OF THE CALIFORNIA DENTAL ASSOCIATION

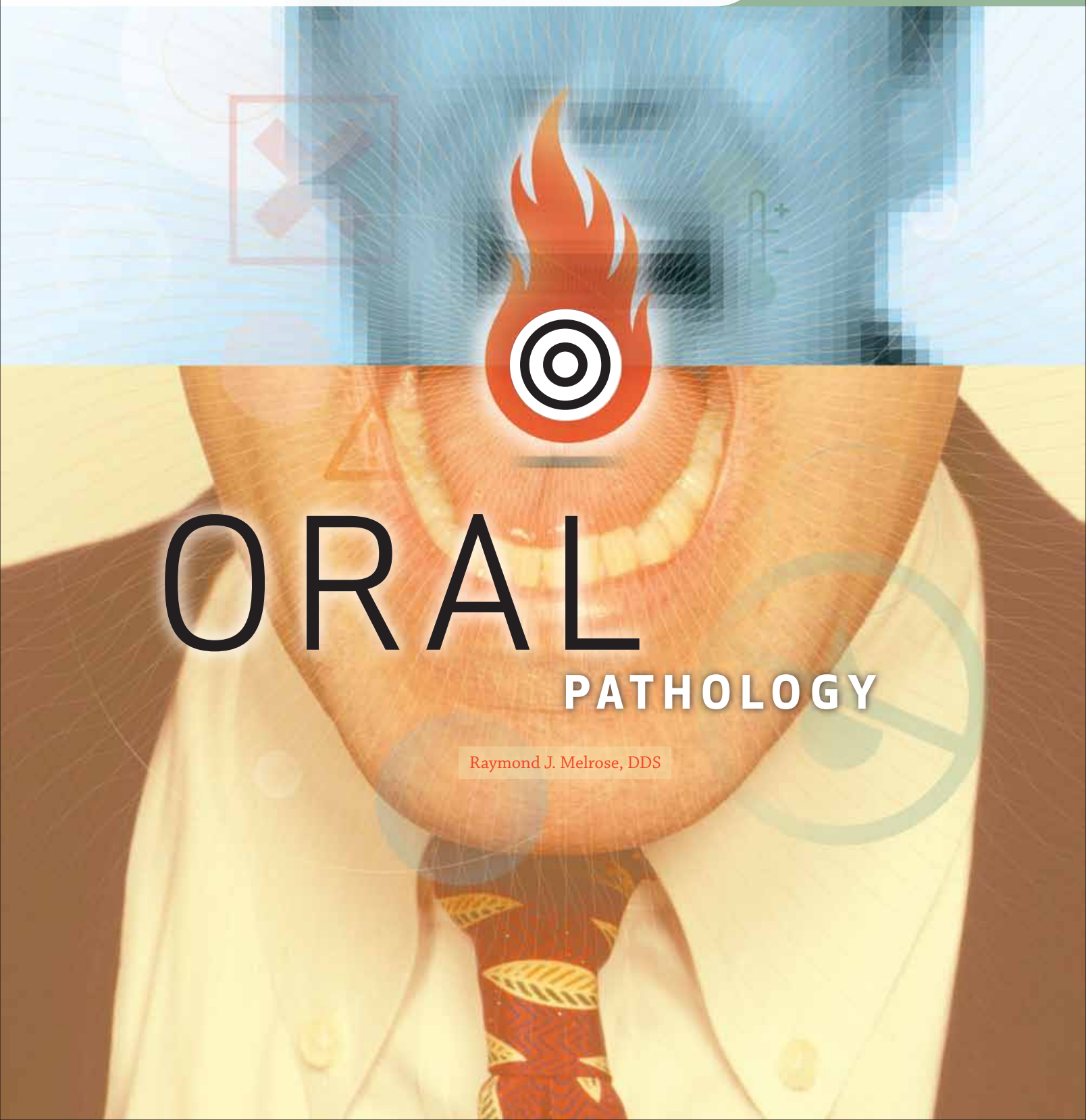
Journal

JUNE 2007

The Burning Mouth

Oral Lichenoid Reactions

Managing Xerostomia



ORAL PATHOLOGY

Raymond J. Melrose, DDS

OF THE CALIFORNIA DENTAL ASSOCIATION
Journal
CDA Journal
Volume 35, Number 6
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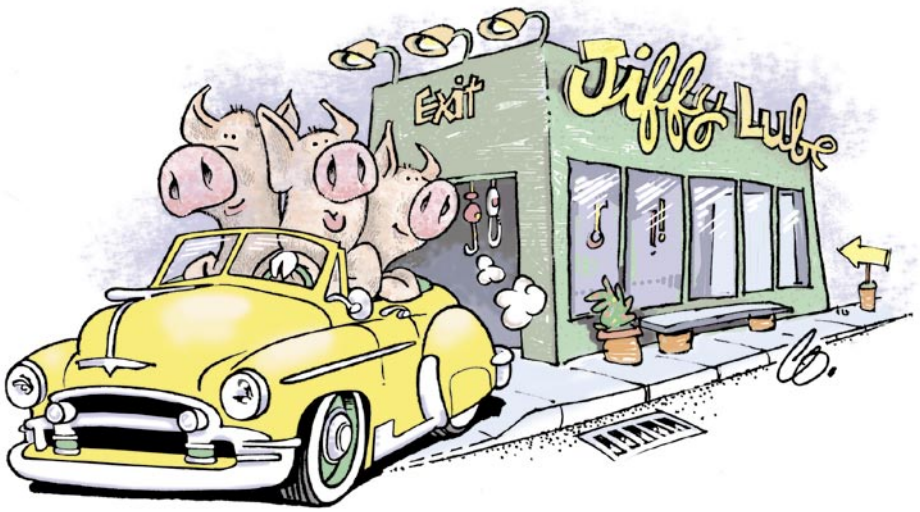

Open Wide: Here Comes IntelliDrug

"This thing," he continues, indicating his teeth, "automatically solves all my problems of memory lapse and noncompliance.

Robert E. Horseman, DDS

ILLUSTRATION BY CHARLIE O. HAYWARD

Manfred and Jacob are having lunch at a small sidewalk café in Stuttgart. The bratwurst is good, the matzo soup excellent, and the Heinekens cold. Suddenly Manfred cocks his head slightly to one side mid-chew, listens intently. "What's that noise?" he asks.

"What noise?" Jacob queries.

"That clicking, topockita-pockita noise. Don't you hear it?"

"Oh, *that*," Jacob says, brightening. He reaches in his mouth with thumb and forefinger and pries out two of his lower molars that resemble a unilateral partial denture from dentistry's distant past. "This is my IntelliDrug Device. I am diabetic; I need four kinds of heart medications and six prescription drugs I don't even know what they're for."

"This thing," he continues, indicating his teeth, "automatically solves all my problems of memory lapse and noncompliance. It is the lingerie du chat, as we say in Tel Aviv."

"French for 'cat's pajamas,'" Manfred says. "You're not French."

"I know. We just do it to annoy them. Feh!"

We leave the two friends noshing on their vittles to do a little research on what promises to be the biggest thing in dentistry and medicine combined during the last two weeks. Potentially even bigger than the silicone implants and tooth whitening that have become as necessary as oxygen for the under-60 set.

While American dentists were engrossed in discovering shades of white beyond the ability of the human eye to appreciate, and insisting no edentulous space goes unimplanted, European and Israeli experts were hot on the development of a high-tech automatic drug dispensing device they have named IntelliDrug. Because of insufficient space on the product, the runner-up name of Der Schmartzigdruggendrippendiviser didn't make the cut.

Here's the skinny as explained by Roger Cheng of Dow Jones Newswires: Dr. Andy Wolff, an Israeli dentist, initially came up with the concept of an automatic drug-dispensing device, knowing the average patient has the compliance level of a

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preschool toddler when it comes to taking his prescribed medicines. Luckily, Wolff immediately thought of the mouth as the proper site for such a device. No telling where it would have been placed if brain surgeons or proctologists had had a glove in the decision.

Miniaturization being what it is these days, we should not be surprised to learn that the device being prepared for comprehensive tests by a consort of 15 different European and Israeli companies will house the following components: a pump, custom valves, a microprocessor, batteries, and a reservoir for the drugs. There will be a communication port so that the device can be remotely controlled, eventually linking it with cell phones or nearby hospitals.

Political alarmists have been quick to detect a parallel between IntelliDrug and the "Manchurian Candidate." If a man's mediations can be controlled remotely by perfect — or imperfect strangers — what else can it do? So many things to protest, so little time!

Of interest to dentists are reports that the IntelliDrug device, all enclosed in a space the size of two molars is "strapped" in. Strapped in? To what? Ask all the Doubting Thomases among us. It is said to be easily removable by technicians (not exodontists) who can then refill the drug reservoir, change the battery, and give it the standard lube, oil, and filter service at any convenient Jiffy Lube outlet.

Dr. Wolff is pretty excited about this and so are the pigs on which the concept has been successfully tried. Except for the occasional ticked-off porker holding a one-way ticket to Hormel, not a single incident of Mad Pig Disease has been detected. Once the pigs have given the tests a hooves-up, Dr. Axel Schumacher, who is helping design the pumps, declares he hopes to have a prototype ready for human testing by the end of the year. The pigs hope so, too, indicating they would like to get back to their normal activities of truffle hunting and seeking better building materials to thwart big, bad wolves. ■■■■

Revised Guidelines for Heart Patients

Based on a review of new and existing scientific evidence, most dental patients with heart disease do not need antibiotics before dental procedures to prevent infective endocarditis, a rare, but life-threatening heart infection.

According to revised guidelines from the American Heart Association, with input from the American Dental Association, antibiotics are now only recommended for patients at greatest risk of negative outcomes from infective endocarditis, including those with artificial heart valves or certain congenital heart conditions; heart transplant recipients who develop cardiac valve problems; recipients of an artificial patch to repair a congenital heart defect within the past six months; and patients

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Kodak RVG 6100 Digital Radiography System →

Kodak Dental Systems has introduced its RVG 6100 digital radiography system, featuring rounded corners, rear-entry cable, and a new size-0 sensor. The system provides the comfort patients demand, while still capturing the highest quality images in the industry today. The new

size-0 sensor captures clear, accurate images while allowing the practitioner to reduce radiation exposure for pediatric patients. For more information on Kodak's suite of digital imaging products, go to Kodak.com/dental or call 800-944-6365.

Himalayan Dental Relief Project Expands to Guatemala

The Himalayan Dental Relief Project has expanded into Guatemala, making it the fourth country served by the humanitarian organization.

Behrhorst Partners for Development is hosting the Himalayan Dental Relief Project in Guatemala. As a local partner, Behrhorst Partners for Development secures the clinic location, coordinates with local health officials, and organizes the daily flow of children to the clinic in Guatemala. The goal this year is to reach an estimated 800 children for first-time dental care. Volunteer dental health professionals, including a dental hygienist from California, dentists from Maryland, Colorado, and Washington, provide care. Classes emphasizing oral health are taught by Behrhorst Partners for Development local staff and includes hygiene, and toothbrushing demonstrations for children and their parents at each school location.

"I know we were there to help others, but I feel that I am the one who benefited. I came home feeling uplifted and invigorated," said Maria Glashof, a hygienist from California, who participated in the program.

The inaugural clinic held in January included 80 extractions, 453 restorations, and several anterior composite restorations, valued at a U.S. equivalent of $94,670. A second clinic is scheduled for this month.

Guatemala has a population of 14.6 million with more than 40 percent of population made up of children under the age of 14. It is estimated there are 12 dentists per 100,000 people.

For more information about the dental relief project, go to: http://www.himalayandental.com/.

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"We know that it isn't a question of if avian flu will reach the United States, it is a question of when."

SCOTT LAYNE, MD

UCLA Receives Award to Research Flu Viruses with Pandemic Potential

The University of California Los Angeles School of Public Health has been awarded $18.5 million over five years to create the Center for Rapid Influenza Surveillance and Research by the National Institute of Allergy and Infectious Disease.

Physicians, veterinarians, biologists, and researchers from across the country have created a team that will conduct research on influenza viruses with pandemic potential.

"UCLA's School of Public Health has assembled many of our country's leading influenza experts to monitor the path of influenza in the United States and abroad," said Linda Rosenstock, MD, MPH, dean of the school. "CRISAR will be instrumental in early detection of the next influenza outbreak, providing a head start in preventing a pandemic."

Domestic surveillance of wildlife, particularly feral birds, and domestic animals will be conducted along the Pacific Flyway of North America in states including California, Washington, and Alaska. International surveillance also will be conducted in far eastern Russia, Japan, Cambodia, Laos, and Mongolia. Once samples have been collected, the research team will analyze influenza genes from thousands of viruses each year, creating a capacity that is at least 10 times greater and far faster than currently exists to fully characterize influenza viruses as they evolve.

"We know that it isn't a question of if avian flu will reach the United States, it is a question of when," said Scott Layne, MD, a professor at the School of Public Health and principal investigator for CRISAR. "The efforts of UCLA and our partners will allow scientists and health officials to judge the threat posed by particular influenza subtypes and strains, and respond rapidly and decisively."

UPCOMING MEETINGS

2007	
June 27-July 1	Academy of General Dentistry Annual Session, San Diego Convention Center, 888-243-3368.
Aug. 4	31st Annual Scripps Symposium on Oral Medicine, San Diego, scripps.org/conferenceservices, 858-587-4404.
Aug. 22-24	International Society for Breath Odor Research Seventh International Conference, Chicago, Bill Bike, billbike@uic.edu or 312-996-8495.
Sept. 27-30	American Dental Association 148th Annual Session, San Francisco, ada.org.
Nov. 27-Dec. 1	American Academy of Oral and Maxillofacial Radiology 58th Annual Session, Chicago, aaomr.org..
2008	
May 1-4	CDA Spring Scientific Session, Anaheim, 800-CDA-SMILE (232-7645), cda.org.
Sept. 12-14	CDA Fall Scientific Session, San Francisco, 800-CDA-SMILE (232-7645), cda.org.
Oct. 16-19	American Dental Association 149th Annual Session, San Antonio, Texas, ada.org.

To have an event included on this list of nonprofit association meetings, please send the information to Upcoming Meetings, CDA Journal, 1201 K St., 16th Floor, Sacramento, CA 95814 or fax the information to 916-554-5962.

Second Workshop Addressing Oral Health Held in Rwanda

A follow-up workshop dedicated to support the process of developing the first oral health policy for Rwanda was held recently in the country's capital of Kigali.

The event was jointly organized by the Rwanda Dental Association, the FDI World Dental Federation, and the World Health Organizations, and the African Regional Organization, following the first-ever oral health meeting in Rwanda two years ago.

In Rwanda, people travel an average of 300 km to obtain dental care. Additionally the dentist-population is less than 1:800,000.

In her remarks at the event, Charlotte Ndiaye, a professor and WHO AFROs regional adviser for oral health, offered congratulations for the work done so far and for the collaboration between FDI and WHO to support policy development in African countries. She said oral health is important for one's overall well-being and general development. "It is our responsibility to address it with appropriate policies and functioning essential services. WHO is keen to provide the necessary technical support to all countries of the region requesting it," she said.

Habib Benzian, DDS, MScDPH, MSc, FDI Development and Public Health manager, emphasized the importance of considering oral health as a human right. During the landmark Nairobi conference on Oral Health in Africa, organized in 2004 in Nairobi, oral health was recognized as a basic human right. Benzian said it was therefore important to consider it as a key issue for every health policy in every country.

Early Humans Weren't Too Different From Apelike Species

For those of the belief that modern man was more apelike than previously considered weren't half bananas, according to a professor at New York University College of Dentistry.

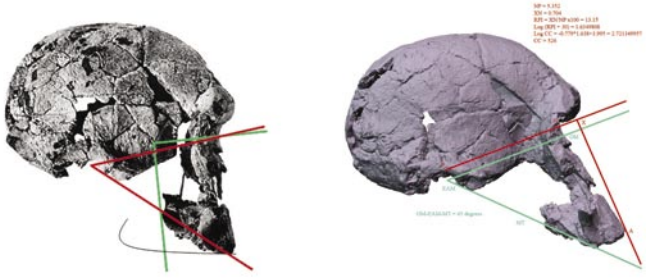
The findings of Timothy Bromage, MA, PhD, a paleoanthropologist and an adjunct professor of Biomaterials and of Basic Science and Craniofacial Biology, call into question the extent to which Homo rudolfensis differed from earlier, more apelike hominid species. Bromage showed a 1.9 million-year-old skull belonging to H. rudolfensis, the earliest member of the human genus, with an astonishingly small brain and markedly protruding jaw, features typically associated with more apelike members of the hominid family living as much as 3 million years ago.

Bromage presented his findings at the annual scientific session of the International Association for Dental Research in New Orleans.

He is the first scientist to produce a reconstruction of the skull that questions renowned paleontologist and archeologist Richard Leakey's depiction of modern man's earliest direct ancestor. Leakey's depiction is of a vertical facial profile and a fairly sizeable brain — an interpretation widely accepted … until now.

Bromage's reconstruction also suggested that humans developed a more vertical face with a less prominent jaw, smaller teeth, and a larger brain at least 300,000 years later than commonly thought, maybe as recently as 1.6 million to 1 million years ago, when two later species, H. ergaster and H. erectus, lived.

"Dr. Leakey produced a biased reconstruction based on erroneous preconceived expectations of early human appearance that violated principles of craniofacial development," said Bromage.



Dr. Richard Leakey's reconstruction, left, shows an erroneous vertical facial profile on a 1.9 million-year-old early human skull. At right, Dr. Timothy Bromage's computer-simulated reconstruction shows the same skull with a distinctly protruding jaw. Bromage used the green and red lines to compare the location of the eyes, ears, and mouth, which must be in precise relationship to one another in all mammals.

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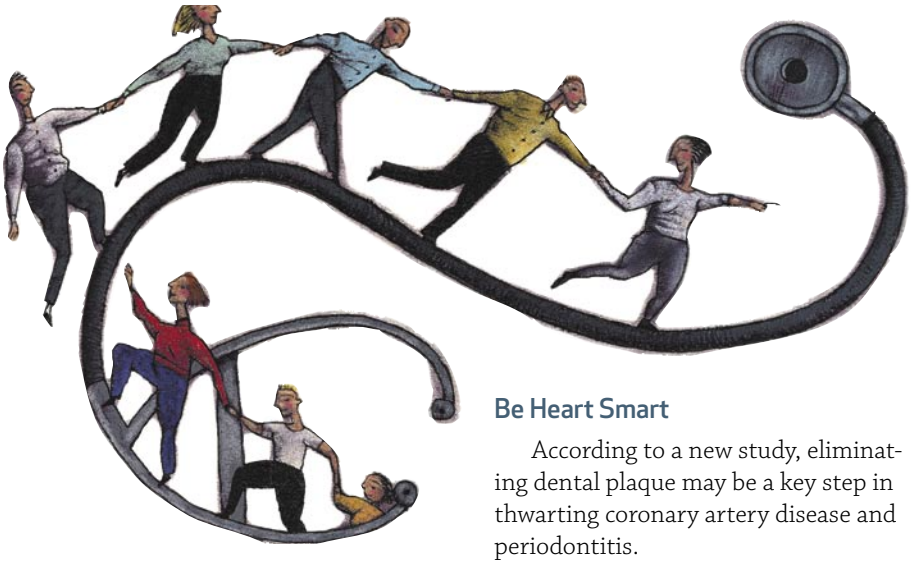


Be Heart Smart

According to a new study, eliminating dental plaque may be a key step in thwarting coronary artery disease and periodontitis.

Because periodontitis is a persistent bacterial infection causing recurrent inflammation in periodontal tissues, it has been suggested that it may travel through the bloodstream and raise the risk of acute cardiac syndrome. Researchers recently examined 20 people with chronic periodontitis. In 13 of those patients, bacterial pathogens most frequently found in severe chronic periodontitis also were found in atherosclerotic plaque of coronary vessels. In 10 cases, those species of bacteria also were present in atherosclerotic plaque and in subgingival plaque."

"We found that patients with periodontal pathogens detected in atherosclerotic plaque had 4 millimeters or greater of deep periodontal pockets and a significantly higher bleeding index," commented study author Dr. Maciej Zaremba, in the February issue of the *Journal of Periodontology*. "This supports the possibility that bacteria associated with periodontitis can permeate into coronary vessels."

"Since periodontal and cardiovascular diseases have several common risk factors, more studies are needed to evaluate the strength of association between the two diseases," said Preston D. Miller, Jr., DDS, American Academy of Periodontology president. "It is very important for people to talk to their dentist or periodontist about their periodontal health and their at-home oral hygiene routine to prevent periodontal disease and maybe even coronary artery disease."

BIOMET 3i's Certain PREVAIL Implant Now Prevails With More Options

BIOMET 3i has introduced the latest addition to its popular Certain PREVAIL Implant Family — a new straight collar design. In clinical situations where the existing expanded collar implant might not fit, the new straight collar design provides an option for narrower interdental spaces or ridge widths.

BIOMET 3i designed this implant system to help clinicians in the pursuit of crestal bone preservation. Certain PREVAIL Implants feature integrated Platform Switching by incorporating a coronal bevel design that medializes the implant-abutment junction. Additionally, the entire length of the implant is dual acid-etched with the industry-proven OSSEOTITE Surface, which is designed to expedite bone-to-implant contact and also offers the Certain QuickSeat Connection. This provides the clinician with an audible and tactile click that confirms the abutment is properly seated.
For more information, go to www.biomet3i.com or call 800-443-8166 or 561-776-6700.

New Venture Assists in Practice-building

ADA Business Enterprises, Inc., a wholly owned subsidiary of the American Dental Association, has partnered with Intelligent Dental Marketing of Salt Lake City to help dentists build and market their dental practices.

ADA Intelligent Dental Marketing will provide a wide range of affordable and effective and marketing services and products that dentists have identified as a need to help them retain and attract patients, said William Zimmermann, ADA BEI chief executive officer.

"We are very excited about this new joint venture with IDM. It will enable us to help meet the needs of ADA members with a high-quality offering," said Zimmerman. "We are confident that the combination of the ADA and IDM will be invaluable to dentists by assisting them in their practice-building efforts."

Current ADA Intelligent Dental Marketing offerings include direct mail, Web site development, logo and identity development, and the TreatmentPRO case presentation system.

"We look forward to continuing to demonstrate to the dental community the compelling nature of our marketing solutions and our ability to help improve new patient flow and profitability within a dental practice," said Joel Harris, chief executive officer and co-founder, Intelligent Dental Marketing.

Honors

Sonia Molina, DMD, MPH, has been selected as a "Woman of Distinction" by California Speaker of the Assembly Fabián Núñez for his 46th Assembly District.

The award recognizes women for their outstanding service, demonstrating courage and providing leadership in improving the quality of life for the residents in their community.

A native of El Salvador, Molina immigrated to Los Angeles, graduated from the Harvard School of Dental Medicine, and received her endodontics degree from the University of California, Los Angeles, School of Dentistry. Her professional affiliations include the California Dental Board, the Los Angeles Dental Society, the Latin American Dental Association, and the Women's Dental Society. Additionally, she is also a House delegate and legislative representative for the California Dental Association, commissioner for the Los Angeles Health Authority Commission, and a board member of the Salvadoran American Leadership and Educational Fund.

Sonia Molina, DMD, MPH, (right) with Speaker Fabián Núñez.

Kenneth F. Hinds, DDS, Laguna Niguel, has been elected secretary of the Academy of Osseointegration. He operates a private practice emphasizing comprehensive, esthetic, and implant dentistry, and is a visiting lecturer (restorative dentistry) at the University of California, Los Angeles. Hinds earned his dental degree from the University of Southern California School of Dentistry.

New Automix Delivery System for Insure →

Cosmedent adds a new dual-cure automix syringe to its top-rated Insure Universal Cementation System line. Insure Clear Lite and Simulcure are now available in a convenient automix syringe. This quick and easy-to-use delivery system is a real time-saver as it eliminates hand mixing and messy cleanups. Insure Lite Automix is ideal for inlays, onlays, and crowns. For more information, go to www.cosmedent.com or call 800-621-6729.

Proposals Requested for Improving Children's Oral Health

The ADA Foundation has issued a request for proposals to help improve children's oral health under its Samuel Harris Fund for Children's Dental Health. The deadline to submit a proposal is July 17.

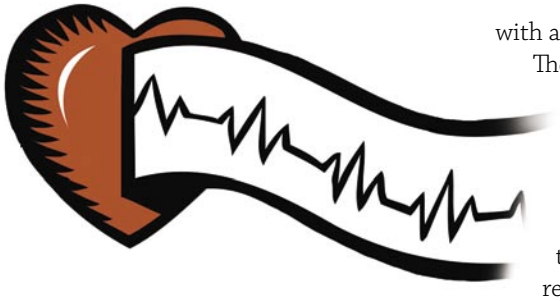
Proposals from community-based, not-for-profit organizations in the United States or its territories will be considered. Examples of qualified oral health promotions include:

- Dental health education conducted at schools, health fairs, and social agencies via mobile dental clinics or outreach programs;
- Dental health education programs in conjunction with preventive programs such as fluoride and dental sealant application programs;
- Oral health and nutrition education materials designed for parents and/or dental professionals;
- Instruction in the proper use of oral care products; and
- Development of public service announcements to increase awareness of, and appreciation for, proper childhood oral care.

More than $300,000 was awarded to 73 programs throughout the country last year.

For more information, contact the ADA Foundation at 312-440-2547 or e-mail adaf@ada.org.

HEART PATIENTS, CONTINUED FROM 387



with a history of infective endocarditis.

The American Heart Association's latest guidelines were published in its scientific journal, *Circulation*, in April. The guidelines apply to a range of medical and dental procedures. The ADA has published those portions of the new guidelines relevant to dentistry on its Web site, www.ada.org/goto/endocarditis, and in this month's issue of the *Journal of the American Dental Association*.

For decades, the American Heart Association recommended that patients with certain heart conditions take antibiotics shortly before dental treatment. This was done with the belief that antibiotics would prevent infective endocarditis, previously referred to as bacterial endocarditis. Infective endocarditis is an infection of the heart's inner lining or valves, which results when bacteria enter the bloodstream and travel to the heart. Bacteria are normally found in various sites of the body, including on the skin and in the mouth.

The ADA participated in the development of the new guidelines and has approved those portions relevant to dentistry. The guidelines are also endorsed by the Infectious Diseases Society of America and by the Pediatric Infectious Diseases Society.

The new guidelines are based on a growing body of scientific evidence that shows the risks of taking preventive antibiotics outweigh the benefits for most patients. The risks include adverse reactions to antibiotics that range from mild to potentially severe and, in rare cases, death. Inappropriate use of antibiotics can also lead to the development of drug-resistant bacteria.

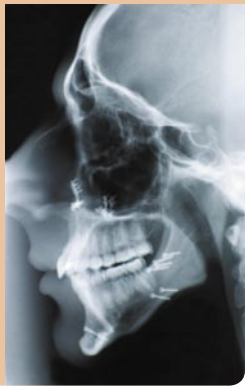
Scientists also found no compelling evidence that taking antibiotics prior to a dental procedure prevents infective endocarditis in patients who are at risk of developing a heart infection. Their hearts are already often exposed to bacteria from the mouth, which can enter their bloodstream during basic daily activities such as brushing or flossing.

Literature Review Now Available on Bone Augmentation Techniques

The American Academy of Periodontology has released its commissioned literature review on bone augmentation techniques.

The review, "Bone Augmentation Techniques," appears in the March issue of the *Journal of Periodontology* and focuses on different techniques that can be used to reconstruct lost alveolar bone before or after tooth extraction, or placement of a dental implant.

"With dental implants being the preferred method of tooth replacement, practitioners are beginning to see more complex cases where bone augmentation is needed," said Preston D. Miller, Jr., DDS, president of the American Academy of Periodontology. "This comprehensive review outlines the situations in which bone augmentation may be needed and offers a great review of different techniques and their proven outcomes."



Explained Brad McAllister, DDS, review author, "It is always important to use an evidence-based approach when developing a treatment plan. … As new bone augmentation techniques utilizing molecular, cellular, and genetic tissue engineering technologies become more mainstream, it will be important for practitioners to keep an eye to the latest research on these techniques."

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Articaine versus Lidocaine: The Author Responds

In the April issue of the *Journal of the California Dental Association*, a letter to the editor, written by Dr. James Dower, was published.[1] The major premise of this letter is that the paper "Local Anesthetics: Dentistry's Most Important Drugs, Clinical Update 2006" appears to be written to promote the use of articaine and nullify the reports of paresthesia rates up to 20x that of lidocaine.[1,2] I would like to address a number of his comments.[3]

In the first paragraph in the articaine section of the paper I stated: "Little to no evidence-based medicine exists demonstrating any superiority of articaine over other available local anesthetics. ... Included in these admittedly anecdotal reports are claims that articaine (1) works faster; (2) works "better"; (3) "I don't miss as often"; and (4) "gets patients numb when other local anesthetics fail." Dr. Dower interprets this as being "written to promote the use of articaine." Let the reader judge. I disagree.

Dr. Dower continued by stating that I ignore the majority of clinical studies that demonstrate that the "efficacy of lidocaine for local anesthesia is unsurpassed" and "only listed a clinical trial where articaine had better results than lidocaine."[1] The reality is somewhat different. I wrote: "Since its introduction in Germany in the early 1970s, articaine has been compared in double-blinded, randomized, controlled clinical trials to each of the other available local anesthetics. To date, only one clinical trial has demonstrated any superiority of articaine to any other local anesthetic.[4] I went on to describe the phase 3, double-blinded, randomized clinical trials mandated by the U.S. Food and Drug Administration requiring that a new drug be evaluated for its safety and efficacy.[5,6] Twenty-nine dental schools in two countries, the United States and the United Kingdom, were involved. Articaine, the new drug, was compared to the "standard of comparison" lidocaine. Results of the studies, in which 1,325 patients were treated, found that "there were no clinically significant differences between articaine and lidocaine, and concluded that articaine was a 'safe and effective local anesthetic' for dentistry."[5,6]

THERE IS ABSOLUTELY no scientific evidence available to support the claim that articaine is associated with a greater incidence of paresthesia.

Lidocaine represented the first amide local anesthetic used in medicine and dentistry, entering the dental market in 1948. It still represents the most used local anesthetic in medicine and dentistry worldwide. Articaine, introduced in Germany in 1973 and the United States in 2000, has rapidly become either the most-used local anesthetic (e.g., Germany, Canada, and Denmark) or second most popular (United States).[7]

These are the scientific facts about the clinical trials regarding articaine and its subsequent use in dentistry.

The second, and major, theme of Dr. Dower's letter is his claim that "the author(s) endeavors to nullify the global findings that the drug is associated with very significant increases in paresthesias with mandibular block injections."[1]

There is absolutely no scientific evidence available to support the claim that articaine is associated with a greater incidence of paresthesia (or stated more correctly, is more neurotoxic) than other local anesthetics.

This claim is addressed in considerable depth in the original paper.[2] The interested reader is also referred to the available statistical analysis of articaine found in the new drug application, NDA, which was reviewed and approved by the FDA.[8]

Yes, there is "buzz" in our profession today about the possibility of 4 percent drugs, specifically articaine, being associated with increased incidences of paresthesia. But as previously stated, there exists absolutely no scientific evidence demonstrating that this may be true. All reports and papers are anecdotal in nature, yet have taken on a life of their own with several insurance carriers and other organizations suggesting that 4 percent local anesthetics be avoided in the mandibular nerve block."[9,10]

An example of the hysteria being generated by some is illustrated by the "Letter of Concern" sent to thousands of U.S. dentists in September 2006 by Emery & Webb, Inc., in which it was stated: "We at Emery & Webb/Ace USA have had a recent increase in anesthetic-related malpractice incidents. They are essentially related to the administration of articaine (Septocaine) as an anesthetic ... we have noticed an increase in reversible and, in some cases, nonreversible paresthesias. These have been mostly limited to the accomplishment of a mandibular inferior alveolar nerve block. ... We are writing you to alert you to these events in hopes that you will not fall victim to one of these incidents."[11]

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LETTER, CONTINUED FROM 240

The letter goes on to recommend: "Limit the use of articaine to infiltration and PDL anesthesia."

Concerned and informed dentists and dental educators across the United States communicated their concerns about the veracity of these statements with Emery & Webb resulting in a "Notice of Retraction" (Oct. 31, 2006) reading, in part: '"Unfortunately, we at Emery & Webb discovered upon further review, and subsequent to the mailings, that both documents contained certain inaccuracies and an alarmist tone, which was not warranted."[12] "Emery & Webb has not noted an increase in malpractice claims or lawsuits in connection with articaine as referred to in the e-mails and further, it is not aware of any increase in claims at ACE USA. It should be made clear that Emery & Webb has not conducted any scientific investigation, sampling, testing, or other investigation of the articaine anesthetic, and has no independent knowledge or data which would restrict the use of the product."

In a paper published in the *International Journal of Oral and Maxillofacial Surgery* in 2006, Hillerup and Jensen reported on 52 cases of paresthesia reported in Denmark.[13] Of these, 42 involved only the lingual nerve, yet, the authors concluded by stating "Until factual information is available, a preference of other formulations to articaine 4 percent may be justified, especially for mandibular block analgesia" despite having made this important comment, "Thus, there is an urgent need for further studies focused on the problem of neurotoxicity of local analgesics with specific focus on articaine 4 percent."

Responding to an inquiry concerning the Danish paresthesia paper, the European Union's Pharmacovigilance Working Party re-evaluated the incidence of adverse effects, especially the hypothesis that nerve injuries (paresthesias, sensory impairment) may be caused by local anesthetics used in relation with dental care and, specifically, that articaine was responsible for an increased risk of nerve injuries compared with other local anesthetics.[14] Their report included international experiences from 57 countries, estimating the annual number of patients treated with articaine at approximately 100 million.[14] The European Union's investigation reviewed experimental studies and clinical trials with healthy volunteers and patients, and included all local anesthetics used in dentistry, not only articaine.

THIS REPORT from the European Union's Pharmacovigilance Working Party represents the most careful scientific analysis of the perceived "problem" of articaine-related paresthesia to date.

The report concluded that the "safety profile of the drug (articaine) has not significantly evolved since its initial launch (1998). Thus, no medical evidence exists to prohibit the use of articaine according to the current guidelines listed in the summary of product characteristics" (the drug package insert).

This report from the European Union's Pharmacovigilance Working Party represents the most careful scientific analysis of the perceived "problem" of articaine-related paresthesia to date.

In a recent review of local anesthetic associated paresthesia, Missika and Khoury stated that "a clear causal relationship has not been established in the literature between the anesthetic agent and neurological complications such as paresthesia."[15]

In the April *Journal of the California Dental Association*, coincidentally, the same issue in which Dr. Dower's letter appeared, Dr. Pogrel reported on the first well-documented review of local anesthetic associated paresthesia.[16] His review included examination of all patients (n = 57), questioning of their dentists, and a review of their medical records. He concluded that "we do not see a disproportionate nerve involvement for articaine."

Thus, I remain firmly of the opinion that given the present level of scientific evidence or, more accurately, the lack thereof, linking 4 percent local anesthetics with an increased risk of neurotoxicity, it seems that advisories to dentists from agencies suggesting it might be prudent to avoid the use of articaine in mandibular nerve blocks is unjustified at this time.

To further debunk the statement that the primary focus of my paper was "to promote the use of articaine and nullify the reports of paresthesia rates up to 20x that of lidocaine," I offer the concluding statement in my paper: "However, as in all dental treatments and therapies, it is you, the doctor, who must make the ultimate decision as to whether or not to use a 4 percent local anesthetic, such as articaine, in mandibular block anesthesia. This decision should follow assessment of the benefits to be accrued from use of the drug versus the potential risks associated with its administration. Only when, in the mind of the doctor, the benefit clearly outweighs the risk should the drug be administered."

"Remember, that prior to the introduction of articaine into the United States in 2000, local anesthesia in dentistry was not a problem. Successful pain control can be achieved with other drugs."[2]

To the readers of the *Journal* I would recommend that you carefully evaluate the quality of science presented in publications, including peer-reviewed journals such as the *Journal*, or in statements made by continuing education "gurus" before making decisions on whether or not to use a drug, or any other dental material or procedure.

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ORAL PATHOLOGY

The Diagnosis and Management of Patients with a Dry, Burning or Painful Mouth

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Among the most difficult clinical problems dentists are faced with are those related to patients who complain of a dry, painful, or burning mouth. These problems are especially difficult because they are frequently chronic and have resisted various treatment modalities. Further, they may be complicated by systemic illness, medications, previous dental care, habits, hypersensitivity, and other variables that require individual assessment and modification. Therefore, developing a diagnosis and a satisfactory treatment regimen often requires a painstaking approach to history, physical examination, and diagnostic testing. All of this is daunting for a busy general dentist or even a specialist, but it can be done, and when done properly may result in a most satisfying result for patient and doctor alike.

In this issue of the *Journal*, four outstanding oral and maxillofacial pathologists contribute their expertise in the diagnosis and management of several conditions, which, when taken together, account for the most probable causes of a patient complaint of a dry, painful, and/or burning mouth. Dr. John S. McDonald discusses a rational and methodical approach to diagnosis of a patient with a chief complaint of burning mouth. No group of patients can present a more difficult challenge, so Dr. McDonald's wisdom and experience in this area should be carefully regarded and retained.

The symptom of a burning mouth can be a common denominator for more specific conditions. Among these are oral lichen planus and oral lichenoid reactions. These diseases may have quite similar clinical characteristics and can sometimes be confused microscopically. Yet, they have separate and distinct etiologies, treatments and prognoses. Dr. John R. Kalmar discusses oral mucosal lichen planus while Dr. John Wright addresses the compound problem of oral lichenoid reactions and hypersensitivity. Lastly, Dr. Cynthia L. Kleinegger rounds out the topic by carefully discussing xerostomia in its varied clinical presentation, complex etiologies, diagnosis, and management.

All told, the depth of knowledge and experience manifested by these excellent clinicians in such a difficult area of clinical practice makes this issue of the *Journal* one which should be carefully read and saved for future reference.

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The Burning Mouth

JOHN S. MCDONALD, DDS, MS

ABSTRACT Burning in the mouth in and of itself is not all that uncommon. It may result from a variety of local or generalized oral mucosal disorders, or may be secondary to referred phenomena from other locations. Primary burning mouth syndrome, on the other hand, is relatively uncommon. Burning mouth syndrome is an idiopathic pain disorder, which appears to be neuropathic in origin. Thoughts on management of secondary and particularly primary burning mouth syndrome are discussed.

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Burning mouth syndrome is one of the more enigmatic oral pain complaints that present in clinical practice. Although not a terribly common clinical complaint in the average private practice, it is in fact frequently encountered in an oral and maxillofacial pathology or oral medicine clinical practice. It is a chronic dysesthetic orofacial pain condition known under a variety of names such as stomatodynia, stomatopyrosis, glossodynia, and glossopyrosis along with a number of other names. It frequently presents as a symptom complex, which may also include xerostomia and/or dysgeusia. It has been grouped along with other idiopathic orofacial pain disorders and other idiopathic pain conditions with a primary complaint of pain that is disproportionate to the evident clinical findings.[1-4]

Problematic is the fact that burning mouth syndrome is characterized by symptoms that can result from a number of local or systemic disorders, some of which can be readily diagnosed while other times no obvious etiology can be found. From a clinicopathologic standpoint two forms of burning mouth syndrome will be discussed: primary burning mouth syndrome, the idiopathic form of the disorder, and secondary burning mouth syndrome, which results from local or systemic disorders that may respond to appropriately directed therapy.[5]

Burning mouth syndrome is usually described as a burning quality, which may vary in severity from aggravating or annoying to agonizing as if the affected area had been scalded or had touched a hot griddle. Tingling and numbness are other features that may be experienced. Affected areas are most commonly said to be the dorsum of the tongue, primarily the anterior tip and lateral borders; the mucosal surfaces of the lips, most often the lower lip; the palate, primarily the anterior

FIGURE 1 Evaluation of the patient with BMS-like symptoms.

hard palate; and gingival tissues. These symptoms, which may occur individually or in combination, are usually bilateral but may be unilateral.[6] Occasionally, the patient will complain the entire mouth burns. The complaint of burning and numbness may be noted concurrently.

The estimated prevalence rate of burning mouth in the general adult population varies widely from 0.7 percent in the U.S. adult civilian population to 15 percent in a Finnish adult population.[7,8] Of note, however, is that on examination of the patients in the Finnish study, half were said to have some clinically observable oral mucosal lesion or candidosis. Burning mouth syndrome affects women much more commonly than men, primarily peri- and postmenopausal females.

Classification

As previously indicated, burning in the mouth can take on two different forms: a primary or idiopathic form of the disease for which there is no evident clinical explanation, and a secondary form derived from the presence of local or systemic factors. In evaluating a patient for burning mouth syndrome, the first and probably most important step is obtaining an accurate clinical history (**FIGURE 1**). Not just that "Doctor, my mouth burns," but the specific areas to which the pain is localized, the pattern of the complaint as to episodic or continuous, time(s) of the day it may be better or worse, if there is such a pattern, sleep pattern (is the sleep disturbed by pain), and the presence or absence of other complaints such as dry mouth or altered taste. A thorough clinical history of the chief complaint then needs to be taken, including a description of the initial presentation, how it has changed over time, a chronological listing of other practitioners who have evaluated the patient for the condition, the various therapies that have been employed, tests that have been done, and the results of any previous tests or therapies. From this the practitioner may then begin to put together in his or her mind a provisional differential diagnosis for the problem. An in-depth health history interview is necessary that includes a history of all medications the patient is taking, previous medications they have taken, the presence of known allergies to any drugs, medications, mouthrinses, dentifrices, chewing gums, cosmetics, etc. A social history is also important and should be geared particularly at present and past psychosocial factors going on in the patient's life. The patient should be questioned as to the use of tobacco, alcohol, caffeine, and the use of any recreational drugs. After all of

TABLE 1

Local factors that may result in burning mouth syndrome-like symptoms

Fissured tongue
Geographic tongue
Hairy tongue
Foliate papillitis
Trauma ■ Physical, i.e., traumatic ulceration, denture irritation, etc. ■ Chemical ■ Thermal, i.e., pizza burn, reverse smoking, etc.
Aphthous stomatitis (RAS) ■ Herpetiform aphthae ■ Aphthae minor ■ Aphthae major (Sutton's disease, PMNR)
Herpes simplex virus infections (HSV) ■ Recurrent labial or intraoral HSV infection ■ Herpes zoster (varicella zoster virus) infection
Oral premalignancy or malignancy

this, a thorough examination of the oral cavity, oropharynx, and adjacent and associated structures should be performed. These are all necessary preliminary steps in determining a diagnosis whether it is suspected the complaint is primary or secondary burning mouth syndrome.

SECONDARY CAUSES OF BURNING MOUTH SYNDROME

Burning in the mouth may arise from a variety of disorders, which may be local or generalized in nature. **TABLE 1** lists many of the local factors that may result in burning mouth syndrome-like symptoms. **TABLE 2** provides an outline of more generalized appearing disorders that may produce burning mouth syndrome-like symptoms. Many of the disorders listed in these two tables may be fairly obvious clinically while others require a differential diagnosis from even a skilled diagnostician and, ultimately, diagnostic testing.

While the list of potential causes for burning in the mouth listed in these tables is long, and even a bit ponderous, a few are much more commonly encountered as secondary causes of burning mouth syndrome than others. For example, fissured and geographic tongues are commonly encountered conditions that may produce a complaint of burning of the tongue. Although far more often asymptomatic, they can produce pain in some individuals, most commonly associated with eating or drinking, particularly spicy foods or liquids. Oral candidiasis is also a frequent cause of burning symptoms in the mouth. Predisposing factors for candidiasis include xerostomia, possibly in combination with gastroesophageal reflux disease, which is either undiagnosed or poorly controlled, and separate or concomitant antibiotic therapy.

If an oral candida infection is suspected and does not respond to initial

TABLE 2

More generalized disorders that may produce burning mouth syndrome-like symptoms

Physical, chemical, drug-induced
- Parafunctional habits
- Contact stomatitis/allergy, i.e., cinnamon allergy, allergy to dentifrices, mouthwashes, cosmetics, denture base allergy, amalgam, gold or other metals
- Fixed drug eruption
- Radiation mucositis and its long-term sequellae
- Chemotherapy

Infection
- Candidiasis, pseudomembranous, acute and chronic erythematous candidiasis including median rhomboid glossitis
- Coliform bacteria, Fusospirochetal infections, Helicobacter pylori
- Gonococcal infection
- HIV infection
- HSV, primary or recurrent (particularly in immunocompromised individuals), VZV infections
- ANUG

Nutritional disorders
- Vitamin B-1, B-2, B-6
- Vitamin B-12
- Iron deficiency
- Folate deficiency

Dermatologic disorders
- Lichen planus, particularly atrophic lichen planus
- Erythema multiforme
- Benign mucous membranes (cicatricial) pemphigoid
- Pemphigus vulgaris
- Lupus erythematosus

Systemic diseases
- Diabetes mellitus
- Uremia
- Crohn's disease
- Blood dyscrasias

Referred pain from other disorders
- Myofascial pain dysfunction, orofacial and paracervical neck musculature, i.e., CN V and cervical nerve distributions
- Gastroesophageal reflux disease
- Trigeminal and glossopharyngeal neuralgia
- Pain referred from tissues in the CN V, CN IX, CN X and cervical nerve distributions

Burning mouth syndrome-like symptoms secondary to disorders of the central nervous system
- Multiple sclerosis
- Parkinson's disease
- Tardive dyskinesia
- Mass lesions involving the brain and CNS

conservative therapies, such as the use of a nystatin rinse or clotrimazole troches, a fungal culture also ordering a mean inhibitory concentration will confirm the diagnosis and provide information on the sensitivity of the fungal organism to other antifungal agents the practitioner may want to utilize. Although xerostomia is often described as part of the symptom complex of idiopathic burning mouth syndrome, its presence alone may produce oral burning. Salivary flow rate can be measured objectively using a modified Schirmer test to confirm the subjective complaint of xerostomia.[9,10] This is important as some patients with a complaint of xerostomia will have objectively measured normal rates of salivary flow.

PRIMARY OR IDIOPATHIC BURNING MOUTH SYNDROME

Although the cause or causes of the primary or idiopathic form of burning mouth syndrome are not truly known, there is an increasing body of evidence pointing to a neuropathic origin. Specific changes in peripheral or central nervous system sensory function and not a psychogenic origin were suggested as early as 1987 by Grushka et al.[11] Ship et al. felt it was likely that burning mouth syndrome reflected a neuropathic condition involving the peripheral and/or central nervous systems.[12] Alterations in sensory function pointing to a possible neuropathic etiology of burning mouth syndrome were also demonstrated by Svensson et al. who reported sensory thresholds as being significantly higher and ratios between pain and sensory thresholds significantly lower on all tested regions.[13] Some objective evidence for a neuropathic etiology for burning mouth syndrome was demonstrated using the eye blink reflex evoked by stimulation of the trigeminal cutaneous nerve branches.[14] Forssell et al. used quantitative sensory testing in addition to the blink reflex to study possible neural mechanisms of burning mouth syndrome pain.[15] They reported abnormal findings in 89 percent of the patients studied by both blink reflex and quantitative sensory testing.

The occurrence of burning mouth syndrome has long been associated with a patient's psychological status. The readers are referred to a paper by Lamb et al. that cited 19 references prior to their 1988 paper addressing the psychological aspects of burning mouth syndrome with the earliest reference dating to 1920.[16] In their critical review of the literature on burning mouth syndrome, Scala et al. pointed out there is little or tenuous evidence to support this view, stating that scientific evidence has generally not supported this belief with the reverse being the case.

THERE IS AN increasing body of evidence pointing to a neuropathic origin.

They interpreted their results as evidence for a generalized, possibly multilevel, abnormality in the processing of somatosensory information in burning mouth syndrome. Of the patients tested with quantitative sensory testing, 76 percent demonstrated abnormal findings in one or more sensory thresholds indicating small fiber dysfunction. More recently, a study was performed comparing superficial biopsies from the lateral aspects of the anterior two-thirds of the tongue in patients with burning mouth syndrome for at least six months with healthy controls.[17] Patients with burning mouth syndrome had a significantly lower density of epithelial fibers than controls with epithelial and subpapillary nerve fibers showing diffuse morphological changes that were thought to reflect axonal degeneration. They concluded that burning mouth syndrome was caused by small-fiber sensory neuropathy. Granot and Nagler hypothesized that the mechanism for development of the idiopathic sensory disturbances of burning mouth syndrome, dysgeusia, and xerostomia is based on a regional neuropathy.[18] They suggested that a regional small fiber neuropathy might affect salivary secretion and oral sensation or alternatively that a primary idiopathic salivary dysfunction might result in sensory neural dysfunction at the receptor level by changing the oral environment.

Burning mouth syndrome, or as also termed in the literature as stomatodynia, has been included in the taxonomy of idiopathic orofacial pain disorders, which includes also atypical odontalgia, atypical facial pain, and facial arthromyalgia.[2-4] It has been proposed these conditions may correspond to a single disease expressed in different tissues characterized by similar or common mechanisms.[2-4] In their recent review of idiopathic pain disorders, Diatchenko et al. suggested that two major contributors to the predilection to develop common idiopathic pain disorders are enhanced pain sensitivity or amplification and psychological distress with genetic variants mediating the activity of physiologic pathways that underlie both of these domains.[1] They believe that as it is highly likely that idiopathic pain disorders share underlying pathophysiological mechanisms and that

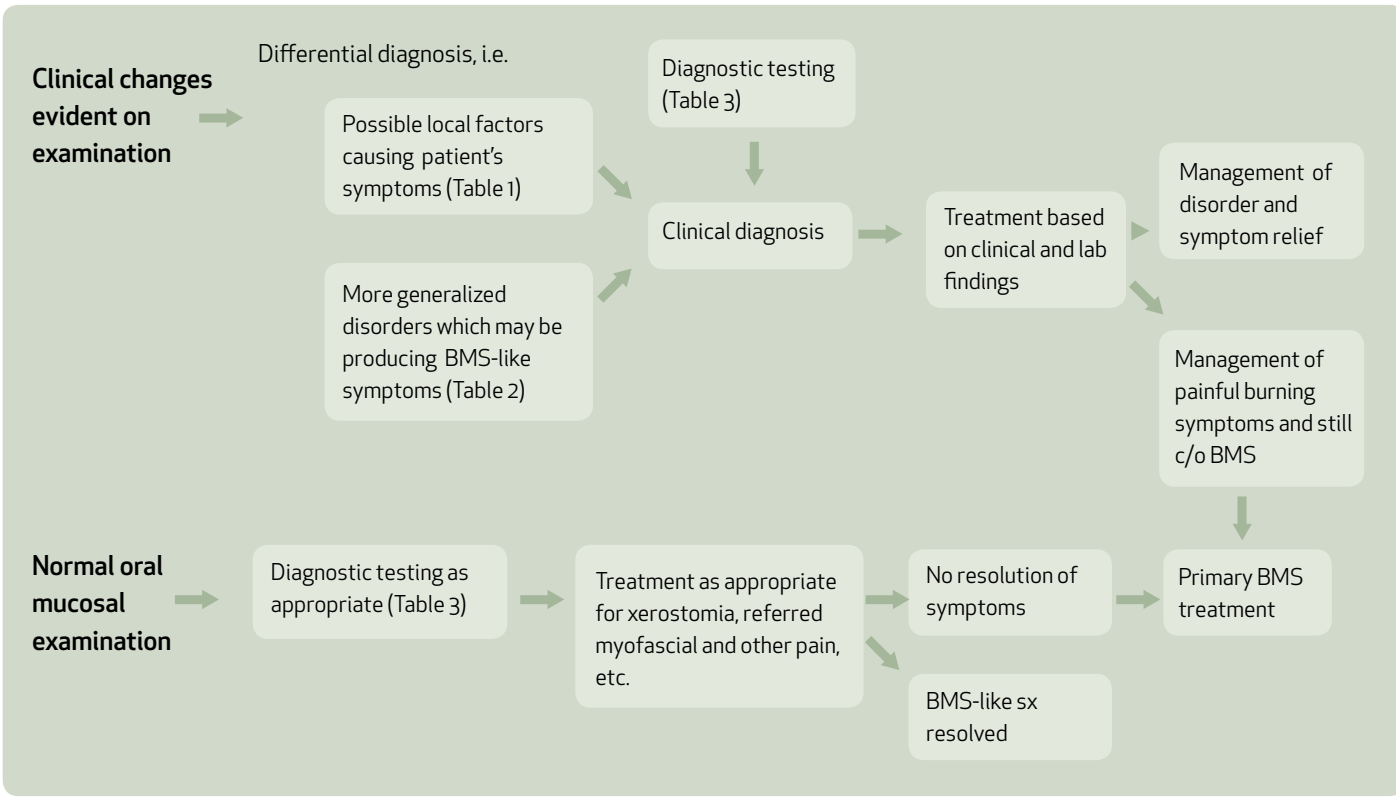

FIGURE 2. Clinical examination.

the same functional genetic variants will often come into play in mediating other types of idiopathic pain disorders.[1,19]

Again, it should be remembered that before entertaining a diagnosis of primary or idiopathic burning mouth syndrome, all secondary factors must be ruled out. Also, it is important to remember there may be apparent secondary factors that overlie true idiopathic burning mouth syndrome that, when resolved, reveal the underlying primary condition.

Treatment

The first step in treating a patient with burning mouth syndrome is an accurate diagnosis. **FIGURE 1** provides an outline for the initial work-up of any chronic pain patient and is a necessary first step in evaluating the patient with a burning mouth. **FIGURE 2** provides an algorithm for the differential diagnosis of the patient's condition. The first step is determining if there are clinical changes evident, either local or generalized, that may produce a burning sensation in the mouth. **TABLE 1** provides a list of local factors that may result in burning mouth syndrome-like symptoms while **TABLE 2** lists more generalized disorders that may also produce these symptoms.

As previously indicated, in some cases where clinical changes are evident, the diagnosis will be fairly obvious. Other times, the cause of the disorder is far less clear-cut, particularly in the case of contact stomatitis or allergy, nutritional and systemic disorders, and when the pain is referred from another site. In many cases, diagnostic testing as outlined in **TABLE 3** is necessary to either confirm the provisional clinical diagnosis or to provide the diagnosis when the underlying disorder is unknown. Without a clear and concise plan to the diagnostic process, the correct diagnosis may not be considered and the clinician is left to take an incorrect approach at managing the disorder. In the case of burning mouth syndrome secondary to other factors and after establishing a clinical diagnosis, the appropriate treatment is pursued, aimed at resolution of the symptoms. In some cases, it will become apparent the evident clinical disorder was overlying and not related to the burning symptoms, and the diagnosis of primary burning mouth syndrome is then made.

When the oral mucosal examination is normal, then diagnostic testing may still be appropriate. This should include, first and foremost, salivary testing, particularly measuring salivary flow rate. A quick, easy, and reliable test in this regard is the modified Schirmer test.[9,10] Salivary pH testing may also be employed. In some patients with a complaint of oral burning and objectively established xerostomia, improving hydration by increasing water intake to normal levels, generally considered to be 64-fluid ounces qd, and decreasing or eliminating caffeine will significantly or com-

TABLE 3

Diagnostic testing for burning mouth syndrome-like symptoms

Salivary testing, including but not limited to ■ Objective testing of salivary flow rate (modified Schirmer test) ■ Salivary pH testing
Fungal and possibly bacterial or viral cultures
Laboratory studies ■ CBCD ■ B-1, B-2, B-6, B-12 levels ■ Blood glucose followed by a fasting glucose tolerance test if high
Oral biopsy with immunofluorescence testing in the case that one or more of the mucocutaneous disorders are suspected
Allergy testing
Clinical assessment ■ Cranial nerve examination ■ Musculoskeletal examination ■ Gastrointestinal consult to R/O GERD if suspected
CT or MRI scans as necessary, depending on the differential diagnosis and clinical findings

pletely mollify the patient's complaint.

In the end, after potential specific etiologies for burning in the mouth with normal clinical evaluations have been ruled out, the clinician is faced with an enigmatic situation. First and foremost, the patient needs reassurance that the tissues are clinically healthy and their condition is not related to any form of cancer or other serious disease. The patient needs reassurance that their condition is not imaginary, i.e., it is not just in their head. The practitioner needs to express cautious optimism and discuss that while there is no one effective treatment regimen, there are a variety of potential treatment protocols that may be employed. The patient needs to understand the chronic nature of their condition with a goal of successful management.

As there is no definitive therapy for primary or idiopathic burning mouth syndrome, the concept of symptomatic therapy should be embraced. Because of the chronic nature of this condition and the fact that recent literature points to the neuropathic nature of this disorder, pharmacologic therapy, either topical or systemic, may naturally be considered. As in assessing other chronic pain complaints, a 10 cm visual analog scale, can be used to assess the severity of the patients pain (0 = no pain; 10 = the worst pain imaginable) and their overall improvement (0 = no improvement; 10 = complete resolution of symptoms). Severity of pain should be assessed at the time of the initial examination, i.e., asking the patient to rate their pain at it worst and at its usual level, and determine if there is a daily pattern to their pain. The patient's pain should also be rated at the start of therapy and assessed at follow-up intervals.

It is also appropriate to employ the concept of escalation of therapy, i.e., topical versus systemic therapy, using the alternative with the fewest side effects first. With a possible neuropathic etiology in mind, the use of topical capsaicin should be considered. It has been shown that topical application of capsaicin can partially or completely mollify the pain in primary burning mouth syndrome.[20]

The effect of capsaicin on the pain in burning mouth syndrome will depend on the underlying pathophysiological mechanism of the process involved in the patient's pain. The effect of the capsaicin is to desensitize the c-fiber nociceptors, thus exciting significant effects on painful disorders arising from these afferents.[21] The authors in this study proposed that capsaicin would be most suitable for treating neuropathic pain symptoms characterized by exaggerated heat pain sensation. Their data also reflected a resistance of A-delta nociceptors to capsaicin. From this it may be inferred that the lack of consistent results from capsaicin therapy points out the heterogeneity of the underlying neuronal mechanisms producing the patient's pain.[22]

For a capsaicin rinse, a Tabasco sauce/water mixture using one part Tabasco sauce (approximately 300 ppm capsaicin and two parts water is rinsed around the mouth for approximately 15 seconds and then expectorated.[23] A 1:3 ratio may be used if the recommended concentration is too objectionable. This procedure is repeated every two to three waking hours for three to four days. If relief is achieved, the interval between rinses may be increased according to the length of pain relief is achieved. A pilot study using systemic capsaicin has also been reported.[24] It was shown to be therapeutically effective for short-term management of burning mouth syndrome, although major gastrointestinal side effects were noted.

Topical or systemic uses of a variety of medications have been considered as treatment for primary burning mouth syndrome. Woda et al. studied the effect of local application of clonazepam for patients with burning mouth syndrome.[25] The subjects were to suck on between one-quarter and one-half of a 0.5 mg

tablet, taking care not to swallow, and expectorating after three minutes. Following their proposed treatment protocol, one-third of patients had experienced total relief of pain, one-third had partial improvement, and one-third had no improvement. The average outcome of all patients' improvement was 52 percent.

Zakrzewska et al. undertook a Cochrane review of interventions for burning mouth syndrome.[26] Nine trials were included in their review. They reported on three interventions as demonstrating a reduction in burning mouth syndrome symptoms: alpha-lipoic acid (thioctic acid), clonazepam, and cognitive behavioral therapy. Two randomly controlled trials were performed comparing alpha-lipoic acid to cellulose starch controls as efficacy against burning mouth syndrome. In the first study, a 20-day trial using 600 mg per day followed by 200 mg per day for 10 days, significant improvement was said to be noted in up to two-thirds of patients receiving alpha-lipoic acid compared to about 15 percent of those using a placebo.[27] In the second study, 200 mg of alpha-lipoic acid was used three times a day for 60 days, again using a cellulose starch pill for control.[28] A statistically significant improvement was noted in 97 percent of patients who used alpha-lipoic acid over two months compared to 40 percent for the placebo group. Follow-up at 12 months showed improvement was maintained completely in 73 percent of patients compared to controls where all patients had noted some deterioration in their improvement. A trial was then undertaken comparing alpha-lipoic acid to bethanacol, lactoperoxidase, or placebo (xylitol in distilled water).[29]

Gremeau-Richard et al. studied the effect of topical clonazepam on burning mouth syndrome.[30] This study demonstrated that sucking a 1 mg tablet of clonazepam three times daily for 14 days resulted in an improvement of pain symptoms in two-thirds of the included patients. They also noted the treatment was not effective in all patients and concluded that like other idiopathic pain, burning mouth syndrome probably results from several mechanisms and topical administration of clonazepam may only be effective when the primary mechanisms are peripheral. Finally, it has been pointed out that in cases of burning mouth syndrome resistant to other therapies, a psychological origin should be considered. Bergdahl et al. in the last study accepted in this review, reported on the effect of cognitive therapy in patients with resistant burning mouth syndrome after odontological and medical treatments were employed.[31] Odontological treatment consisted of diseases diagnosed on estimation of saliva secretion rate and candidal investigation. The control group of patients received attention/placebo therapy. Of the patients receiving cognitive therapy, 27 percent of patients were "cured" during a six-month follow-up period and a reduced intensity of symptoms was noted in almost all of the patients. The attention/placebo group did not show any decrease in intensity of burning mouth syndrome. The authors concluded that if burning mouth syndrome remains after the patient had been appropriately treated from a dental and medical standpoint, their pain was most likely of psychological origin.

IN CASES OF burning mouth syndrome resistant to other therapies, a psychological origin should be considered.

To reiterate, treatment of primary burning mouth syndrome is usually directed at symptomatic relief. As there is evidence it is by and large a neuropathic pain disorder, then, if topical therapies are ineffectual, systemic medications aimed at other neuropathic conditions may be considered. These may include the use of benzodiazepines such as clonazepam as already mentioned, tricyclic antidepressants such as amitriptyline or nortriptyline (side effects of xerostomia may preclude their use), and anticonvulsants such as gabapentin used alone or in combination.[32]

Grushka et al. reported on the use of clonazepam taken orally in escalating doses on burning mouth syndrome.[33] Their dosages ranged from 0.25 mg at sleep to a total dose of 2 mg per day taken in three divided doses. Of the 30 patients in their study, 13 (43 percent) reported at least some improvement and continued to use the medication; eight (27 percent) had noted at least some improvement but had chosen to discontinue its use because of side effects or for other reasons; and nine (30 percent) had reported no benefit from using clonazepam. More recently, Grushka et al. reported a retrospective study using "polypharmacy" consisting of various combinations of low-dose anticonvulsant medications in combination for management of burning mouth syndrome.[34] Medications used included clonazepam, gabapentin, baclofen, and lamotrigine in various combinations. The average maximum pain rating reported was 60.6 prior to treatment, with the average maximum pain rating said to be 32.1 after therapy.

Finally, the rate of spontaneous

remission of burning mouth syndrome has been studied. Grushka et al. reported at least partial remission in nearly 50 percent of patients with burning mouth syndrome with seven years of onset of their symptoms.[34] They also reported a change from constant to cyclic burning during the same time period for some patients still experiencing some pain. More recently, Sardella et al. in a retrospective study looked into the spontaneous remission rate of patients with this disorder.[35] Their data showed complete spontaneous remission in 3 percent of patients within five years after the onset of burning mouth syndrome. They speculated the wide range in remission rate between patients in the previously cited study and their study might be explained through a larger follow-up period in the earlier study.

Conclusion

Burning in the mouth is a most nefarious complaint that may be a challenge to diagnose and, dependent on the ultimate diagnosis, treatment may be even more enigmatic. The first step in management is in arriving at an accurate diagnosis and determining if the burning is secondary to local factors or more generalized disorders as listed in **TABLES 1** and **2**. Initial therapy includes addressing any of these factors that may be present to attempt to mollify the burning. Even in the presence of secondary factors, the primary form may be uncovered.

In its primary form, there are a variety of potential treatment options that may be employed as discussed in this paper. Throughout, the patient must be treated with reassurance and great care using, in the context of its benign but chronic nature, escalation of therapy combined with the principle of doing no harm. Treatment requires almost as much patience on the clinician's part as on the patient's often with less-than-hoped-for results for both parties. ■■■■

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Diagnosis and Management of Oral Lichen Planus

JOHN R. KALMAR, DMD, PHD

ABSTRACT Oral lichen planus is a relatively common mucosal autoimmune disease that may be initially detected and diagnosed in the dental office. For asymptomatic patients, clinical characteristics including a generalized involvement of the oral mucosa are often sufficient to establish a working diagnosis. Symptomatic presentations of oral lichen planus, however, can mimic a variety of other potentially serious conditions and scalpel biopsy is recommended to determine an accurate diagnosis. Treatment strategies for the symptomatic patient are discussed.

AUTHOR

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Lichen planus is a chronic, immunologically mediated condition first described as a disease of the skin that can also affect mucosal surfaces, including those that line the oral cavity. Oral lichen planus has been estimated to affect from 0.1 percent to 4 percent of the population.[1] Interestingly, while more than one-third of patients with cutaneous lichen planus will reportedly have oral involvement, only about 15 percent of patients with oral lichen planus ever develop skin lesions.[2,3] Although the etiology is unknown, most authorities agree it represents a form of autoimmune disease in which dysregulation of T lymphocyte function results in damage to, or destruction of, basal cells of the surface epithelium.[4,5]

The relatively high prevalence of oral lichen planus makes it likely that virtually every dentist who treats adult patients will encounter this condition. The fact that the mucosal changes in oral lichen planus can occasionally mimic oral precancerous lesions or other significant conditions makes it important for all dentists to be aware of its clinical features. Practitioners should also know the additional steps that can be taken to confirm a clinical diagnosis of oral lichen planus, including incisional biopsy for routine histopathologic evaluation and direct immunofluorescent examination. Finally, as some patients with oral lichen planus are symptomatic and desire treatment, clinicians should be aware of current management strategies.

Clinical Presentations of Oral Lichen Planus

Since a significant percentage of oral lichen planus patients will also have cutaneous involvement, skin lesions can be used to help support the clinical or working diagnosis. The classic skin lesions of lichen planus have been described as purple, polygonal, pruritic papules that are usually found in small clusters on the flexor aspects of the extremities (**FIGURE 1**).

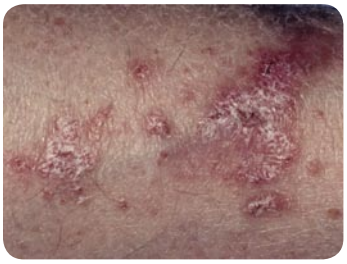


FIGURE 1. Erythematous cutaneous papules and plaques of lichen planus on the lower leg of a female patient. *(Courtesy of Doug D. Damm, DDS, Lexington, Ky.)*

Fine, interlacing whitish lines known as Wickham's striae can occasionally be observed on the surface or periphery of the flat-topped papules and plaques. Dystrophic nail changes develop in some patients and females can have vulvo-vaginal involvement that may be symptomatic.[3,6]

Oral lichen planus usually develops in middle-aged adults, and women are affected more often then men. It is quite uncommon in childhood, although affected patients often have associated cutaneous disease and a predisposition among children of Asian descent has been reported.[7-9] Several variants of oral lichen planus have been described, however, two major forms are recognized: reticular and erosive.

RETICULAR

Reticular oral lichen planus represents the most common clinical pattern of this disease. The word reticular refers to the net-like or lacy pattern of interlacing keratotic lines (also denoted as Wickham's striae) that is characteristic of oral lichen planus. Reticular oral lichen planus is usually asymptomatic and bilateral involvement of the posterior aspects of the buccal mucosa that may extend into the vestibules is virtually pathognomonic for this condition (**FIGURES 2A-B, FIGURE 3**). Some cases are predominated by small keratotic papules that may be interconnected by thin keratotic striae. With involvement of the dorsal aspect of the tongue, a lace-like quality may not be present and lesional tissue will often appear as single or multiple keratotic plaques with loss or coalescence of the filiform papillae (**FIGURE 4**).

The lesions of oral lichen planus tend to wax and wane in their clinical severity without any treatment. Many patients report nothing more than a vague awareness of tissue "roughness." Concomitant involvement of other mucosal sites, most often the gingivae, the dorsal and lateral aspects of the tongue and vermilion border, may be noted.

EROSIVE

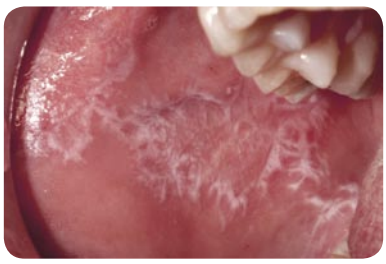
The erosive form of oral lichen planus is much less common than the reticular form and differs in that most patients report symptoms with their oral lesions. Affected mucosa usually presents as an area of atrophy and erythema with variable zones of central erosion or ulceration and a peripheral border of fine, radiating keratotic striae. Affected sites are similar to those seen with reticular oral lichen planus and it is not uncommon to see both forms of the disease manifest in the same patient (**FIGURES 5A-B**). Occasionally, lesional changes are relatively confined to the attached gingival or alveolar mucosa, producing a clinical pattern that has been termed "desquamative gingivitis" (**FIGURE 6**). Rarely, the erosive aspect of the disease is so severe that epithelial separation may occur and vesicle or bulla formation may be observed clinically.

As with the reticular form, erosive oral lichen planus tends to have a bilateral or multifocal mucosal presentation with periods of remission and exacerbation rather than steadily progressing course (**FIGURES 5A-B**). Symptoms can vary from mild discomfort to severe pain that interferes with normal mastication or speaking.

Diagnosis: Clinical

Even without a history or evidence of cutaneous lichen planus, reticular oral lichen planus with bilateral involvement of the buccal mucosa has such a characteristic pattern that clinical diagnosis alone is usually sufficient. It should be emphasized that even in "classic" cases, periodic patient re-evaluation would be warranted to detect any progressive tissue changes, and the patient should be advised to consider tissue biopsy in order to provide a firm, baseline histopathologic diagnosis.

The finding of a single area or an isolated mucosal lesion with a reticular or lichenoid appearance is not characteristic of oral lichen planus and is



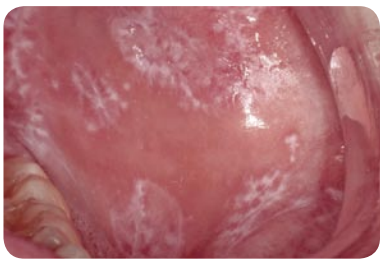


FIGURE 2. Reticular oral lichen planus affecting right (a) and left (b) buccal mucosa. Note scattered small whitish papules and interconnected keratotic striations *(Wickham's striae)*.

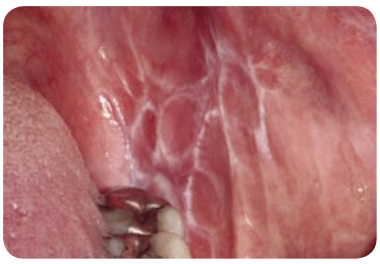


FIGURE 3. Reticular oral lichen planus of the posterior right buccal mucosa with well-defined lace-like pattern.

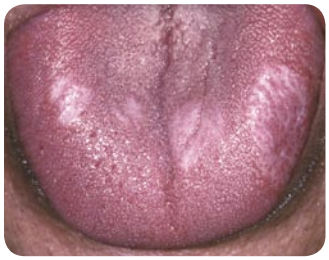


FIGURE 4. Reticular oral lichen planus of the dorsal tongue. Keratotic plaques can be seen on patient's right side and mid-dorsum while fine, internal striations are visible within the lesion on the left dorsolateral aspect.

more suggestive of conditions such as a lichenoid drug or contact hypersensitivity reactions (see related manuscript in this issue). To complicate matters, some oral lichen planus patients with generalized mucosal involvement may also have similar lesions localized to areas in direct contact with amalgam restorations (lichenoid amalgam reaction).[10] Careful history taking and clinical correlation may be helpful in assigning a working diagnosis and a biopsy is usually warranted. In presentations limited to keratotic plaque(s) of the dorsal, and especially dorsolateral, tongue, a biopsy would be mandatory to exclude the possibility of dysplasia (precancerous epithelial change) or squamous cell carcinoma.

For patients with suspected erosive oral lichen planus, the differential diagnosis can be quite broad. A biopsy should be recommended to support or confirm the clinician's working diagnosis and exclude other and potentially more serious conditions. Depending upon the precise clinical setting, the differential could include epithelial dysplasia, squamous cell carcinoma, lichenoid reactions to drug, foreign body, amalgam, or other contact agents (such as artificial cinnamon flavoring), lupus erythematosus and chronic ulcerative stomatitis.[11,12] In patients with a history of bone marrow transplantation, the complication known as graft versus host disease can closely mimic the clinical features of oral lichen planus.[12]

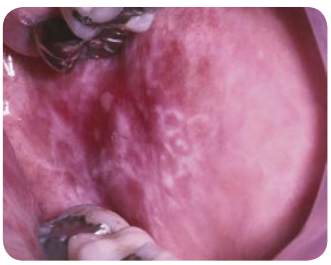
If a desquamative gingivitis-like presentation predominates, conditions such as lichenoid foreign body reaction (possibly to dental prophylaxis materials), mucous membrane (cicatricial) pemphigoid, chronic ulcerative stomatitis and pemphigus vulgaris would need to be considered. Therefore, a biopsy should be considered for any case of persistent desquamative gingivitis that does not respond to conservative local hygiene measures. Submission of tissue for both routine and direct immunofluorescent examination will permit the exclusion or confirmation of a specific autoimmune disease, such as pemphigus vulgaris, as quickly as possible.

It should also be noted that oral lichen planus, reticular and erosive forms alike, may become complicated by the acquisition of superficial fungal microorganisms, usually *Candida albicans*. In most cases, this probably represents an opportunistic infection since *Candida* consume keratin and this substance is readily available in the keratotic papules and striae produced by oral lichen planus.

Superimposed candidiasis may lead to mild "burning" discomfort of the affected mucosa, even in reticular oral lichen planus, and can further complicate the diagnosis by masking the classic net-like pattern of the keratotic striae. Cytologic or culture studies can aid in the management of these cases by providing positive identification of the microorganisms. Even without diagnostic tests, an empirical course of appropriate antifungal therapy (such as clotrimazole troches or fluconazole tablets) may unmask the characteristic clinical features of the underlying oral lichen planus and help reduce candidiasis-related symptoms.

Diagnosis: Routine Biopsy and Direct Immunofluorescence

The final diagnosis of oral lichen planus, especially in cases of erosive disease, often rests with a tissue biopsy of affected mucosa. Following appropriate local anesthesia, an elliptical wedge should be obtained that extends from lesional tissue into adjacent normal mucosa. Use of cautery methods is not recommended for this purpose due to artifactual changes they often induce within the specimen. In addition, erosive or ulcerated lesions must be handled gently to minimize the chance of peeling or splitting the surface epithelium from the underlying connective tissue, greatly degrading the diagnostic usefulness



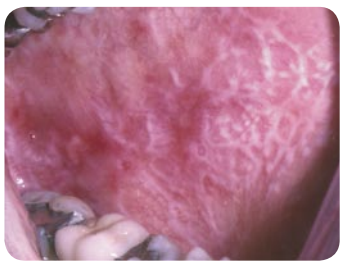


FIGURE 5. Erosive oral lichen planus affecting left buccal mucosa (a) and same area seven months later (b). Bilateral involvement was noted at both time periods and patient reported a waxing and waning course. *(Courtesy of Carl M, Allen, DDS, MS, Columbus, Ohio.)*

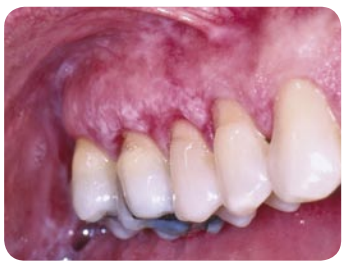


FIGURE 6. Erosive oral lichen planus presenting as desquamative gingivitis in the canine-molar region of the right maxilla. All quadrants were similarly affected.

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of the specimen. When it is important to exclude specific vesiculobullous conditions such as mucous membrane pemphigoid, a separate sample must be obtained for direct immunofluorescent examination because the routine formalin fixative interferes with direct immunofluorescent processing.

This can be accomplished with two separate biopsies, but can also be managed through careful planning and harvest of a single incisional specimen. Ideally, a "double-duty" biopsy should extend from just within the border of lesional tissue to several millimeters into normal-appearing mucosa. An overall length of 8 mm to 10 mm ensures adequate sampling for both studies. Once the tissue is removed, it can be carried to a table or sterile gauze and split across the short axis with a sharp scalpel. The "lesional" half of the specimen should be placed in formalin for routine histopathologic examination. The "normal" half can then be placed in Michel's solution, a special liquid medium designed for direct immunofluorescence.

Oral lichen planus has several characteristic histopathologic features, including hyperkeratosis, vacuolar degeneration of the basal cell layer and degenerating keratinocytes termed colloid or Civatte bodies. Rete ridges may be absent or elongated with a pointed or "saw-tooth" appearance. A band-like infiltrate of small lymphocytes is seen immediately subjacent to the epithelium, occasionally destroying the epithelial-connective tissue interface. Unfortunately, these features are not specific to oral lichen planus and can be seen in several other conditions, such as lichenoid amalgam reaction, lichenoid drug reaction, mucosal cinnamon reaction, lupus erythematosus, graft versus host disease, and chronic ulcerative stomatitis. As a result, oral lichen planus is a diagnosis that demands careful correlation of the clinical setting with the results of routine biopsy examination.

Many practitioners are familiar with oral vesiculo-bullous diseases like mucous membrane (cicatricial) pemphigoid or pemphigus vulgaris. In contrast, most dentists and physicians are unfamiliar with chronic ulcerative stomatitis, a specific mucocutaneous autoimmune disease first described in 1990 that can mimic the clinical features of oral lichen planus.[12-14] Chronic ulcerative stomatitis is associated with the development of circulating autoantibodies to a nuclear antigen in stratified squamous epithelium known as p63. For this reason, chronic ulcerative stomatitis has also been compared to both oral lichen planus and lupus erythematosus, another autoimmune disease that is characterized by the production of anti-nuclear antibodies.

ORAL LICHEN PLANUS is a diagnosis that demands careful correlation of the clinical setting with the results of routine biopsy examination.

The majority of chronic ulcerative stomatitis patients have been older adult women, and some patients have also presented with erosive or bullous skin lesions. Intraorally, the most commonly affected site is the tongue, followed by the labial or buccal mucosa and gingiva.[14] Similar to erosive oral lichen planus, lesions appear as shallow, irregular ulcerations but peripheral keratotic striae, if present, are usually abbreviated or vaguely formed. Gingival involvement produces a clinical presentation of desquamative gingivitis.

Direct immunofluorescent testing of oral lichen planus specimens is similar to routine histopathologic examination in that the results can be suggestive of or consistent with the diagnosis of oral lichen planus, but they are not specific to oral lichen planus alone. Most lesions demonstrate an irregular linear band of fibrinogen deposition at the basement membrane zone, a feature shared with other forms of lichenoid mucositis (see related manuscript is this issue), graft versus host disease, lupus erythematosus and chronic ulcerative stomatitis. The distinguishing feature for chronic ulcerative stomatitis patient specimens is the additional finding of punctuate (dot-like), intranuclear deposits of IgG in the basilar cells of the surface stratified squamous epithelium.

Patients with chronic ulcerative stomatitis have been shown to respond best to treatment with hydroxychloroquine (Plaquenil) and are usually resistant to initial treatment measures recommended for oral lichen planus patients. This provides a persuasive rationale for obtaining both routine and direct immunofluorescent examination in all cases of erosive oral lichen planus. Although chronic ulcerative stomatitis has been described as an uncommon or even rare autoimmune disease, the number of cases masquerading as oral lichen planus could be substantial due to similarities in their clinical and even routine histopathological features. Patients should be advised that the benefit of a correct diagnosis (including exclusion of other forms of autoimmune disease like pemphigoid or pemphigus) and early initiation of effective treatment for the patient more than justifies the added cost of baseline direct immunofluorescent testing.

Management

Unlike cutaneous lichen planus, which is usually self-limited and spontaneously resolves within one to two years,

oral lichen planus is more commonly a chronic condition that often persists for multiple years, if not decades.[11,17] As with most forms of autoimmune disease, there is no cure for oral lichen planus. The primary goals of treatment are to reduce the length and severity of disease during periods of activity and, if possible, increase the periods of disease quiescence.

As mentioned, patients with asymptomatic reticular oral lichen planus do not require therapeutic intervention. Conservative measures to improve oral hygiene and minimize local tissue irritation may help reduce periods of notable tissue "roughness." These could include decreasing the interval between professional dental prophylaxis (every four months instead of every six months), recommending the use of bland toothpaste or mouthrinse formulas and smoothing/repairing sharp or broken teeth, restorations, or prostheses. In the case of superimposed candidiasis, antifungal therapy would be appropriate to relieve associated symptoms.

Treatment of symptomatic erosive oral lichen planus is largely based on the use of topical corticosteroids, especially the higher potency formulations such as fluocinonide (Lidex) 0.05 percent, augmented betamethasone (Diprolene) 0.05 percent and clobetasol (Temovate) 0.05 percent. Gel formulations are preferable to creams or ointments as the latter are more hydrophobic and adhere poorly to the normally moist oral mucosa. Patients should be advised to apply the corticosteroid gel in a thin film directly to the lesional tissue four to five times daily. Emphasis should be placed on the use of tiny amounts of the gel multiple times a day rather than large amounts less often. After symptoms subside, patients can simply stop applying the gel without tapering the dosing schedule. Since oral lichen planus has a natural waxing/waning course, patients should be instructed to re-institute their topical therapy at full strength whenever symptoms return. Dentists and hygienists should also encourage patients to improve or maintain excellent oral hygiene measures as this step leads to decreased disease activity, with or without topical corticosteroid treatment.[16,18]

In addition, it is important to inform the patient that while this treatment has not been approved in the United States by the Food and Drug Administration, it is considered a well-documented "off-label" use for formulations originally marketed to treat skin conditions such as cutaneous lichen planus. More than three decades of scientific studies have shown these agents to be safe and efficacious in managing patients with oral lichen planus, yet no pharmaceutical company has pursued the costly process required by the FDA to receive formal approval for this application. It can be pointed out that significant complications from topical corticosteroid treatment of oral lichen planus have been rare, and only in cases where the patient substantially and improperly overused their medication. On the other hand, clinicians should also be aware that oral candidiasis is not an uncommon minor complication of topical corticosteroid therapy. These opportunistic infections (probably resulting from mild local immunosuppression), however, are readily resolved with concomitant antifungal therapy.

PATIENTS WITH asymptomatic reticular oral lichen planus do not require therapeutic intervention.

For patients with widespread symptomatic disease or who have limited manual dexterity, possibly secondary to underlying conditions such as arthritis, aqueous corticosteroid solutions may be an effective alternative to gel formulations. Options include dexamethasone (Decadron) elixir, 0.5 mg/5 ml and prednisolone (Prelone) syrup, 15 mg/5 ml. Patients should be instructed to swish the solution over affected areas for a minute or so and expectorate without rinsing after meals and before bedtime.

A variety of other medications have been used in treating oral lichen planus, including other topical immunosuppressives (tacrolimus, retinoids, cyclosporine), systemic agents (corticosteroids, retinoids, dapsone, azathioprine, griseofulvin, thalidomide, levamisole), and PUVA (oral psoralen and low-dose ultraviolet A) or laser therapy.[1,6,11,12,16] Although encouraging results have been reported, these agents are typically more expensive than topical corticosteroid therapy without clear evidence of superior efficacy. Currently, their use should be reserved for erosive oral lichen planus patients who prove recalcitrant to topical corticosteroid treatment and prescribed under the guidance of a dental (i.e., an oral and maxillofacial pathologist) or medical specialist, i.e., a dermatologist.

Does Oral Lichen Planus Represent a Premalignant Condition?

Numerous studies have addressed this important question; however, a definitive answer remains elusive.[11,16,19] Evidence from some reports indicates that patients with oral lichen planus, particularly those with erosive or atrophic forms, have an increased risk for the development of oral squamous cell carcinoma. Others have suggested that case reports or case series

of oral lichen planus that have undergone "malignant transformation" probably represent cases of oral epithelial dysplasia (precancerous change) that were misdiagnosed (clinically, microscopically or both) as oral lichen planus. In their recent review, Lodi et al. pointed out that oral lichen planus could be confused, both clinically and microscopically, with the condition known as proliferative verrucous leukoplakia.[16] Patients with proliferative verrucous leukoplakia may present with multiple leukoplakic areas throughout the oral cavity. Lesions of proliferative verrucous leukoplakia are considered precancerous with a significant rate of malignant transformation.

Obviously, the distinction between oral lichen planus and premalignant lesions is critical. For this reason, oral biopsy specimens should be interpreted by oral and maxillofacial pathologists, who are specifically trained in both the microscopic and clinical diagnosis of mouth diseases. With their experience in clinicopathologic correlation, oral and maxillofacial pathologists are uniquely suited to provide an accurate diagnosis for these challenging cases and, if needed, to assist in patient management or follow-up.

Science has known for years that cancer is essentially a genetic disease that results from nonlethal damage to cellular DNA. Different patterns of damage can be seen in different forms of cancer and several chromosomal sites have been recognized as important to the development of epithelial dysplasia and oral squamous cell carcinoma. To date, the only molecular studies to address the issue of DNA damage in oral lichen planus have been presented by Zhang et al. using comparative genetic analysis of biopsy material to detect evidence of allelic loss or loss of heterozygosity at three different chromosomal sites related to oral squamous cell carcinoma.[20] Analysis of multiple examples of different oral mucosal lesions, including cases of oral lichen planus, benign reactive hyperplasia, various degrees of dysplasia and oral squamous cell carcinoma was performed. Among the oral lichen planus specimens, evidence of loss of heterozygosity was lower than that for reactive hyperplasia (6 percent versus 14 percent) and was significantly lower in comparison to mild, moderate, or severe dysplasia/carcinoma-in-situ (40 percent, 46 percent, and 81 percent, respectively) as well as oral squamous cell carcinoma (91 percent). The follow-up study examined dysplastic lesions that mimicked oral lichen planus under the microscope (so-called lichenoid dysplasia) and found high levels of loss of heterozygosity in these cases that were essentially identical to dysplastic lesions lacking a resemblance to oral lichen planus.[21]

ORAL AND MAXILLOFACIAL pathologists are uniquely suited to provide an accurate diagnosis for these challenging cases

Confirmation of these results by other scientists is needed. It is possible that DNA damage occurs in oral lichen planus, but not in areas of the chromosomes that would have been detected by the panel of probes used by Zhang and co-authors. Overall, however, their molecular findings would argue that oral lichen planus is probably not a premalignant condition. The problem, particularly with erosive oral lichen planus, is that lesional tissue can occasionally resemble areas of erythroplakia, a clinical presentation that is suspicious for precancerous or cancerous change. As mentioned previously, baseline biopsy with direct immunofluorescent is recommended in all cases of erosive oral lichen planus to establish the diagnosis. Subsequently, any lesional tissue that appears to worsen progressively despite appropriate therapy should be viewed with suspicion and undergo biopsy (or re-biopsy) as soon as possible. Oral lichen planus may not be a premalignant condition, but neither does it preclude a patient from developing a second disease, including oral cancer.

Conclusion

In patients with classic reticular oral lichen planus, the diagnosis can often be made on the basis of clinical features alone. Patients should be advised as to the chronic nature of their disease and its tendency to exhibit periods of activity that alternate with times of relative quiescence or remission. Biopsy confirmation of oral lichen planus should be considered, especially with symptomatic erosive disease, and the use of direct immunofluorescent is strongly recommended to exclude more specific forms of autoimmune disease. Most cases of oral lichen planus can be managed through the use of topical corticosteroids and good oral hygiene measures. While the most current molecular evidence does not suggest oral lichen planus to be a precancerous condition, clinicians are advised to closely monitor their oral lichen planus patients for any intraoral lesion that does not respond to normal therapeutic measures. Regardless of a previous diagnosis of oral lichen planus, tissue biopsy and histopathologic evaluation should always be recommended for any persistent or progressive area of mucosal abnormality. ■■■■

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Diagnosis and Management of Oral Lichenoid Reactions

JOHN WRIGHT, DDS, MS

ABSTRACT Lichen planus is one of the most common mucocutaneous conditions seen in dental practice. A variety of other conditions known as lichenoid reactions can simulate lichen planus either clinically or histologically. This paper will discuss the more common lichenoid reactions seen in clinical practice and review the diagnosis and management of these conditions.

AUTHOR

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Lichen planus is a well-known mucocutaneous disorder with well-defined clinical and histologic features. Lesions are typically keratotic (white), often in a striate or reticular pattern (**FIGURE 1**) that may be mixed with erythema (redness) that commonly affects the buccal mucosae and gingivae. Microscopically, lichen planus is characterized by hyperkeratotic epithelium, often with angular rete ridges (saw tooth). There is a band-like infiltrate of small lymphocytes just subjacent to the epithelium and the basal keratinocytes usually show "liquefactive degeneration." (**FIGURE 2**).

It is now well-documented that other conditions can mimic lichen planus clinically and/or histologically, and this has led to the concept of lichenoid reaction. Dental restorative materials, especially amalgam, will produce lichenoid reaction as well as other allergens producing hypersensitivity reactions. Numerous systemic medications produce lichenoid drug reactions. Premalignant lesions may share clinical and/or histologic features with lichen planus. Other less common conditions producing lichenoid reactions are graft versus host disease, lupus erythematosis, and chronic ulcerative stomatitis.

Further complicating the controversy is the fact that in most instances, lichen planus and lichenoid reaction cannot be distinguished by their histologic features alone. One of the most common lichenoid reactions is amalgam-associated lichenoid reaction, and a recent study concluded the uncertainty of the diagnostic histological differences.[1]

It is also known that true lichen planus evolves through cycles of exacerbation and quiescence, and patients may actually have lichen planus, but depending on when and where the biopsy is taken, the histologic features may not confirm the diagnosis. Pathologists will use variable terminology such as "lichenoid mucositis," "chronic mucositis with lichenoid features," etc. This can be frustrating to the clinician and the patient since the patient is subjected to the time, discomfort, and expense of a surgical procedure that does not provide a definitive diagnosis. However, such a biopsy is useful because it does confirm and communicate that the patient has an inflammatory condition that has some but not all diagnostic

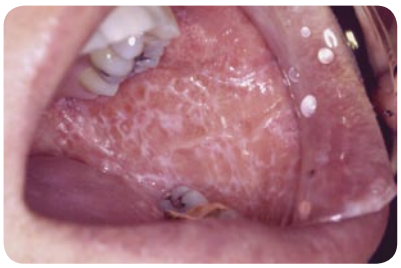


FIGURE 1. Characteristic clinical pattern of intraoral lichen planus.

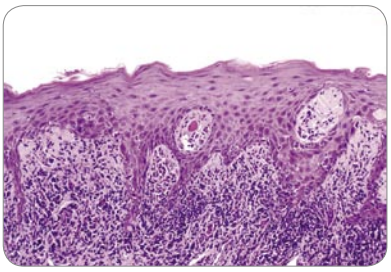


FIGURE 2. Characteristic histologic features of lichen planus showing angular rete ridges with basal cell degeneration and a band-like infiltrate of small lymphocytes.

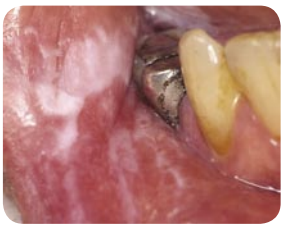


FIGURE 3. Lichenoid reaction to amalgam.

features of lichen planus. Such lesions may represent lichen planus or lichenoid reaction, and the distinction is often based on the clinical features of the condition.

When a patient presents with lichenoid tissue change clinically, a biopsy should be submitted to board-certified oral pathologists, who, because of their advanced training in diagnosing changes indigenous to the oral cavity, would have the greatest likelihood of rendering an accurate and definitive diagnosis.[2] It should be noted that distinguishing lichen planus from lichenoid reaction should not rely on histologic features alone, but should be based on clinical correlation to include history, physical findings, and, occasionally, patch testing.

Lichenoid Reactions to Amalgam

Amalgam is the most common dental restorative material to elicit a chronic mucosal reaction similar to lichen planus. Lesions can be plaque-like or striate and may be erosive (**FIGURE 3**). Lesions tend to be persistent and only affect the mucosa in contact with the amalgam, most commonly posterior buccal mucosa, lateral tongue, and, occasionally, gingiva, if the amalgam is placed into the sulcus.

The reaction most likely represents a hypersensitivity reaction, most commonly to mercury. However, depending on the study design, the percent of patients who test positive by patch testing ranges from 6 percent to almost 80 percent.[5-6] The better-designed studies show patch test reactivity to mercury or amalgam in the 70 percent range.[5,7] Lack of reactivity may be due to false negative skin reactions or hypersensitivity to constituents other than mercury. Sensitivity to other materials such as gold or palladium chloride is well-documented.[5] Dermatologists or allergists would be the appropriate referral for patch testing if one suspects amalgam sensitivity. However, because the materials must be placed in solution, they have a limited shelf life and are therefore not readily available unless the referral office routinely tests for dental materials. However, offices familiar with patch testing will know the commercially available sources for patch testing constituents. They can be instructed to purchase the appropriate testing material for amalgam which is included in **TABLE 1.**

Lichenoid reactions to amalgam should be considered for isolated, persistent mucosal reactions of soft tissue in direct contact with amalgam. Patch testing to mercury can be considered, but it is important to remember that while a positive reaction confirms the diagnosis of hypersensitivity, many patients are nonreactive and a negative patch test does not preclude a diagnosis of amalgam hypersensitivity. One can fabricate a full-coverage mouthguard, which should be worn as often as possible and re-evaluate the lesion for resolution. Otherwise, the amalgam should be removed and replaced with an alternative restoration. Resolution of lichenoid reactions to amalgam following replacement of the amalgam is also highly variable depending on study design and ranges from below 50 percent to 90 percent. Many studies also do not distinguish between resolution and significant improvement with amalgam removal. The best designed studies show a significant improvement/resolution to amalgam replacement in the 90 percent range.[5-8] Some studies show a better response rate in patients who are patch test positive.[8] For true lichenoid reaction to amalgam, only the amalgam contacting the lesion needs to be removed. Resolution can be prolonged, and one study showed a mean resolution of 6.4 months.[8]

TABLE 1

Amalgam Metals Patch Test

1%	Copper sulfate solution
5%	Cupric nitrate
1%	Stannous chloride
0.01%	Mercury chloride
0.1%	Silver nitrate
5%	Zinc sulfate
5%	Amalgam

Other Lichenoid Hypersensitivity Reactions

Besides amalgam, there are numerous other allergens capable of inducing hypersensitivity. One of the most common offenders seen in dental practice today is the flavoring agent cinnamon. Cinnamic aldehyde is widely distributed in various foods and drink, but reactions are more common with prolonged chronic use such as toothpaste, gum, or mints. Toothpaste hypersensitivity is seen most frequently with tartar control toothpaste and the most characteristic clinical presentation is desquamative gingivitis.[3]

The cinnamon in gum and mints

TABLE 2

Drugs Causing Lichenoid Reactions

Allopurinol
Amiphenazole
Amlodipine
Atorvastatin
Beta blockers
Bismuth
Captopril
Carbamazepine
Chloroquine
Chlorpropamide
Cyanamide
Dapsone
Enalapril
Erythromycin
Fenclofenac
Furosemide
Gabapentin (Neurontin)
Gold
Hydroxychloroquine
Interferon-Alpha-N1
Ketoconazole
Labetalol
Mepacrine
Mercury
Methyldopa
Metopromazine
NSAID
Oxyprenolol
Palladium
Para-amino salicylic acid
Penicillamine
Phenothiazines
Practolol
Propanolol
Pyrimethamine
Quinidine
Quinacrine
Sildenafil
Spironolactone
Streptomycin
Tetracycline
Thalidomide
Thiazides
Tolbutamide
Triprolidine
Zoloft

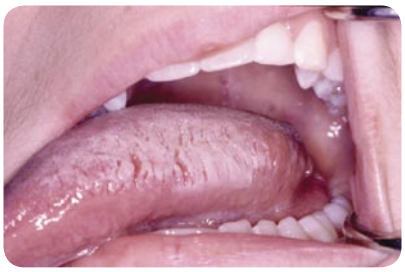
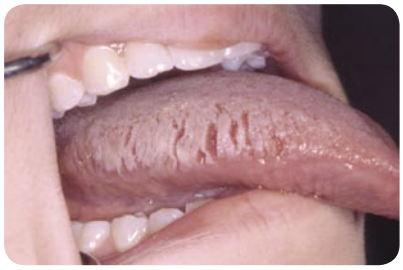


FIGURE 4.



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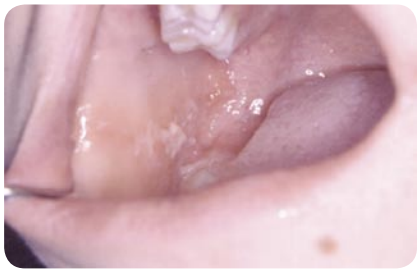

FIGURE 6.

FIGURES 4-6. Eighteen-year-old white female with reactions on her lateral tongue and cheek to cinnamon-flavored gum.

dissolves in saliva and typically produces lesions on the cheek and lateral tongue (**FIGURES 4-6**). In fact, any lesions discovered on the buccal mucosa and ipsilateral tongue is highly suggestive of hypersensitivity. Reactions to allergens can be Type I hypersensitivity (anaphylactoid reactions) or Type IV (delayed T-cell mediated hypersensitivity). These reactions can produce any combination of red and white tissue change. Patients are usually symptomatic and complain of sensitivity, burning, or mild pain.

Because hypersensitivity reactions are nonspecific in their clinical presentation, a biopsy is often performed. The pattern of inflammation in many hypersensitivity reactions is remarkably lichenoid. While not definitively diagnostic, deep extension of the inflammatory infiltrate, presence of occasional eosinophils or particularly deep perivascular inflammation is very suggestive of hypersensitivity.[4]

Withdrawal of the allergen produces resolution of the clinical reaction.

Lichenoid Drug Reaction

A variety of medications have been documented to produce oral mucosal reactions that are similar clinically and microscopically to lichen planus.[9-11] A full list of drugs producing lichenoid reactions is presented in **TABLE 2**, but the most common offenders are the nonsteroidal anti-inflammatory drugs, angiotension-converting enzyme inhibitors, and gold salts. Lichenoid drug reactions can be identical to lichen planus but have a tendency to produce more full thickness ulceration and more commonly affect sites not frequently affected by lichen planus, such as ventral tongue (**FIGURES 7-13**). Lichenoid drug reaction should be suspected when a new oral reaction follows the administration of a new medication. While there are some histologic and immunofluorescent findings that might suggest lichen planus or lichenoid drug reaction, these are not invariably present and biopsy often cannot distinguish between the two conditions.

The ultimate confirmation of lichenoid drug reaction is resolution of the condition following withdrawal of the drugs. Dentists should never withdraw a medication prescribed by another health care provider, but consultation with the prescriber will often lead to a trial of drug substitution.

Premalignant Lesions Producing Lichenoid Reactions

The most controversial and often confusing of the lichenoid lesions are the ones associated with premalignant lesions. As normal oral mucosa evolves to oral cancer, it progresses through a premalignant stage, which produces clinically detectable lesions. This tends to produce a color change to tissue, which can be a combination of white (leukoplakia) and/or red (erythroplakia). While these lesions

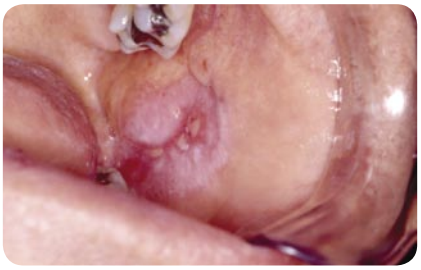

FIGURE 7.

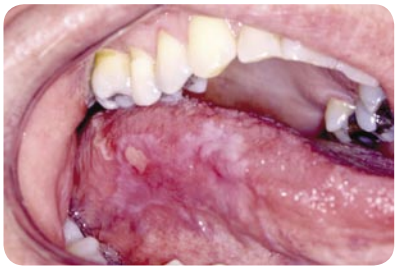

FIGURE 8.

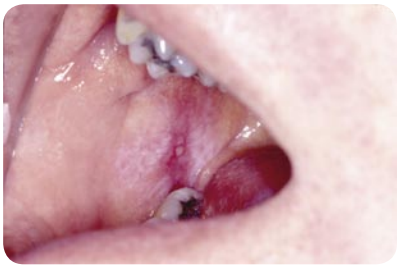

FIGURE 9.

FIGURES 7-9. Lichenoid drug reaction to azulfadine for the management of Crohn's disease.

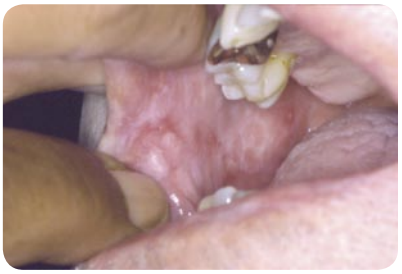

FIGURE 10. Lichenoid reaction to gold salts for the management of rheumatoid arthritis.

are almost never striate, the pattern of redness and whiteness will have similar features to lichen planus (**FIGURE 14**). At the cellular level, the morphological cellular changes that characterize premalignancy are known as epithelial dysplasia. The further from normal the dysplastic cell evolves, the more foreign, and therefore antigenic, it becomes. Microscopically, dysplastic cells often induce an immune response. The immune cells are found just under the epithelium, often in a "band-like pattern," which bears a remarkable resemblance to lichen planus (**FIGURE 15**).

It is common for pathologists to misinterpret the immune reaction to dysplasia as lichen planus. The resemblance microscopically between the body's immune reaction to dysplasia and true lichen planus has led some authorities to define the former as "lichenoid dysplasia."[12] Because lichenoid dysplasia has nothing to do with lichen planus, the author believes the use of the term adds only controversy and confusion to the debate on the malignant potential of lichen planus. However, it is imperative for pathologists who interpret oral mucosal biopsies to know that reactions to dysplasia will often show histologic features of lichen planus.

There are clearly premalignant lesions that occur orally that show some clinical as well as histological features of lichen planus. These are usually isolated white and/or red lesions that commonly affect the lateral or ventral tongue, or floor of the mouth. True lichen planus is almost always multifocal, and lateral/ventral tongue and floor of mouth are not common sites affected. If one were to biopsy a red and/or white isolated lesion of the lateral/ventral tongue or floor of mouth, and your pathologist renders a diagnosis of lichen planus, that diagnosis must be viewed with the greatest caution as it most likely represents misinterpretation of dysplasia.

Other Rare Lichenoid Reactions

Several other conditions show clinical and/or histologic similarity to lichen planus.

Twenty to 70 percent of patients who survive allogenic bone marrow or stem cell transplantation will develop graft versus host disease, which resembles lichen planus clinically and microscopically.[13-14] The clinical history of transplantation, however, should provide the definitive diagnosis.

Patients with lupus erythematosis also have oral mucosal involvement that clinically and histologically resembles lichen planus. The clinical lesions are usually red and white with characteristic short striae oriented perpendicularly in the margin. While the microscopic features are lichenoid, there are microscopic features to distinguish lupus from lichen planus.[15] Additionally, on direct immunofluorescent testing, lupus shows a deposition of immunoglobulin, usually IgG, at the basement membrane zone and lichen planus usually shows fibrinogen.[16]

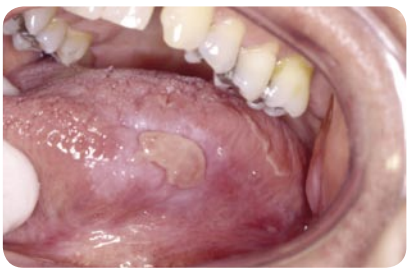

FIGURE 11.

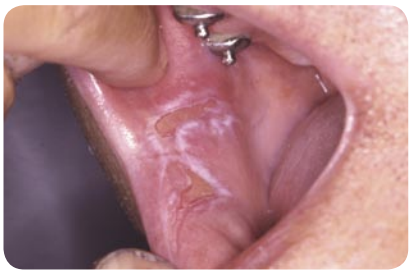

FIGURE 12.

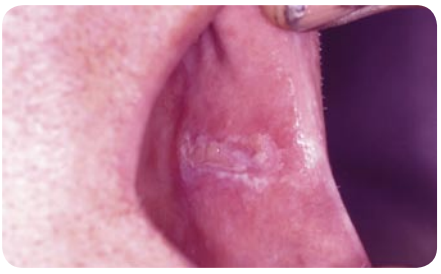

FIGURE 13.

FIGURES 11-13. Lichenoid reaction to allopurinol for the management of gout.

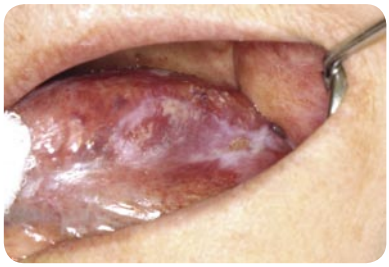

FIGURE 14. Premalignant lesion of lateral tongue with some features of lichen planus. Note lack of striae and the lack of multifocal involvement.

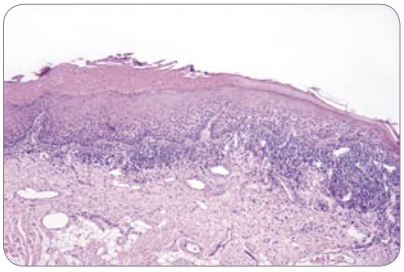

FIGURE 15. Photomicrograph depicting immune reaction to mildly dysplastic epithelium. Such features could easily be misinterpreted as lichen planus.

Lastly, chronic ulcerative stomatitis is a relatively new oral mucosal disorder that shows remarkably similar microscopic features to lichen planus. It can only be diagnosed by immunofluorescence because it has circulating as well as tissue bound antinuclear antibodies.[17] Chronic ulcerative stomatitis is exceedingly rare.

Summary

A variety of conditions show clinical and/or histologic features of lichen planus. There are several pathologic conditions seen orally that are not always diagnosed by histologic features alone, but by clinicopathologic correlation, suggesting that at times the clinical findings and medical/dental history are as important as the histologic features in determining the definitive diagnosis. The author believes this is true of lichen planus and lichenoid reactions. Biopsy, as a means of diagnosing lichen planus, remains the gold standard. Clinicians, at the same time, need to be aware that microscopic features that can definitively separate lichen planus from the various lichenoid reactions are not clearly defined and universally accepted. It is extremely important when performing a biopsy to provide the pathologist with the entire clinical history and accurate description of the clinical tissue change, including which site was chosen to biopsy. "Oral lesion" is not particularly helpful. It makes a significant difference to the pathologist to know that the lesion is a 1 cm white plaque on the ventral surface of the tongue versus a lesion from a patient with bilateral striate keratoses of the buccal mucosae with multifocal erosive and keratotic change of the gingiva.

Clinical correlation is extremely important. Because of the cyclical nature of lichen planus, it is not uncommon for the biopsy to fail to definitively confirm the diagnosis. However, the biopsy is invaluable if it can rule out other conditions such as pemphigus vulgaris, epithelial dysplasia, etc., and confirm the pathologic process is at least inflammatory. In such cases, it would be appropriate to use clinical judgment and, as long as the patient's clinical disease is compatible with lichen planus, the author would treat the patient for lichen planus. Conversely, if the biopsy is from a solitary white plaque on the lateral border of the tongue and a diagnosis of lichen planus is rendered, it is appropriate to question the pathologic diagnosis rendered and even ask for a second opinion by consultation.

The clinical features of this group of conditions are as important as the microscopic features. Any condition diagnosed as lichen planus, "lichenoid mucositis," "chronic mucositis with lichenoid features" etc. could represent any of the conditions discussed. If isolated to tissue contacting restorations, reaction to restorative materials, especially amalgam, should be considered. Patients should be questioned about oral allergens, particularly about products they use that may contain cinnamon. Any patient suspected of having lichen planus should be questioned about systemic medications. If a drug reaction is suspected, consultation with the prescriber can often lead to a trial of cessation or drug substitution. It is important to remember that premalignant lesions can sometimes share clinical and histological features with lichen planus. The clinician's experience with various oral lesions is invaluable in ensuring a dysplastic lesion is not confused with lichen planus. ■■■■

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Dental Management of Xerostomia — Opportunity, Expertise, Obligation

CYNTHIA L. KLEINEGGER, DDS, MS

ABSTRACT Xerostomia often goes undiagnosed and unmanaged. Failure to properly deal with this condition leaves patients at greater risk for other problems. Dentists have the opportunity, the expertise, and the obligation to identify and manage xerostomia and its complications. This article presents a practical approach to diagnosis and treatment of xerostomia and its complications.

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The term xerostomia comes from the Greek words "xeros" meaning dry and "stoma" meaning mouth. It is defined in Stedman's medical dictionary as "A dryness of the mouth, having varied etiology, resulting from diminished or arrested salivary secretions, or asialism."[1]

It is unfortunate the term has been commonly adopted to refer only to the perception of dry mouth. This has led to a difficulty in describing the epidemiology of xerostomia as some studies have been based only on the subjects' perceptions rather than on objective findings of dry mouth.[2]

The prevalence of xerostomia in population-based samples has been reported to vary from 0.9 percent to 64.8 percent.[2] Dry mouth is a more common complaint in the elderly. Its prevalence has been estimated to be 30 percent in those 65 years and older.[3] It is generally accepted this is mainly due to medical problems and their treatments rather than to any age-related physiologic changes.[3]

Etiology

Familiarity with the causes of xerostomia will help the clinician identify those patients at greatest risk for the problem. Most cases of xerostomia are the result of decreased saliva production or hyposalivation.[4] The most frequent cause of this is medication use.[5]

A wide variety of prescription and over-the-counter medications may cause hyposalivation.[6] The categories of medications most often associated with xerostomia are listed in **TABLE 1**. Many medications not included in these categories may also cause dry mouth, although less frequently.

Several medical conditions are known to affect the salivary glands and result in decreased saliva production (**TABLE 1**).[3,5] The most well known is Sjögren's disease, a chronic autoimmune disorder that is thought to affect more than 1 million people in the United States.[7] It is most common in middle-aged females. It may occur as a primary disorder, also known as Sicca syndrome, affecting only the salivary

and lacrimal glands. It more often occurs as a secondary disorder in association with other conditions such as rheumatoid arthritis or lupus erythematosus.

Radiation therapy for the management of head and neck cancer is a well-recognized cause of xerostomia.

TABLE 1

Causes of Xerostomia

Medications
- Anticholinergics
- Antiparkinsonian
- Antidepressants
- Antineoplastics
- Antipsychotics
- Antihypertensives
- Central nervous system stimulants
- Diuretics
- Systemic antihistamines

Medical Conditions
- Sjögren's disease
- Connective tissue disorders
- Diabetes mellitus
- Diabetes insipidus
- Sarcoidosis
- HIV-disease
- Hepatitis C virus infection
- Graft versus host disease
- Parkinson's disease
- Psychogenic disorders

Radiation Therapy

Other
- Inadequate fluid intake
- Excessive caffeine or alcohol use
- Vomiting and diarrhea
- Mouth breathing
- Decreased mastication
- Smoking

Developmental Abnormality
- Salivary gland aplasia

TABLE 2

Patient History in Evaluation for Xerostomia

Medical History	Past and present medical diagnoses Past and present medical treatments Undiagnosed symptoms
Medication History	Name of medication Dosage/change in dosage Reason for taking How long taken
Dental History	Types of dental treatment Extent of dental treatment Oral home care practices Dietary habits
Patient Perception of Oral Condition	Do you have a sticky, dry feeling in your mouth? Do you have trouble chewing, swallowing, tasting, or speaking? Do you have trouble wearing a denture? Do you have a sore or burning feeling in your mouth? Do you have bad breath?

Radiation therapy causes transient or permanent damage to salivary gland tissue, which results in decreased or, in some cases, loss of saliva production. The severity and duration of radiation-induced xerostomia depends on the type of therapy, the dosage, and the specific area being irradiated.[5]

In some patients, xerostomia may be a side effect of dehydration. Dehydration may be due to inadequate fluid intake. Elderly patients who suffer from incontinence may underhydrate in an attempt to self-manage the problem. Dehydration may also be due to excessive use of caffeine or alcohol, both of which act as diuretics resulting in a net fluid loss. Vomiting and diarrhea are other causes of fluid loss that may result in xerostomia. Mouth breathing also may cause xerostomia as a result of superficial dehydration of oral soft tissues.

Mastication normally plays an important role in stimulating saliva flow. Loss of this stimulus may be a cause of xerostomia in patients who are unable to masticate due to dental, neuromuscular, or other problems. Smoking commonly contributes to dry mouth. Although rare, developmental abnormalities such as salivary gland aplasia cause xerostomia.

Complications

The roles of saliva are numerous and varied.[6,8] They include cleansing, buffering, remineralizing, moisturizing, lubricating, and fighting infection. It follows that the more common complications of hyposalivation include dental caries, periodontal disease, candidiasis, mucositis, and halitosis.[8] Other complications such as difficulty chewing, swallowing, tasting, and wearing oral prostheses often interfere with eating, which decreases one's quality of life and may lead to nutritional deficiencies. With severe xerostomia even speaking may be difficult. In some cases, problems with speaking, eating, wearing prostheses, halitosis, or chronic mucosal pain may have significant negative psychosocial effects.

Diagnosis

Establishing a diagnosis of xerostomia is dependent on a thorough patient history and clinical evaluation.[9,10] The

possibility of xerostomia should be considered even for patients who do not complain of dry mouth. Furthermore, the possibility of xerostomia should be considered not only upon initial evaluation but on an ongoing basis for all patients.

Specific information obtained in the medical history may raise concern for xerostomia (**TABLE 2**). In addition to information about diagnosed medical conditions, a complete medical history should include discussion about any undiagnosed symptoms. A thorough medication history with identification of potentially xerogenic agents is an essential part of every patient work-up.

The patient's dental history may also raise concern for xerostomia (**TABLE 2**). For example, xerostomia should be seriously considered in the patient who has required extensive dental treatment in spite of a good oral hygiene practices and a diet low in sugar and refined carbohydrates.

Every patient interview should include questions to determine the patient's perception of their oral condition (**TABLE 2**). Positive responses to these questions indicate further evaluation for xerostomia.

A wide variety of clinical abnormalities may be associated with xerostomia (**TABLE 3**).[6,9-11] While most of the these findings are nonspecific, when combined with appropriate historical information they can be supportive of the diagnosis and some, such as dry mucosa and an inability to stimulate saliva flow, may even be considered diagnostic.

Although a thorough history and clinical examination may be sufficient to diagnose xerostomia in most patients, specific diagnostic evaluations such as the measurement of unstimulated and stimulated saliva flow, labial salivary gland biopsy, salivary gland imaging, or blood studies may be required to establish a definitive diagnosis or to determine the cause.[5,10,11]

TABLE 3

Clinical Findings in Xerostomia

Major Salivary Glands	Visible or palpable enlargement Tender to palpation Unable to express clear saliva on massage Purulent material expressed from ducts
Mucosa	Dry to touch Unable to stimulate saliva on manipulation Ulcers Atrophy Erythema White plaques Fissured tongue
Lips	Dry, chapped, or cracked
Dentition	High caries rate Heavy accumulation of plaque and debris
Other	Halitosis

Collection and measurement of whole saliva requires no specialized equipment and can be accomplished easily in the dental office.[10] Patients should be instructed to avoid all forms of oral stimulation such as eating, drinking, smoking, chewing gum, or performing oral hygiene for 90 minutes prior to testing. To collect whole saliva, the patient is seated upright with eyes open, head tilted forward, and the mouth positioned over a funnel that sits within a test tube. For unstimulated saliva, the patient is asked to swallow first and then allow saliva to passively flow over the lower lip into the funnel. At the end of the five-minute collection period, the patient is asked to spit any saliva remaining in the mouth into the funnel. Collection of stimulated whole saliva is similar; however, the patient is given a piece of gum to chew at approximately 45 chews per minute and asked to clear the mouth of saliva by spitting into the funnel every minute for five minutes. The flow rate for each sample is calculated in milliliters per minute by dividing the volume collected by 5.

It is generally considered that an unstimulated flow rate of 0.2 mL/minute or less and a chewing stimulated flow rate of 0.7 mL/minute or less are abnormally low.[10] To control for the affects of circadian rhythm on salivary flow, it is recommended that unstimulated whole saliva tests be performed at a fixed time point or in a limited time interval early in the morning.[12]

Imaging studies are not routinely performed to diagnose xerostomia; however, scintigraphy (scintiscanning) has been demonstrated to provide useful information about functional capabilities of major salivary glands.[13] The technique is based on uptake and secretion of ^{99m}Tc-technetium pertechnetate (Tc-99), a pure gamma emitting radionucleotide, which is injected intravenously. Tc-99 is taken up by the salivary glands and then secreted with the saliva into the oral cavity. Uptake and secretions phases are detected on scans and a grading scale is applied to assess secretory function. Demonstration of secretory function could be used to predict effectiveness of secretatogue therapy.

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Management

Management of a patient with xerostomia has many components. The ideal treatment plan would identify and eliminate the cause or causes of the problem; however, this is not always possible. Realistically, treatment is geared toward improving saliva flow, relieving symptoms, and preventing the complications of the disorder.

Medical Consultation

Often a consultation with the patient's physician is the first step in managing a patient with xerostomia. A medical evaluation may be necessary to identify or rule out an underlying systemic disorder. In the case of medication-induced xerostomia, the physician may be able prescribe an alternative medication that would be less xerogenic or may recommend that the patient take a lower dose of the current medication. In many cases of medication-induced xerostomia, the patient is taking multiple xerogenic medications and it may be necessary to make multiple adjustments before any benefits can be seen. Unfortunately in some cases, medication adjustments cannot be made.

Patient Education

Education is a critical component of patient management in xerostomia. Patients need to be educated regarding the cause of their problem; what, if any, measures can be taken to reduce xerostomia; and what actions will be taken to minimize its consequences. Patients must be made aware that xerostomia is a condition that can have a significant negative impact on oral health and can result in irreversible damage. They must understand they are at increased risk of developing dental caries, periodontal disease, and candidosis. Importantly, they need to recognize they must play an active role in minimizing the detrimental effects of xerostomia (TABLE 4). Patient information brochures and Web resources serve to reinforce education provided in the dental office. The following Web sites are good examples of Web resources for information regarding xerostomia:

- http://www.nidcr.nih.gov/HealthInformation/DiseasesAndConditions/DryMouthXerostomia/DryMouth.htm
- http://www.niams.nih.gov/HI/topics/sjogrens/index.htm
- http://www.laclede.com

Saliva Stimulation

Unless there has been total destruction of salivary gland tissue, saliva stimulants are usually effective in improving saliva flow (TABLE 5). There are many systemic agents that may be used for this purpose, but pilocarpine (Salagen) and cevimeline (Evoxac) are the most well-studied and the most widely used.[5,14]

Both drugs act on muscarinic receptors to produce parasympathetic stimulation. Pilocarpine is a nonselective muscarinic agonist and interacts with M2 and M4 receptors of lung and cardiac tissues, as well as with the M3 receptors of salivary and lacrimal glands. Cevimeline is reported to have M1 and M3 selectivity. Theoretically, this should decrease the risk of cardiac and pulmonary side effects; however, the safety and adverse event profiles of pilocarpine and cevimeline are very similar.[3,14]

As with any systemic medication, medical contraindications, precautions, drug interactions, and side effects need to be considered. As there are many such considerations for both pilocarpine and cevimeline, it is prudent to consult with the patient's physician before prescribing them. Pilocarpine ophthalmic solution, taken orally, is a particularly cost effective means of stimulating saliva flow and it can easily be titrated to the minimum effective dose.[8]

A number of studies have addressed the management of xerostomia in Sjögren's disease via use of medication to modify the underlying disorder. These have included studies with interferon α (IFN-α), corticosteroids, and hydroxychloroquine.[5] The most promising results have been with low dose IFN-α. Administered as 150 IU lozenges three times daily, IFN-α has increased salivary output with minimal side effects and adverse events.[5,14]

Saliva may also be effectively stimulated by chewing sugar-free gum or sucking on sugar-free candy. Several chewing gums on the market are sweetened with xylitol, which have been shown to have cariostatic effects.[15]

Biotene Dry Mouth Gum (Laclede, Rancho Dominguez, Calif.) not only contains xylitol but also antibacterial enzymes normally found in saliva. When selecting sugar-free candy, patients should be cautioned against those with cinnamon or strong mint flavoring that may irritate soft tissues. While lemon-flavored candies are very effective in stimulating saliva flow, the citric

TABLE 4

The Role of the Patient in Xerostomia Management

Ensure adequate hydration by frequently sipping water
Limit caffeine
Avoid alcohol
Use a cool air humidifier (clean daily)
Sleep on side if possible to reduce mouth breathing
Avoid sugars and refined carbohydrates
Practice optimal oral homecare (plaque control)
Use supplemental fluoride as directed
Seek professional dental care at least every six months

acid they contain may irritate soft tissue or cause dental erosion with long-term use. An excellent option for safely stimulating saliva flow is SalivaSure (buffered citric acid lozenges, Scandinavian Formulas, Sellersville, Pa.). Since they are buffered, they do not irritate soft tissues or cause dental erosion. They also are sweetened with xylitol.

Moisture Replacement

Adding moisture to the oral environment is particularly important for patients in whom saliva cannot be stimulated. While there are numerous saliva substitutes on the market, they are variably well-received by patients and their benefits tend to be short-lived. Many patients prefer sipping water to using a saliva substitute. Not only is water sipping the most cost-effective means of improving oral moisture in the short-term, it has the added advantage of contributing to improved hydration. Oral Balance Gel (Laclede), which may be spread on soft tissues or in dentures, provides longer-lasting moisture and also contains antibacterial enzymes.

Patients with dry mouth often suffer from dry lips. Hydrous lanolin and aloe vera products are very effective in managing this problem. Oral Balance Gel may also be used to relieve dry lips.

General Oral Hygiene

Optimal oral hygiene, including regular tooth brushing and flossing or other interdental cleaning, is essential for patients with xerostomia. These patients should use fluoridated

TABLE 5

Saliva Stimulants

Agent	Directions for Use	Approximate Cost	Medical Considerations
Pilocarpine 5 mg tablet (Salagen or generic)	1 tablet PO TID	TID x 30 days Salagen ≈ 175.00 Generic ≈ 136.00	Contraindications ■ Hypersensitivity ■ Uncontrolled asthma ■ Narrow angle glaucoma ■ Acute iritis ■ Patient taking beta-blockers ■ Patient taking anticholinergics Precautions ■ Cardiac disease ■ Controlled asthma ■ Chronic bronchitis ■ Chronic obstructive pulmonary disease ■ Cholelithiasis ■ Biliary tract disease ■ Nephrolithiasis Drug interactions
Cevimeline 30 mg capsule (Evoxac)	1 capsule PO TID	TID x 30 days ≈ 183.00	
Pilocarpine 4% ophthalmic solution = 2 mg/drop (generic)	2 drops TID, in 1-2 tablespoons water, swish and swallow, or two drops placed on sugarless gum	TID x 30 days ≈ 7.00	
SalivaSure buffered citric acid lozenge, (Scandinavian Formulas)	Dissolve one lozenge slowly in mouth up to every hour as needed	90 lozenges ≈ 9.00	None

TABLE 6

Prescription Neutral Sodium Fluoride Supplementation

Brush-On One Step ■ Prevident 5000 Plus ■ Fluoridex ■ Control Rx	Brush with pea-sized amount twice daily. Spit out excess. NPO ½ hour after.
Brush-On Two Step ■ Prevident 1.1% NaF Gel ■ NeutraCare 1.1% NaF Gel	Brush with pea-sized amount twice daily after cleaning teeth. Spit out excess. NPO ½ hour after.
Custom Fluoride Trays ■ Thera-Flur-N 0.5% NaF Gel	Apply thin film to inner surface of trays and hold on clean, dry teeth five to six minutes daily. Spit out excess. NPO ½ hour after.

TABLE 7

Management of Oral Candidiasis

Medication	Dosage and Directions[1]
Chlorhexidine 0.12% alcohol-free aqueous[2]	15 ml mouthrinse and expectorate TID. NPO ½ hour after use.
Nystatin 100,000 units/ml sugar-free oral suspension[3] or amphotericin-B 25 mg/ml sugar-free oral suspension[3]	5 ml mouthrinse 1 min and expectorate[4] QID (PC and HS). NPO ½ hour after use.
Nystatin 100,000 units/ml oral suspension[5]	5 ml mouthrinse 1 min and expectorate[4] QID (PC and HS). NPO ½ hour after use.
Ketoconazole 2% cream (Nizoral) or clotrimazole 1% cream (Lotrimin)	Apply thin film to inner surface of denture(s) and/or corners of mouth QID (PC and HS). NPO ½ hour after use.
Clotrimazole 10 mg oral troches (Mycelex)	Dissolve 1 troche slowly in mouth 5x daily. NPO ½ hour after use.[6]
Ketoconazole 200 mg tablets (Nizoral)	1 tablet PO QD for 7 to 10 days. Do not take antacids within two hours of this medication.[7]
Fluconazole 100 mg tablets (Diflucan)	1 tablet PO BID for first day, then 1 tablet PO QD for 10 to 14 days.

1. In most patients, decreased frequency and dosages may be used if maintenance therapy is required.
2. Available from Sunstar-Butler for in-office dispensing or can be prepared by experienced compounding pharmacist. Causes extrinsic staining and may cause dysguesia.
3. Must be prepared by a compounding pharmacist.
4. May be swallowed for pharyngeal involvement.
5. Should not be used in dentate patients.
6. May be difficult to use in moderate to severe xerostomia.
7. Acidic environment is required for absorption.

toothpaste that is free of sodium lauryl sulfate, a detergent used as a foaming agent in most commercial toothpastes. Biotene toothpaste (Laclede) is SLS-free and contains antibacterial enzymes normally found in saliva.

Patients with xerostomia who use mouthwash should use a product that is alcohol-free. They should also avoid cinnamon and strong mint flavoring, which may irritate the soft tissue. Biotene mouthwash (Laclede) is alcohol-free and contains xylitol, as well as antibacterial enzymes normally found in saliva.

Fluoride Supplementation

Topical fluoride supplementation is a key component of the management of xerostomic patients and should be implemented before caries become a problem. Patients with mild xerostomia may be directed to use an over-the-counter fluoride mouthrinse daily. Patients with more significant xerostomia should use a prescription-strength topical fluoride, which may be delivered in custom fluoride trays or in a brush-on preparation. To avoid soft tissue irritation and excessive staining, neutral sodium fluoride is the best choice for patients with xerostomia (TABLE 6).[8]

Mucositis Management

Patients with xerostomia may require management for candidiasis or nonmicrobial forms of mucositis, such as aphthous stomatitis, traumatic ulcers, or nonspecific mucositis.[8] Often, mucositis management is required on an ongoing basis. It is important to establish a definitive diagnosis before initiating treatment. In most cases, a clinical diagnosis of candidiasis can be confirmed with cytologic preparations.[16] Although the diagnosis of aphthous stomatitis is typically based on clinical and historical

TABLE 8

Management of Non-microbial Mucositis

Medication	Dosage and Directions[1]
Triamcinolone acetonide (Kenalog) 0.1% or 0.2% aqueous suspension[2,3]	5 ml mouthrinse and expectorate QID (PC and HS). NPO ½ hour after use.
Triamcinolone acetonide (Kenalog) 0.1% or 0.5% ointment or gel[4]	Apply thin film to inner surface of medication tray(s)[5] and seat for 30 minutes BID-TID or apply to involved area QID (PC and HS). NPO ½ hour after use.
Fluocinonide (Lidex) 0.05% ointment or gel[4] or clobetasol (Temovate) 0.05% ointment or gel[4]	Apply thin film to inner surface of medication tray(s)[5] and seat for 30 minutes BID or apply to involved area BID-QID (PC and HS). NPO ½ hour after use.
Triamcinolone acetonide (Kenalog) 0.5% ointment 1:1 with Orabase	Apply thin film to dried mucosa BID-TID. Do not rub in. NPO ½ hour after use.
Fluocinonide (Lidex) 0.05% or clobetasol (Temovate) 0.05% 1:1 with Orabase	Apply thin film to dried mucosa BID. Do not rub in. NPO ½ hour after use.
Misoprostol[2,6]	May be compounded in various topical forms and dosages with or without corticosteroids and/or antifungals.
Triamcinolone acetonide (Kenalog) injectable 40 mg/ml diluted to 10-20 mg/ml with local anesthetic with vasoconstrictor[7]	Anesthetize area first and inject 10 to 40 mg into base of lesion.
Prednisone	30 to 60 mg PO QD (AM 1½ hour after arising) for five days, then 5 to 20 mg QOD (AM1½ hour after arising) for 10 days.

1. In most patients decreased frequency and dosages may be used if maintenance therapy is required.
2. Must be prepared by a compounding pharmacist.
3. May be compounded in nystatin (edentulous patients only), nystatin sugar-free suspension or amphotericin-B sugar-free suspension.
4. May be mixed 1:1 with clotrimazole 1 percent or ketoconazole 2 percent cream or prepared by a compounding pharmacist in ointment form or mucoadhesive base to provide full strength of both medications.
5. Custom tray(s) fabricated by a dentist for management of gingival mucositis. Gel is best for medication tray use. Brush teeth after removing medication trays.
6. Contraindicated in women of childbearing age. Decreases pain and increases rate of healing of ulcerated mucosa.
7. For management of recalcitrant solitary lesions.

features, a biopsy may be required to rule out other types of ulcerative mucositis.

There are many treatment options for oral candidiasis (TABLE 7) and nonmicrobial mucositis (TABLE 8).[8,16] Use of topical agents is preferred as it minimizes the risks of systemic side effects and drug interactions. However, some contain sugar, which should be avoided in dentate xerostomic patients, and/or alcohol, which should be avoided in all xerostomic patients. Fortunately, compounding pharmacists can prepare formulas that are both sugar-free and alcohol-free.

Conclusion

The assessment of salivary gland function should be a routine part of initial and ongoing evaluation for every patient. When signs or symptoms of xerostomia are identified, they should be proactively managed to minimize potential complications. As with any other medical or dental problem, detailed information regarding the assessment, management and follow-up evaluation should be documented in the patient record. Establishing, implementing, and documenting protocols for the diagnosis and management of xerostomia will not only eliminate potential liability from

failure to diagnose this common oral disease, but will also assure the highest quality of patient care. ■■■■

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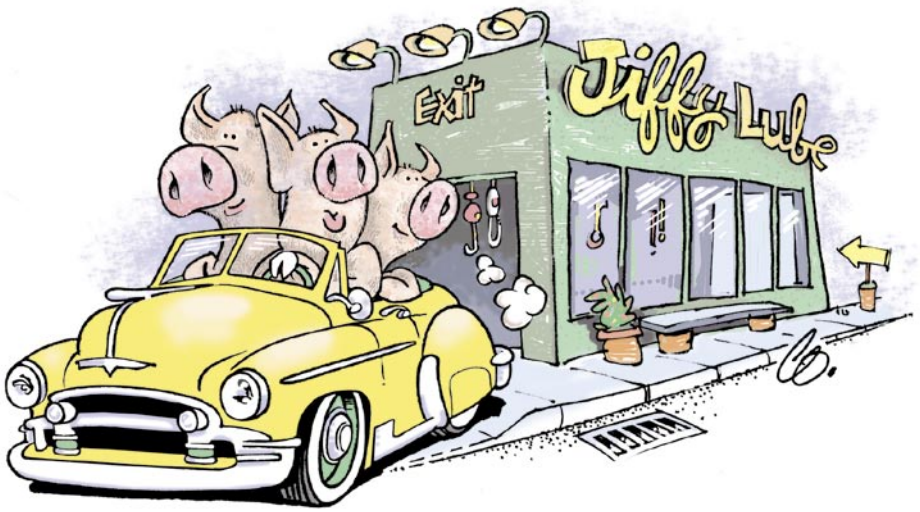

Open Wide: Here Comes IntelliDrug

"This thing," he continues, indicating his teeth, "automatically solves all my problems of memory lapse and noncompliance.

Robert E. Horseman, DDS

ILLUSTRATION BY CHARLIE O. HAYWARD

Manfred and Jacob are having lunch at a small sidewalk café in Stuttgart. The bratwurst is good, the matzo soup excellent, and the Heinekens cold. Suddenly Manfred cocks his head slightly to one side mid-chew, listens intently. "What's that noise?" he asks.

"What noise?" Jacob queries.

"That clicking, topockita-pockita noise. Don't you hear it?"

"Oh, *that*," Jacob says, brightening. He reaches in his mouth with thumb and forefinger and pries out two of his lower molars that resemble a unilateral partial denture from dentistry's distant past. "This is my IntelliDrug Device. I am diabetic; I need four kinds of heart medications and six prescription drugs I don't even know what they're for."

"This thing," he continues, indicating his teeth, "automatically solves all my problems of memory lapse and noncompliance. It is the lingerie du chat, as we say in Tel Aviv."

"French for 'cat's pajamas,'" Manfred says. "You're not French."

"I know. We just do it to annoy them. Feh!"

We leave the two friends noshing on their vittles to do a little research on what promises to be the biggest thing in dentistry and medicine combined during the last two weeks. Potentially even bigger than the silicone implants and tooth whitening that have become as necessary as oxygen for the under-60 set.

While American dentists were engrossed in discovering shades of white beyond the ability of the human eye to appreciate, and insisting no edentulous space goes unimplanted, European and Israeli experts were hot on the development of a high-tech automatic drug dispensing device they have named IntelliDrug. Because of insufficient space on the product, the runner-up name of Der Schmartzigdruggendrippendiviser didn't make the cut.

Here's the skinny as explained by Roger Cheng of Dow Jones Newswires: Dr. Andy Wolff, an Israeli dentist, initially came up with the concept of an automatic drug-dispensing device, knowing the average patient has the compliance level of a

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DR. BOB, CONTINUED FROM 454

preschool toddler when it comes to taking his prescribed medicines. Luckily, Wolff immediately thought of the mouth as the proper site for such a device. No telling where it would have been placed if brain surgeons or proctologists had had a glove in the decision.

Miniaturization being what it is these days, we should not be surprised to learn that the device being prepared for comprehensive tests by a consort of 15 different European and Israeli companies will house the following components: a pump, custom valves, a microprocessor, batteries, and a reservoir for the drugs. There will be a communication port so that the device can be remotely controlled, eventually linking it with cell phones or nearby hospitals.

Political alarmists have been quick to detect a parallel between IntelliDrug and the "Manchurian Candidate." If a man's mediations can be controlled remotely by perfect — or imperfect strangers — what else can it do? So many things to protest, so little time!

Of interest to dentists are reports that the IntelliDrug device, all enclosed in a space the size of two molars is "strapped" in. Strapped in? To what? Ask all the Doubting Thomases among us. It is said to be easily removable by technicians (not exodontists) who can then refill the drug reservoir, change the battery, and give it the standard lube, oil, and filter service at any convenient Jiffy Lube outlet.

Dr. Wolff is pretty excited about this and so are the pigs on which the concept has been successfully tried. Except for the occasional ticked-off porker holding a one-way ticket to Hormel, not a single incident of Mad Pig Disease has been detected. Once the pigs have given the tests a hooves-up, Dr. Axel Schumacher, who is helping design the pumps, declares he hopes to have a prototype ready for human testing by the end of the year. The pigs hope so, too, indicating they would like to get back to their normal activities of truffle hunting and seeking better building materials to thwart big, bad wolves. ■■■■