and oral infections.

elevated pro-inflammatory cytokines in response to periodontal pathogens have not been fully investigated until recently. Insulin resistance occurs in both diabetic and nondiabetic patients during acute infections. In chronic infections, insulin resistance increases by 28 percent.32 One suggested mechanism for the increase in insulin resistance is the release of cytokines such as of IL-1b and TNF-a in response to infections. Two suspected periodontal pathogens, P. intermedia and P. gingivalis have been shown to increase insulin resistance. The suggested mechanism for the increase in insulin resistance is the release of cytokines such as IL-1b and TNF-a in response to a bacteroides infection.

As previously discussed in this review, investigators have suggested that elevated cytokine levels in response to periodontal pathogens may also have detrimental effects to the fetus whose mother has periodontitis.33 Others have hypothesized that elevated levels of cytokines may participate in atherosclerosis and coronary heart disease.34

The biologic basis for periodontal disease and diabetes mellitus has been summarized here. The following questions need to be addressed to determine a definitive link between diabetes and periodontal disease.

- Do diabetics have increased susceptibility to periodontal disease?
- Will metabolic control of diabetic patients have a beneficial effect on their periodontal status?
- Will the treatment of periodontitis result in improved glycemic control?

Do diabetics have increased susceptibility to periodontal disease?

Extensive supporting evidence indicates that there is a relationship between poor glycemic control and periodontal disease. Investigators have determined that type 1 diabetics have an increased risk of developing periodontal disease with age, and the severity of periodontal disease increases with duration of diabetes.35,36 Significantly more attachment and bone is lost in type 1 diabetics who have poor glycemic than in those who are well-controlled or nondiabetics. **Figure 1** demonstrates the severe gingival inflammation of a poorly controlled diabetic.

Multiple studies on the Pima Indian population in Arizona who have an unusually high prevalence of type II diabetes indicate that diabetics have a higher prevalence of periodontal disease.37,38 Additionally, poorly controlled diabetics have more severe disease with an increased risk of progressive bone loss. 39 These findings have been corroborated in other populations. Turkish NIDDM patients had more severe periodontal disease than nondiabetics.40

One team of investigators has hypothesized that increased accumulation of AGEs and their interaction with RAGE in the gingiva of diabetic patients increases vascular permeability, loss of tissue integrity, and barrier function. The increase in AGEs in the tissue may also attract and immobilize monocytes with the release of pro-inflammatory cytokines and MMPs. Additional cells such as fibroblasts affected by AGEs may lead to an increase in MMPs and a decrease in collagen production. This cascade of events may contribute to an exaggerated response to periodontal pathogens with accelerated connective tissue and bone destruction seen in patients with diabetes.14

Will metabolic control of diabetic patients have a beneficial effect on their periodontal status?

In one study, the effect of improved metabolic control of diabetes on periodontitis without periodontal therapy over a period of eight months resulted in no significant improvement in periodontal status.41 There appears to be no conclusive evidence suggesting strict metabolic control will improve periodontal status without treatment. A cause-and-effect relationship has not been established. What has been well-documented is that diabetics with good glycemic control will respond as well to periodontal treatment as nondiabetic patients.42,43,44 Poorly controlled patients may show an improvement in their periodontal status after therapy, but with less favorable

results and recurrence of periodontitis over the long term.45

Will periodontal treatment result in improved glycemic control?

Review of the literature in answering the third question provides equivocal results. Two recent investigations provided evidence that treatment for periodontitis in type 2 diabetics resulted in an improvement in glycemic control. Both used glycated hemoglobin (HbA1c) as a measure of glycemic control, which measures the amount of glucose irreversibly bound to the hemoglobin molecule. The first study provided mechanical therapy to the test group and no periodontal therapy to the control group.46 After three months, the reduction in HbA1c was significantly greater for the test group than the control group, 21 percent vs. 9 percent.

A second investigation combined ultrasonic scaling with systemic doxycycline and/or irrigation with water, chlorhexidine, or povidone-iodine.47 At three months, the test groups receiving doxycycline had significantly greater reductions in HbA1c that approached 10 percent. Those groups not receiving doxycycline had smaller and nonsignificant reductions in HbA1c. The authors suggested the use of doxycycline was beneficial in two ways, first in part to its antimicrobial effects and second due to the ability of the drug to modify the host response. Doxycycline, a modified tetracycline, may modify the host response by suppressing collagenolytic activity, increase protein synthesis and secretion, inhibit matrix metalloproteinases, inhibit nonenzymatic glycation, and block protein kinase C activity, a step in the secretion of IL-1b and TNF-a .48

Other studies have found that periodontal therapy did not have a statistically or clinically significant change in HbA1c.42,44 Two reviews of the literature suggest the current research available is insufficient to ascertain if periodontal therapy can contribute to the metabolic control of either type 1 or 2 diabetes.21,49

Several investigators have developed hypotheses to address the relationship between diabetes and periodontal disease. One hypothesis proposes "that periodontal infection-mediated cytokine synthesis and secretion may amplify the magnitude of the AGE-mediated cytokine response and vice versa. The relationship between diabetes and periodontal disease becomes a two-way relationship."48 A second group of investigators hypothesizes that AGE monocytes RAGE interaction results in chronic monocyte generation of pro-inflammatory mediators such as IL-1b , TNF-a , and IL–6, mediators whose ultimate effects may result in activation of osteoclasts and collagenases/matrix metalloproteinases, thereby leading to bone and connective tissue destruction."50

Additional research is needed to answer the question, will the treatment of periodontitis result in improved glycemic control. It will be important to determine if improved insulin resistance accompanies a decrease in the concentration of cytokines after periodontal therapy.

Conclusion

Evidence is mounting that there is a connection between periodontal disease and diabetes as well as other systemic conditions on a molecular level. Poorly controlled diabetics have an increased risk for periodontal disease and periodontal disease has the potential to effect glycemic control. It would be prudent to determine glycemic control in periodontal patients with diabetes prior to treatment to correct poor control to reduce complications during treatment. Additionally, this may provide for improved therapeutic results after periodontal therapy. The potential exists to influence the course and management of systemic disease and health through periodontal therapy. Conversely, a poor healing response to periodontal therapy may indicate a systemic disease influencing healing and warrant a medical consultation to rule out systemic influences on the periodontium.

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As Good as It Gets

Robert E. Horseman, DDS

Apparently the late Peggy Lee was right when she lamented in song years ago "Is That All There Is?" At least that is the position taken by Professor Steve Jones of University College London in presenting his argument at a Royal Society Edinburgh debate "Is Evolution Over?"

"Things have simply stopped getting better, or worse, for our species," claims Professor Jones. He is one of a group of biologists who believe our species has reached its biological peak and is no longer capable of changing. "If you want to know what Utopia is like, just look around -- this is it," says the professor, who has possibly been narcotized by long-term exposure to British television.

His view is controversial, however. In the first place, how much credibility can you give to a highly placed professor named Steve Jones? This is a name for a salt-of-the-earth guy running a back hoe for Municipal Maintenance in Cleveland. To make profound statements that carry any weight in the scientific community, you need an improbable name such as Professor Heinrich Krautzmeyer, followed by a string of initials, to bolster your hypothesis.

Another Brit, with the plebian moniker of Professor Chris Stringer of the Natural History Museum, London, represents the opposite camp. If we were counting on Stringer's view to cheer us up, however, we are doomed to disappointment. He demurs, "Evolution is going on all the time. For example, brain size has decreased over the past 10,000 years. We are punier and smaller-brained compared with our ancestors only a few millennia ago. - Evolution does not automatically mean an improvement in our lot." Which is exactly what many of us puny, small-brained people have been demonstrating since the evolution of music into present-day cacophony.

It might be held that London's dismal weather is responsible for both these depressing views, but along comes biologist Christopher Wills of the University of California, San Diego, where California's most salubrious climate is said to prevail. He postulates that ideas are driving our evolution and that there is a premium on sharpness of mind and the ability to accumulate money. Intellect, he claims, is the defining characteristic of our species and is what is still driving our evolution. If that were so, one would expect to see a diminishment of simple knuckleheadedness over the past century or so, a phenomenon not in evidence.

Not so fast, says Peter Ward, of the University of Washington in Seattle, where the sun last appeared in 1947, "I don't think we are going to see any changes -- apart from ones we deliberately introduce ourselves." He means the

bioengineering of people by introducing genes into their bodies so they live longer or are stronger and healthier. With Cher and Michael Jackson as examples, this approach does not augur well.

In summary, the wisdom of people who have spent upwards of 25 years in study distills to this:

- Evolution has come to a halt; this is as good as it gets.
- Evolution is ongoing with the speed of library paste, but things are not necessarily going to improve and, in fact, might get worse.
- Evolution is a hoax perpetuated by unconscionable opportunists. Everything was created in six days and that's that.

It would seem that biologists are no more trustworthy than economists. It's the TMI syndrome (too much information) that has addled the pates of both professions. For all of us who were lucky to get out of high school chemistry and biology with a "C," the answer is clear -- discount completely the opinions of anybody bearing the title "professor."

Cherish the hope that morons who drive 20 mph in the fast lane with a right-turn blinker flashing will eventually evolve into, at the very least, pedestrians. Believe with all your diminishing intellect that good manners will make a comeback, that society will no longer tolerate willful boorishness and that baseball caps will eventually return to their correct alignment even though the brain of the wearer is visibly shrinking. If you like, hold fast to the notion that evolution will eventually mold the idiotic pros and imbecilic cons of society into one mind. Go gently into that good night -- you should live so long.