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Managing Disorders

New Advances

Burning Mouth Syndrome

CHRONIC OROFACIAL PAIN UPDATE

GLENN T. CLARK, DDS, MS

OF THE CALIFORNIA DENTAL ASSOCIATION
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DEPARTMENTS

FEATURES

Steven A. Gold, DDS

An Obligation Unmet?

We have commented previously on the positive impact the Give Kids a Smile program has made on many individuals throughout our state and the country. The improvement in the quality of life of those children who received treatment cannot be underestimated or understated. Indeed, one positive dental experience facilitated by one caring individual can prove to be a turning point in a young person's life. It has the power to elevate their awareness of oral health and establish attitudes and habits that will improve their chances of maintaining optimum oral health for a lifetime.

Behind these success stories and the many photos of smiling kids, dentists, hygienists, dental assistants, corporate sponsors and other volunteers, is a deeper and broader story. Some call it "access to care" and it is has appeared at the front of every major dental publication and on the agenda of every major and minor dental organization. Give Kids a Smile and access to care are often talked about in the same breath, yet they are entirely different. Our profession does an admirable job donating dental services to the needy. In addressing the access to care problem, we have been less successful. It is the latter that warrants a focused, proactive, and collaborative effort that is led by the dental profession. And perhaps, a somewhat different tack than the one we've been taking.

One reason access to care is a difficult issue for us as a profession to get our hands around, is that it is poorly defined. Many in our profession have opined about whether there is a shortage of dentists, an unequal distribution of dentists, or both, that is limiting dental care in certain populations. For many living in California and across the nation, the problem may not be due to access. Rather, it would be more accurately defined as "unmet dental needs."

Unmet dental needs in our population have two root causes. One of them is true access to dental care limited by geography, cost, or both. The other is personal neglect, either through conscious lifestyle decisions, lack of education about proper oral care, or unaddressed fear of dental treatment. When we as a society look for solutions to America's unmet dental needs, both of these potential causes must be considered.

Tulare County in California's San Joaquin Valley may very well be the epicenter of unmet dental needs in the state, and possibly the nation. It is not surprising then that local newspaper *Valley Voice* recently published an article, "Tooth Decay Most Common Health Problem Among Valley Children." The statistics are sobering: Tooth decay in California's children tops 60 percent; the next most common health condition, asthma, is slightly over 10 percent. Most will certainly agree that the health fallout from this epidemic is unacceptable. Yet, is the response of the dental profession proactive, reactive, or a little of both? Surprisingly, the article did not once mention the California Dental Association. And it mentioned the ADA only as a source of demographic statistics. Why do our profession's efforts go unnoticed once the buzz of excitement from Give Kids a Smile wears off?

Many are by now aware of the ADA's lawsuit against the Alaskan Native Tribal Health Consortium to halt the delivery of care by dental health aide therapists. While

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helping to uphold each state's dental practices act is likely a necessary and appropriate pursuit, some within our profession question its direction and timing. Ronald Hsu, DDS, said it quite succinctly in a letter published in the April 17, 2006, *ADA News*. "As long as we the dentists continue to ignore the access to care problem, creative means of getting care to those who need it the most will continue to spring up." Others wonder why the response seemed a bit reactionary; a response evoked because someone else came up with a solution that we did not like.

Regardless of one's personal feelings, continued support of our profession's efforts to address unmet dental needs is imperative. To our ADA leaders' credit, the recent proposition to create a new category of allied dental health professional — community dental health coordinator — is right on target. This will likely pave the road to real long-term results in getting dental care to the underserved. Yet, this is a vision that may have a tortuous path to fruition. The final report to the ADA House of Delegates this year is months away. The development of educational curricula and the amending of dental practice acts are years away. Creating an actual impact on the dental health of underserved populations will take even longer.

What can we do in the meantime? One suggestion made recently by one of our CDA leaders seems to have merit. It would call for the creation of a paid staff position for a dentist within CDA, a "Dental Czar," if you will, who could better coordinate local efforts that are taking place right now. We often hear of the great work being done by community clinics and individuals. Yet some gaps remain. A full-time dental staff person, devoted solely to our state's unmet dental needs could help to fill in some of those gaps. For example, care could certainly reach more individuals if patients' transportation needs were addressed. And placing at least one full-time health professional, such as a dental hygienist, at every school will give all children the opportunity to be educated about oral health care and screened for dental disease. Not to be overlooked is the fact that the public will see the dental profession put its money where its mouth is to make a tangible difference in the lives of those who need our assistance.

We do not need to seek to thrust ourselves into a leadership role on this issue. We, as dentists, are already looked upon by the public as the pivotal player in addressing unmet dental needs. We must, however, coordinate and maximize our efforts and be more proactive as a profession so that we live up to that role and meet our obligation. ■■■■

Resist the 'Quick-fix Mentality'

I am writing to express my complete agreement with Dr. Steven Gold's editorial "A Bitter Pill" in last May's issue.

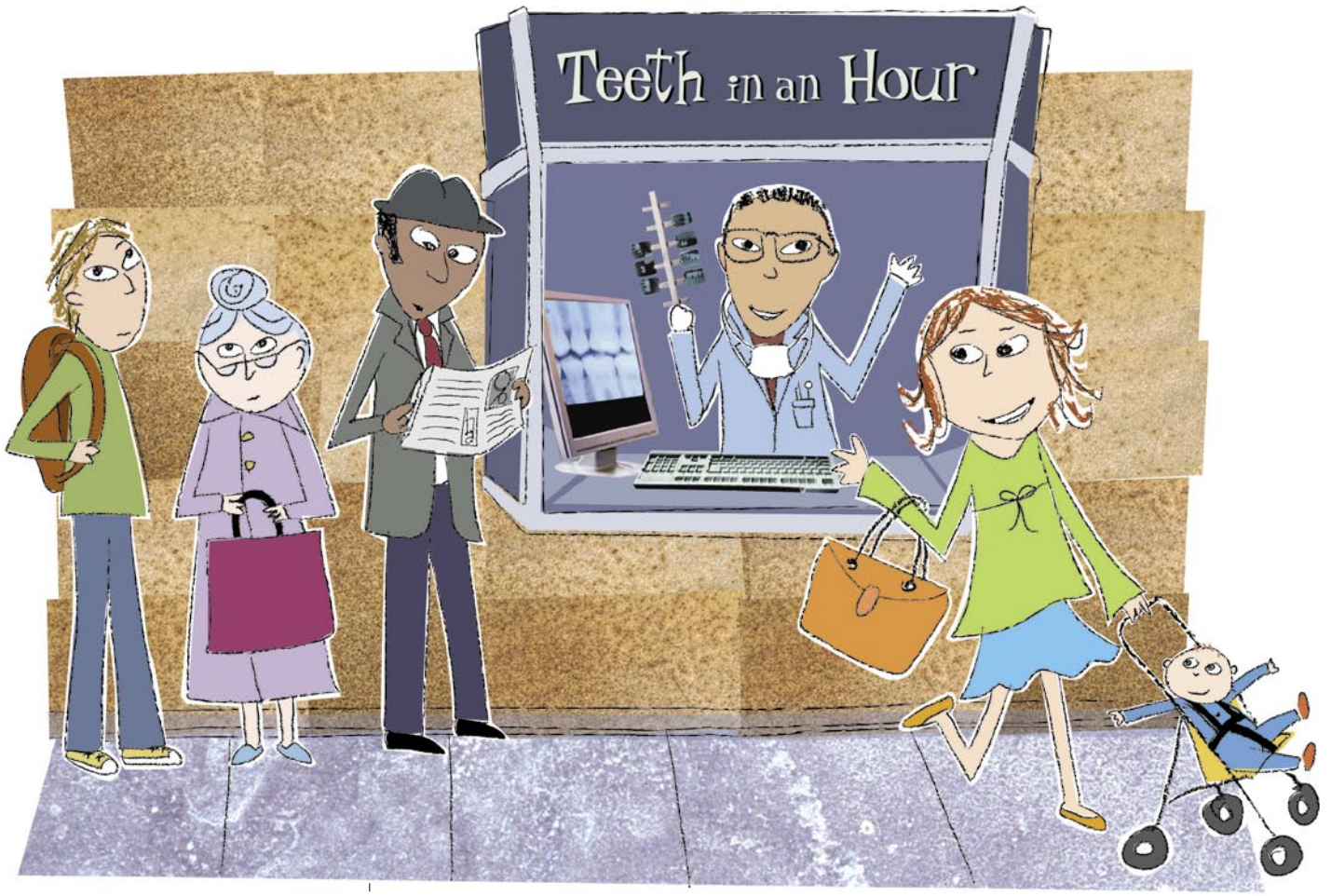
I think it is disgusting how the drug companies "push" drugs onto the public in the name of education. This has only happened over the last few years when a legal judgment allowed advertising/education by pharmaceutical companies to go forward. And forward they went with Hollywood images and soft music that tries to encourage all viewers to ask their doctor about "this particular medication" that can solve all problems. It encourages, aids and abets the capricious increased use of a pill to solve life's problems. The latest ads are so slick and present with such authority that you get the impression this information is coming from the American Medical Association and should be acted upon.

It is incumbent upon all physicians and dentists to counter this easy drug fix message with careful thought and diagnosis before that prescription is written.

It is incumbent upon all physicians and dentists to counter this easy drug fix message with careful thought and diagnosis before that prescription is written. It is not easy to resist a persistent patient who seems certain of their self-diagnosis and need for medication. But, hey, who is the doctor here? It certainly is not the profit-motivated drug company or a naïve and unsuspecting patient. The patient should trust your judgment and you must honor that trust in doing what you think is truly right for the patient.

Thanks Steve, for the editorial. This message of resisting "… a quick-fix mentality …" will need to be repeated often.

John W. Burk, DMD
Santa Barbara



Lee Ann Engle

Looks, Ease Driving Use of Mini-implants

By Dell Richards

While technology constantly adds new choices to implants, patient demands also are driving some of the changes. Mini-implants as well as software templates for implant placement are just two of the latest innovations. Some dentists proceed with caution, others are pushing ahead.

Like many dentists, prosthodontist Jeffrey Y. Nordlander, DDS, is using mini-implants for people who want immediate results and for some edentulous cases. "If patients want something implant-supported right after surgery, we use them," said Nordlander. "They can be immediately loaded."

The minis protect the other implants during the healing process.

"We only use them in selected cases when the patient is willing to accept the added risk and cost of doing the procedure in a more convenient way."

JEFFREY Y. NORDLANDER, DDS

He uses mini-implants primarily as a temporary solution, however, "We put temps in between the permanent ones," said the partner with Prosthodontic Dental Group. "So you need more sites."

For the patient, this means more bone, more money, and more risk.

"We only use them in selected cases when the patient is willing to accept the added risk and cost of doing the procedure in a more convenient way," Nordlander said.

For Nordlander, who handles the complex cases referred to him by dentists throughout the Central Valley, protecting the patient is of paramount importance.

Even Victor J. Sendax, DDS, inventor of the IMTEC-Sendax mini-dental implant system — the only FDA-approved implant currently on the market — spoke of the risk. In a 2004 posting for the *Osseo News* blog, Sendax gave a tip on how to use minis so that dentists avoid exposing them "… to lateral force overload."

Meanwhile, others are forging ahead, using minis on a permanent basis. Sandy Kim, DDS, went into practice in Los Angeles with her father, John Kim, when she graduated from dental school more than a decade ago. They both have been using mini-implants on a permanent basis for more than three years. For their patients, the lower cost is a big factor.

"We have a lot of full-denture cases and the lower dentures are a problem after a while," said the associate of Dr. Kim's dental office, who also has her own practice in Garden Grove. "Implants stabilize the dentures and keep them from floating in the mouth. An implant is great, but some patients still cannot afford it."

Which bring in the minis. "The minis are cheaper — by a lot."

Because they advertise in Korean newspapers, the father-daughter team has patients flying in from as far away as Hawaii. To date, only one patient has had problems, a woman with rheumatoid arthritis.

Kim is not alone. Stephen Hadwin, executive vice president of IMTEC Corporation, said minis are flying out the door. "They are one of our biggest products at the moment."

Because minis allow dentists to reach a consumer who can't afford the conventional system, or elderly patients who can't bear surgery, minis have experienced phenomenal growth in sales since they were introduced in 1999. "Sales have been very healthy for the past five years," Hadwin said. "They have experienced 40 to 50 percent growth."

While minis have given patients more choice, recently approved software and scanning systems help dentists with time and accuracy when placing any kind of implants, mini or regular.

Using software that scans X-rays helps Nordlander plan the placement of implants. "We use implant analogues for planning," said the dentist whose practice has three offices and two satellites. "With 3-D implant forms, you can superimpose your X-ray to see where the best placement would be."

Because of the cost, few dentists have adopted the system. And Nordlander said that the new guides help "translating the 2-D image on a computer screen into a patient's 3-D mouth."

Peter K. Moy, DMD, is one of the dentists currently using one of those guides: Nobel Biocare's "Teeth in an Hour" system. This treatment planning software and CT scanning create a 3-D image of the patient's mouth. The Nobel Biocare guide, as it's called, allows dentists to determine the placement of implants digitally while having an exact match made for the denture.

"The software helps identify where the implants go," said Moy, adjunct associate professor of Oral and Maxillofacial Surgery, Diagnostic and Surgical Services

at the University of California, Los Angeles, School of Dentistry. "That way, dentists can fabricate the bridge before the implants are placed and put them in the exact location they planned."

"Teeth in an Hour" refers to surgical time, not prep time. For dentists, the major benefit for is doing the CAD-CAM planning at the same time as fabrication. "You spend less time because the work is done during the work-up that you would do anyway," said Moy, who uses the software and templates for 80 percent of his implant patients at the UCLA Dental Implant Center. "You're eliminating two to three hours, which is quite a bit of savings, quite a bit of time you could be seeing other patients."

The one-time software cost is about $5,000. Each template fabrication also adds about $2,000 to the cost.

However, the restoration can be loaded immediately after surgery. "It's easier on the patient because all the work is done beforehand," said Moy, who helped introduce the guide in the United States and now also teaches its use. "It's a more predictable, more accurate way of treating patients."

"The procedure had been performed numerous times in Sweden," said Moy, who is a consultant to Nobel Biocare, adding the company paid him to fly over and watch the surgeon who had the most experience placing it. "That's when I came back and was one of the first to use the guide in this country."

While Moy thinks the future of this technology as "huge," Nordlander said patients still want to look good. Whether the dentist is doing the planning on a computer or using mini-implants, the teeth — and gums — need to look real. "The big issue with implants, at least with front teeth, is making the tissue around the implant look natural," Nordlander said.

The problem is the papilla between the front teeth. "Re-creating that peak is an area where more work is needed," Nordlander said. "People are more conscious of having teeth — and gums — that look nice. We need to improve the contour and form of gums around the restoration."

When they do, dentists and patients undoubtedly will have even more options to consider.

A practicing journalist, Dell Richards runs Dell Richards Publicity, a public relations firm specializing in dentistry and health care.

"You're eliminating two to three hours, which is quite a bit of savings, quite a bit of time you could be seeing other patients."

PETER K. MOY, DMD

Diabetic Patients May Improve Sugar Control With Periodontal Therapy

The results of a recent study support the hypothesis that periodontal therapy may help metabolic control (lower HbA1c) in patients with diabetes.

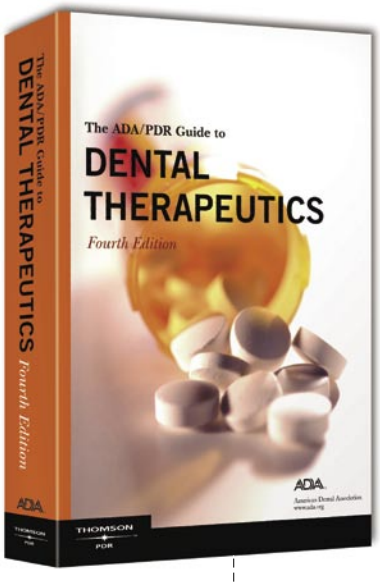
The results suggest that the therapy may decrease a diabetic patient's HbA1c count by as much as 20 percent at three and six months following treatment. According to the American Diabetes Association, HbA1c provides patients with a snapshot of their average blood sugar changes in the past two to three months and gives them a good idea of how well their diabetes treatment plan is working. A healthy HbA1c count ranges between 4.0 to 6.0. This study appeared in the April issue of the *Journal of Periodontology.*

"We found that conventional treatment for chronic moderate generalized periodontitis, which included a simple, nonsurgical procedure called Scaling and Root Planing (SRP) lowered the study group's HbA1c count from 7.2 to 5.7," said study authors Antonio Bascones, a professor, and Dr. Ricardo Faria-Almeida, both of the Department of Medicine and Buccofacial Surgery of the Complutense University in Madrid, Spain. "This could significantly put diabetic patients who are just above the normal HbA1c range into the healthy range and reduce their risk of serious complications from diabetes."

Bascones warned these findings should not be considered definitive or universally generalizable because of the study sample size. Additionally, this study compared the response to conventional periodontal treatment between type 2 diabetic and nondiabetic patients with chronic moderate generalized periodontitis and did not include a group of diabetics that was not undergoing periodontal treatment. The absence of this information is a limitation because it is unknown how diabetic patients who were not undergoing periodontal treatment would have progressed.

"For a long time we've known that diabetic patients have a higher risk of developing periodontal disease compared to nondiabetics," said Kenneth A. Krebs, DMD, and president of the American Academy of Periodontology.

For more information about periodontal disease and treatment is available online, www.perio.org. A brochure, "Diabetes & Periodontal Diseases" is available by calling (800) FLOSS-EM.



ADA and Thomson PDR Partner to Publish Guide

A new dental therapeutics guide will help provide dentists with readily accessible and timely information for making medication decisions.

The American Dental Association recently announced its partnership with Thomson PDR to publish *The ADA/PDR Guide to Dental Therapeutics*, fourth edition. PDR, a part of the Thomson Corporation, provides integrated information tools and authoritative drug information to health care professionals across the globe.

The guide, written by a team of experts, includes the work of dentistry's leading clinicians and academicians. Sebastian G. Ciancio, DDS, a distinguished service professor and chair at the Department of Periodontics and Endodontics at the University of Buffalo, State University of New York, edited the guide, which will be available next month.

"We are very pleased to collaborate with Thomson PDR and be able to bring our profession's unique perspective and latest clinical information to the guide," says James B. Bramson, DDS, ADA executive director. "We also view this collaboration as an opportunity for ongoing enhancements to the publication to continually provide the dentist with the latest patient-care information in a readily accessible format."

"It is noteworthy that this book has been prepared at the request of the ADA Council on Scientific Affairs and is the only dental therapeutics book published by the ADA," Ciancio said. "This provides dentists with timely information on making the best medication decisions for patients."

The guide underwent a redesign for quick access of vital data needed to treat patients.

Thomson PDR and the ADA are discussing additional electronic and printed products to further enable dentists to provide better care for their patients.

Girls Find the Thrill of the Grill

Chalrlie O. Hayward

Getting grilled about grills? The latest oral fad, those snap-on supposed smile enhancers, has resulted in a national upswing of patients peppering their dentists with questions about tooth covers.

Typically made of real yellow or white gold, and from 14 karats up to 24, the one-piece grills can cover two to six teeth or the entire smile. Buyers can choose a solid look, "open face" featuring cutouts to expose the natural teeth, or even fangs. They also can opt for a diamond-encrusted version or those made with etched words, initials, and symbols.

Once sported only by male rappers and street toughs, grill-wearing has reached a wider following, from college students and grandparents to teenagers, according to an article in the *San Francisco Chronicle* newspaper. In fact, the paper also reported that last year, San Francisco Bay Area grill makers said teenage girls were the fastest-growing segment of grill-wearers.

In a recent issue of *Today's FDA*, the Florida Dental Association's journal, Alyssa Brown, associate editor, wrote about the trend in adorning one's choppers. Quoting members and spokespeople from the ADA, Brown offered some tips should patients ask them about grills:

- Keep to the facts. Wearing grills even for a few hours can cause periodontal disease.
- Focus on the oral health of the patient. Avoid commenting on esthetics so as to not alienate the patient.
- Educate patients about maintaining good oral health if they choose to wear the toothy accessories. Demonstrate how to clean the devices and advise them to wear them for only abbreviated periods of time. Discourage the patient from obtaining permanent grills.

Declutter 101

Mistakenly thought of symbols of busyness or an active mind, clutter strewn around an office and on a desk keeps a person "living in the past," said Janice Goodman, DDS, in an issue of *Oral Health* (Canada).

Those are pretty lame excuses and coping strategies to help clutterers avoid cleaning up their work spaces, said Goodman. What's more, it makes it difficult to keep work projects organized and finished on a timely basis.

Four simple guidelines can help quickly declutter an office. Among them, Goodman suggested:

- List the most pressing issues, i.e., clear papers off the desk, read the mail, return calls, recycle old journals.
- Start small, clear out a cluttered drawer.
- Be ruthless. Sort through things immediately. Don't get overwhelmed by thinking over possible uses an item might have in the future.
- Neaten up. For items you feel you can't toss but contribute to the clutter, make a place for it. For example, keys should be placed in the same spot each time. This makes it easier to find as opposed to typically getting lost in the clutter.

Practice Advisory for Intraoperative Awareness Published

The American Society of Anesthesiologists has announced the publication of a practice advisory for member physicians that addresses intraoperative awareness and the role of brain function monitoring. Unintended awareness under general anesthesia, sometimes called "anesthesia awareness," is a rare occurrence in which a patient may regain consciousness and be able to recall events during surgery while under general anesthesia. The ASA Practice Advisory is being published to disseminate critical patient safety information and guidance on this topic.

"Practice Advisory for Intraoperative Awareness and Brain Function Monitoring" appeared in the April issue of *Anesthesiology* and represents the most thorough document to date that assists hospitals and anesthesiologists to minimize the risk of awareness under general anesthesia. Similar information for clinicians is provided in a joint statement produced by the Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland.

The advisory documents that awareness occurs in 1 to 2 cases per 1,000 surgeries performed under general anesthesia. Examples of awareness may include feeling sensations, pain, or hearing sounds. It is more likely to occur in individuals whose condition is unstable or during surgery for emergencies or trauma. Some episodes of awareness cannot be prevented, including instances in which the patient's injury or health requires lighter anesthesia to keep the patient safe. Intraoperative awareness is not an issue for those patients who undergo procedures with moderate sedation, regional or local anesthesia, as these patients are expected to be aware during some or all of the procedure.

With the goal of reducing awareness, the advisory makes recommendations for managing patients. These recommendations are summarized in four major areas — preoperative evaluation of patient risk for awareness; use of equipment checklists; monitoring depth of anesthesia; and drug selection.

Honors

The Alumni Association of University of the Pacific, Arthur A. Dugoni School of Dentistry paid tribute to its namesake dean with an inaugural award during the association's 107th annual meeting. "The Arthur A. Dugoni Lifetime Achievement Award," which will be granted on an infrequent basis, recognizes individuals for exceptional achievement, commitment and service to the dental school and the profession.

William Carpenter, DMD, MS, chair of the Department of Pathology and Medicine at University of the Pacific, Arthur A. Dugoni School of Dentistry, received the Distinguished Alumnus of the Year Award from University of Pittsburgh School of Dental Medicine.

Additionally, **Nader Nadershahi, DDS, MBA**, associate professor and chair of the Department of Dental Practice and Community Services at the University of the Pacific, Arthur A. Dugoni School of Dentistry, was elected president of the American Dental Education Association's Leadership Institute Alumni Association.

Electronic Transactions Easier With National Provider Number

The American Dental Association has recommended that all of its members apply for a National Provider Identifier because of the many advantages it offers. Health care providers who use standard electronic transactions, such as electronic claims, are required by federal law to have a unique NPI number by May 23, 2007.

The NPI replaces existing identifiers such as Social Security numbers and tax IDs for health care electronic transactions, and dentists no longer have to maintain multi-identifiers required by dental plans.

According to an article in the April-June issue of the *Journal of the Philadelphia County Dental Society*, even dentists who use paper, voice, and fax to transmit these communications may find NPIs necessary or useful. Highmark Blue Shield, for example, has announced it plans to use the NPI as the identifier for all providers.

For more information, go to http://nppes.cms.hhs.gov. Simply read the instructions, fill out the questionnaire, and submit the application. After confirmation of the data, an NPI will be e-mailed in one to five business days.

Upcoming Meetings

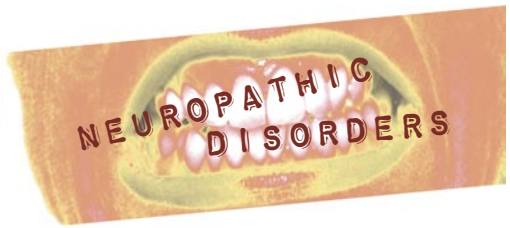
2006

Sept. 15-17	CDA Fall Session, San Francisco, 800.CDA.SMILE (232.7645).
Sept. 28-30	17th International Congress of Head and Neck Radiology, Budapest, Hungary, Eva Schiff at Redhill Travel, (415) 924-3229.
Oct. 7-11	Pacific Coast Society of Orthodontists 70th Annual Session, Honolulu; post-meeting program, Poipu Beach, Kauai, www.pcsortho.org, (415) 674-4500.
Oct. 16-19	ADA Annual Session, Las Vegas, (312) 440-2500.
Nov. 2-4	Hispanic Dental Association 14th Annual Meeting, Universal City, www.hdassoc.org or (217) 793-0035.
Nov. 5-11	United States Dental Tennis Association, Palm Desert, www.dentaltennis.org.
Nov. 12-18	57th American Academy of Oral and Maxillofacial Radiology 57th Annual Session, Kansas City, MO., www.aaomr.org.
Dec. 3-6	International Workshop of the International Cleft Lip and Palate Foundation, Chennai, India, (91) 44-24331696.

2007

April 15-21	United States Dental Tennis Association, Sarasota, FL, www.dentaltennis.org.
May 3-6	CDA Spring Session, Anaheim, 800.CDA.SMILE (232.7645).
Nov. 27-Dec. 1	American Academy of Oral and Maxillofacial Radiology 58th Annual Session, Chicago, www.aaomr.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.



Persistent Orodental Pain, Atypical Odontalgia, and Phantom Tooth Pain: When Are They Neuropathic Disorders?

Glenn T. Clark, DDS, MS

ABSTRACT

Patients with unrelenting pain in the teeth, gingival, palatal or alveolar tissues often see multiple dentists and have multiple irreversible procedures performed and still have their pain. Up to one-third of patients attending a chronic facial pain clinic have undergone prior irreversible dental procedures for their pain without success. In these cases, if no local source of infectious, inflammatory, or other pathology can be found, then the differential diagnosis must include a focal neuropathic pain disorder. The common diagnoses given include the terms atypical odontalgia, persistent orodental pain, or if teeth have been extracted, phantom tooth pain. One possibility is that these pain complaints are due to a neuropathic alteration of the trigeminal nerve. There are several diagnostic procedures that need to be performed in any patient suspected of having a trigeminal neuropathic disorder including (1) cold testing of involved teeth for pulpal nonvitality; (2) a periapical radiograph examining the teeth for apical change; (3) a panoramic radiograph examining for other maxillofacial disease; (4) a thorough head and neck examination also looking for abnormality; (5) a cranial nerve examination including anesthetic testing which documents any increased or decreased nerve trigeminal nerve sensitivity and rules out other neurologic changes outside the trigeminal nerve; and (6) MRI imaging in some cases. Finally, when a nonobvious atypical toothache first presents, direct microscopic examination of the tooth for incomplete tooth fracture is also suggested.

The majority of these patients are women over the age 30 with pain in the posterior teeth/alveolar arch.

Multiple causes exist for sustained neuropathic pain including direct nerve injury (e.g., associated with fracture or surgical treatment), nerve injection injury, nerve compression injury (e.g., implant, osseous growth, neoplastic invasion) and infection-inflammation damage to the nerve itself. Sustained nerve pain is commonly seen in patients with psychiatric impairment. It may be that the unrelenting nature of the pain itself alters the patient's personality.

Treatment includes pharmacologic medications which suppress nerve activity. The common medications used for atypical odontalgia and phantom tooth pain include gabapentin, tricyclics, topical anesthetics, and opioids. A list of these medications is provided in table form. Data suggest that once the patient has failed dental treatment and pain persists, the long-term outcome is less than 25 percent will have complete pain relief with treatment. With earlier treatment, better pain control, and improved nerve activity suppression medications, this should also prevent secondary psychiatric disease from developing and lower the number of inappropriate treatments.

Guest editor / Glenn T. Clark, DDS, MS, is a professor and program director, Orofacial Pain and Oral Medicine Center at the University of Southern California School of Dentistry.

This article focuses on the diagnosis, etiology, and pharmacologic management of unrelenting pain in the teeth, gingival, palatal, or alveolar tissues that do not respond to the usual and customary dental-medical treatments. One possibility is that these pain complaints represent a neuropathic disorder of the trigeminal nerve.

Patients with this disorder often see multiple dentists, have multiple irreversible procedures performed, and still have the pain in spite of scaling, curettage, antibiotics, NSAIDs, corticosteroids, endodontics, extractions, and even apical and alveolar surgical debridement. One recent case report in 2005 described a patient who had had multiple failed treatments performed because of unrelenting orodental pain.[1]

An article in 2003 described the prevalence of failed invasive therapies in a case series of 120 consecutive patients who attended a hospital center for treatment of their orofacial pain.[2] The report categorized patient self-reports of prior treatment and the success or failure of those treatments. The study reported that 38 out of the 120 (32 percent) patients with chronic oral pain had undergone prior irreversible dental procedures for their pain (e.g., endodontics (30 percent), extractions (27 percent) and apicoectomies (12 percent). All 38 patients still had pain, and 21 of 38 (55 percent) of the patients reported that these interventions actually exacerbated their pain. This article did not address whether psychiatric illness was co-morbid in this population.

Psychiatric assessment of chronic pain subjects with failed treatment was described in an earlier case series report (21 patients) on atypical facial pain.[3] These patients had a total of 65 irreversible dental and oral surgical treatments (3 per patient) trying to solve their pain and only one patient reported showing less pain as a result of the treatment. Each of the patients in this report also had a full psychiatric assessment. Based on these data, these authors concluded that failed treatment patients with chronic orodental pain suffered a high degree of psychiatric illnesses. The authors recommended psychiatric assessment before repeated dental and surgical procedures are performed in this population. While the need for a psychiatric assessment with a mental health professional is easy to comprehend and implement in the chronic multiple treatment failure patient, it is harder to justify and implement if the patient has not yet failed treatment and presents with a single symptom such as toothache and no obvious behavioral abnormalities. Whether psychological pathoses in this population precedes or is a consequence of chronic pain is unknown.

The authors recommended psychiatric assessment before repeated dental and surgical procedures are performed in this population.

Definition and Terminology

Neuropathic orodental pains are not new phenomena. In 1932, Wilson described a group of patients with atypical facial neuralgia and among them were patients who had dental pain of unknown origin.[4] Since then, many others have coined terms for these patients such as idiopathic periodontalgia and atypical odontalgia.[5-9] The term phantom tooth pain, PTP, was applied for the subgroup of these patients who had unexplained persistent dental pain even after the suspected tooth was extracted.[10-13] As such, phantom tooth pain is best described as a syndrome of persistent, unexplained pain at the site of the extracted tooth. While the mechanism is debated, it also is most likely a neuropathic pain process, which is defined by the International Association for the Study of Pain as "pain initiated or caused by a primary lesion, or dysfunction in the nervous system."[14] These specific changes that occur in the nervous system peripherally and centrally are described later in this article.

Differential Diagnosis of Chronic Orodental Pain

For most persistent orodental pain patients, unless a psychiatric illness is obviously necessitating immediate referral for mental health assessment, the dentist seeing a patient with chronic orodental facial pain would begin by first ruling in or out infection and/or inflammation as a source of the pain. If the teeth and surrounding oral tissues have a healthy appearance and probing of the gingival tissues reveals no obvious pathology, the next consideration is that there is pathology under the site of pain. This can usually be evaluated with periapical dental films and a panoramic film of the jaw. When this is also negative, the dentist must consider further a field disorders (e.g., sinus infection, myofascial pain and temporomandibular joint pain) and any local maxillofacial pathology (e.g., neoplastic disease).

Depending on the situation, sometimes irreversible diagnostic treatments (e.g., root canal or extraction) are performed to see if they will have any beneficial effect. These are labeled diagnostic treatments when they are performed, even though the usual and customary signs of infection or inflammation being not present. If these treatments

Table 1

Three Phases of the Diagnostic Work-up for Suspected Dental Neuropathic Pain

Phase I: Problem: Pain in a vital tooth

Step 1 **Action**: Progressively perform the following tests:
(1) Cold testing for pulpal nonvitality
(2) Periapical radiographic examination for apical change
(3) A panoramic radiograph looking for other maxillofacial disease
(4) A thorough head and neck examination looking for other causative diseases
(5) A cranial nerve examination which assess any sensory alterations

1.1a **Response**: Positive evidence of nonvitality or new periapical lucency would lead to recommendation of immediate endodontics treatment; positive evidence of other disease in the maxillofacial region evident on panoramic radiograph, clinical examination or as a result of a cranial nerve examination would lead to treatment of this other disease or referral to the appropriate specialist.

1.1b **Response:** No evidence of "nonvitality" or other disease in the maxillofacial region. Proceed to phase II.

Phase II. Problem: Lingering (>3 weeks) pain in a vital tooth without periapical lucency

Step 2.1 **Action**: Remove all fillings, examine under microscope (or loops) for crack. (Note: Most cracks are mesial-distal in direction and U>L; M>P>>A). If the tooth has already been extracted, see step 3.

2.1a **Response**: Positive evidence of crack on close inspection, perform endodontics treatment on tooth and fabricate crown; if a cracked tooth already has endodontic treatment, extract tooth. (Note: Odds of success if definite crack identified is 90 percent, however, 1/10 will still fail to improve.)

2.1b **Response**: No evidence of crack on close inspection, restore tooth and see step 2.2

Step 2.2 **Problem**: Lingering pain in a vital tooth without periapical lucency and no evidence of crack on close inspection with all restorative materials removed; pain continues.
Action: Adjust tooth slightly out of occlusion or make a full-arch orthotic device to examine for excessive tooth loading pattern during sleep. This is done by waiting one month and after delivering the appliance and re-examining the orthotic surface for dents or grooves. Make it on the arch that hurts and try unloading most painful teeth. (Note: If, during the removal of the restoration, the tooth was difficult to anesthetize with local anesthetic injection, this indicates a lower prognosis for this being a reversible process and central neuropathic changes are more likely.)

2.2a **Response**: If occlusal splint is positive for tooth loading during sleep and pain reduces, continue using orthotic device for as long as needed and try to adjust device so that the painful area is not in heavy contact. (Note: Because sometimes teeth undergo slow degenerative changes, re-examine, X-ray, and pulp-test at intervals.)

2.2b **Response**: If occlusal splint is negative for evidence of tooth loading and pain continues, discontinue splint use and see step 2.3.

Step 2.3 **Problem**: Persistent pain in a tooth, with or without prior endodontics treatment, or in a tooth site if an extraction was performed. If nonendodontic-treated tooth present, there is no evidence of cracks, tooth is vital to cold test, no periapical lucency evident, occlusal appliance surface shows no bruxism or sustained clenching during sleep.
Action: Perform anesthetic test protocol which involves topical, infiltration, and get pain diary (one week).

2.3a **Response**: If topical stops pain, use a neurosensory stent with topical anesthetic as long as needed.

2.3b **Response**: If topical unsuccessful but local helps reduce pain, start medication protocol (see below). Re-examine, radiograph, and pulp-test vital teeth at intervals.

Phase III: Problem: Lingering pain in a vital tooth, that shows no evidence of nonvitality, cracks or fractures, and radiographic, clinical examination for other pathology is negative. Moreover, it does not respond to occlusal adjustment/occlusal splint treatment, topical or local anesthetics have no effect and patient is not responsive to anticonvulsant medications. Note: Phase III can be initiated earlier if psychosocial issues or neurological signs and symptoms dictate these tests.

Step 3.1 **Action**: Perform the following tests:
(1) MRI of brain
(2) Psychological consultation

3.1a **Response**: Positive evidence of CNS lesion or positive report psychiatric impairment that could explain the symptoms would lead to treatment of this other disease by referral to the appropriate specialist.

3.1b **Response**: No evidence of "nonvitality" or other disease in the maxillofacial region. Return to phase I and reassess, or if pain is substantial, referral to a medical or dental pain specialist for pain management.

fail to help, before performing a second diagnostic treatment on a second tooth or oral tissue site, the possibility that the patient has a neuropathic basis to their pain must be considered.

There are three phases of diagnostic testing that may be needed in a patient suspected of having a persistent orodental pain that might have converted into a neuropathic disorder (**Table 1**). Phase 1 is a baseline work-up for all patients that would likely include: (1) cold testing for pulpal nonvitality; (2) periapical radiographic examination for apical change; (3) a panoramic radiograph looking for other maxillofacial disease; (4) a thorough head and neck examination looking for other potentially causative diseases; and (5) a cranial nerve examination which documents any altered sensory alterations (especially the trigeminal nerve). Phase 2 is for those patients who have no obvious causation found with the above baseline examination protocol. This involves three additional steps that should be taken to assess the patient who has a suspected orodental neuropathic pain disorder (**Table 1**). These three steps include microscopic inspection of the tooth with all restorations removed, occlusal adjustment/orthotic device use, and anesthetic testing of the intraoral pain site. While the first step of the process is the most expensive and the last step (anesthetic testing) is the least expensive, anesthetic testing cannot be considered as a definitive test. In contrast, if a crack in the tooth is identified after removing all restorations, this is definitive. Phase 3 is considered when the above three procedures fail to identify a cause of a treatment method. This phase involves ordering an MRI examination to screen for central or peripheral pathology, and, if clinical history is suggestive of any psychopathology or a mood disorder order (e.g., depression, anxiety), a behavioral assessment by a trained psychologist is needed. These last two tests are especially indicated if the pain does not respond to treatment.

An index of suspicion for all deadly diseases, including cancer, should elevate when dental professionals are dealing with any patient with a history of prior cancer, when dealing with a patient with exposure to risk factors (e.g., smoking) or when the pain disorder is not within the expected sites or age group of the commonly affected.

CT imaging of the tooth may not pick up the partial tooth fracture which leaves direct microscopic examination of the tooth for cracks as the best method.

The common site and age of first presentation for atypical odontalgia was described in a study on atypical odontalgia patients. In a study, 74 percent of the sufferers were women in their 40s at initial onset, and the pain was usually present in posterior teeth/alveolar arch with molar teeth affected 58.8 percent of the time, premolars 26.8 percent, canines 4.2 percent, and incisors 12 percent.[15] In another study that evaluated 120 subjects complaining of atypical odontalgia, they had 80.8 percent of women between the ages of 23 and 60 years, with a mean age of 43 ± 13.9 years[16] (**Table 1**).

Other Trigeminal Neuropathic Pains

While this article focuses on orodental neuropathic pains (atypical gingival pain, atypical odontalgia, and phantom tooth pain), there are several trigeminal pains that have a neuropathic basis to the pain. For example, burning mouth syndrome is now thought to have clear neuropathic pain causation. In addition, some patients with chronic temporomandibular joint pain develop a persistent, anti-inflammatory medication-resistant TMJ pain, which may be neuropathic.

Sensitization of the auriculotemporal nerve may account for the reason some patients have sustained unchanging pain even after direct corticosteroid injection into the joint itself. In general, NSAIDs and corticosteroid injections do not strongly suppress neuropathic pain. Proof of auriculotemporal nerve change was provided in recent study that used quantitative sensory testing on 72 patients (44 who had arthralgia and 28 who had chronic myalgia) and 22 health controls.[17,18] Testing of nerve response threshold was achieved with electrical stimulation applied bilaterally in three trigeminal nerve sites (cheek, temple, and chin). By comparing the affected side threshold to the control (nonaffected) side, they found the electrical detection threshold ratio for the three sites, which did not vary from the expected value of 1 in the controls.

However, the patients with arthralgia the mean ratio obtained for the stimulation at the temple region site was significantly lower compared to the other sites and this was not so for the cheek or chin sites. These data suggest that the auriculotemporal nerve which innervates both the TMJ and also the temple was sensitized and had a lower threshold.

Microscopic Inspection of Teeth With Persistent Orodental Pain

Incomplete tooth fracture is a rational alternative explanation for persistent toothache without definitive evidence of dental-pulpal disease, such as a periapical radiolucency.

Incompletely fractured teeth will show evidence of vitality (responsiveness) to thermal and electrical pulp testing. Unfortunately, both the partially fractured tooth and the neuropathically sensitized tooth will show increased sensitivity to testing (e.g., palpation, percussion, cold, and electrical stimulation). Of course this theory can be tested by performing what has been termed a diagnostic root canal or diagnostic extraction. If the root canal or extraction abruptly stops the pain, then the pulpal tissues were the source of the pain, and hopefully any fractures will be confirmed, and if salvageable, neutralized by a full-crown restoration after the root canal. If these procedures do not stop the pain, the possibility of a neuropathic change in the nerve supplying the area is elevated. Since an irreversible procedure is not the first choice of the diagnostic process, it is necessary to discuss alternative methods for diagnosis beyond pulp testing and periapical imaging. These methods include computerized tomography and microscopic examination for tooth cracks. Unfortunately, CT imaging of the tooth may not pick up the partial tooth fracture which leaves direct microscopic examination of the tooth for cracks as the best method.

One recent study assessed the value of direct visual examination of 46 chronically painful teeth in 32 patients after removal of all restorations was performed for evidence of an incomplete fracture.[19] They found evidence of incomplete tooth fracture in one or more teeth from 29 of the 32 patients. While this study suggests that if one looks hard enough, 90 percent of teeth with persistent pain will have a incomplete tooth fracture as the underlying cause. This finding is not consistent with the literature since the long-term outcomes for patients seeking care in a chronic orofacial pain clinic suggests that less 25 percent have complete relief with irreversible dental and oral surgical treatment (see section on prognosis below). Clearly, additional data on this method of diagnosis (direct visualization using an operating microscope) and the long-term results needs more research, but in the meantime, this method should be considered to confirm the presence of a structural abnormality of the tooth before a diagnostic root canal or diagnostic extraction is performed.

If there are neuropathic changes that result in persistent tooth site pain, this is commonly called phantom tooth pain.

Evidence for True Hyperalgesia in Phantom Tooth Pain

When tooth pain becomes persistent and root canal treatment is unsuccessful in stopping the pain, the treating dentist commonly elects to extract the tooth, hoping that the pain symptoms will stop. If the tooth is the source of the pain and extrapulpal trigeminal neuropathic changes have not occurred, then the pain should stop. If there are neuropathic changes that result in persistent tooth site pain, this is commonly called phantom tooth pain. Eide and Rabben were the first to conduct quantitative sensory testing in the trigeminal region on symptomatic continuous neuropathic pain cases.[20] Specifically, they reported on eight cases with spontaneous onset continuous trigeminal neuropathic pain. Moreover, four of these had unsuccessful endodontic treatment or extraction for their pain. They determined the threshold for mechanosensory detection and first pain threshold detection using von Frey filaments applied to the painful facial skin area. They compared the pain patient results with a similar test performed on the contralateral nonpainful side. They reported that in the group of eight spontaneous onset trigeminal neuropathic pain cases, they found no difference between sides for tactile threshold using von Frey filaments. Of course, it should be noted there were no control (nonpain) subjects, these cases were a mixture of probable atypical odontalgia and phantom tooth pain cases and the mechanosensory testing was performed at an extraoral facial skin site. In one study, the authors performed threshold level measurements for light touch sensation using an intraoral site in clearly defined group of phantom tooth pain subjects. They did this using a case-control experimental on 10 phantom tooth pain patients (mean age 56, range 32-71, nine females) and 10 controls.[21] They found the phantom tooth pain complaints were predominantly reported in the upper jaw (ratio 8:2) with the majority in the molar region (ratio 5:3). In addition, phantom tooth pain subjects showed significantly lower threshold levels for light touch sensations on the affected side. While limited in quantity, the above data suggests that PTP subjects demonstrate measurable mechanical hyperalgesia, and among all tests performed, mechanical pain threshold was significantly altered on both sides with the greatest change being on the pain side.

Etiology and Co-morbid Psychological Diseases

There are case reports of sustained neuropathic pain after direct traumatic (e.g., fracture or surgical) injury, nerve injection injury, implant compression injury, osseous growth compression

Table 2

Medications Used for Trigeminal Neuropathic Pain

Medication/Dosage	Action	Rating/Efficacy	Issues to consider with use of this drug
Sodium channel-blocking medications: ■ Benzocaine 20% ■ Lidoderm Patch 5% ■ EMLA cream (all three are applied topically to area of pain)	MOA: Blocks nerve transmission along the axon by blocking sodium channels	First-line tx for chronic trigeminal neuropathic pain	■ All three are FDA-approved as an aid for minor surgical procedures but benzocaine and EMLA are used off-label for neuropathic pain. Lidoderm Patch is approved for allodynia and chronic pain associated with postherpetic neuralgia.
Mild anticonvulsant medications: ■ Gabapentin (Adults: 300 mg; 3-5/day) (range: 1800-3600 mg/day, daily doses >1800 mg do not generally show benefit) ■ Pregabalin (Adults: 50 mg; 3/day)	■ MOA: Not known, for gabapentin but has properties in common with anticonvulsants ■ MOA: Pregablin binds to subunit of voltage-gated Ca+ channels in CNS and inhibits excitatory neurotransmitter release	First-line tx for chronic neuropathic pain	■ FDA-approved as an adjunctive medication for epilepsy. Gabapentin is frequently used for neuropathic pain but this is an off-label use of this medication. ■ Pregabalin is FDA-approved for both diabetic neuropathic pain and postherpetic neuralgia. Both medications yield infrequent and benign side effects at high doses, but total dosage must be lower in individuals with renal compromise. There is generally no necessity to monitor blood levels and no significant drug/drug interactions.
Tricyclic antidepressants ■ Amitriptyline (Adults: 50-150 mg/day at bedtime or in divided doses; maximum suggested dose is 300 mg/day) ■ Nortriptyline (Adults: 10-25 mg; 3-4 times/day up to 150 mg/day)	■ MOA: Inhibits paroxysmal neuronal activity; blocks sodium and calcium channels; decreases sensitivity of adrenergic receptors on injured nerve sprouts; blocks the reuptake of norepinephrine and serotonin	First-line medication for neuropathic pain	■ FDA approves of TCAs for depression. Amitriptyline and nortriptyline are also used off-label commonly for chronic neuropathic pain in temporomandibular dysfunction (TMD); for CDH and postherpetic neuralgia, traumatic nerve injury, diabetic neuropathy, tension-type headaches, migraine prophylaxis and fibromyalgia. They generally have a high side effect profile with sedation, dry mouth, constipation, urinary retention, weight gain being common.
Nonopioid analgesics ■ Acetaminophen (Adults: 325-650 mg every 4-6 hours or 1000 mg 3-4 times/day) ■ Tramadol (Adults: 50-100 mg every 4-6 hours, not to exceed 400 mg/day)	■ MOA (Acetaminophen): Inhibits the synthesis of prostaglandins in the CNS and peripherally blocks pain impulse generation in axons ■ MOA (Tramadol): Binds to μ-opiate receptors in CNS and inhibits reuptake of norepinephrine and serotonin	Second-line medication for neuropathic pain	■ FDA approves acetaminophen for treatment of mild-to-moderate pain and fever. ■ FDA approves tramadol for relief of moderate to moderately-severe pain.

NNT	NNH
■ Lidocaine patch 5% has a 4.4 NNT for PHN	■ NNH: All three medications would likely have a high NNH with essentially no major systemic adverse effects
■ NNT for gabapentin use in various neuropathic pain conditions at high doses (2400 mg/day) was 3.8 ■ NNT for pregabalin use in treating PHN and DN at dose ranging from 150 to 600 mg/day was 4.2	■ NNH for withdrawal for gabapentin is 26.1 ■ NNH for pregabalin was 11.7 indicating a higher high withdrawal rate than gabapentin
■ NNT ranges from 2 to 3	■ NNH is not known for neuropathic pain
■ NNT for less potent opioid medication (tramadol) is 3.9	■ NNH for tramadol use in neuropathic pain is not known

(Table continues on Page 606)

injury, neoplastic perineural invasion injury, and infection damage to the nerve itself such as with a trigeminal herpes zoster and herpes simplex infection.[22] Neuropathic pain also can be caused by diabetic-related neural injury and altered sympathetic nervous system-related neuropathy. Medications and other chemical toxins as well can cause neuropathic pain along with idiopathic neuropathies. All branches of the trigeminal nerve can be involved including the lingual, inferior alveolar, mental nerve, auriculotemporal and infraorbital nerves.[23]

Regardless of the cause or which nerve branch is damaged, neuropathic pain and psychiatric impairment are common co-morbid problems.[24] The fact that two problems are associated strongly, does not prove that one is the cause of the other.

In fact, pretreatment depression or anxiety as a psychological characteristic does not dictate that the individual to become a neuropathic pain sufferer in the future. An alternate explanation for the strong association between psychological disturbance and neuropathic pain is that the unrelenting nature of the pain itself alters the patient's personality.

Another recent study examined the relative contribution of catastrophic thinking (i.e., rumination, magnification, helplessness) to the pain experience in 80 neuropathic pain patients.[25] Those individuals who scored higher on a measure of catastrophic thinking also rated their pain as more intense, and rated themselves to be more disabled due to their pain. Catastrophizing thinking predicted pain-related disability over and above the variance accounted for by pain severity and combined, these data suggest that unrelenting pain without highly effective treatment methods may induce helplessness in patients and shift them to express more psychopathology and mood disorders.

Mechanism of Neuropathic Sensitization Conversion

The mechanisms that turn a normal sensory signal into neuropathic pain occur because of multiple alterations e.g., the type and number of sodium channels on an affected nerve. These alterations increase the nerve's sensitivity. The sensitivity of some nerves can be increased to such a degree that they will fire with no obvious physical stimulus. The various mechanisms responsible for these changes include spontaneous ectopic discharge of peripheral nerves, sensitization of sensory nerves from altered receptors, and an increased excitatory neurotransmitter release. Cross-excitation of these nerves occurs after demyelination. Sometimes the sympathetic nervous system can stimulate the sensory system directly after sustained pain causes the sensory system to start upregulating sympathetic neurotransmitter (i.e., adrenergic) receptors. With any peripheral nerve injury or substantial pain nerve activity, the spinal cord undergoes reorganization. An alteration in the descending modulatory nerves also develops that increases the excitability of spinal and trigeminal neurons and with loss of interneurons after injury, there is a reduction of inhibitory activity. Finally, the brain itself can and does change and these supraspinal influences are potent amplifiers and even generators or pain.[26-29]

Medications for Chronic Trigeminal Neuropathy

There still exists no clear choice as to the best medication for the treatment of neuropathic pain. This is due to the large number of pharmacologic medications that can be used to treat both pain symptoms and the co-morbid diseases. There are no neuropathic-activity suppressing medications that affect only the damaged, sensitized nerves without having a powerful effect on normal sensory nerve systems. This

Table 2

Medications Used for Trigeminal Neuropathic Pain *(continued)*

Medication/Dosage	Action	Rating/Efficacy	Issues to consider with use of this drug
Atypical antidepressants ■ Venlafaxine (Adults: 75 mg/day, tid and taken with food; maximum dose is up to 225-375 mg/day) ■ Duloxetine (Adults: 20 mg bid. Maximum dose is 60 mg/day)	■ MOA: Both medications are serotonin and norepinephrine reuptake inhibitors (SNRIs)	Second-line medication for neuropathic pain	■ FDA has approved venlafaxine for major depression; generalized anxiety disorder (GAD), social anxiety disorder (social phobia); panic disorder. ■ Duloxetine is FDA-approved for depression and diabetic neuropathy. In general, SNRIs have fewer anticholinergic properties than TCAs. Adverse effect profile is similar to that of SSRIs and blood pressure must be monitored regularly.
Moderate and strong opiods: ■ Oxycodone ■ Hydrocodone ■ Morphine (These medications have a variable dose for chronic pain use and they have titrated to effect.)	■ MOA: Agonist for opioid receptors	Third-line medication for neuropathic pain	■ FDA has approved opioids for pain. Oral long-term treatment with opioids. More relevant in chronic pain, has only been tested using placebo-controlled designs in peripheral neuropathic pain conditions and was found superior to placebo in patients with postherpetic neuralgia, phantom limb pain, and painful diabetic neuropathy.
Moderate anticonvulsant medications: ■ Valproic acid (Adults-migraine): 500 mg/day for 7 days; then increase to 1000 mg/day	■ MOA: Increase GABA neurotransmission	Third-line medication for neuropathic pain, but first-line medication for CDH	■ FDA approves of valproic acid for treatment of seizures and bipolar disorder and for migraine prophylaxis. It is off-label when used for neuropath ic pain. This medication needs frequent hematologic, hepatic, and blood level monitoring, and it has multiple drug-drug interactions.
Strong anticonvulsant medications: ■ Carbamazepine (Adults: 400-1200 mg/day using divided dose [bid])	■ MOA: Depresses thalamic activity and temporal stimulation by limiting influx of sodium ions across cell membrane	Third-line tx for chronic neuropathic pain but is a first-line tx for episodic trigeminal neuralgia	■ FDA approves of carbamazepine for treatment of seizures and bipolar disorder and trigeminal neuralgia. It is off-label when used for neuropathic pain and this medication is not commonly used for sustained neuropathic pain. This medication needs frequent hematologic, hepatic, and blood level monitoring, and it has multiple medication-medication interactions.
Benzodiazepines ■ Clonazepam (Adults: 0.25-3 mg/day in two divided doses)	■ MOA: This medication binds to the GABA receptor and function as an anticonvulsant and anxiolytic	Third-line medication for neuropathic pain but first-line medication for BMS	■ FDA-approved for general anesthesia sedation and analgesia. It is off-label when used for neuropathic pain, anxiety. Clonazepam also may be useful in managing the co-morbid anxiety that may amplify pain symptoms. It is thought to act by potentiating inhibitory GABA transmission, but its analgesic effects may be more related to its anti-anxiety and anti-spasticity properties.

NNT	NNH
■ NNT for duloxetine for DN was 4.1 (at 60mg/d and 120mg/d) ■ NNT for venlafaxine for painful polyneuropathies is 4.0	■ NNH for SNRIs used in neuropathic pain is not known
■ NNT for P.O. opioids when used for chronic pain is 2.5 to 3.0	■ NNH for tramadol was 9.0 and was very low (nonsignificant) for oxycodone and morphine
■ NNT is not known for neuropathic pain	■ NNH is not known for neuropathic pain but will be much higher than gabapentin
■ NNT for trigeminal neuralgia of 1.7 ■ NNT for painful diabetic neuropathy was 2.3	■ NNH for neuropathic pains is 21.7
■ NNT for clonazepam as a neuropathic medication is not known	■ NNH for clonazepam as a neuropathic medication is not known

(Table continues on Page 608)

means that high side effects are likely to be associated with these medications. Direct medication-to-medication trials are not commonly performed, and therefore it is difficult to compare medications for relative efficacy. It is common to use two numbers calculated from randomized blinded-controlled clinical trials to help rate and compare drugs. The first is the number needed to treat, NNT, which is defined as the number of patients needed to treat with a certain medication to obtain one patient with a defined degree of pain relief (usually 50 percent).[30,31] The second one is the number needed to harm, NNH. This is defined as the number of patients that need to be treated for one patient to drop out due to an adverse effect. The characteristic of a good medication is one that has a low NNT and a high NNH. Several meta-analyses of medication trials have reported these two numbers for medications commonly used in the management of neuropathic pain.[32-39]

Using the above meta-analysis information, plus the NNT and NNH calculations, this paper has ranked neuropathic suppressing medications as first-, second-, third-, or fourth-line medications (**Table 2**). Using these rankings, the first and safest approach for persistent neuropathic orodental pain is to apply topical anesthetics (a first-line medication) for a prolonged time to attempt to suppress nociceptive activity and reverse the neuropathic changes. Usually these medications are applied to the focal pain site using a tissue-covering oral stent as a holding device. The most common topical anesthetic medication is benzocaine 20 percent in orobase paste. This agent is very helpful controlling the patient's pain.[40] Two other first-line oral medications that might be added to the treatment protocol would be either a tricyclic antidepressant type medication (e.g., nortriptyline) and/or a mild anticonvulsant type medication (gabapentin or pregabalin). If adequate control is not achieved with these two agents and the topical anesthetics, another second-line medication would be an atypical antidepressant (e.g., duloxetine).

This medication is used if the tricyclic antidepressant/anticonvulsant combination does not work or the side effects are not acceptable to the patient. In all situations, the above medications would be supplemented with a nonopioid analgesic for breakthrough pain (another second line medication). In some cases, a moderate or strong opioid (third-line medication) is used if the nonopioid analgesic is not adequate. In some select neuropathic pain conditions (e.g., trigeminal neuralgia, CDH, BMS) individual neuropathic medications that would be third- or fourth-line medications for orodental pain might be first-line medications, these medications are not the focus of this review article but are included in the table for completeness. Finally, in cases were the patient has substantial comorbid depression a fourth-line neuropathic pain medication, such as an SSRI, would be used as part of the treatment protocol.

As a general rule, the clinician also must try to avoid polypharmacy, which sometimes is impossible in the treatment of chronic pain. Theoretically, the use of a single medication that is directed toward the responsible pain receptor is preferred over a combination of medications that are nonspecific for the condition being treated. Likewise, the use of multiple medications with different mechanisms of action should increase effectiveness for conditions where more than one receptor needs to be targeted. The clinician's goal should be to alleviate pain and distress while keeping medications to a minimum effective dose. This article has not covered the nonpharmacologic methods used to treat pain (e.g., behavioral and

Table 2

Medications Used for Trigeminal Neuropathic Pain *(continued)*

Medication/Dosage	Action	Rating/Efficacy	Issues to consider with use of this drug
Antidepressants - Serotonin selection reuptake inhibitors: ■ Fluoxetine ■ Paroxetine ■ Sertraline ■ Citalopram (variable dosing, tritrate to effect)	■ MOA: All SSRIs act via potentiation of the serotonin system pathways	Fourth-line medications for neuropathic pain	■ FDA has approved SSRIs for major depression. They are used off-label for pain. Overall these medications have been very disappointing for pain but useful for managing the co-morbid symptoms of depression

physical medicine methods) but without question a comprehensive approach to assessment and treatment of pain is paramount (**Table 2**).

Long-term Prognosis for Atypical Odontology and Phantom Tooth Pain

All patients with a neuropathic pain disorder ask about the future in that they wish to know: (1) How long with the pain last? and (2) Will it go away with time? In addition, when they are having irreversible treatments, they usually want to know the odds of the treatment working. Extensive data on the prevalence of how often irreversible dental treatments (e.g., endodontics and extractions) completely solve a patient with persistent orodental pain without pretreatment evidence of nonvitality and or periapical lucency is based only on retrospective analysis of cases. While such reports are valuable because they are retrospective studies on complex "chronic pain" patients, they make it difficult to reliably predict the future for an individual patient. There are only two studies that examine the long-term prognosis of patients suffering facial pain that does not fit with the traditional diagnostic criteria and which does not respond to dental treatment was examined in a recent study. One recent article described the long-term results of a cohort of 74 patients suffering chronic idiopathic facial pain who were seen a minimum of nine to 19 years prior.[41] Of the 74, 13 had died and 16 did not wish to participate. Of the 45 remaining study participants 10 (22 percent) were free of orofacial pain. In a subset of 14 of these patients who had undergone multiple extractions (7.1 per patient), only 3 (21.4 percent) reported permanent pain relief, which is no higher than the rate seen in non-extraction cases.

Overall, these authors reported a very low success rate for the invasive dental treatments that were performed and suggested they may be contraindicated in patients suffering from idiopathic orofacial pain.

These data were consistent with a prior study on persistent facial pain.[42] This study followed up 109 consecutive patients seen in a dental school pain clinic. The patients had between four to nine years of time from their first visit to the follow-up and of the 109, 85 percent responded to the questionnaire. The data suggested only 27 percent of the patients experienced total disappearance of pain. These two studies suggest that between 21 percent and 27 percent of patients who have chronic orofacial pain will have pain relief with time. It may also suggest that the treatments provided in the late 1980s and early 1990s were not highly effective. Based on these data, assuming no obvious dental infection or cracked tooth is identified, the odds of pain stopping in a atypical odontalgia case or in a phantom tooth pain case (after failed root canal therapy or extraction has not stopped the pain) is 25 percent for full-pain remission in five-plus years.

Moreover, the odds of a positive psychiatric diagnosis being made (e.g., anxiety, depression, somatization) in a failed treatment atypical odontalgia or phantom tooth pain case is 67 percent. It seems logical to hope that with a logical plan, a more defined diagnosis and with some of the newer medications and methods of treatment that the percent of patients having full remission will increase and more patients overall will feel better managed. Hopefully with earlier treatment and pain control with the best neuropathic suppressing medications (**Table 2**) this should also prevent secondary psychiatric disease from developing. ■■■■

NNT	NNH
■ NNT for SSRIs for neuropathic pain is almost 7	■ NNH for SSRI as a neuropathic medication is not known

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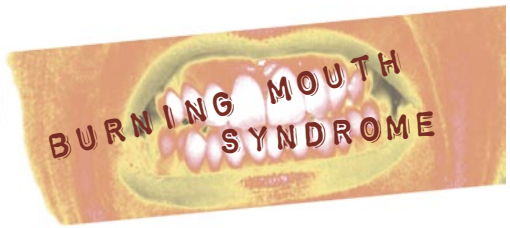

Burning Mouth Syndrome: An Update on Diagnosis and Treatment Methods

Piedad Suarez, DDS, and Glenn T. Clark, DDS, MS

ABSTRACT

Burning mouth syndrome is characterized by both positive (burning pain, dysgeusia and dysesthesia) and negative (loss of taste and paraesthesia) sensory symptoms involving the lips and tongue, mainly the tip and anterior two–thirds. BMS patients report a persistently altered (metallic) taste or diminished taste sensations. Acidic foods such as tomatoes and orange juice cause considerable distress. Most of the common laboratory tests suggested for BMS patients will be negative as well. BMS is best subcategorized as primary BMS, no other evident disease, and secondary BMS, which is defined as oral burning from other clinical abnormalities. The presence of BMS is very uncommon before the age of 30; 40 years for men. The onset in women usually occurs within three to 12 years after menopause, and is higher in women who have more systemic disease. Quantitative assessment of the sensory and chemosensory functions in BMS patients reveals that the sensory thresholds (significantly higher) are different than in controls.

Tongue biopsies have shown that there is a significantly lower density of epithelial nerve fibers for BMS patients than controls. The above data generally support the idea that BMS is a disorder of altered sensory processing which occur following the small fiber neuropathic changes in the tongue. BMS patients frequently have depression, anxiety, sometimes diabetes, and even nutritional/mineral deficiencies, but overall these co-morbid diseases do not fully explain BMS. The management of BMS is still not satisfactory, but because BMS is now largely considered to be neuropathic in origin, treatment is primarily via medications that may suppress neurologic transduction, transmission, and even pain signal facilitation more centrally. Finally, spontaneous remission of pain in BMS subjects has not been definitely demonstrated. The current treatments are palliative only, and while they may not be much better than a credible placebo treatment, few studies report relief without intervention.

Imagine the frustration of having a continuous painful disorder that cannot be definitively diagnosed with any known test or X-ray, interferes with eating, becomes progressively worse with time, has no known cause, and for which there is no highly effective treatment. This is what patients with burning mouth syndrome deal with every day of their lives. BMS typically has a spontaneous onset, although its intensity will increase gradually over time. It is characterized by both positive (burning pain, dysgeusia and dysesthesia) and negative (loss of taste and paraesthesia) sensory symptoms. The primary location for these symptoms are the lips and tongue, mainly the tip and anterior two–thirds. BMS patients complain also of sensory discomfort in the hard palate and alveolar ridges.

Conversely, the buccal mucosa and the floor of the mouth are almost never involved.[1] At least for the tongue, the anatomic distribution of the burning pain in BMS patients corresponds to a great degree where taste bud density

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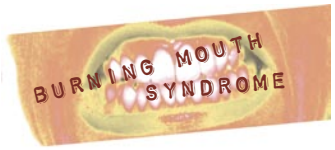


is greatest in the mouth. For example, Miller examined taste bud density on the tongue and found that taste bud density was 4.6 times higher on the tip than the mid-tongue region.[2] However, since taste buds are not commonly located on the inner lip mucosa, anterior hard palate or alveolar ridges, this association between taste buds and BMS is not absolute. Nevertheless, most BMS patients report a persistently diminished taste or altered (metallic) taste sensations. Acidic foods such as tomatoes and orange juice cause considerable distress with an increase in burning sensations. These descriptions vary but often include a stinging-burning sensation as if they have scalded the mucosa. Finally, in spite of the vividly described irritated or raw feeling in their oral tissues, most of the time, the tissues appear normal to visual inspection. Most of the common laboratory tests suggested for BMS patients (described later) will be negative as well.[3]

BMS has various synonyms such as stomatopyrosis, glossopyrosis, stomatodynia, glossodynia, sore mouth, sore tongue, and oral dysesthesia. These terms are used to emphasize the quality and/or the location of pain in the oral cavity. The International Association for the Study of Pain has identified BMS as a distinctive named entity characterized by oral burning pain episodes lasting at least four to six months.[4] The International Classification of Disease (version 9) has assigned the term glossodynia, which included the subterms glossopyrosis and painful tongue a specific identity code number (ICD-9 #529.6).[5]

A recent paper suggested that a subpopulation of BMS cases presents with a common triad of symptoms including idiopathic sensorial disturbance of burning mouth, taste disturbance (dysgeusia), and dry mouth.[6] Another paper suggested three subgroups with type 1 being characterized by burning pain increasing throughout the day and reaching its peak in the evening. Type 2 was characterized by complaints of continuous sensory disturbances, and type 3 had intermittent symptoms with free-pain periods during the day.[7] The most pragmatic method of grouping BMS is by dividing patients into the primary BMS sufferers (no other evident disease) and secondary BMS sufferers (defined as oral burning from other clinical abnormalities). In fact, using this classification scheme, one paper examined 69 BMS patients (83 percent female) and asked them to fill out both the Multidimensional Pain Inventory and Symptom Checklist 90-Revised.[8] They found that the primary BMS patients and the secondary BMS patients showed no differences with respect to age, pain duration, pain intensity, or levels of psychologic distress. The only substantial difference was that if the associated clinical abnormality was treatable, then the burning sensations would improve in the secondary BMS group, whereas the primary BMS group did not demonstrate remarkable symptom cessation with treatment.

In spite of the vividly described irritated or raw feeling in their oral tissues, most of the time, the tissues appear normal to visual inspection.

Epidemiology

Burning mouth symptoms are reported in up to 4 percent of adults, and this percentage increases with age being more prevalent in the fifth to seventh decade. One study surveyed 669 men and 758 women randomly selected from 48,500 individuals between the ages of 20 and 69, and reported 53 individuals (3.7 percent) exhibited BMS (11 men or 1.6 percent and 42 women or 5.5 percent).[9] The presence of BMS is very uncommon before the age of 30; 40 years for men. The onset in women usually occurs within three to 12 years after menopause and is higher in women who have more systemic disease.[10] Another epidemiologic study surveyed U.S. adults and estimated the overall prevalence of burning mouth to be 0.7 percent of the adults up to age 65.[11] This study was repeated on a subset of more than 5,800 individuals aged 65 or older in southern Florida.[12] They reported a prevalence of 1.7 percent for burning mouth pain in this elderly group. Clearly the differences in these prevalence figures are related to sampling bias in surveyed populations and disease definition being used.

Quantitative Sensory Testing in BMS

The frequent occurrence of numbness, pain and dysesthesia in BMS has prompted researchers to perform a quantitative assessment of the sensory and chemosensory functions in these patients. Until recently, researchers have not consistently found a statistically significant alteration in the sensory perception (touch and temperature) of BMS patients. For example, one study carefully examined 20 BMS patients versus 20 controls for different abilities to perceive different shapes of objects with

their tongue.[13] No systematic disparity was evident in the two groups regarding object size perception ability. Of course, detecting the shape of objects with one's tongue is not the only test of sensory acuity. Several years ago researchers used argon laser stimulation to examine 23 BMS subjects versus 23 age-matched controls for differences in their sensory and pain thresholds.[14] This study used brief laser stimulation to six test sites (tongue tip, lower lip mucosa and skin, buccal mucosa, anterior hard palate, and dorsum of the hand).

They reported the sensory thresholds were significantly higher and the ratios between pain and sensory thresholds significantly lower in patients with BMS at all tested sites. The resulting widespread sensory threshold differences seen in this study argues for a centrally mediated sensory amplification abnormality. Another study used an objective electrophysiological examination of the trigeminal-facial nerve system using the blink reflex response in 11 BMS subjects and 10 controls.[15] They reported BMS patients have clear-cut alterations in their blink response to applied stimulation. Finally, a study examined evoked brainwave potentials following lingual nerve stimulation in 22 BMS patients with pain, 10 BMS patients with reported numbness, and six controls.[16] They found that pain thresholds were significantly lower and evoked potential response latencies were significantly different (i.e., shorter) in the BMS with pain group. The latencies in the BMS with numbness group were significantly longer. Overall, these sensory data suggest that peripheral and/or central nervous system changes are clearly present in BMS but they do not pinpoint where in the somatosensory system changes are to be found.

Biopsy Evidence of BMS changes

Until recently, the primary site of pathology in BMS was not identified; therefore, no diagnostic test was available for this disorder. However, a new study investigated the innervation of the epithelium of the tongue in 12 chronic BMS cases and nine healthy controls using tongue tissue biopsies to assess whether damage of peripheral nerve fibers underlies the pathogenesis of the disease.[17] These researchers used immunohistochemical and microscopic methods to examine for nerve damage in the tongue. They reported a significantly lower density of epithelial nerve fibers for BMS patients than controls. The authors described epithelial and subpapillary nerve fibers changes suggestive of axonal degeneration. They concluded that BMS is caused by a trigeminal small-fiber sensory neuropathy.

BMS patients frequently report a positive taste sensation, which they describe as a persistently altered (metallic) taste.

Taste Changes and BMS

Dysgeusia is a term used to describe a distorted gustatory perception or persistent gustatory sensation in the absence of gustatory stimulants.[18] As mentioned earlier, BMS patients frequently report a positive taste sensation, which they describe as a persistently altered (metallic) taste. They also have a diminished ability to detect bitter flavors, and spicy and acidic foods increase their burning sensations. One recent study examined 50 patients with BMS (study group) and 50 healthy subjects (control group), and analyzed their ability to taste three flavors: bitter, acid, and spicy substances.[19] They found that taste sensation was normal in all controls, but in 30 of the BMS patients, they had a diminished response to bitter taste. The use of a spicy substance, pepper sauce, applied to the tongue produced a strong burning to the tongue in 28 patients of the BMS group but the same response was only seen in 10 of the controls.

Another study examined 180 subjects with complaints of BMS, xerostomia, and taste disturbances versus 90 age- and gender-matched healthy controls.[20] They also reported that the BMS patient group had clear-cut taste acuity differences compared to the controls with more of the BMS patients reporting sweet abnormality than with the other three taste substances: salt, bitter, and sour. Lastly, a study examined taste acuity in 73 BMS patients (57 women and 16 men) and 52 control subjects (38 women and 14 men) who were age- and gender-matched to the BMS group.[21] They used various concentrations of sweet, salty, sour, and bitter solutions, and asked subjects to rate the intensity and quality of each solution. They found that the 57 women in the BMS group gave lower intensity ratings for salty and sweet test solutions than the 38 women controls. They also found no group differences for these women on sour or bitter test solutions, but the men in this study showed no group differences on any of the substances tested. The above studies document that taste is consistently altered, although not in a consistent direction in BMS patients.

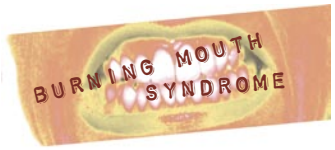


Table 1

Primary and Secondary BMS

Presumed Etiology	Clinical Presentation
PRIMARY BMS TREATMENT	
Nerve atrophy	**Focal neuropathic pain involving small fiber atrophy of the oral tissues.**
SECONDARY BMS TREATMENT	
Dry mouth (xerostomia)	Several medications cause decreased salivary flow (tricyclic antidepressants, central nervous system depressants, lithium, diuretics, and medications used to treat high blood pressure). It can also occur with aging or Sjögrens syndrome.
Oral infection	Yeast infections (thrush) have been seen in BMS patients and may be related to immune dysfunction (e.g., HIV), uncontrolled diabetes, poorly maintained/cleaned denture and certain immunosuppressive medications.
Autoimmune mucosal Rxns	Lichen planus and geographic tongue are conditions that are usually painless but sometimes cause a mucosal Rxns stomatitis and a sore, patchy tongue.
Nutritional deficiencies	Being deficient in nutrients, such as iron, zinc, folate (vitamin B-9), thiamin (vitamin B-1), riboflavin (vitamin B-2), pyridoxine (vitamin B-6) and cobalamin (vitamin B-12), may affect oral tissues and cause a burning mouth. These deficiencies can also lead to vitamin deficiency anemia and oral stomatitis.
Allergies	The mouth burning may be due to allergies or reactions to foods, food flavorings (especially cinnamon), other food additives, fragrances, dyes, or other substances. Similarly, direct chemical irritation and allergic reactions to dental materials may be a factor in burning mouth syndrome.
Reflux of stomach acid	The sour- or bitter-tasting fluid that enters the mouth from the upper gastrointestinal tract may cause irritation and pain.
Certain medications	Angiotensin-converting enzyme (ACE) inhibitors, used to treat high blood pressure, may cause side effects that include a burning mouth.
Endocrine disorders	Endocrine disorders such as diabetes and underactive or overactive thyroid are known to produce peripheral neuropathic pain and generalized hyperalgesia.

Since metallic dysgeusia is a common early symptom of a BMS disorder, it would be appropriate to review a recent article that describes medication induced dysgeusia.[22] This recent paper reported that the most commonly reported medications linked to metallic dysgeusia are those used to treat bacterial infections, psychosis, arthritis, and hypertension. Specifically, they found case reports for metallic dysgeusia linked with tetracycline, lithium carbonate, D-penicillamine, and catopril.[23-27] The Doty and Bromley review paper in 2004 also pointed out that sometimes the underlying medical problems for which medications are being prescribed are the real problem, especially when the disease affects the brain (e.g., epilepsy, migraines, hypothyroidism, schizophrenia).[28] Lastly, one 1985 paper described a link between metallic dysgeusia and Crohn's disease that is manifesting oral effects as well as the usual intestinal changes.[29]

In summary, metallic dysgeusia is not well understood, but in the absence of medications or a brain disease causing it, the possibility remains that it may be related to damaged peripheral nerves, especially considering the information already presented about small sensory fiber neuropathic changes in the tongue. The hypothesis that pain

Table 2

Diagnostic Test Used as Part of the BMS Diagnostic Process

Complete blood cell count (CBC)	This common blood test provides a count of each type of blood cell in a given volume of blood. The CBC measures the amount of hemoglobin, the percentage of blood that's composed of red blood cells (hematocrit), the number and kinds of white blood cells, and the number of platelets. This blood test may reveal a wide variety of conditions, including infections and anemia, which can indicate nutritional deficiencies.
Other blood tests	Because nutritional deficiencies are one cause of a burning mouth, running a test on the blood levels of iron, zinc, folate (vitamin B-9), thiamin (vitamin B-1), riboflavin (vitamin B-2), pyridoxine (vitamin B-6) and cobalamin (vitamin B-12) is important. Also, because diabetes causes neuropathic pain, a check may be done of the fasting blood sugar level.
Allergy tests	While it is not common, occasionally, testing to see if the patient may be allergic to certain foods, additives or even substances in dentures can be ordered through an allergist.
Oral swab culture or cytologic smear	If a fungal infection is suspected, a small tissue sample (biopsy) or an oral swab of the mouth for culture and examination may be ordered.
Tongue tissue biopsy	With the recent suggestion that small nerve fibers are depleted in the affected area, some special tests may be ordered when a biopsy is taken.

and taste pathway are both affected and interact is reasonable and certainly worthy of further testing, especially if an animal model could be developed.

Other Local Oral Factors and BMS

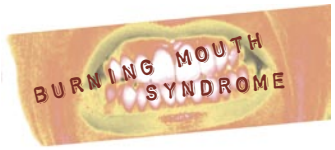
Many local and systemic precipitating factors have been suggested beyond the salivary changes and sensory dysfunction changes previously mentioned. The local factors included other diseases that may cause burning sensations such as oral candidal infections, autoimmune mucosal reactions like lichen planus and geographic tongue, and tissue trauma from ill-fitting dentures. Of course, there are always case reports of burning-type pain occurring from oral carcinomas that invade the trigeminal nerve and from a variety of local oral mucosal tissue irritants.[30] These local oral conditions have been seen often enough to suggest that some cases of BMS are secondary BMS cases.[31] Estimates are that more than one-third of all BMS patients presenting for diagnosis have multiple causes and the most common causes of secondary BMS are listed in **Table 1**.

Other Common Co-morbid Systemic Diseases

Various systemic conditions have been associated with BMS, including diabetes, hormonal changes and nutritional/mineral deficiencies. Because the condition is more prominent in female patients over age 40, most suffering from BMS are perimenopausal or postmenopausal at this stage in life.[32] Whether or not the hormonal changes in women that occur with menopause is causally related to BMS is not clear. One study examined this issue by looking at the effect of hormonal replacement therapy, HRT, on BMS. They found that HRT helped in 15 of 27 of their postmenopausal women with BMS.[33] Unfortunately, this study was an open label study and not a randomized, blinded, placebo-controlled study and thus the data are not convincing proof of a causal link between hormone alterations and BMS. Patients with BMS often have high blood glucose levels, but this does not occur on a consistent basis so no causal relationship has been demonstrated.[34] Next, nutritional deficiencies (vitamins B-1, B-2, B-6, B-12, iron, folic acid, zinc, etc.) is yet another reported systemic abnormality associated with BMS. Like hormonal status and diabetes, these suggested nutritional deficiencies are not consistently supported by the literature. Nevertheless, local and systemic factors must be ruled out before final diagnosis of BMS is made. The common diagnostic tests used for BMS are listed in **Table 2**.

Psychological Factors

Various psychological disorders, including depression, anxiety and soma-



tization, have been mentioned as playing a role in BMS.[35] One study examined 25 patients with a diagnosis of primary BMS and 25 age- and gender-matched patients with organically based painful disorders of the mouth and reported a positive psychiatric diagnosis in 44 percent (11/25) of the BMS patients but only in 16 percent (4/25) of the non-BMS controls of the patients with BMS. This study involved an interview by a psychiatrist and a questionnaire that screens for psychiatric disorders. While 44 percent seems a high number when compared to other chronic pain patients, this rate is not unusual or even high. For example, the same 28-item psychiatric screening questionnaire (general health questionnaire (GHQ-28)) used in the prior study was given to 31 consecutive primary BMS subjects. These authors found that although 51.9 percent of the patients showed evidence of psychiatric illness using the GHQ-28 questionnaire, this rate was similar or lower than what had been reported for other chronic pain subjects, except those attending a psychiatric clinic.[36] Anxiety is another often-reported feature of BMS patients and one study examined 74 BMS using a psychiatric interview plus the Hamilton's Depression and Anxiety Scales, HADS.[37]

This study reported a positive psychiatric diagnosis (mostly depression) was established in 38 of the 74 cases (51.4 percent). The HADS questionnaire data suggested that when anxiety was present, it strongly influenced the psychiatric condition of these patients. Findings of an elevated rate of positive findings when a systematic psychometric analysis of BMS patients is performed was confirmed again in a recent study, which examined 32 BMS patients and 32 matched control subjects using a comprehensive, reliable, and validated inventory.[38] Like the studies previously mentioned, results showed highly significant differences between the BMS group and the non-BMS controls with regard to several personality factors. Unfortunately, findings of high levels of anxiety, depression or even somatization tendencies are not unusual or unique to BMS patients.

Chronic pain patients in general have elevated findings when compared to age- and gender-matched nonpain patients. The question remains whether the pain is etiologically related to these personality characteristics or visa versa. In fact, recently, a report on 33 BMS patients suggested that psychological factors are not consistently elevated over control subjects in this population.[39] These authors used the revised Symptom Checklist (SCL-90R) and the Multidimensional Pain Inventory (MPI) on their BMS cases and compared the resulting data to data from population samples that included both non-BMS chronic pain patients and a normal nonclinical sample. They concluded the BMS patient scores were not significantly elevated on the measures of depression, anxiety, and somatization. They did note that 21 percent of the BMS cases (7/33) had a substantially elevated psychologic distress. Of course, the presence of co-morbid psychological disease would suggest treatment of these problems but is not evidence of causality.

Unfortunately, findings of high levels of anxiety, depression or even somatization tendencies are not unusual or unique to BMS patients.

Current Etiologic Theories

Searching for the causal link is one of the more difficult endeavors in science. It is a well-known scientific principle that association does not prove causality. Unfortunately, many authors have not made this point clear when reporting on clinical findings that are seen in association with BMS symptoms. For example, it is just as likely that the observed elevated depression and anxiety traits and the elevated somatic focus on their burning pains is an effect of the pain symptoms and not a causative factor. The same could be said about diabetes, menopause, candida infections and their relationship to BMS. For example, it is just as likely that the patients do not clean their mouth as well because of the burning and this causes candida overgrowth.

Other local factors and systemic factors could also be coincidental findings that may have no specific relationship to the causation of the BMS. To establish a causal link between two factors, one must have good consistency of data. This means that the association is present in all cases, no matter how many ways it is studied. The association should be strong and it should account for most of the variability seen in the data. There should be a positive dose-response relationship between the two associated factors. This means that when you have a small amount of the predictor, you see only a small amount of outcome. As the predictor increases so does the outcome response. A bio-

logically plausible explanation must be available regarding how the predictor variable causes the outcome and the suggested association must be independently verified.

Given the mentioned caveats, there are two current hypotheses for BMS worth discussing. The first deals with the interplay of sensory and taste systems which innervate the tongue. The anterior two-thirds of the tongue send taste sensations centrally via the chorda tympani nerve. Nontaste sensations are supplied by the trigeminal nerve (lingual branch). The essential theory is that burning mouth pain symptoms occur when there is an abnormal interplay between lingual nerve function and chorda tympani function.[40,41] These authors have further speculated that there is a specific group of patients at risk for developing burning mouth pain who have a large number of fungiform papillae. They speculate that individuals with increased fungiform papillae innervation (labeled as supertasters) are more at risk for disturbance of the balance between these two nerves (trigeminal and chorda tympani). In other words, if there is damage to the chorda tympani nerve over time, they have the greatest potential to develop pain and taste alterations (dysgeusia). At present, this theory is lacking definitive data that a high prevalence of BMS patients are indeed supertasters.

Their second theory is similar but does not require a disturbed interplay between taste nerves and sensory nerves. It is based on two new studies that suggest that BMS is due to small fiber neurologic damage in the oral cavity. Of course, the idea that a neuropathic change may underlie BMS is not new, but strong evidence supporting this idea has been lacking. The first study of significance is one that examined 52 BMS patients using quantitative sensory tests (QST) in addition to the blink reflex (BR) recordings.[42] They suggested that while BMS patients have different types of neural change (some with diminished neural responses and some with elevated neural responses, the majority (90 percent) of those tested had some form of an altered sensory thresholds or reflex reaction. The other critical study supporting a neuropathic etiology for BMS is by Lauria et al. (2005) and it was described earlier in the section on biopsy evidence for BMS. In combination, the QST and the tongue biopsy data suggest that small diameter nerve fibers progressively deteriorate causing the BMS symptoms.

Altered central nociceptive signal processing is an expected consequence with all neuropathic disease processes, not just BMS.

Finally, neuropathic pain phenomena are not limited to peripheral neural changes altering transduction and transmission of impulses into the brain. Most neuropathic disorders also have ongoing altered central modulation of nociceptive information as an integral part of the disease process. In this regard, two additional studies have examined BMS patients for more central neural changes, specifically on dopamine receptors in the basal ganglia.[43] The study measured dopaminergic function of the putamen in 10 BMS patients and 14 healthy controls using positron emission tomography. They reported that the presynaptic dopaminergic function was significantly decreased (between 17 percent and 20 percent) in the putamen of the BMS patients compared to control subjects. The above data was supported by a subsequent study using a more specific ligand which specifically bound to dopamine D1 and D2 receptors in these patients.

Again, they examined 10 BMS cases and 11 healthy controls. They concluded from the ligand uptake data that a decline in endogenous dopamine levels in the putamen was present in burning mouth patients.[44] The number of available striatal D2 receptors are thought to dictate the extent of central pain suppression.[45] All in all, these studies suggest that brain function changes occur along with peripheral nerve changes and support the idea that central modulation of sensory signal occurs in BMS cases. In fact, altered central nociceptive signal processing is an expected consequence with all neuropathic disease processes, not just BMS.

Management

In 2003, a systematic review of the treatment literature for BMS was conducted.[46] These authors examined Medline publications and conference proceedings up to September 2001 which contained quality research on interventions used for the treatment of BMS in comparison to a placebo. The authors identified several trials that tested antidepressants, cognitive behavioral therapy, analgesics, hormone replacement therapy, and vitamin complexes used to provide relief of the burning and discomfort in BMS. They found that none of the trials examined was able to provide conclu-

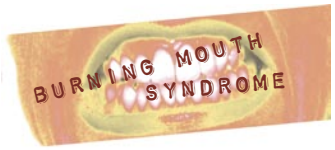


Table 3

Medications for BMS

Medications (class of drug)	Common Dosage Range	Prescription	Mechanisms of Action/ FDA Approval Status
Nortriptyline (tricyclic antidepressant)	10 to 75 mg per day	10 mg at bedtime; increase dosage by 10 mg every four to seven days until oral burning is relieved or side effects occur.	Tricyclic antidepressants inhibit the activity of such diverse agents as histamine, 5-hydroxytryptamine, and acetylcholine. It increases the pressor effect of norepinephrine. This drug is approved for use of the symptoms of depression, but is used off-label for neuropathic pain.
Oral clonazepam (benzodiazepine)	0.25 to 2 mg per day	0.25 mg at bedtime; increase dosage by 0.25 mg every four to seven days until oral burning is relieved or side effects occur. As dosage increases, medication is taken as full dose or in three divided doses.	Mechanism is unknown, although it is believed to enhance the activity of gamma aminobutyric acid (GABA), the major inhibitory neurotransmitter in the CNS. This agent is approved by the FDA for seizures and for panic disorders. It is used off-label for neuropathic pain and BMS in particular.
Topical clonazepam (benzodiazepine)	1 mg tablet tid, after meals	Let tablet dissolve and hold fluid in mouth in area of most intense burning for three minutes, then spit.	Same as above
Gabapentin (anticonvulsant)	300 to 2,400 mg per day	100 mg at bedtime; increase dosage by 100 mg every four to seven days until oral burning is relieved or side effects occurs. As dosage increases taken in three divided doses.	Anticonvulsant action is unknown, gabapentin is known to prevent seizures as do other marketed anticonvulsants. This drug is FDA-approved for partial seizures and for post-herpetic neuralgia pain.
Pregabalin (anticonvulsant)	100 mg PO tid	100 mg PO tid	This is a new drug that is being suggested for use in neuropathic pain patients. Its mechanism of action is thought to be similar to gabapentin. It is approved by the FDA as an adjunctive agent in adult patients with partial onset seizures and for post-herpetic neuralgia and diabetic neuropathy.
Topical lidocaine (anesthetic)	Viscous gel 2%	5 ml qid. Rinse for two minutes and expectorate.	This agent is a sodium channel-blocking agent and provides analgesic effects when applied topically. It is FDA-approved as a topical anesthetic agent but its use is specified as an aid for minor surgeries or skin abrasions.

Evidence Basis for Use
No published evidence for BMS but used commonly for neuropathic pain.
Open clinical trials show some efficacy for BMS. No randomized, blinded placebo-controlled study (note exception below).
RBCT is available showing this approach is helpful in many BMS patients and is better than placebo.
Case report data suggests this agent may be helpful in some patients. No RBCT study performed.
No data for BMS is yet available, but it should work similar to gabapentin and it thought to have better pharmacokinetics. No RBCT study performed.
No data for BMS is yet available. No RBCT study performed.

(Table continues on Page 620)

sive evidence of high effectiveness. They reported that cognitive behavioral therapy may be beneficial in reducing the intensity of the symptoms, that the clinician needs to provide support and understanding when dealing with BMS sufferers, and that psychological interventions help patients cope with symptoms. A random, controlled test demonstrating benefit when compared to placebo suggests that psychotherapy or cognitive therapy sessions of one hour per week over 12 to 15 weeks have beneficial effects on reducing BMS pain intensity for up to six months.[47] An additional study showed some improvement resulting from psychotherapy over two months with significant improvement when combined with alpha lipoid acid therapy.[48]

Even though definitive curative treatments cannot be demonstrated in randomized, controlled, blinded trials, the current standard of practice for neuropathic pain disorders involves medications that may suppress neurologic transduction, transmission, and even pain signal facilitation more centrally. The most common medications used in BMS cases are presented in **Table 3**. These medications include but are not limited to tricyclic antidepressants, clonazepam, trazodone, serotonin-norepinephrine reuptake inhibitor (duloxetine), sodium channel-blocking agents, antipsychiotic medications (olanzapine, amisulpride), anticonvulsants (gabapentin, pregabalin) and alpha-lipoic acid, a nutritional supplement (alpha-lipoic acid).[49-52]

Among these medications, the most widely accepted treatment for BMS is clonazepam. This drug has been evaluated in open-label studies on BMS with reported positive results.[53] Recently, a randomized, double-blind, placebo-controlled multicenter clinical trial was performed on the efficacy of topical clonazepam for BMS.[54] This study reported on 48 patients (four men and 44 women) who were given either a placebo tablet or a 1 mg tablet of clonazepam to suck on and hold the saliva in the area of burning for three minutes, then spit. This was done three times per day for 14 days. They reported that pain intensity decreased significantly more in the clonazepam group and blood levels of clonazepam were extremely low. They hypothesized that clonazepam, which is classified both as an anticonvulsant and an anxiolytic agent, acts locally to disrupt the mechanism(s) underlying stomatodynia.

The newer drugs, on which there is preliminary data assessing efficacy for possible use in BMS, include gabapentin and alpha-lipoic acid. Gabapentin was approved by the Food and Drug Administration in the United States in May 2002 for treatment of postherpetic neuralgia. Even before this, gabapentin has been used off-label for many types of neuropathic pain disorders including BMS. A meta-analysis of gabapentin shows it to be a promising medication in the treatment of sustained continuous pain, but no good, high-quality study has examined it specifically for BMS.[55] A recent case report showed that at least in one patient, this medication was helpful at reducing burning pain.[56] Another agent that has been suggested as potentially helpful in BMS is alpha-lipoic acid. This is a common nutritional supplement that is promoted for its pain-suppressing effect on diabetic neuropathic pain. The best study on alpha-lipoic acid involved assessment of the short-term effect (three weeks) of 600 mg of alpha-lipoic acid per day for diabetic polyneuropathy.[57] This study was a multicenter, randomized double-blind placebo-controlled trial on

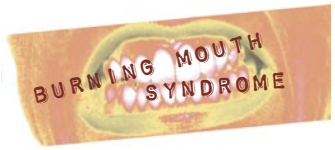


Table 3

Medications for BMS *(continued)*

Medications (class of drug)	Common Dosage Range	Prescription	Mechanisms of Action/ FDA Approval Status
Alpha-lipoic acid (antioxidant)	200 mg tid	200 mg tid for two months in association with gastroprotector.	This agent is not a drug and it is described as an antioxidant. It is not regulated by the FDA and therefore requires no prescription since it is considered a nutritional supplement.
Duloxetine (serotonin, norepinephrine reuptake inhibitor)	60 mg PO qd	Start with 30 mg for one week then increase to 60 mg qd	Mechanism unknown. The antidepressant and pain inhibitory actions are believed to be related to its potentiation of serotonergic and noradrenergic activity in the CNS. This agent is approved by the FDA for major depression and for treatment of diabetic neuropathic pain.
Tramadol (analgesic, non-narcotic)	50 mg taken up to 4/d	50 mg in the evening is the starting dose, but if needed, the dose can be increased up to four tablets per day or more (depending on side effects).	While it is classified as a nonopioid medication, most consider tramadol as an opiod since it does bind to opioid receptors. It also inhibits reuptake of norepinephrine and serotonin similar to tricyclic antidepressants. It is FDA-approved for moderate to severe pain relief.
Hydrocodone (narcotic analgesic)	5/500	One tablet q6h	Used primarily for chronic pain control. It is FDA-approved for moderate to severe pain relief.
Olanzapine (atypical anti-psychotic agent)	5 mg/day	5 mg once a day	Antipsychotics decrease unusually high levels of brain activity. This drug is FDA-approved for schizophrenia.
Amisulpride (atypical anti-psychotic agent)	50 mg/day	50 mg tablets up to three times per day. Maximum dose not to exceed 400 mg/d	Same as above, but not available in the United States.

509 outpatients with neuropathic pain symptoms in the feet. The subjects were randomly assigned to receive either 600 mg alpha-lipoic acid once daily intravenously, 600 mg alpha-lipoic acid three times a day orally for six months, or a placebo in various sequences. Using the total symptom score as an outcome, the study found no significant difference between the alpha-lipoic acid group and the placebo group. In contrast, in BMS patients, there was one double-blind, randomized controlled study that involved 60 BMS patients who were given either alpha-lipoic acid or an inert control substance.

This study reported significant improvement in the alpha-lipoic acid group compared with placebo with the majority showing at least some improvement after two months.[58] Finally, a three-treatment randomized, single-blind comparison study examined amisulpride (50 mg/day), paroxetine (20 mg/day) and sertraline (50 mg/day) over an eight-week period on 76 BMS patients. The study demonstrated beneficial effects on reducing BMS pain intensity for all three agents although amisulpride was the fastest acting of the three agents and no subject assigned to this agent stopped participation in the study.[59] No serious

Evidence Basis for Use
RBCT shows that this agent is helpful for BMS.
No RBCT study performed so no data specific to BMS available.
One RBCT study showed that tramadol was ineffective for BMS.
No RBCT study performed so no data specific to BMS available. Obviously this is a powerful pain-relieving agent.
Only a single case report has reported it is helpful for BMS. No RBCT study performed to date.
One RBCT study showed that amisulpride was ineffective for BMS.

adverse events were reported, and the incidence of side effects did not differ among the three groups. It is interesting to note that amisulpride is an antipsychotic that is disinhibitory at low doses (<10 mg/kg), with specific dopamine D2 and D3 receptor-blocking and little effect on other receptors.[60] Unfortunately, this study had no placebo-control condition and amisulpride is not available in the United States.

Prognosis

In spite of the many behavioral and medication-based treatments, the management of BMS is still not satisfactory, and there is no definitive cure, although help is provided with these methods. Untreated BMS represents a disorder with a very poor prognosis in terms of quality of life, and the patient's lifestyle may worsen when psychological dysfunctions occur. Spontaneous remission of pain in BMS subjects has not been definitely demonstrated, the current treatments are palliative only, and while they may not be much better than a credible placebo treatment, few studies report relief without intervention. ■■■■

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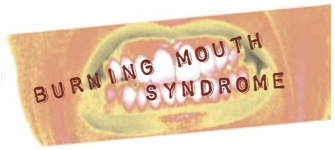

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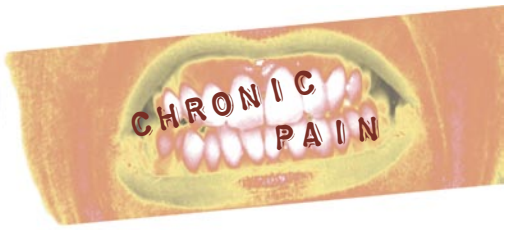

Orofacial Muscle Pain: New Advances in Concept and Therapy

Ana Cristina Lotaif, DDS, MS; Somsak Mitrirattanakul, DDS, PhD; and Glenn T. Clark, DDS, MS

ABSTRACT

This manuscript focuses on chronic myogenous pains affecting the masticatory muscles. The differentiation of myogenous masticatory pain into subcategories is proposed by separating myogenous pains according to their location and anatomic extent. Focal myalgia, regional myalgia, myofascial pain, and fibromyalgia are classified based on specific historical and clinical examination criteria. The probable mechanisms underlying chronic myogenous pains and trigger points phenomena are discussed. Treatment options of the myogenous masticatory pain conditions including physical medicine modalities, as well as several types of pharmacologic agents, are presented.

Pain in the masticatory musculature is broadly classified as masticatory myalgia or myogenous masticatory pain. The anatomic approach to myogenous masticatory pain classification includes focal masticatory myalgia; regional craniocervical myalgia, involving several muscles of the jaw and neck on the same side; and widespread chronic myalgia.

Focal Myalgia Due to Direct Trauma

Focal masticatory myalgia can result from a direct trauma, such as an inadvertent anesthetic injection into muscle tissue during dental treatment.[1-4] When direct trauma results in cellular damage and inflammation within the muscle, the term myositis is used.[5,6] Patients



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typically exhibit strong focal pain and limited jaw opening due to secondary trismus.[7] This trismus of the jaw occurs as an acute response in an attempt to prevent painful movement, but if prolonged, it can lead to chronic loss of jaw motion due to contracture development.[8,9] The standard treatment for traumatic myalgia is jaw rest, ice application, nonsteroidal anti-inflammatory drugs, NSAIDs, and frequent daily active mobilization of the jaw until normal range of motion is achieved.[10]

Primary Myalgia Due to Stress and/or Parafunction

Focal and regional myalgias are often associated with stress and/or parafunction. A diagnosis of primary myalgia due to oral parafunctions includes both waking and sleeping clenching and tooth grinding, as well as other oral habits.[11,12] With regard to stress, current research cannot determine if the chronic pain is influencing the psychologic factors or vice versa.[13-15] If these behaviors are persistent, then a behavioral modification approach to treatment is recommended, which include use of an occlusal appliance and avoidance training. Psychological-based treatments which address the patients etiology will be helpful, especially when the patient is medication-resistant or side effect intolerant.

Secondary Myalgia Due to Active Local Pathology

Sometimes focal and even regional myalgia can develop in response to a local painful pathologic process such as an acute pulpal pain or a painful arthritis or internal derangement of TM joint.[16] When the myogenous process is a secondary myalgia, it is logical and appropriate to manage or minimize the local pathology first and then re-examine the myogenous pain for resolution or persistence.

Myofascial Pain

The term myofascial pain can be used for focal or regional muscle pain when specific criteria are satisfied. Myofascial pain was classified by the International Association for the Study of Pain Subcommittee on Taxonomy as pain in any muscle with trigger points that are very painful to compression during palpation and cause referred pain.[17] The subjective (history-based) criteria that patients should endorse include spontaneous dull aching pain and localized tenderness in the involved muscle(s); stiffness in the involved body area; and easily induced fatigability with sustained function. The objective (examination-based) criteria are a hyperirritable spot within a palpably taut band of skeletal muscle or muscle fascia; upon sustained compression of this hyperirritable spot, the patient reports new or increased dull aching pain in a nearby site; decreased range of unassisted movement of the involved body area; and weakness without atrophy and no neurological deficit explaining this weakness.

Different from traumatic myalgia, myofascial pain is not associated with any histologically evident tissue damage or inflammation. Several authors in recent years have offered explanations for this referred pain phenomena.[18-23] Myofascial pain therapeutic methods includes stretching of the taut bands and direct stimulation of the trigger point via needling or injection of a local anesthetic.[24] Also, methods to reduce stress either behaviorally or pharmacologically are indicated.

With regard to stress, current research cannot determine if the chronic pain is influencing the psychologic factors or vice versa.

Fibromyalgia

Fibromyalgia is a widespread chronic myalgia disorder with specific published criteria and it is less common with a prevalence of 2 percent in the community.[25] The American College of Rheumatology, ACR, has set forth criteria for the diagnosis of fibromyalgia.[26] These criteria include specific duration, location, and examination findings that must be satisfied. The duration criteria specify that a history of widespread pain has to be present for at least three months. Moreover, for pain to be considered widespread, it must involve both sides of the body and be located above and below the waist. The location criteria states that the pain must involve the multiple areas of the axial skeleton including the cervical spine, anterior chest and thoracic spine or lower back regions. Finally, the examination findings criteria specify that a "painful" response must be elicited in 11 of 18 tender point sites on digital palpation. The ACR criteria specify the exact location of these tender point sites and they also specify that a manual finger palpation force of approximately 4 kg is to be used during the examination and the allowable responses to palpation are no pain, tender, and painful.

There is substantial evidence that fibromyalgia sufferers have central neuronal changes in their pain system.[27-29] In general, fibromyalgia is treated using multimodal approaches that simultaneously target the biological, psychological and environmental/social factors that maintain the pain.

Chronic Myogenous Pains Mechanisms

The pathophysiologic mechanisms underlying various types of muscle pain have only recently become better understood, although many of the details remain controversial or unknown. At this time, it is reasonable to say that muscle pain could be grouped according to one of the following mechanisms: (1) local cellular and humoral inflammation, i.e., myositis; (2) accumulation of endogenous chemicals within the contractile elements of the muscle proper or within the soft tissues in and around the muscles; (3) altered neurogenic tissues within the muscle, e.g., sensitized muscle nociceptors; and (4) central sensitization and plasticity of the pain pathways from trigeminal nucleus or spinal cord to the cortex.

Muscle Hyperactivity

For many years it was hypothesized that stress caused an elevated level of background waking, resting or background muscle hyperactivity in jaw muscles, and this in turn caused chronic human jaw or neck muscle pain.

This concept developed because many electromyographic data collected on patients with muscle pain compared to nonpain subjects showed that the former had elevated resting muscle activity in their painful muscles.[30,31] However, current data do not support the concept that stress causes elevated nonfunctional muscle hyperactivity, which then causes muscle pain or even episodic tension-headache pain.[32,33]

Muscle Hypoperfusion

The hypothesis that nontraumatic primary myogenous pain could be due to intramuscular hypoperfusion was recently reviewed in detail.[34]

Dynamic muscle blood flow in fibromyalgia has been studied by numerous researchers using different methods to monitor blood flow.[35-37] These studies have found there is a significantly reduced intramuscular perfusion in the focal myalgia subjects. These differences in vasodilative response in focal myalgia cases might be related to desensitization of beta-adrenergic receptors, which occurs with long-term exposure to stress-associated neurotransmitter epinephrine.[38] Overall, these studies suggest there are demonstrable changes in intramuscular perfusion of chronic regional myalgia involving the masseter and trapezius muscles. This hypoperfusion occurs in these subjects both during and after muscle activity.

There is substantial evidence that fibromyalgia sufferers have central changes in their pain system.

Muscle Pain Location

Non-traumatic primary myogenous pain occurs in roughly the same anatomic locations from patient to patient in the masticatory and craniocervical systems. It was recently described that the slow time to peak motor units, which are presumably the slow twitch type 1 fibers, are clearly more sensitive to ischemia than the "fast" time to peak group.[39] What would explain why postural muscles, which have a much higher proportion of slow twitch (type 1 fibers), are much more likely to exhibit diminished perfusion and show ischemic injury sites.[40-42] Studies have shown that pH values of 6 or lower can be reached during ischemia and sustained contractions or exhaustive exercise.[43,44]

Muscle Nociceptor Sensitization

Considering what is now known about muscle pain mechanisms, specifically about jaw muscle activity, intramuscular blood flow and the effect of prolonged stress on masticatory muscle blood flow, the following hypothesis can be suggested: Prolonged stress may be causing local intramuscular hypoperfusion, which seems to selectively target muscles with higher proportions of type 1 (slow twitch) fibers that are involved in postural maintenance. Secondly, this focal hypoperfusion induces an ischemic condition and local muscle pain. Thirdly, once the pain develops to a sufficient level in the muscle or fascial tissues, this causes a reactive muscle activation (taut bands and even whole muscle splinting or trismus), which is most evident when the patient actually attempts to function. Fourthly, depending on the type and amount of algesic chemical released, the focal muscle pain can produce a peripheral nociceptor sensitization and even a more central pain pathway sensitization. Lastly, when this occurs, myo-

fascial pain trigger points are likely to develop and some susceptible patients will develop more widespread pain.

Chronic Myogenous Pains Treatment

Self-directed Treatments

Self-directed means nonmedical office-based treatments and include nutrition (e.g., herbs, nutritional supplements); relaxation-meditation techniques (e.g., yoga, relaxation exercises, breathing techniques, aromatherapy); daily exercise (e.g., gentle aerobic exercise and stretching); avoidance of stimulants (e.g., caffeine, sugar, and alcohol); participation in a local support group; and thermal therapy for pain relief.[45,46]

Physical Medicine Treatments

Physical medicine treatments include manual physical therapy procedures including therapeutic massage, myofascial release therapy and acupressure; local trigger point injections therapy; botulinum toxin injections; acupuncture therapy; and other forms of manual therapy as osteopathic or chiropractic manipulation.

A review on trigger-point therapy does offer an endorsement of this method, but it suggests that dry-needling is a viable therapy and injecting a local anesthetic or corticosteroid solution into the trigger point was not needed for improved efficacy.[24] Moreover, they suggested the needling effect may not be more than a powerful placebo treatment.

Botulinum toxin was examined in a randomized double-blind study.[47] They were not able to demonstrate statistically significant improvement between the group receiving normal saline and the other two groups receiving either 50 or 100 units of botulinum toxin injections, and it cannot be endorsed as evidence-supported treatment for trigger points based on current research.

One systematic review on acupuncture that focused on fibromyalgia endorses acupuncture as better than sham acupuncture.[48] However, a review on acupuncture for management of acute and chronic low back pain examined 11 clinical trials but stated that only two were of high quality.[49] It also concluded that the available studies were not of sufficient methodological quality to offer an endorsement.

Deciding which medication and how much to use is difficult especially since many of the medications suggested are being used off FDA label.

Pharmacologic-based Treatments

Pharmacologic-based treatments include: nonsteroidal anti-inflammatory drugs; opioid pain medications; antidepressants medications (e.g., tricyclic antidepressants and selective serotonin reuptake inhibitors); benzodiazepines and other muscle relaxants; and sleep modifying medications. Deciding which medication and how much to use is difficult especially since many of the medications suggested are being used off FDA label, which means being used in a way not approved by the FDA.

Medications with enough literature where systematic review have been performed are the topical pain medications, muscle relaxants, and antidepressants. Of these, none demonstrate high efficacy and most of the reviews were based on chronic nonspecific musculoskeletal pain disorders, not masticatory specific myalgia, but all show some promise.[50-53]

A systematic review of topical medications contained NSAIDs for chronic muscle pain concluded they were effective and safe in treating chronic musculoskeletal conditions for two weeks.[50] A review on topical capsaicin for the treatment of chronic musculoskeletal and/or neuropathic pain concluded it was not shown to be an effective stand-alone topical treatment.[51]

A systematic review of muscle relaxants for myofascial face pain concluded that the use of muscle relaxants in patients with myofascial pain involving masticatory muscles seems to be justified but that current research can only be judged as weak, and consideration must be made of the risk-benefit ratio of these medications.[52]

A systematic review on the use of various antidepressants for fibromyalgia endorsed the use of antidepressants as having enough evidence to support their use in fibromyalgia.[53]

Behavioral Treatments

Behavioral treatments include various forms of therapy with a psychologist with the most common being cognitive behavioral therapy. Sometimes these methods are a component of a combined multidisciplinary program and sometimes they are stand-alone treatments.

A systematic review of behavioral therapy for both fibromyalgia and for chronic musculoskeletal pain suggest stand-alone behavioral therapy is not a powerful treatment and in fact, exercise

therapy was equal or better in efficacy.[54] The use of a multidisciplinary approach for fibromyalgia was reviewed and found not to be highly efficacious either.[55] A third review in this area concluded that nonpharmacologic treatments (mostly behavioral in nature) were better than pharmacologic treatment when compared directly.[56]

Conclusion

Deciding which treatment is appropriate for chronic myogenous pain of the masticatory system begins with having a correct diagnosis. To do this, it is necessary to understand the etiology and the mechanism underlying the pain. If the correct etiology-mechanism-based diagnosis were available, then the appropriate treatment choice should logically follow.

Treatment Recommendations Summary

■ Traumatic onset local myalgia with secondary trismus: jaw rest, ice application, NSAIDs and frequent daily active mobilization of the jaw until normal motion is achieved.

■ Local myalgia secondary to self-reported parafunctions: use of an occlusal appliance and avoidance training seems indicated.

■ Secondary local or regional myalgia: manage or minimize the local pathology first and then re-examine the myogenous pain for resolution or persistence.

■ All forms of nontraumatic chronic myogenous pain:

- Aerobic exercise will be beneficial and this exercise program could be supervised or self-directed, but a daily activity is recommended.
- Whole body thermal therapy (i.e., spa therapy or even hot baths daily) should be considered in those who can tolerate the heat without other medical consequences. Thermal therapy may also involve local hot packs applied to the local or regional areas, but less evidence is available on this version of thermal therapy.

If the correct etiology-mechanism-based diagnosis were available, then the appropriate treatment choice should logically follow.

- Low-dose tricyclic antidepressants may be helpful as an adjunctive pain medication and to improve sleep.
- Muscle relaxants such as cyclobenzaprine and various benzodiazepines appear logical for acute myogenous pain, but long-term effects of these treatments in chronic myogenous pain are questionable.

■ Myofascial pain: the use of injections with a local anesthetic or dry-needling of the most hyperirritable spots appears better than no treatment, but may not be better than a credible placebo.

■ Chronic myogenous pain that is associated with anxiety and/or depression: psychological-based treatments which address the patients etiology will be helpful, especially when the patient is medication-resistant or side effect intolerant. ■■■■

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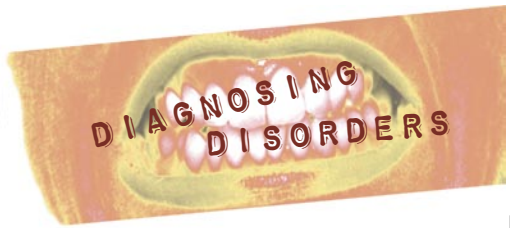

Diagnostic Imaging for Chronic Orofacial Pain, Maxillofacial Osseous and Soft Tissue Pathology and Temporomandibular Disorders

Werner Shintaku, DDS, MS; Reyes Enciso, PhD; Jack Broussard, DDS; and Glenn T. Clark, DDS, MS

ABSTRACT

Since dentists can be faced by unusual cases during their professional life, this article reviews the common orofacial disorders that are of concern to a dentist trying to diagnose the source of pain or dysfunction symptoms, providing an overview of the essential knowledge and usage of nowadays available advanced diagnostic imaging modalities. In addition to symptom-driven diagnostic dilemmas, where such imaging is utilized, occasionally there are asymptomatic anomalies discovered by routine clinical care and/or on dental or panoramic images that need more discussion. The correct selection criteria of an image exam should be based on the individual characteristics of the patient, and the type of imaging technique should be selected depending on the specific clinical problem, the kind of tissue to be visualized, the information obtained from the imaging modality, radiation exposure, and the cost of the examination. The usage of more specialized imaging modalities such as magnetic resonance imaging, computed tomography, ultrasound, as well as single photon computed tomography, positron electron tomography, and their hybrid machines, SPECT/CT and PET/CT, are discussed.

When faced with a patient who has a new onset sustained or episodic orofacial pain, orodental pain, or headache that is not easily explained by local dental or periodontal disease, the dentist must make two determinations. First, he or she must




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decide if the pain is due to a life-threatening cause and if so, make immediate referral to the proper specialist or emergency room. If a life-threatening cause for the symptoms (e.g., pain or headache) is not likely and urgent action is not indicated, the standard of practice suggests that a dentist perform a thorough medical history and a good examination of the intraoral and extraoral structures which often include appropriate radiologic imaging methods (see Sections I.a-b). This examination and the imaging are taken to make sure local maxillofacial osseous or soft-tissue pathology is not overlooked. Sometimes, neuroimaging is required and this assessment can be ordered by the dentist or by a specialist referral for additional diagnosis and possible treatment (see Sections I.c-d).

I.a. Diagnostic Radiologic Imaging Choices

The minimum set of images needed when ruling out maxillofacial pathology in a patient with jaw or facial pain of unknown origin would be to take a panoramic radiographic. Of course, the value of the panoramic film as a routine screening tool for asymptomatic young adults is not of proven value.[1] However, panoramic films increase their value when diagnostically complex cases are under consideration. In recent years, the panoramic screening films are rapidly being replaced by cone-beam computerized tomographic, CBCT, assessment of the jaw and face as a first-line diagnostic test when assessing pain of unknown origin.[2] CBCT is a technology that uses a cone-shaped X-ray beam that goes around the object acquiring volumetric data in one rotation. This allows a shorter scanning time and lesser radiation exposure compared with conventional CT scans.[3,4] The advantages of the CBCT technology are based on the patient's comfort, that information is rapidly acquired, that data can be manipulated and seen in a versatile manner, and that it has the option of magnification, simultaneous multiplanar display, density measurements, the possibility for linear, angular and area measurements and 3-D display of the image if needed.[5] Examples of how CBCT is used for osseous imaging are presented later in this article. When more accurate imaging of the nonosseous orofacial or brain tissues are needed, this is typically achieved with magnetic resonance imaging, MRI.[6] Finally, there are also several other imaging modalities including ultrasound and radionucleotide bone scans when specialized questions are being asked. These methods will be discussed in Sections II.c and III.a-b.

One frequent problem dentists face is how to deal with a patient who has an atypical toothache.

I.b. Imaging for Chronic Orodental Pain

One frequent problem dentists face is how to deal with a patient who has an atypical toothache. This is a persistent toothache *without* definitive evidence of dental-pulpal disease such as periapical radiolucency and/or a thermal or electrical pulp test that shows complete nonresponsiveness (an indicator of nonvitality) of the tooth to stimulation. Note that atypical toothaches may have a hyper-responsiveness to stimulation, but would not test as being "nonvital." There are three main causes of these symptoms including (1) irreversible pulpitis; (2) pain due to a spontaneously active branch of the trigeminal nerve that has become sensitized and the pulpal tissues are not irreversibly altered; and (3) pain due to an incomplete crack or fracture of the tooth. It is quite difficult to distinguish between these three problems. In practice, most dentists believe that a pulpal origin of the pain can be definitively proven or disproven by performing what has been termed a diagnostic root canal or diagnostic extraction. If the root canal or extraction abruptly stops the pain, then the pulpal tissues were indeed the source of the pain. However, if these procedures do not stop the pain, the possibility of neuropathic changes in the nerve supplying the area is elevated. Since no one would elect to have an irreversible procedure as the first choice of diagnosis, discussion of alternative methods for diagnosis beyond pulp testing and periapical imaging is needed. These methods include CT imaging and microscopic diagnosis of tooth cracks.

One recent study assessed the value of direct visual examination of 46 chronically painful teeth in 32 patients after removal of all restorations was performed on the teeth in question to better examine them for evidence of incomplete fracture.[7] They found evidence of incomplete tooth fracture in all examined teeth and in produced pain relief in 29 of the 32 patients, 90 percent, who had endodontics or full-crown restorations. Unfortunately, extensive data on the prevalence of how often endodontic/extraction treatments completely resolve a persistent orodental pain without evidence of nonvitality and no periapical lucency is not available. Clinical experience at

the University of Southern California Orofacial Pain Center suggests that the likelihood of full resolution of tooth pain with endodontics treatment in a tooth with persistent symptoms (>1 year) may not be as high as this prior study suggests. Additional data on this method of diagnosis (direct visualization using an operating microscope) and more long-term studies with careful pain assessment at follow-up is needed. In the meantime, this method should be considered before a diagnostic root canal or diagnostic extraction is performed.

On the horizon is the possibility that incomplete tooth fractures might be detected using either digital dental radiographic images or using conventional CT or CBCT images but this has not yet been proven. One study used 201 extracted teeth (100 fractured and 101 nonfractured) in which they created vertical or oblique root fractures and then imaged these roots with a digital dental imaging system.[8] The radiologists viewing the images had to decide if the image showed evidence of root fracture or not. The resulting data showed a sensitivity for this determination which ranged between 79 percent and 81 percent. The specificity was found to be 86.1 percent and magnification did not help. While these data are interesting, the level of sensitivity and specificity needs to be established for an in vivo situation and for incomplete tooth fractures or cracks, not complete root fractures. With regard to CT as a tooth crack detection method, there is one recent study that reported on the value of a specialized conventional CT device in Germany that was used to visualize vertical root fractures.[9] These authors examined five extracted teeth that had prior root canal fillings yet had chronic pain symptoms and were suspected to have vertical fractures because of the presence of isolated periodontal pockets >/= 8 mm but standard dental radiographs were not able to visualize the fracture. All teeth were carefully extracted and then submitted to imaging using a CT technique.

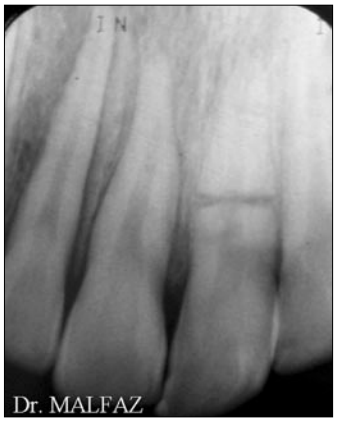

Figure 1a. Periapical image of a horizontal root fracture of tooth No. 9 *(courtesy of Dr. Jose Maria Malfaz, University of Southern California).*

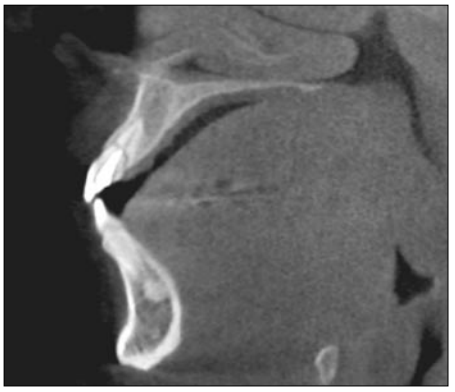

Figure 1b. CBCT images (sagittal view) of the same tooth seen in Figure 1a. In both views, the fracture line is evident *(courtesy of Dr. Malfaz).*

In all cases the authors claimed that they could easily detect the vertical root fractures or crack lines, but no actual blind testing was done. For this reason, whether or not conventional CT or the new CBCT devices can routinely detect incomplete vertical tooth cracks and fractures has not been proven yet. Of course CBCT can be used to detect more substantial tooth complete fracture cases (those where the teeth components have some physical separation). The figures below show a tooth that has a complete horizontal fracture examined with both a periapical film and a CBCT film (**Figures 1a-c**). No study has yet been performed using CBCT imaging to find its sensitivity and specificity for detecting incomplete vertical fractures in vivo. In such a research project, the gold standard would have to be teeth either examined with a microscope during endodontics treatment or after careful extraction to see if the CBCT prediction was correct (**Figures 1a-b**).

I.c. Neuroimaging for Dangerous Intracranial Pathology

Diagnosis of intracranial pathology typically involves MRI-based neuroimaging, however, the likelihood of a new onset orofacial/headache pain without positive neurologic findings resulting in a positive imaging study for intracranial or other pathology is less than 0.7 percent.[10] This figure comes from a study where 306 patients with normal neurologic findings but with chronic or recurrent headaches were imaged with MRI. They found that 169 (55.2 percent) had no MRI evident abnormality, 135 (44.1 percent) had minor unrelated MRI abnormalities evident and 2 (0.7 percent) had clinically important intracranial abnormalities that were probably related to the chronic or recurrent headache. This rate is consistent with prior literature reports on positive findings when imaging headache patients with negative neurologic examination.[11]

Of course, telling a patient he or she does not need imaging does not necessarily convince them since they may worry about being in the group who does have a positive finding. On this very point, one recent study examined

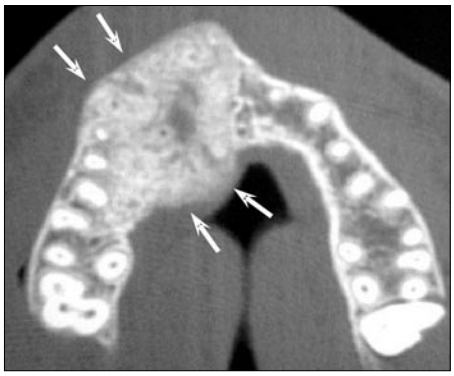

Figure 2a. CT image (axial view) of a fibrous dysplasia showing a unilateral, ill-defined and radiolucent-radiopaque lesion *(courtesy of Dr. Roman Carlos, Centro de Medicina Oral de Guatemala).*

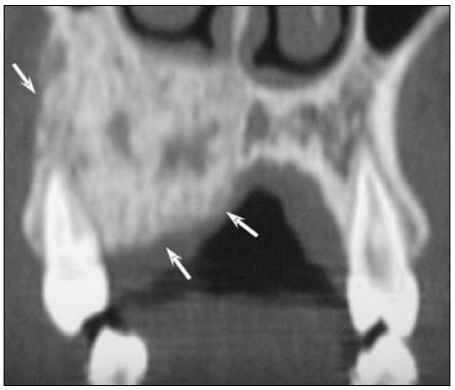

Figure 2b. CT image (frontal view) of the same fibrous dysplasia seen in Figure 2a *(courtesy of Dr. Carlos).*

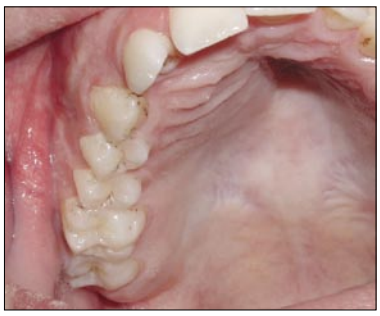

Figure 2c. Clinical aspect of the same fibrous dysplasia seen in Figure 2a. Note the expansive pattern of the lesion *(courtesy of Dr. Carlos).*

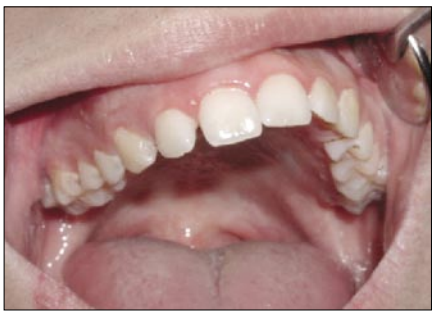

Figure 2d. Clinical aspect of the same fibrous dysplasia seen in Figure 2a. Note the modification in normal occlusion *(courtesy of Dr. Carlos).*

if ordering neuroimaging in patients with chronic daily headache reassured them or increased their anxiety.[12] They measured this by tracking the number of doctor visits and overall costs of health care for a one-year period after imaging. Prior to imaging the subjects in this study were rated on their level of depression and anxiety using the Hospital Anxiety and Depression Scale, HADS.[13] The study was performed at a specialty referral-based headache clinic in South London and included 150 patients who had a negative neurologic examination and had a diagnosis of chronic daily headache. They were randomly assigned to either have a MRI brain scan or not. One year after imaging, the case noted 137 of the 150 enrolled patients were examined and it was determined that the more anxious patients (those with a high HADS score) who had been offered a MRI brain scan said they were less worried about a serious cause for their chronic headaches and they had significantly less health care costs than the group with high anxiety (HADS score >11) who did not have a MRI scan. Based on these findings it seems prudent to suggest that in "negative neurological examination" patients, a MRI scan is not usually required as the odds of intracranial pathology is very low although anxious chronic pain patients may need the reassurance a negative MRI scan provides.

I.d. Neuroimaging and Trigeminal Neuralgia

Neuroimaging is routinely performed for patients who have a clinically confirmed diagnosis of trigeminal neuralgia and who do not fit the following profile: over the age of 60 with unilateral brief severe light-touch triggered divisional pain of the trigeminal nerve and no other neurologic findings. It is also routinely performed for those patients who are medication intolerant and/or wish to consider surgical treatment options. One article examined 51 patients using a MRI-based trigeminal nerve imaging protocol and found that 17 (33 percent) of the patients had nonvascular abnormalities while 27 (53 percent) had vascular contacts or compressions of the trigeminal nerve.[14]

While the 33 percent figure these authors report for nonvascular nerve pathology is much higher than other studies on trigeminal neuralgia, which usually report a prevalence of <15 percent for tumors or multiple sclerosis, the trend they identify is important.[15] Specifically, they found that in younger patients, the rate of tumor or multiple sclerosis was much higher than in those over the age of 60. In addition, these authors reported that if the trigeminal neuralgia involved more than one branch of the trigeminal nerve, one-third of those imaged had tumors. Recently, the question of how often does an MRI detect neurovascular compression abnormalities at the trigeminal root entry zone in patients with persistent idiopathic facial pain, PIFP, sometimes described as atypical

trigeminal neuralgia or atypical facial pain, has been addressed. The study involved examination of 12 patients with unilateral PIFP and compared the neurovascular image finding on the symptomatic side to the asymptomatic side. They found no statistically significant difference between the two sides and reported MRI detection of neurovascular compression had 58 percent sensitivity and 33 percent specificity when they used the presence of symptoms as the gold standard. Obviously this raises the issue of false-positive MRI findings as a problem.

II. Assessing Maxillofacial Osseous Pathology

While pain is illusive and the source of the pain is not always visible, osseous pathology is certainly visible and imaging is critical to any assessment. There are a variety of asymptomatic and sometimes symptomatic osseous lesions of the jaws and temporomandibular joints that require advanced radiologic-based imaging to better document the disorder/pathology, and even to determine proper treatment. Examples of these conditions include any large cyst or expansive lesion of the jaw. The same holds for suspected osteomyelitis or asymptomatic osteonecrosis of the jaws and osteoarthritis of the temporomandibular joint.

When dealing with growing lesions of the bony structures and soft tissue such as might occur with tumors, fibrous dysplasia of the jaws and even normal bony tissues that are potentially undergoing hyperplasia, this may require radionucleotide-based imaging methods. For example, sometimes it is critical to know if the abnormal temporomandibular joint image is a reactive proliferative osseous healing in response to a trauma or a progressively growing neoplastic process such as an osteochondroma (**Figures 2a-d**).

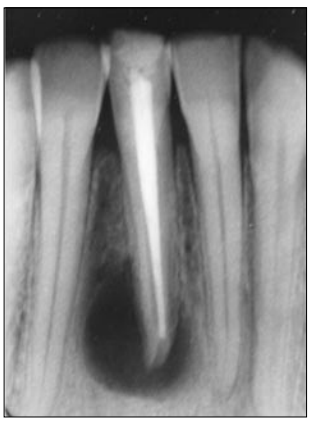

Figure 3a. Radiographic aspect of a periapical lesion showing a typical well-defined round image *(courtesy of Dr. Ali Vaziry, University of Southern California).*

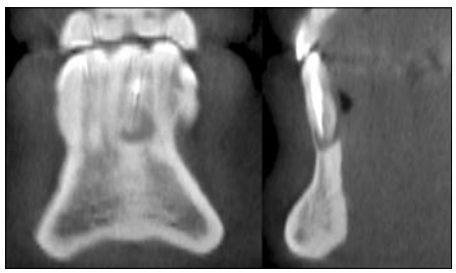

Figure 3b. CBCT views of mandibular incisor periapical lesion from the same patient pictured in Figure 3a *(courtesy of Dr. Vaziry).*

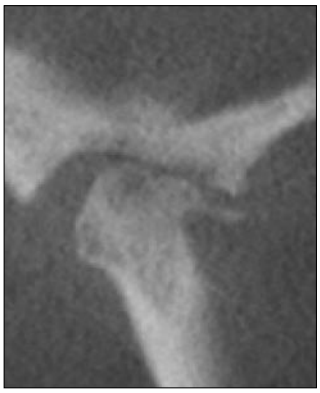

Figure 4a.

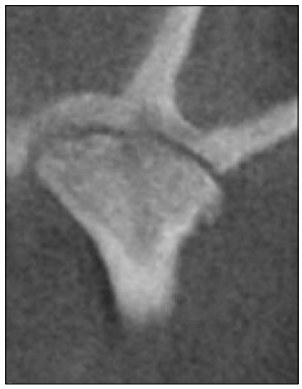

Figure 4b.

Figures 4a (sagittal view) and 4b (coronal view). CBCT exam of an arthritic TMJ. Note the lack of normal contour, decreased intra-articular space and increased radiographic density *(courtesy of USC Orofacial Pain and Oral Medicine Center).*

II.a. Radiologic Imaging for Maxillofacial Osseous Pathology

When attempting to detect osseous lesions (radiopaque or radiolucent) in the maxillomandibular tissues, the dentist needs to know what is the correct radiograph to best image the lesion. For example, standard pulpal-pathology-related periapical lesions are best imaged with standard periapical view dental radiographs (**Figure 3a**). However, as a periapical film represents a bidimensional view of a tridimensional structure, there are some instances when this projection does not correctly capture the area of concern because of tooth malposition or abnormal anatomy of the patient, or a superimposed structure (e.g., maxillary sinus). In other instances, the patient cannot open their mouth adequately, they are uncooperative, or have a strong gag reflex preventing usual and customary imaging approaches.

In these cases, it may be necessary to consider either sedating the patient or ordering a panoramic film, a conventional CT or CBCT scan. The two last ones provide multiple planar views from different directions, which is sometimes required before action is taken (**Figure 3b**). The accuracy of conventional CT

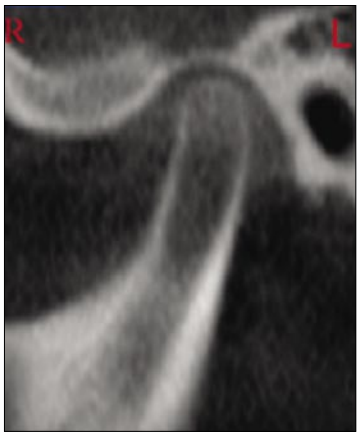

Figure 5a.

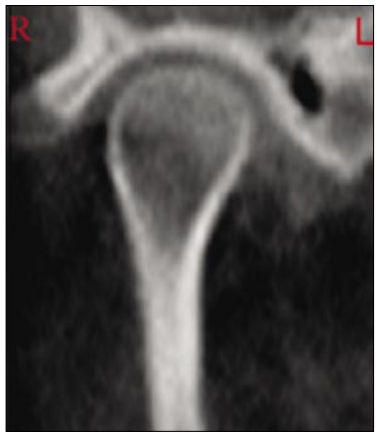

Figure 5b.

Figures 5a (sagittal view) and 5b (coronal view). CBCT of a more normal TMJ showing a better contour and intra-articular space *(courtesy of USC Orofacial Pain and Oral Medicine Center).*

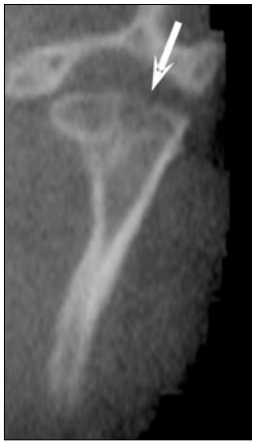

Figure 6a.

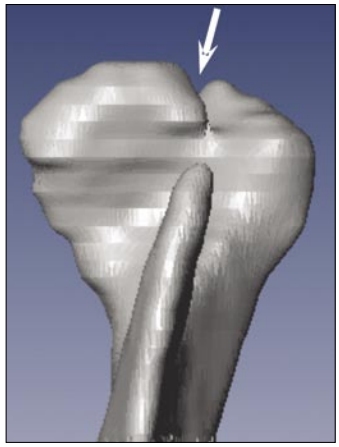

Figure 6b.

Figures 6a and 6b. CBCT image of fractured condyle and 3-D image of same condyle *(courtesy of USC Orofacial Pain and Oral Medicine Center, School of Dentistry).*

films versus standard dental films at detecting periapical lesions was actually evaluated in one study.[16] The authors examined 50 patients (80 roots) with a persistent apical lesion that was referred for apical surgery in the molar or premolar region using both a CT scan and one periapical radiograph. The apical lesion was confirmed (gold standard) at surgery. The results showed that of the 78 lesions diagnosed during surgery, all were visible (100 percent) with the CT scan while the conventional periapical films detected only 61 (78 percent) of these lesions. Obviously, larger lesions of the mandible or lesions below or above the apices of the teeth cannot be imaged with standard dental periapical films, and CT is a preferred method in these situations. For diagnosis of routine periapical lesions in cooperative patients, CT imaging is a far more expensive method and provides far more radiation to the patient than a periapical film. On the positive side, conventional CT and CBCT have the advantage of increased accuracy and they can find the exact relative location of the lesion to the sinus or mandibular canal and therefore should be considered when indicated (**Figures 3a-b**).

II.b. Panoramic Versus CBCT Imaging for TMJ Pathology

Even with a careful clinical examination, some TMJ cases are hard to diagnose accurately.[17-21] For example, patient cases of osteoarthritis that also have severe movement limitations or do not yet present with crepitation on movement. In either case, the most telling clinical sign of osseous TMJ changes, crepitation on motion, is not present. A widely used technique, the panoramic projection can provide information about the condyles, rami, and body, as well as the surrounding structures, including the neck, TMJ, zygomatic arches, maxillary sinus and nasal cavities. It serves as a screening projection to identify possible disorders that may be related to TMJ symptoms making possible the identification of gross osseous changes in the condyle such as asymmetries, extensive osseous erosions, osteophytes, or displaced fractures and neoplasia.

To better visualize the TMJ on a panoramic projection, it should be taken with a partly open mouth and even then the condyle shape is distorted.[22] One recent study examined the prevalence of panoramic TMJ changes in a serologically positive juvenile population (n=97) known to have juvenile idiopathic arthritis (JIA).[23] They found 45 percent of this population had clear TMJ involvement. JIA has a variety of arthritic subtypes, but those children with a polyarticular course, irrespective of their disease onset, had a higher TMJ involvement compared to the oligioarticular group (55 percent

vs. 31 percent). Positive clinical examination findings of pain and dysfunction in the lower jaw exhibited a good specificity but a low sensitivity for radiographically proven TMJ involvement in this population. Moreover, the study revealed that a positive panoramic type radiographic finding of TMJ involvement in JIA patients can occur without having clinical signs.

If a positive finding is seen on a panoramic projection often additional views (usually with CBCT) can be obtained later.[24] A disadvantage of the CBCT is cost, and higher radiation exposure compared to panoramic films, although both of the cost and the radiation exposure are much lower with CBCT than conventional CT.[25] For the TMJ, the CBCT gives spectacular 2-D images, however at present, the 3-D reconstructed views from CBCT images are not quite as smooth as seen in medical computed tomography and, sometimes, artifacts can be misunderstood as degenerative changes (**Figures 4a-b, 5a-b, 6a and 7a-b**). When imaging the TMJ, the most common findings are osteoarthrotic changes but occasionally, a neoplastic change is evident. For example, osteochondroma is a benign tumor arising from the condyle and it is slow growing but can cause progressive deformities of the jaw (**Figures 7a-c**).[26] When a proliferative alteration of the condyle is evident on a film, the differential diagnosis would be a reactive condylar hyperplasia, osteoma, chondroma, osteoblastoma, and osteochondroma. In these cases, patients usually complain of pain, facial asymmetry, and sometimes malocclusion.[27] When active growth is suspected, repeat CBCT imaging is one way of assessing whether the growth is active, and another is a bone scan using a radionucleotide-based image described later (**Figures 4a-b, 5a-b, 6a-b, and 7a-b**).

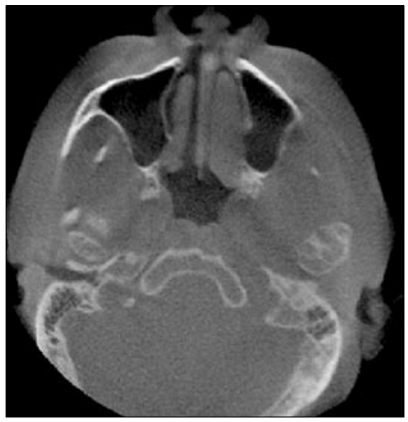

Figure 7a. CBCT of an osteochondroma in the left TMJ (axial view). Note the irregular condylar bulbous or globular expansion *(courtesy of USC Redmond Imaging Center).*

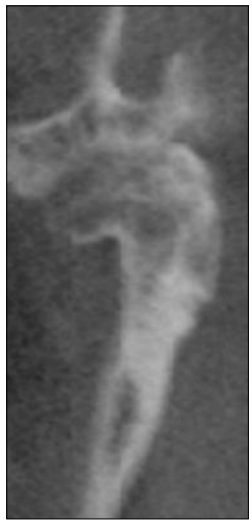

Figure 7b. CBCT image (frontal view) of the same osteochondroma of Figure 7a.

II.c. Radionucleotide-based Imaging vs. MRI for Osseous Disease and Growth Activity

When an unusual osseous disease is seen on a panoramic, CT, or CBCT, additional imaging with MRI has been used to better understand the soft-tissue changes and visualize the disease in question. For example, osteonecrosis of the maxillofacial structures is rapidly becoming a substantial concern in diagnosis with the increased use of bisphosphonates and more recently, some of the anti-retroviral drugs. One study has recently examined the value of MRI at detecting osteonecrosis of the TMJ with painful internal derangements.[28] T1-(proton density) and T2-weighted MR images were correlated with the histological observations from the marrow of the mandibular condyles showing 78 percent sensitive and 84 percent specificity. This yielded a positive predictive value of only 54 percent due to a high number of false-positive MRI diagnoses and thus, this method has limited value as a diagnostic test. Another study examined the relationship of bone marrow edema pattern and the MRI findings in the mandibular condyles of patients who had a diagnosis of TMJ pain and dysfunction, and who also showed a positive MRI-based finding of condylar bone marrow edema.[29] This study involved repeat MRI images (17 months later) taken after relief of joint pain following arthrocentesis and other nonsurgical treatments (behavior modification, manipulation of the joint and nonsteroidal anti-inflammatory drugs, followed by a stabilization-type splint). The authors report that four of the 14 joints (28.6 percent) showed a normal bone marrow signal, whereas 10 joints (71.4 percent) showed a persistent bone marrow edema pattern.

This finding raises the issue of whether a MRI finding of bone marrow edema is clinically significant. Another interesting feature of MR images is their ability to identify calcification and ossification in tissues that do not normally ossify (e.g., muscles).[30] This rare condition known as myositis ossificans and related to fibrodysplasia ossificans progressive syndrome has an unknown pathogenesis but can be related to an autosomal dominant mutation and trauma. Fibrodysplasia ossificans progressive is certainly a possibility in

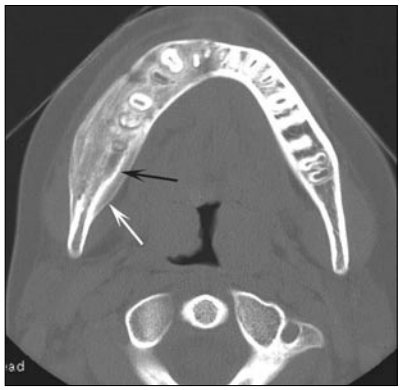

Figure 8a. CT of osteomyelitis with a characteristic onion-skin appearance in the posterior body of the mandible *(courtesy of Dr. Michael Pharoah, University of Toronto).*

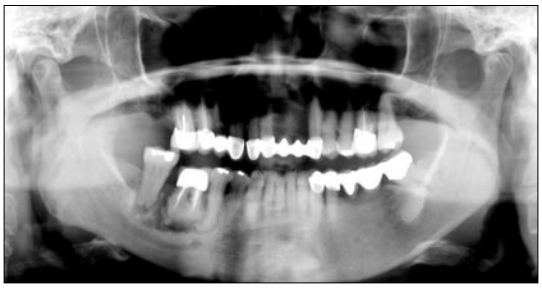

Figure 8b. Panoramic projection of an osteomyelitis in the mandible *(courtesy of Dr. Parish Sedghizadeh, University of Southern California).*

those patient cases that never open fully after a jaw muscle trauma or injury has occurred. Prolonged jaw trismus can and does turn into a permanent contracture when an inadvertent intramuscular injection of anesthetic containing epinephrine has caused a severe myositis, and even though the patient has had plenty of time for this injury to resolve, they still cannot open wide.

For maxillofacial diseases where an active growth is suspected (e.g., neoplasia) bone scans are increasingly used for diagnosis. Bone scans use a radionucleotide and show areas with increased uptake providing additional information helpful in confirming whether a suspicious lesion is growing or not. In the case of osteochondroma, or even fibrous dysplasia, it is helpful in confirming the diagnosis without a biopsy.[31] There are two recent radionucleotide imaging methods that have a potential value in dental osseous disease detection, including single proton emission computed tomography bone scans, SPECT, and positron emission tomography, PET. Both involve the injection of radionucleotide isotopes and a bone scan to detect the site of its chemical uptake. These methods cannot distinguish between benign or neoplastic growth as this will require a biopsy. One problem with bone scans is that they also show increase nucleotide uptake in sites of active inflammation, which causes false-positives results.

SPECT and PET offer the advantage over traditional planar bone scanning in that they can use CT technology to provide detailed anatomical and 3-D images. In the past, because of the lack of anatomical information, it was not possible to reliably delineate a tumor within the oral cavity due to superimposition. For example, one study compared and contrasted SPECT with standard planar film bone scans in determining growth patterns in the mandibular condyle and reported that while both methods were acceptable in accuracy, the SPECT method was easier to perform with better reproducibility than the standard planar technique.[32] SPECT bone scanning has recently been used for confirmation of the diagnosis of fibrous dysplasia.[33]

One study compared standard radiographs with radionucleotide bone scans of 42 histopathologically proven fibrous dysplasia cases and found that while the fibrous dysplasia patients showed a nonspecific increased 99m-Tc MDP uptake, its appearance was different than bone metastases and other bone diseases. The authors suggested that combining radionuclide bone scanning with standard radiographs provides the best results. Another more controversial study has actually looked at the potential of SPECT bone scans to the diagnosis of idiopathic jaw pain.[34] The study included 20 patients with a diagnosis of chronic idiopathic jaw pain and compared them to 20 age-matched and gender-matched normal controls. Nineteen of 20 patients with jaw pain showed increased signal uptake, and 15 of them showed uptake in the area of the pain. However, 12 out of the 20 controls also showed uptake and the uptake site in these subjects was correlated with previously detected jaw pathoses that had long since healed. Overall, this method showed an unimpressive sensitivity and specificity for detecting painful sites of 0.79 and 0.68, respectively.

One clear drawback of SPECT for diagnosis of atypical pain is that there are a high number of false-positives

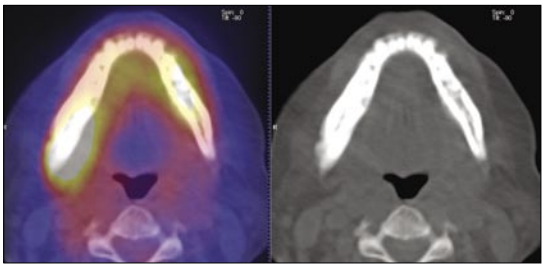

Figure 9a. PET/SPECT of a 54-year-old female with a history of breast cancer with metastases to bone and lung, and multiple chemotherapies. PET/CT images demonstrated intense hypermetabolic activity in the right mandible greater than the contralateral side. These findings are consistent with Zometa-associated biopsy-proven osteonecrosis *(courtesy of Dr. Peter Conti, PET Imaging Science Center, USC University Hospital).*

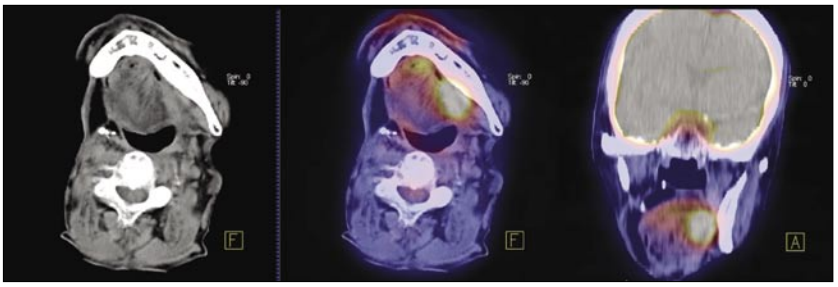

Figure 9b. PET/SPECT of a 53-year-old male with a right tonsillar fossa squamous cell carcinoma. PET/CT images show a focal increased activity internal to the midline of the mandible suspicious for a second focus of malignancy *(courtesy of Dr. Conti).*

which clearly limits its application as a diagnostic test. On the issue of using SPECT for the determination of condyle growth, a recent paper described the case of a 14-year-old girl suffering from condylar hyperplasia and enlargement of ipsilateral jaw body.[35] They described how the SPECT bone scan was used to plan when to perform surgical intervention (i.e., condylectomy) in the management of this case. More importantly, there is a third report on a series of cases were the authors found that the SPECT was able to separate "active growth" from "growth cessation" of the condyle.[36] Finally, PET-based bone scans use 18 fluorodeoxyglucose, FDG, a glucose-based tracer that has become a routine diagnostic tool for staging and restaging patients with pathologies in the oral cavity and lymph nodes, as well as to identify distant metastases. In a systematic review of diagnostic techniques available for excluding or confirming chronic osteomyelitis, FDG-PET imaging demonstrated to be the most sensitive technique, with a sensitivity of 96 percent compared with 82 percent for bone scintigraphy, and 84 percent for MRI.[37] New PET-CT fusion machines are available, allowing both examinations to be performed without having to move the patient. A study evaluating its use for the identification of tumor and metastases found an accuracy rate of 98.4 percent for 18F-FDG PET when compared to CT (87.1 percent) and MRI (99.2 percent); a sensitivity for the identification of nodal metastases of 74.7 percent (52.6 percent for CT/MRI), and a specificity of 93.0 percent (94.5 percent for CT/MRI).[38] Although PET is less sensitive in detecting small tumors (less than 1.0 cm) and tumors of low metabolism, it is showing a good potential to provide information that conventional exams cannot, and with technological advances it may allow improved patient care in the near future (**Figures 8a-b, and 9a-b**).

III. Imaging for Maxillofacial Soft-tissue Disease

Today, the most accessible and commonly used technique when one wants to evaluate the articular soft tissues (i.e., disk) of the TM joint is the MRI. MRI is also indicated for assessment of the salivary and lymph glands in the maxillofacial and submandibular/cervical region (See Section III.a). Another example where MRI is important is when there is a suspected disk displacement without reduction, DDWR, case with limited opening motion. The limitation of motion in these cases could just as easily be due to trismus, so imaging can help confirm one's clinical suspicions (see Section III.b).

III.a. Imaging for Salivary and Lymphatic Glands

Salivary pathologies of concern include sialoadenitis, sialolithiasis and glandular, and extraglandular tumors. Chronic inflammatory disorders of these glands such as sarcoidosis and Sjögrens syndrome also need exploring with imaging before aspiration, cytologic biopsy, and traditional biopsy procedures are undertaken. With the rise of CT and MRI for imaging salivary gland tissues, the need to infuse a radiopaque dye into the gland to image them declined. In the last 15 years, multiple authors have described the value of MRI for diagnosis of salivary pathology. For example, one study on 162 patients with clinically suspected diseases of the major salivary glands

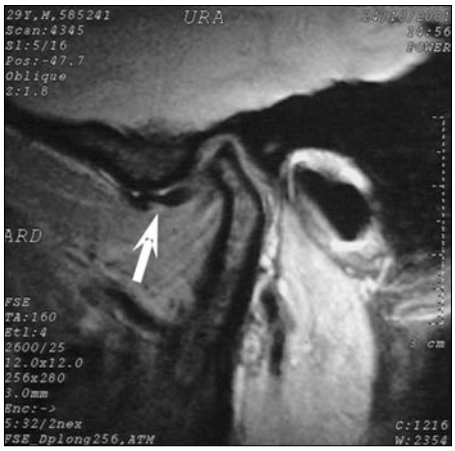

Figure 10. MRI of a TMJ with the displaced articular disk *(courtesy of USC Orofacial Pain and Oral Medicine Center, School of Dentistry)*.

compared ultrasound (sonography), sialography and CT-based-sialography.[39] As the gold standard, they compared the image-based diagnosis with histologically (70 percent), cytologically (26 percent) and clinically proven diagnoses in the remaining subjects. The study reported that sialoadenitis was diagnosed via sonography and sialography with a sensitivity of 58 percent and 54 percent, respectively. Salivary gland tumors were correctly diagnosed by sonography and CT-sialography in 76 percent of the cases, and by sialography in 83 percent of cases. In a second comparative study, the salivary glands of 80 patients with clinically suspected diagnoses of sialoadenitis and/or sialolithiasis were examined using both MRI and digital subtraction sialography.[40]

The gold standard was based on clinical follow-up and biopsy or surgery. The authors reported that digital subtraction sialography provided greater detail than MRI, and the sensitivity and specificity to diagnose chronic sialoadenitis was 70 percent and 98 percent with MRI and 96 percent and 100 percent with digital subtraction sialography. In addition, MRI enabled diagnosis of sialolithiasis with a sensitivity of 80 percent and a specificity of 98 percent versus 90 percent and 98 percent for each with digital subtraction sialography. The authors concluded that while MRI was not as accurate as sialography, the latter, which is an invasive technique, had a substantial procedural failure rate, particularly for the submandibular duct. A third comparative study was published in 2005, which examined 135 patients with various salivary gland diseases using ultrasonography, sialography, CT, and MRI.[41]

The authors used histopathologic examination as the gold standard and reported that ultrasonography was better at detecting neoplastic and inflammatory processes in small lesions (<5 mm diameter) while CT and MR were better at evaluating large tumors. Since that time, MRI has become the standard method since the method itself has increased its accuracy and it is far easier to perform. Final diagnosis is performed by cytology or biopsy, if needed. In fact, it is now almost impossible to find a radiologic laboratory that still performs sialography. Ultrasound combined with MRI is currently the standard of practice for evaluating salivary, lymphatic, and extraglandular palpable pathology.[42]

III.b. MRI for Temporomandibular Disk Position

MRI was initially introduced in the early 1980s and is used most often because it is noninvasive and does not result in patient exposure to ionizing radiation. Multiple digital slices can be manipulated and formatted like the CT information but with superior image detail of soft tissues.[43] Osseous changes can also be evaluated but a more detailed study of bone is usually reserved for CT.[44] Oblique sagittal and coronal images are usually required to evaluate the TMJ.[45] The slice thickness and the pixel size also can be manipulated to improve the image resolution.[46] Typically, a TMJ exam consists of both open- and close-mouth views in an oblique sagittal plane with the sections oriented perpendicular to the long axis of the condyle. These images are useful to evaluate the disk position with respect to the condyle. Images in coronal plane can also be used to identify lateral or medial displacement of the disk.[47] One of the main TMJ-based reasons to order an MRI is to discover the position and form of the disk. The problem with this is that disk displacement (in the closed-mouth view) is frequently seen in asymptomatic volunteers.[48] This problem (false-positives) would not be a concern if all patients could open wide since asymptomatic volunteers almost never show a nonreducing disc displacement in the open-mouth view.

Unfortunately, many of the patients who have a TMJ MRI assessment made cannot open wide thus, clinical correlation with image results are required to make the final determination as MRIs do give false-positives at times. In addition to disk-positioning abnormalities, MRI has value in detecting joint effusion and mandibular condyle marrow abnormalities. In a recent study, the authors reported that nearly 15 percent of TMD patients consecutively referred for TMJ MRI had joint effusion, and 30 percent of those will have bone marrow abnormalities.[49] They also reported that patients with TMJ effusion and/or abnormal bone marrow in the mandibular condyle seem to constitute only a minor portion (less than one-fourth) of consecutive TMD patients referred for diagnostic TMJ imaging and patients with rheumatoid arthritis and other arthritides TMJ involvement may

mimic the more common TMDs. What is lacking from the MRI-based diagnoses is a proper gold standard for effusion and/or abnormal bone marrow signals to see if this diagnosis also suffers from false-positive (**Figure 10**). ■■■■

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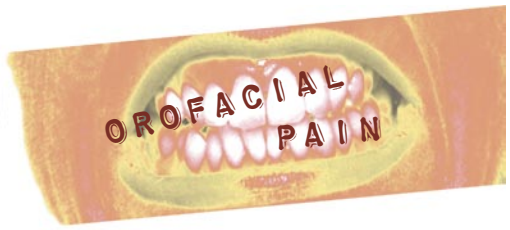

Using Oral Medications, Infusions and Injections for Differential Diagnosis of Orofacial Pain

Saravanan Ram, BDS, MDS; Satish K.S. Kumar, BDS, MDSc; and Glenn T. Clark, DDS, MS

ABSTRACT

Chronic orofacial pain is a rapidly evolving and challenging field that deals with the management of pain originating from neurogenic, osseous, muscular, or vascular structures of the head and neck. The challenge lies in the accurate diagnosis of orofacial pain conditions, which may be difficult to differentiate in many clinical situations. As pain cannot be "seen" or precisely located or its intensity measured with any device, clinicians must rely heavily on the patient's own description of type, duration and location of pain, and thus, history plays a crucial role in diagnosis. Advances in neuroscience, pharmacology, and pain management have made medications one of the primary therapeutic modalities in the management of pain including orofacial pain conditions.

Despite this, these medications will not help patients if the origin and nature of pain is not accurately diagnosed. Hence, diagnosis is critical for successful management of orofacial pain conditions. Experience and knowledge of practice in pain management have led clinicians to devise several clinical diagnostic tests using medications in various forms (topical, oral, injections, intravenous infusions) to differentiate certain orofacial pain disorders where the nature of pain is unclear and the presentation of pain is at multiple sites. Although the diagnostic tests are not 100 percent accurate, they are very effective in many clinical scenarios, especially in orofacial pain conditions. Topical medications such as anesthetics and anti-inflammatories, oral medications such as anti-inflammatory drugs and skeletal muscle relaxants, injections such as local anesthetics and corticosteroids, and vapocoolant sprays are some examples of the modalities used by clinicians to manage orofacial pain conditions.

These medications may also be used for diagnostic tests to aid in accurate diagnosis of some orofacial pain conditions. In addition, there are special cases where medications such as triptans, carbamazepine and indomethacin may be used as diagnostic tests to confirm diagnosis of migraines, neuralgias, or stabbing headaches, respectively. Based on the concept of using medications to predict which treatment would be best for certain pain conditions or to aid in better diagnosis, diagnostic intravenous infusions of lidocaine, morphine, and ketamine have been studied to test the response to adjuvant analgesics and oral dextromethorphan. Paradoxically, taking the patients off their current medications can be of diagnostic significance in conditions like medication overuse headache and serotonin selective reuptake inhibitor-induced clenching. In summary, this paper focuses on the use of medications in different forms as useful diagnostic tests for differential diagnosis of orofacial pain conditions that are difficult to diagnose or are refractory to past or current treatment.



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There are many different reasons for pain in the orofacial region and some of these problems are very difficult to differentiate.[1] For example, when a patient has jaw pain and a limited opening, it could be due to an intracapsular disorder (disk derangement) or an extracapsular disorder (trismus). Determining the exact cause of a restricted jaw opening is not always easy, and if one pursues the causation in an aggressive fashion with computerized tomography and magnetic resonance imaging, it can be expensive. An alternative and faster diagnostic procedure might be to inject an anesthetic solution into the most painful area to see if the patient then can open their mouth. Of course while this is a "low-tech" approach, it certainly is more pragmatic. What is not known is whether these low-tech methods compare to the "higher-tech" imaging approaches, MRIs, CTs. Using injectable, or even oral medications, to assist in the diagnosis of jaw locking is one example, but there are other examples of diagnostic dilemmas that can be evaluated with medications. Research can and should address the validity and predictive values of all proposed tests. This article focuses on how various medications might be used as diagnostic tests in dealing with difficult-to-diagnose orofacial pain problems.

Pain Is Not Visible On X-rays or MRIs

To quote the National Institute of Neurologic Disorders and Stroke website, "There is no way to tell how much pain a person has. No test can measure the intensity of pain, no imaging device can show pain, and no instrument can locate pain precisely. Sometimes, as in the case of headaches, physicians find that the best aid to diagnosis is the patient's own description of the type, duration, and location of pain."[2] These sentences capture one of the major frustrations that is inherent in being a diagnostician specializing in pain disorders, namely that pain is not visible on a radiograph or standard MRI image. Of course, functional MRI images can show you what areas of the brain are activated by experimental pain, but these images are not specific to the diagnosis and will not work in chronic pain since they need a none-pain baseline to compare against. Because most pain disorders are without an incontrovertible physical examination finding or image-based gold standard, gathering a careful history to distinguish between migraine and a tension-type headache, for example, is still critical to the process. However, once a diagnosis has been formulated, it is logical to test the correctness of this theory. Most of the time, proof-of-concept testing is done with treatment and, for neuropathic pain in particular, with medications.

"No test can measure the intensity of pain, no imaging device can show pain, and no instrument can locate pain precisely."

Diagnostic Tests Are Not 100 Percent Accurate

An experienced diagnostician knows that diagnostic tests are rarely infallible, and this is just as true in the field of orofacial pain as it is for any other area of medicine. For example, in 1996, the following statement was issued by the National Institutes of Health regarding diagnostic testing and temporomandibular disorders: "Although numerous assessment methods are available, lack of evidence of the diagnostic value of these tools (i.e., their validity, reliability, specificity, sensitivity, and cost-effectiveness) contributes to this ambiguity."[3] The diagnostician, like a good investigative journalist, should insist upon having at least two sources (positive tests) for any conclusion they make. For example, a positive radiograph showing arthritic change in the temporomandibular joint, palpation findings demonstrating capsular pain plus reduction in pain with an anti-inflammatory drug all lead to the conclusion that arthritis-associated inflammation is the pain source. Of course, the same cautionary note voiced above needs to be put forth about medications as diagnostic tests; namely that they should be only one piece of information and must be used in combination with other available examination, history and imaging data. For example, it is common to give antibiotics to patients with a toothache, even when the tooth has no obvious signs of infection. One conclusion that could be made if the pain is decreased as a result of the antibiotic is that the patient has an infection. This conclusion is not always true, however, since it is known that some antibiotics are potent analgesics, some patients are potent placebo responders, and some antibiotics also suppress transportation of the potent pain inducing neurotransmitter glutamate.[4,5]

The Effect of Inactive Substances (Placebos and Nocebos) in Diagnosis

Certainly, some patients are more responsive to medications than others. In fact, some patients are labeled as placebo responders, which imply they have a personality that is different from nonplacebo responders. One recent study examined the effect of personality traits on a patient's responsiveness to

opioids.[6] This study exposed 34 healthy volunteers to an experimental cold pain (ice water) test and give them 0.5mg/kg oral morphine sulphate (n=21) or 0.33mg/kg oral active placebo (diphenhydramine) (n=13) in a randomized, double-blind design. They reported that high "harm avoidance-" oriented personalities predicted significantly larger pain relief following the administration of morphine sulphate, but not for the placebo. In contrast to patients who are placebo responders, there are an equal number of patients who experience every side effect possible when a drug is given. These patients will often say they do not want to take medications and these patients are usually labeled as "pharmacophobics." One recent study examined this response to see if it was simply the flip side of the placebo response.[7] Negative placebo responders are called nocebo-responders, which means they experience untoward reactions following the administration of an inactive substance. This study looked at the occurrence of nocebo effects in patients with a prior history of adverse drug reactions. It involved 600 patients, seen in three different centers in Italy, with a history of reactions to drugs. All underwent a blind oral challenge with the administration of an indifferent substance and active drugs. The administration of an inert substance in this population provoked untoward reactions in 27 percent of these patients, and the occurrence was significantly higher in women.

Stopping Medications as a Diagnostic Test

There are many situations where taking a patient off a medication might be a valuable diagnostic test. For example, if a patient presents with a chronic daily headache and is using analgesics multiple times a day to try to suppress the pain, one possibility in their diagnosis is that they have a medication overuse headache or MOH.[8] Withdrawal of the analgesics to improve the pain seems paradoxical, but if the MOH diagnosis is correct, this is proof of the diagnosis.[9] Another example where medication withdrawal will confirm the diagnosis is face and jaw pain in a patient caused by a selective serotonin reuptake inhibitor, SSRI, which is causing a dystonic extrapyramidal reaction affecting the jaw muscles.[10]

There are many situations where taking a patient off a medication might be a valuable diagnostic test.

Local Anesthetic Use in Orodental Pain

Local anesthetics act to selectively block sodium channels in the nerve fibers and increase the threshold for spontaneous firing of the nerves. Occasionally, nerve blocks are used diagnostically for facial pain. For example, when it is not clear if the pain is emanating from the TMJ, an auriculotemporal nerve block can be performed to block a majority of the sensory fibers supplying the joint. Another example is the use of local anesthetic injections to assess chronic orodental pain of possible neuropathic origin. In this situation, if the pain does not diminish as expected after local infiltration of 2 percent lidocaine in the area, the neuropathic changes are considered more central. The conclusions made as a result of a failed dental anesthesia is that patients will require systemic, usually anti-convulsant, medications in addition to topical anesthetics to manage the chronic pain. Whether they are used diagnostically or therapeutically, nerve blocks have associated risk in that sometimes the nerve can be aggravated by the injection. This was described in a case series of 83 patients (55 women and 28 men) who were referred to a tertiary care center with permanent alterations of the trigeminal nerve (sometimes painful and sometimes paraesthesia) after an inferior alveolar nerve block.[11] Most of these cases involved the lingual nerve (79 percent) more frequently than the inferior alveolar nerve (21 percent). The authors concluded that, while rare, an inferior alveolar nerve block can result in increased activity of the nerve.

Injection of Local Anesthetics Into Trigger Points

Trigger point injections have both therapeutic and a diagnostic values. This technique uses a small needle (usually 27-gauge); the syringes are luer-lock disposable plastic syringes (either 1 cc or 3 cc size). The commonly used anesthetic solutions injected are procaine (Novocain) and lidocaine (Xylocaine). Because procaine has reports of higher allergic reactions, lidocaine is usually preferred to reduce this risk.[12] In addition to anesthetics, sometimes botulinum toxin A (Botox) is used to treat resistant trigger points associated with taut bands. Of the anesthetic solutions, 0.5 percent procaine and 0.5 percent lidocaine are the least myotoxic, and lidocaine is clearly more myotoxic than procaine. Most physicians and dentists use the anesthetic to provide some transient pain relief associated with immediate post-injection soreness and more importantly to ensure that any referred pain coming from a trigger point is suppressed as a result of the injection. It is unlikely that solutions stronger than 0.5 percent are more effective when injecting trigger points, and higher concentrations of these local anesthetic solutions increase the risk of myotoxicity.[13] Epinephrine is never used

Table 1

USC Orofacial Pain and Oral Medicine Clinic Anesthetic Test Protocol

- Use a cheek retractor and cotton rolls to isolate the painful area.
- Dab the painful area dry with 2-by-2 gauze.
- Record the patient's level of pain on a VAS scale of zero to 10.
- Apply benzocaine 20 percent topically to the painful area.
- Every three minutes, record the patient's pain level on the VAS scale.
- If there is incomplete pain relief, infiltrate the painful site with 2 percent lidocaine.
- Again, record the pain level on the VAS scale after three minutes.

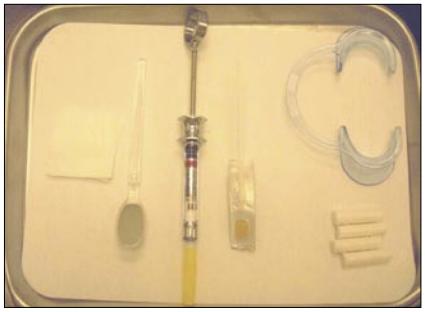


Figure 1a.

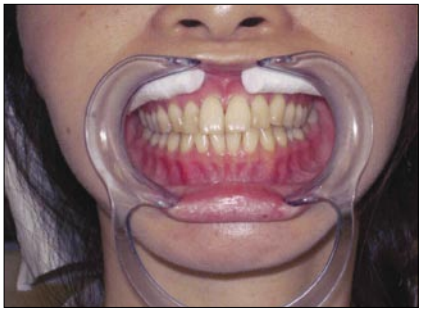


Figure 1b.

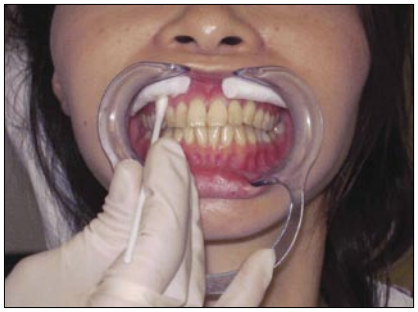


Figure 1c.

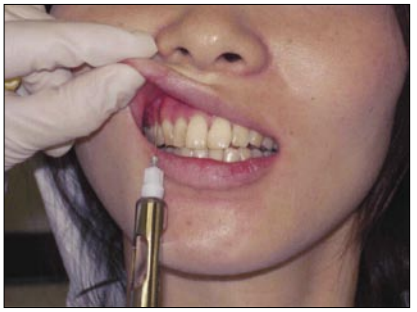


Figure 1d.

Figure 1. Anesthetic test. (A) Armamentarium containing 2-by-2 gauze, mouth mirror, 2 percent lidocaine syringe, 20 percent topical benzocaine swab, cheek retractor, cotton rolls. (B) Isolation using cotton rolls and cheek retractor. (C) Application of 20 percent topical benzocaine. (D) Infiltration anesthesia using 2 percent lidocaine with 1/100,000 epinephrine.

with these injections as it greatly increases mytoxicity.[14] Trigger point injections have been around for a long time, and were described in some detail by Travell in 1952.[15] Limited data beyond open label studies exist on the efficacy of this method of treatment. One study examined the relative efficacy of trigger point injections within the context of a randomized double-blind protocol.[16] The subjects were 63 low-back pain patients, and all had normal lumbosacral radiographs. They were assigned to one of four treatment procedures: (1) lidocaine; (2) lidocaine combined with a steroid; (3) acupuncture; and (4) vapocoolant spray with acupressure. The results indicated injection (with or without medication) was effective and that the injected substance was not critical to the effect. A systematic review of the myofascial trigger point literature concluded that direct needling of the trigger point was an effective treatment, but whether the effect is related to changes induced by needling the trigger point or nonspecific suppression of pain is not clear.[17]

The diagnostic value of trigger point injections is realized when they are used to assess whether the trigger point in the muscle is responsible for the patient's more distant pain complaint. This assessment can be done in three ways. First, pain can be elicited by manual compression of the trigger point, which will often elicit not only focal pain at the trigger point site but distant pain in a referred pain zone. Second, pain of the trigger point and sometimes at the referred sites can be suppressed briefly following stretching of the involved muscle.[18] Third, trigger point pain and usually pain at the referred sites can be suppressed with a trigger point injection. The procedure is done by identifying the trigger point by palpation and then injecting it with 0.5 ml of 0.5 percent lidocaine. This provides prompt, symptomatic pain relief and helps to stretch the involved muscle.[13,16,19]

Local Anesthetic Challenge Test in Neuropathic Pain Diagnosis

It is not uncommon when a root canal is completed on a tooth and the patient still has pain. The typical diagnostic dilemma is to distinguish between a residual dental pulpal-periapical infection causing tooth pain and a sensitized alveolar nerve causing tooth pain. The latter is called a chronic trigeminal neuropathy. Sometimes a peripheral nerve neuropathy will induce secondary central sensitiza-

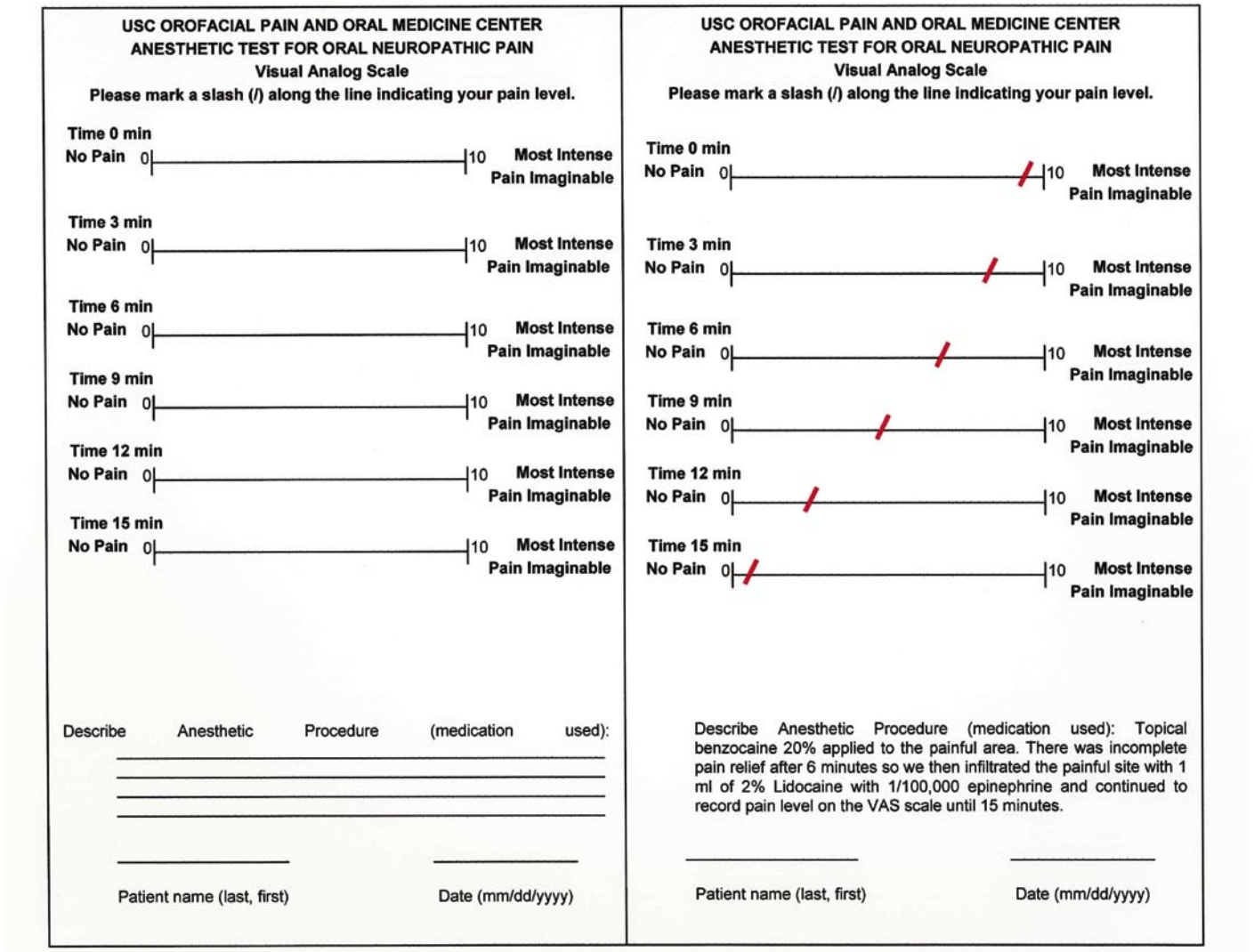


Figure 2. VAS scale for anesthetic test. The left side of the figure shows a blank form and the right side shows one filled out.

tion as well. This means that neural alterations extend into the trigeminal nucleus at the level of the pons, as well as in the third-order neurons and above.[20-25] In these cases, topical anesthetics may help establish that the pain is a neuropathic disorder. The best approach is to perform a local anesthetic challenge test (**Table 1**). This involves isolating the area, rating the pain, and then applying either a topical anesthetic or a nonanesthetic placebo to the painful site (**Figure 1**). The patient will rate the pain change using the VAS scale (**Figure 2**) and the painful site is marked on a mouth map (**Figure 3**). Complete resolution of the pain with topical anesthetic (e.g., benzocaine 20 percent) indicates neuropathic pain with peripheral sensitization. If such is the case, a custom-fabricated vacuum-formed tissue stent that covers the painful area can be made to hold the topical benzocaine in orabase (Colgate Orabase or Orabase-B).[26,27] The purpose of the stent is to hold the medication at the painful site.[28-31] If the pain does not resolve with topical anesthetic, this lowers the chances of sustained application being therapeutic and even reversing the neuropathic changes. In these cases, the next step is to perform a local infiltration of 2 percent lidocaine with 1:100,000 epinephrine in the area to see if the pain can be stopped. As mentioned earlier, the neural changes are considered more central when anesthetics fail, and systemic medications are considered.

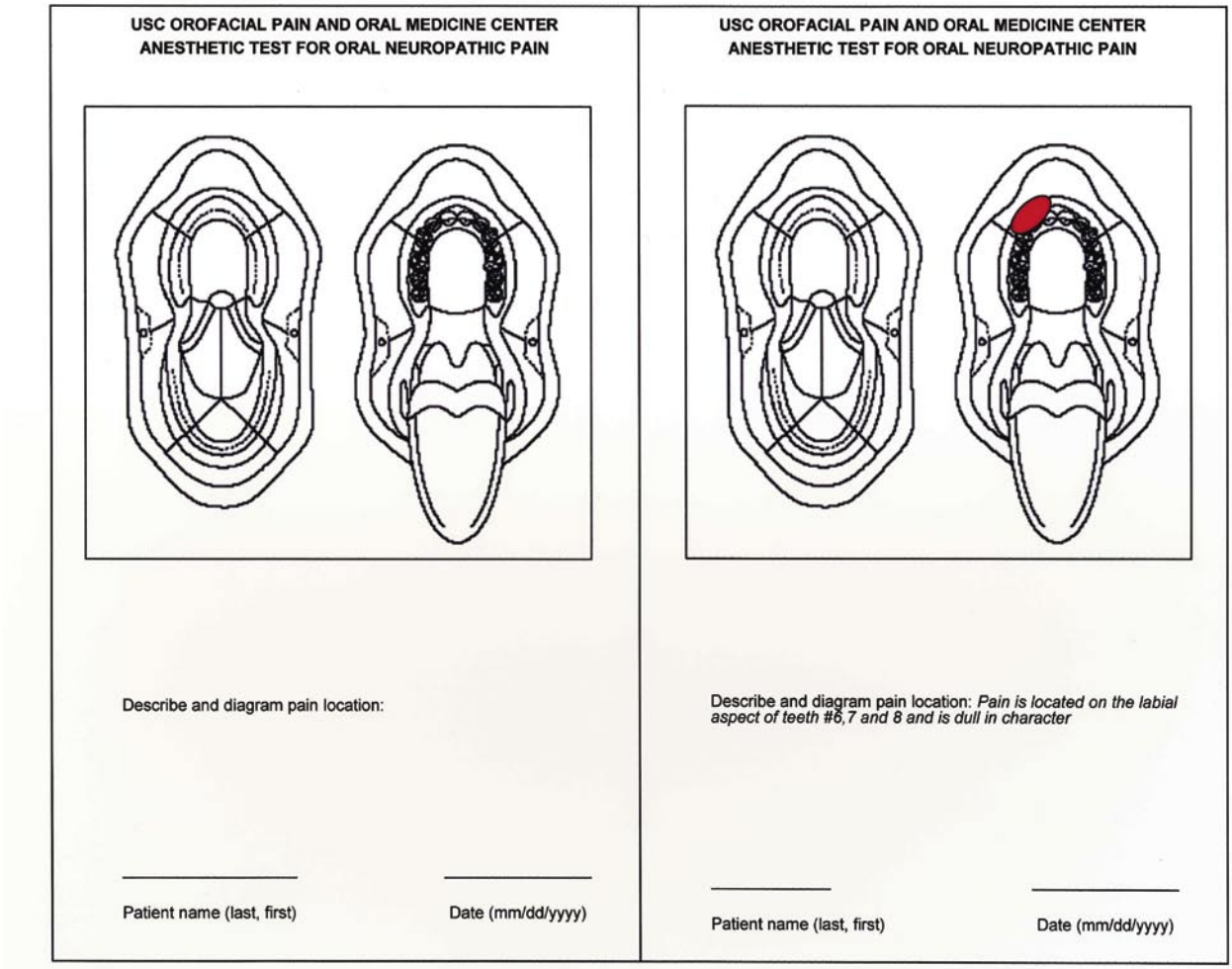


Figure 3. Diagram for anesthetic test. The left side of the figure shows a blank form and the right side shows one filled out.

Corticosteroid and Anti-inflammatory Use in Orofacial Pain

Nonsteroidal anti-inflammatory drugs, NSAIDs, exert their anti-inflammatory and analgesic actions by inhibiting cyclooxygenase enzymes (COX-1 and COX-2) and thereby reducing prostaglandin synthesis.[32] The orofacial pain conditions for which NSAIDs are often prescribed initially are arthralgia, capsulitis, arthritis, myofascial pain, and a locked TMJ. The commonly used NSAIDs are ibuprofen (Motrin and Advil) and nabumetone (Relafen). The recommended oral dosage for ibuprofen is 600 mg qid or 800 mg tid, not to exceed 3200 mg/day. The recommended dosage for nabumetone is PO 500 mg to 750 mg bid or tid, up to 1500 to 2000 mg/day. In suspected cases of tension-type headaches, NSAIDs such as ibuprofen or naproxen sodium (220 mg in divided doses up to a maximum of 660 mg per day) may be used as the first line of choice. In addition, triamcinolone acetonide (Kenalog) is a commonly used corticosteroid medication for intra-articular injection purposes.[33] The primary indication for this procedure is substantial tenderness of the joint capsule. Usually a corticosteroid injection in a small joint such as the TMJ is not performed more frequently than 10 times total and no more often than once every three months (maximum of four injections a year).

Topical NSAIDs as a Diagnostics Test for Inflammation

NSAIDs are effective for both acute and chronic pain conditions and are associated with a numbers needed to treat (NNT) of between three and five for musculoskeletal and joint pain problem.[34] Topicals offer the advantage

of reduced gastrointestinal side effects compared to their systemic counterparts, and a decreased plasma concentration of the drug with high concentrations at the site of application.[35,36] Among the available NSAIDs, to yield a final concentration of 10 percent to 20 percent ketoprofen mixed into a carrier vehicle like pluronic lecithin organogel, PLO, has been extensively used as an effective topical NSAID owing to favorable chemical properties such as lipophilicity, rapid absorption and therapeutic response of the PLO vehicle.[37] Recently, a topical ketoprofen patch has been developed and it may prove more convenient to apply on the skin than the gel in terms of better control of dosage and ease of use.[38] Topical ketoprofen 20 percent in PLO gel is indicated for patients with longstanding capsulitis or arthritis of the TMJ where systemic NSAIDs are contraindicated because of adverse gastrointestinal side effects. NSAIDs are used to treat mild-to-moderate pain of acute or chronic nature caused by trauma, surgery, or inflammatory conditions. As with other joints, the TMJ nerves (e.g., the auriculotemporal) are susceptible to neuropathic changes. If this is determined to be so, a typical method of treating a sensitized nerve is to use a topical sodium channel-blocking agent like lidocaine. In these situations, a 5 percent lidocaine patch (Lidoderm) can be applied to the skin over the painful joint, or lidocaine can be applied topically in a skin-penetrating cream like PLO.

Injectable Steroids as a Diagnostic Test for Inflammation

Intra-articular corticosteroids are occasionally used as a diagnostic test to assess whether the joint palpation pain is neuropathic or inflammatory in character. Partial or incomplete pain relief may indicate a central neuropathy of the auriculotemporal nerve. Even though a long-lasting suppression of joint pain after an intra-articular injection of a corticosteroid is thought to indicate inflammatory pain, this may not be a fully valid assumption.

One study recently examined the effect of corticosteroids on neuropathic pain.[39] Specifically, the corticosteroids act by suppressing ectopic neural discharges from the injured nerve fibers. When the joint pain is chronic in nature and is not associated with arthritis, and is not relieved with the NSAIDs, then one should suspect an underlying neuropathic pain process. In this clinical situation, a local anesthetic can be injected into the joint space and pericapsular region. If the joint pain is not relieved with the anesthetic and the corticosteroid did not provide long-lasting relief, then it signifies that the patient potentially has a complex peripheral and central neuropathic pain condition affecting the region.

Evidence is weak that these muscle relaxants are beneficial for individuals with chronic muscle pain affecting the neck and lower back.

Limited Opening Testing

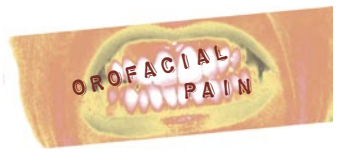
When a patient presents with acute-onset limited opening, one consideration is whether the limitation is due to involuntary active contraction (e.g., trismus) or disk displacement without reduction in the TMJ. Using vapocoolant sprays and muscle relaxants are potential diagnostic assessment tools for this differentiation.

Skeletal Muscle Relaxant Use in Orofacial Pain

There are numerous drugs that are used for relief of chronic regional musculoskeletal pain, including carisoprodol (Soma), chlorzoxazone (Parafon Forte DSC), cyclobenzaprine hydrochloride (Flexeril), metaxalone (Skelaxin), methocarbamol (Robaxin), and orphenadrine citrate (Norflex).[40] These medications are now generally used only for acute clinical proven spasm and not long term. This is because the evidence is weak that these muscle relaxants are beneficial for individuals with chronic muscle pain affecting the neck and lower back.[41,42] For example, when acute muscle spasm is suspected, cyclobenzaprine hydrochloride (5 mg to 10 mg bid) is often administered for short periods of time to see if the jaw pain decreases and mobility increases. Cyclobenzaprine is structurally similar to tricyclic antidepressants and demonstrates similar anti-cholinergic effects.[43] One study compared the efficacy of cyclobenzaprine hydrochloride at 2.5 mg, 5 mg and 10 mg tid over a one-week period in patients with acute muscle spasm of the lumbar and cervical region.[44] Patients who received cyclobenzaprine 5 mg reported experiencing discernable relief more rapidly than those receiving placebo, but not as rapidly as those receiving cyclobenzaprine 10 mg. Somnolence was the most common adverse effect, followed by dry mouth. The incidence of somnolence increased at higher cyclobenzaprine doses. In those cases where the diagnostician is unsure if a muscle spasm is present, a prescription of a muscle relaxant is given to see its effect.

Using Vapocoolant Sprays for Diagnostic Purposes

Vapocoolant spray followed by stretch is a widely used and effective



noninvasive modality for the management of myofascial trigger points. It involves passively stretching the target muscle while simultaneously applying a vapocoolant spray to the skin over the taut muscle band. The sudden drop in skin temperature and tactile stimulus of the stream of vapocoolant spray inhibits the pain and the reflex motor and autonomic responses in the central nervous system. This pain-suppressing effect now permits more effective stretching or lengthening of the muscle.[13] Currently, a new spray has been introduced to replace the fluorimethane spray used in the past.[45,46] This spray contains pentafluoropropane and tetrafluoroethane (Gebaeur's spray and stretch) which is nonflammable and environment friendly. The most likely cause of limited mouth opening of a short duration is acute muscle spasm. In cases of limited mouth opening, the spray and stretch is used diagnostically to differentiate between limited mouth opening due to muscle spasm and that caused by a disk derangement or extracapsular restriction. An increase in mouth opening on using the spray and stretch is indicative of limited mouth opening secondary to trismus.

Comparative Intravenous Infusions for Diagnostic-Predictive Purposes

Over the years, several authors have looked at the concept of using medications to predict which treatment would be best, and/or whether such pharmacologic tests could help distinguish better the diagnosis. For example, intravenous infusion tests have been used to predict subsequent responses to oral analgesics. This is an increasingly popular method used to enhance medical care and conserve resources.

Because no infusion test is completely accurate, the potential benefits of these tests must be weighed against the frustration and waste in resources encountered with false-positives and the failure to use a potentially beneficial treatment with false-negatives.

Lidocaine Challenge Test

One of the earliest pharmacologic based "diagnostic tests" used in decision-making for pain treatment was the intravenous lidocaine (Xylocaine) infusion challenge test. The main purpose of this test was to assess whether the oral sodium channel-blocking agent mexiletine (Mexitil) would alleviate pain. A recent meta-analysis of nine controlled clinical trials on the effect of oral mexiletine for neuropathic pain reported that mexiletine (median dose, 600 mg daily) was superior to placebo and equal to morphine, gabapentin, amitriptyline, and amantadine.[47] The common adverse effects were drowsiness, fatigue, nausea, and dizziness, which makes mexiletine a difficult drug to tolerate. It is also proarrhythmic and known to cause hepatic injury; therefore, it is common for pain specialists to perform a lidocaine infusion to see if it produces a substantial reduction in pain before using oral mexiletine.

One study examined if the lidocaine challenge infusion would predict response to oral mexiletine in nine subjects with chronic neuropathic pain.[48] A single lidocaine infusion was followed with a four-week protocol using oral mexiletine. The results study showed that responses to oral mexiletine were significantly correlated with those to the lidocaine infusion challenge. Mexiletine dose and blood levels were not correlated with pain relief. Another study examined the efficacy of lidocaine infusion as a predictor of the response to other oral drug therapies (antidepressants, channel blockers and anticonvulsants) in 183 inpatients diagnosed with central and peripheral neuropathic pain.[49] Here , intravenous lidocaine was infused at a dose of 4 mg/kg and based on a visual analogue scale, VAS, rating taken before, and at every five minutes during the infusion, patients were categorized as lidocaine responders (n=85) or nonresponders (n=71). All patients were then put on pain medications as their symptoms dictated (irrespective of lidocaine test results).

A VAS pain rating was taken one month after the drug therapy, and it was reported that 90 percent of the lidocaine responders reported substantial pain reduction with the oral drug therapy. In contrast, only 15 percent of the lidocaine nonresponders had similar pain relief. The authors concluded that intravenous lidocaine was a very good predictor of response to adjuvant analgesics in neuropathic pain patients.

The authors concluded that intravenous lidocaine was a very good predictor of response to adjuvant analgesics in neuropathic pain patients.

Intravenous N-methyl-D-asparate Blocking Agents for Diagnosis

Ketamine is a NMDA receptor antagonist used clinically use as a general anesthetic. It exhibits multiple pharmacological actions, including NMDA receptor block, sodium and calcium channel block, block of cholinergic receptors, inhibition of biogenic amine reuptake, and interactions with opioid systems. The chronic use of intravenous ketamine (Ketalar) is usually limited by its psychomimetic side effects. One recent study examined if the effect of dextro-

methorphan, an oral NMDA receptor antagonist as a pain relief agent in cases of chronic pain could be predicted by an intravenous infusion of another NMDA antagonist, ketamine.[50] Specifically, researchers gave 25 patients a small dose (0.1 mg/kg) of IV ketamine before putting them on oral dextromethorphan treatment regimen. By using pain relief of at least 67 percent as a cut off, researchers found that the ketamine test response had a 90 percent positive predictive value and an 80 percent negative predictive value, with the overall observed agreement being 84 percent. These data suggest that IV ketamine test was useful as a diagnostic test for response to oral dextromethorphan. Unfortunately, dextromethorphan is known to produce substantial side effects and is poorly tolerated in many patients.

Morphine Infusion Challenge Test

As with lidocaine and ketamine, intravenous opioids have been used as diagnostic predictors of treatment response. One recent study examined the analgesic responses to intravenous morphine, lidocaine, and ketamine in chronic neck pain patients.[51] The study used 33 patients with diagnosed whiplash-associated neck pain who were given (in a randomized, double-blind, crossover design) morphine (0.3 mg/kg), lidocaine (5 mg/kg), ketamine (0.3 mg/kg), or placebo (isotonic saline). Pain ratings were made before, during, and after the infusions, and patients were classified as nonresponders, placebo-responders, or responders to the drugs. The authors noted that the groups did not show any clear relationships between pretest pain duration and the test result; they nevertheless speculated these subgroups might be useful for deciding on therapeutic approaches. What they did not do is actually make predictions, implement treatment and see if the predictions were valuable or not.

Special Case Medications

There are three special case medications that have specific diagnostic value in the differential diagnosis of orofacial pain.

Special Case Medications: Triptans as a Diagnostic Test

Triptans, which are selective antagonists, for 5-HT 1B and 5-HT 1D receptor subtypes, reduce both sensory activation in the periphery and nociceptive transmission in the brainstem trigeminal nucleus, where they diminish central sensitization. Triptans also induce cerebrovascular vasoconstriction that counteracts vasodilation believed to be involved in the pathophysiology of migraine. Sumatriptan (Imitrex) is the most commonly used drug of this class to treat migraines; other drugs include zolmitriptan (Zomig), eletriptan (Relpax), frovatriptan (Frova), naratriptan (Amerge), and rizatriptan (Maxalt). When a patient responds with full pain relief to the use of a sumatriptan nasal spray (5 mg to 20 mg per nostril) or tablet (25 mg), this is considered confirmatory evidence of a migrainous pain disorder. The nasal spray has a more rapid onset of action than the tablet. Of course, there are dangers in relying too much on a medication response to make the diagnosis. For example, one article describes a patient with sudden-onset head pain who was given sumatriptan (6 mg subcutaneously) to see if the head pain responded and might be a migraine.[52] The result of the injection was that the pain did subside and the patient went home. Unfortunately, she collapsed at home that evening. After being taken to the emergency room, a contrast CT revealed a subarachnoid hemorrhage. She died five days later due to the underlying cerebral aneurysm. This effect of sumatriptan on pain of subarachnoid hemorrhage was also reported in a second case, suggesting this medication cannot be used as a definitive test for migraine since other intracranial pain responses probably act at the same serotonin receptor blocked by sumatriptan on the trigeminal nerve.[53]

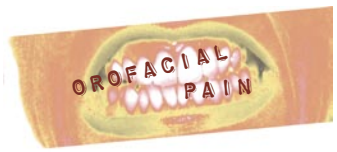
There are dangers in relying too much on a medication response to make the diagnosis.

Special Case Medications: Carabamazepine (Tegretol) as a Diagnostic Test

Carbamazepine is an anticonvulsant that probably acts by a combination of γ–amino butyric acid, GABA, inhibition, neuronal cell membrane stabilization, sodium channel blockade, and NMDA receptor antagonism.[54] Trigeminal or glossopharyngeal neuralgias typically present with an acute episodic lancinating pain that lasts for a few seconds to minutes. Carbamazepine is the drug of choice for treatment of trigeminal neuralgia. When a patient has the correct mix of clinical symptoms and also responds completely to carbamazepine, this response is confirmatory proof of the diagnosis. Usually, clinical symptoms are most important in making the diagnosis, but when a patient has an atypical form of trigeminal neuralgia or several co-morbid symptoms that are confusing the diagnosis, carbamazepine (200 mg to 400 mg bid to a maximum of 600 mg bid) could be helpful in confirming the diagnosis.

Special Case Medications: Indomethacin as a Diagnostic Test

A group of headache disorders are uniquely responsive to the NSAID indomethacin (Indocin).[55] These headaches are primary (no identifiable organic pathologic cause) and are characterized by a prompt and often complete response



to indomethacin. The orofacial pain practitioner must be careful not to overlook this diagnosis, especially since it can be diagnosed easily by simply prescribing a short trial of medication. These indomethacin-responsive headaches fall into three categories: (1) a select group of trigeminal-autonomic cephalgias; (2) valsalva-induced headaches; and (3) primary stabbing headache (ice pick headache or jabs and jolts syndrome). ■■■■

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Medical Management of Oral Motor Disorders: Dystonia, Dyskinesia and Drug-Induced Dystonic Extrapyramidal Reactions

Glenn T. Clark, DDS, MS

ABSTRACT

This article reviews three of the involuntary hyperkinetic motor disorders that affect the orofacial region, namely orofacial dystonia, oromandibular dyskinesia, as well as medication-induced extrapyramidal syndrome-dystonic reactions. Specifically, it discusses and contrasts the clinical features and management strategies for spontaneous primary and drug-induced motor disorders in the orofacial region. The article provides a list of medications reported to cause drug-related extrapyramidal motor activity above and beyond the more commonly known antipsychotics medications. It provides a needed update because the number and use of medications causing involuntary jaw muscle activity are increasing. For example, selective serotonin reuptake inhibitors (SSRI), stimulant medications and illegal drugs have all been reported to induce an orofacial motor activation as adverse reactions.

This article also discusses briefly the genetic and traumatic events associated with spontaneous dystonia. Finally, this article presents an approach for management of the orofacial motor disorders that involves the following three steps: (1) collect a full clinical history and examination, including magnetic resonance imaging of the brain; (2) after ruling out CNS disease, adverse medications reactions and local pathology, try one or more of the motor-suppressive medications that may be helpful in these cases (e.g., cholinergic receptor antagonizers or blockers, and GABA-ergic including benzodiazepines); and (3) if the disorder is severe enough and focal enough to consider, and motor-suppressive medications are not adequate, then consider botulinum toxin injections. The contraindications, side effects, and usual approach for these medications and injections are discussed.

Dentists must be able to recognize and become involved with management of oral motor disorders because such behaviors cause pain and dysfunction of the jaw. If the motor activation abnormality is severe, these disorders can also make it more difficult to perform needed dental care on patients and sometimes dental treatments aggravate these movement disorders. As used in this article, the term "orofacial motor disorders," OMD, encompasses a spectrum of movement aberrations, both hyperactive and hypoactive that involve the muscles of the orofacial complex. Numerous involuntary motor disorders with varying consequences to the patient and can affect the orofacial musculature.[1-3] A partial list of these medications is provided in **Table 1**. The most common motor disorders of concern to dentists everywhere are excessive sleep bruxism and sustained habitual forceful clenching, day or night.

The primary management method for strong bruxism and clenching is still

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Table 1

Partial List of the Hyperkinetic Oral Motor Disorders

Bruxism	Nonfunctional jaw movement that includes clenching, grinding, clicking, and gnashing of teeth during sleep. Based on EMG recording of the jaw closers during sleep, there are two basic patterns of bruxism reported: (1) rhythmic, side-to-side motions and, 2) prolonged, maximal isotonic contractions of the jaw muscles (up to 300 seconds in length). Bruxism has been reported during each stage of sleep; however, the majority of episodes appear during stage II sleep.
Orofacial dyskinesia	Excessive, repetitive, stereotypic oral movements such as facial grimacing, repetitive tongue protrusion, puckering, smacking, and licking of the lips and side-to-side motion of the jaw. The most common form is tardive dyskinesia and it appears in patients who have taken neuroleptic medications. However, dyskinesias may also be spontaneous and can be caused by systemic, metabolic, endocrine, structural, vascular, infectious, psychologic, or inherited degenerative conditions.
Meige's syndrome	Uncontrollable blinking of the bilateral eyelids which makes it appear as if the person is continually winking. When there is no obvious other cause (e.g., dry eyes), blepharospasm is called benign essential blepharospasm. It often affects both eyes at once, but it can also affect only one eye. Severe blepharospasm can cause the eyelids to be forcibly closed for a period which is longer than the typical blink reflex, thus causing a variable interruption in the ability to see. Meige's syndrome is a combination of blepharospasm and oromandibular dystonia (see below).
Oromandibular dystonia	Involuntary, repetitive, sustained muscle contraction, which results in an abnormal posturing of a structure. Depending on the muscle involved, it may produce a twisting movement of the involved structure. Dystonia is typically present throughout the day and disappears during deep sleep. Dystonic spasms typically increase in intensity during stress, emotional upset, or fatigue. If the affected muscles are in the oral region, it can produce involuntary jaw opening, lateral movements of the jaw and/or protrusion of the tongue.
Hemi-facial spasm	Hyperkinetic movement disorder affecting the unilateral facial muscles. It will start with an intermittent periorbital twitching, usually of the inferior orbicularis oculi muscle. Over months to years this abnormality can progress to involve half of the face and the platysma muscle. Since this is a disorder of CN VII, the muscles of mastication are not involved. Sometimes these twitching movements may progress to a sustained, chronic contraction of the involved facial muscles.
Facial and oral tics	Brief, intermittent, repetitive, nonrhythmic, unpredictable, purposeless, stereotyped movements. Rather than a voluntary movement, a tic is a movement which relieves a voluntary urge, and this is the key characteristic which differentiates a tic from another movement disorder. Motor tics of the orofacial area include tongue protrusion, facial grimacing, blinking, and facial twitching, and cheek sucking. Tourette's syndrome include motor and vocal tics and is the most common and severe form of a multiple tic disorder.

a full-arch occlusal appliance, which does not stop the behavior but limits its dental damage.[4] Fortunately, the most severe cases of bruxism and clenching now have several motor-suppressive medications and in extreme cases, botulinum toxin injections that can be added to occlusal appliance treatment. However, this article focuses not on bruxism but on three other vexing disorders of focal orofacial dystonia, oromandibular dyskinesia, and medication-induced extrapyramidal syndrome-dystonic reactions in the orofacial region. When severe, these motor disorders may actually cause strong headaches, damage the temporomandibular joint, or create such motor control difficulty that patients will be unable to eat and may start to lose weight. Sometimes these motor disorders can affect the tongue

musculature to such a degree that it compromises the patient's ability to speak clearly. The social embarrassment, which patients must endure, affects their daily living and many patients will refuse, or strongly avoid, leaving their homes. Fortunately there are various medications, including botulinum toxin injections that can offer partial help (**Table 1**).

Dystonia

Dystonias are involuntary but tend to be more intermittent than dyskinesias and they are a syndrome of short but sustained muscle contractions that produce twisting and repetitive movements or abnormal postures.[5,6] Dystonias are called focal if they involve a single area, e.g., face, oromandibular area, arm, or neck. They are called segmental if two or more contiguous areas are affected, e.g., cranial and cervical areas or the face, jaw, and tongue. They are multifocal if two or more noncontiguous body regions are involved, e.g., an arm and a leg with cranial muscle involvement. Most dentists who have an elderly population have encountered orofacial dyskinesia, but few have seen a true dystonia problem affecting the jaw or tongue area. Focal primary dystonia occurs in 29.5 per 100,000 individuals.[7] Oromandibular dystonia is one of these focal dystonias and it affects the orofacial region and involves the jaw openers (both lateral pterygoids and anterior digastrics), tongue muscles, facial muscles (especially orbicular oris and buccinator), and platysma are involved. When this occurs in association with blethrospasm, this is called Meige's syndrome.[8]

Oromandibular dystonias typically produce intermittent pulling, twisting of the jaw forward or sideways, and if they involve the tongue musculature, it may effect a rolling of the tongue, lips, and cheek or even a spontaneous opening of the jaw. One interesting aspect of the involuntary motor disorders is that patients can partially control or suppress the movement with the use of tactile stimulation, such as touching the chin in the case of orofacial dystonia or holding an object in their mouth. This suppressive effect has been called geste antagonistique.[9] These tactile maneuvers may mislead physicians to the erroneous diagnosis of malingering or hysteria.

One interesting aspect of the involuntary motor disorders is that patients can partially control or suppress the movement with the use of tactile stimulation.

Other examples of sensory tricks include placing a hand on the side of the face, chin, or back of the head, or touching these areas with one or more fingers, which at times will reduce neck contractions associated with cervical dystonia. With some dystonias, patients will have discovered that placing an object in the mouth, such as a toothpick or a piece of gum may reduce dystonic behaviors of the jaw, mouth, and lower face (oromandibular dystonia). Finally, the majority of the focal and segmental dystonias only occurs during waking periods and disappears entirely during sleep.

Dyskinesia

Orofacial dyskinesia occurs as involuntary orofacial movement of the lips, tongue, and sometimes the jaw during the day.[10,11] These problems are characterized as repetitive, stereotypical, orofacial lip, and tongue movements. Sometimes the dyskinesia is medication-induced, called "tardive," or it can occur spontaneously. The spontaneous form of dyskinesia often affects the elderly. The tardive form of dyskinesia typically occurs in mentally ill patients who have taken long-term exposure to medications used to treat the mental illness.[12] Tardive dyskinesia by definition requires at least within three months of total cumulative drug exposure, which can be continuous or discontinuous.

Moreover, the dyskinesia must persist more than three months after cessation of the medications in question. Most dopamine receptor antagonists cause oral tardive dyskinesia to one degree or another. The typical antipsychotics, and in recent years even the atypical antipsychotics, including clozapine (Clozaril), olanzapine (Zyprexa), and risperidone (Risperadal), have been reported to cause both tardive dystonia (see next section) and tardive dyskinesia. No adequate epidemiologic data exist regarding whether any particular psychiatric diagnosis constitutes a risk factor for the development of tardive reactions to medications, but the duration of exposure to antipsychotics required to cause tardive reaction is from months to years. Exposure to antipsychotics need not be long and a minimum safe period is not apparent. This duration of neuroleptic exposure seems to be shorter for women. A longer duration of exposure to neuroleptics does not correlate with the severity of the reaction.

Dystonic-type Extrapyramidal Reactions

There are patients who have developed a medication-induced oral motor hyperactivity which do not fit into the dyskinesia category.[13] These medi-

cations and illegal drugs produce a motor response which is better classified as an unspecified extrapyramidal syndrome, EPS, reaction. These EPS reactions have an international classification of disease (version 9) number of 333.90. EPS responses typically have three presentations: dystonic, akathisia and Parkinsonism. Dystonic reactions consist of involuntary, tonic contractions of skeletal muscles.[14-16] Akathisia reactions occur as a subjective experience of motor restlessness.[17,18] Patients may complain of an inability to sit or stand still, or a compulsion to pace or cross and uncross their legs. Parkinsonian reactions manifest themselves as tremor, rigidity, and akinesia, which shows as a slowness in initiating motor tasks and fatigue when performing activities requiring repetitive movements, bradykinesia. When a medication or drug induces a dystonic EPS reaction, it typically involves the muscles of the head, face, and jaw producing spasm, grimacing, tics, or trismus. Most of the literature has focused on the more severe acute dystonic EPS reactions which occur with use of antipsychotic medications. In addition to the antipsychotics, several antiemetics with dopamine receptor-blocking properties have also been associated with tardive dystonia. These include prochlorperazine (Compazine), promethazine (Phenergan), and metoclopramide (Reglan). Of course, other less severe reaction does occur, which vary in intensity and even wax and wane over time. The most commonly reported offending agents that are not neuroleptics are the selective serotonin reuptake inhibitors, SSRI, and the stimulant medications and illegal drugs.

Serotonergic Agents

Selective serotonin reuptake inhibitors, e.g., fluoxetine, (Prozac), fluvoamine (Luvox), paroxetine (Paxil), sertraline (Zoloft), citalopram (Celexa), escitalopram (Lexapro) are used for depression and a variety of other mental illness. Unfortunately, these drugs are reported to produce the side effect of increased clenching and bruxism.[19-22] Actually, the term SSRI-induced bruxism may not be accurate in that the actual motor behavior does not present as brief, strong sleep state-related contractions as seen in bruxism but more of an increased sustained nonspecific activation of the jaw and tongue musculature. Patients generally describe an elevated headache and tightness in their jaw, tongue, and facial structures and the best information available about the effect of SSRI class medications on oromandibular structures comes from a study in 1999 which examined the acute effects of paroxetine on genioglossus activity in obstructive sleep apnea.[23] They found that 40 mg of paroxetine produced a clear augmentation of peak inspiratory genioglossus activity during NREM sleep. Of course the recent widespread use of SSRIs is based on a perception that these drugs have a lower side effect profile than other categories of antidepressant medications, e.g., tricyclics and monoamine oxidase inhibitors. Unfortunately, only case-based literature exists at this time and further studies, full polysomnographic studies on the motor effects of SSRIs are necessary in order to define prevalence, risk factors, and establish a causal relationship between SSRI use and oral motor disorders.

The recent widespread use of SSRIs is based on a perception that these drugs have a lower side effect profile than other categories of antidepressant medications.

Stimulant Drugs and Medications

Illegal drugs such as methamphetamine; cocaine; 3,4-methylenedioxymethamphetamine (Ecstasy) and legal prescription stimulants such as methylphenidate (Ritalin), phentermine (Adipex-P), pemoline (Cylert), dextroamphetamine (Dexedrine), amphetamines (Adderall), and diethylproprion (Tenuate) have all been reported to induce bruxism and dystonic extrapyramidal reactions.[24-28] All stimulant drugs have the potential to cause extrapyramidal reactions and they are being used in greater numbers to treat obesity and or as stimulants for children with attention deficit hyperactivity disorder or narcolepsy, and even for severe depression[29] (**Table 2**).

Etiology

Certainly in those with a family history of spontaneous dystonia or dyskinesia, genetic factors must be prominent. With the exception of familial idiopathic torsion dystonia, ITD, the specific genetic dysfunction is not known. With ITD, a mutation of the DYT1 gene on band 9q34 has been identified.[30] This gene encodes a protein called torsin A, which binds to adenosine triphosphate. In the absence of any family history, spontaneous dystonia or dyskinesia could be a new mutation. Unfortunately, the pathophysiology of motor disorders is not well understood, partly because it describes a symptom that may arise from a variety of cerebral structures, such as the basal ganglia, cerebellum, thalamus, or brainstem, or cortex. One question not yet answered is whether

Table 2

Partial List of SSRI and Other Stimulants Reported to Cause Jaw Motor Hyperactivity

Selective serotonin reuptake inhibitor medications	
Citalopram (Celexa)	Ellison and Stanziani, 1993; Romanelli et al., 1996; Gerber and Lynd, 1998; Lobbezoo et al., 2001
Fluvoamine (Luvox)	
Paroxetine (Paxil)	
Fluoxetine (Prozac)	
Sertraline (Zoloft)	
Escitalopram (Lexapro)	
Illegal drugs	
Ecstasy	Peroutka et al., 1988; Vollenweider et al., 1998; Fazzi et al., 1999; Winocur et al., 2001; See and Tan, 2003
Cocaine	
Amphetamine	
Stimulant medications	
Pemoline (Cylert)	Malki et al., 2004
Methyphenidate (Ritalin)	
Dextroamphetamine (Dexadrine)	

those susceptible to tardive dyskinesia are individuals who are also vulnerable to drug-induced extrapyramidal dystonia, with the medication serving as a trigger to this mutation.

For a few cases, there is some evidence to support a role of trauma including injury to the head or other body parts. For example, a closed head injury can sometimes result in severe dystonia, but the injury has to be severe enough to result in damage to the basal ganglia, which can be visualized on brain imaging studies. Peripheral, non-CNS, injury to a limb may also result in severe dystonic postures, but the mechanism underlying this "peripheral injury-induced dystonia" is not clear. It is speculated that people who are carriers of the gene for dystonia may be more likely to have trauma as a triggering factor for the development of dystonia. One study reported on the role of peripherally induced oromandibular dystonia.[31] Specifically, they reported on several cases with a history of a recent oromandibular dystonia that: (1) developed within a few days or months, up to a year, after the injury; (2) the trauma was well documented by the patient's history or a review of their medical and dental records; and (3) the onset of dystonia was anatomically related to the site of injury, facial and oral. They found 27 patients identified with an oral motor disorder temporally and anatomically related to prior injury or surgery and nothing else. The mean age at onset was 50 ± 14 year and there was a 2:1 female preponderance.

More important to the dentist was the reported association of new onset cranial dystonias which developed within hours to months following a dental procedure.[32] In these cases, there was no family history of dystonia or prior use of neuroleptics. The authors suggested that the close association in time and location of the procedure and onset of symptoms suggested a causal link between the dystonia and the dental intervention and asked for better epidemiologic studies on the topic.

Management of Disease

Anytime a patient exhibits a new onset involuntary oral motor disorder, a three-step process is suggested. The first step is to collect a full clinical history and examination, including magnetic resonance imaging of the brain. The second step (after ruling out CNS disease, adverse medications reactions, and local pathology) is to try one or more of the motor-suppressive medications that may be helpful in these cases (e.g., cholinergic receptor antagonizers or blockers and GABA-ergic including benzodiazepines). The third step, if the disorder is severe enough and focal enough and motor-suppressive medications are not adequate, is to consider botulinum toxin injections.

History and Examination

The first step in all suspected oral motor disorders is to perform a proper diagnostic work-up for a movement disorder. This involves a full clinical history and examination and magnetic

resonance imaging examination. The history must include a thorough medication and illegal drug history, when tardive induced motor disorders are suspected. The imaging is necessary in order to rule out the possibility that the motor dysfunction may be due to a central degenerative, demyelinating, or sclerotic lesion of the nervous system. Moreover, in addition to a standard MRI, imaging might also include angiographic-type magnetic resonance imaging. These tests will rule in or out a neurologic infarct or tumor or compression of critical nerves or structures. For the most severe forms of bruxism and some sleep-related motor activity problems, it will be necessary to conduct a polysomnogram which includes an electroencephalogram and electromyographic monitoring of the involved structures.

In the absence of a clear-cut history of CNS damage, injury or new pathology, or a family history of similar movement disorders, it should be appreciated that the exact pathophysiologic mechanisms for the spontaneous onset hyperkinetic motor disorders is often not proven by examination or imaging. The two exceptions to this statement would be hemifacial and hemimasticatory spasm, where it is thought that there is a vascular compression of CN V and VII motor roots. Proceed with steps 2 and 3 only after a negative examination and imaging is achieved.

Treatment

Step 2 involves either removing medications, if a suspected drug-related motor disorder is present, or adding medications that effect the motor system.[33] If a patient has a proven tardive dyskinesia which does not stop with withdrawal from the offending medications, or these medications cannot be stopped, this is managed as a spontaneous movement disorders with motor-suppressive medications. These medications work well for acute onset spasms of the jaw, but often only a small effect is seen and side effects can be substantial in patients with hyperkinetic oral movement disorders.

Treatment of Tardive Dyskinesia and Drug-Induced Dystonic Extrapyramidal Reactions

The general rule is that one withdraw the offending medication and hope that the dyskinesia or dystonic reaction will go away.[34] Fortunately, acute dystonic reactions secondary to neuroleptic drugs are infrequent and disappear upon discontinuation of the medication but this may take days to months, depending upon the drug, its dose, and the patient. The same goes for less severe dystonic EPS reactions associated with SSRIs and stimulant drugs. If the suspected medication cannot be stopped or it is severe, the following methods are used to treat them: diphenhydramine (Benadryl) 50 mg; benztropine (Cogentin) 2 mg IV or IM.[35-37] The preferred route of administration is intravenous. If this is not feasible, IM drug administration can be used.

Finally, both amantadine (Symmetrel) 200-400 mg/d po and diazepam (Valium) 5 mg IV have been shown to be effective for recurrent neuroleptic-induced dystonic reactions.[38,39] Some patients with SSRI-induced dystonic EPS have relief when the dose of SSRI or the other stimulant drug is reduced, e.g., fluoxetine (Prozac) changed from 20 mg/day to 10 mg/day. Other patients respond to the addition of buspirone (Buspar) in doses of 5-15 mg per day.[40,41] Some patients developed bruxism within the first few weeks of SSRI therapy, however, they were successfully treated with buspirone in doses of 10 mg twice daily to three times daily. Buspirone appears to be an effective treatment based on a few case reports. This drug may have an additional benefit of relieving anxiety if it is present. It is usually well tolerated and carries a low risk of significant side effects. Finally, switching to antidepressants that have not been associated with bruxism such as the mirtazapine (Remeron) or nefazodone (Serzone).

> The general rule is that you withdraw the offending medication and hope that the dyskinesia or dystonic reaction will go away.

Treatment of Spontaneous Dyskinesias, Dystonias

With any new onset movement disorders without obvious cause, a motor-suppressive medication trial is logical. The commonly used medications are presented in **Table 3**. If the disorder is severe enough and focal enough to consider, and the medications are not adequate then consider botulinum toxin injections (see next page). Finally, for those who cannot be helped with steps 1 through 3, and the scientific evidence-supporting alternative approaches are reasonable, consider neurosurgical therapy or implanted medication pumps that can deliver intrathecal medications. Regarding the prognosis of motor-suppressive medications, a recent meta-analysis of the literature made several conclusions that should be shared with patients before starting treatment.[42] First, this review suggested that botulinum toxin has obvious benefit for the treatment of focal dystonias such as

Table 3

Oral Medications Used for Management of Hyperkinestic Motor Disorders

Drug	Starting dose (mg/day)	Usual dose (mg/day)	FDA: Approved Use	Receptor Action
Trihexyphenidyl HCl (Artane)	1 mg/d	6-15 mg/d	Idiopathic Parkinson's extrapyramidal reactions	Antagonizes acetylcholine receptors
Biperiden (Akineton)	2 mg tid	16 mg/d	Parkinsonism extrapyramidal disorders	Antagonizes acetylcholine receptors
Baclofen (Lioresal)	10 mg/d	30-80 mg/d	Spasticity	Mechanism unclear but most likely a GABA effect
Tigabine (Gabitril)	4 mg/d	8-32 mg/d	Partial seizures	GABA-reuptake inhibitor
Clonazepam (Klonipin)	0.25 mg/d	1-4 mg/d	Seizures, absence anxiety, panic disorder periodic leg movements neuralgia	Binds to benzodiazepine receptors and enhances GABA effect
Buspirone (Buspar)	7.5 mg bid	20-30 mg/d	Anxiety	Non-benzodiazepine but mechanism unclear
Amantadine (Symmetrel)	100 mg bid	100-300 mg/d	Influenza A extrapyramidal reactions Parkinsonism	Mechanism unclear
Benztropine (Cogentin)	1 mg bid	6 mg/d	Parkinsonism extrapyramidal reactions dystonic reaction, acute	Antagonizes acetylcholine and histamine receptors
Diphenhydramine (Benadryl)	25 mg tid	400 mg/d	Antihistamine dystonic reactions	Antagonizes central and peripheral H1 receptors (nonselective)
Botulinum toxin type-A	20-50 units per jaw closer muscle	Max: 200 units every 3 months	Focal dystonia	Blocks release of acetylcholine from motor end plate

cervical dystonia and blepharospasm. Second, trihexyphenidyl (Artane) in high dosages is effective for the treatment of segmental and generalized dystonia in younger patients. Third, all other methods of pharmacological intervention for generalized or focal dystonia, including botulinum toxin injections, have not been confirmed as being highly effective according to accepted evidence-based criteria (**Table 3**).

Anticholinergic Therapy

The anticholinergic drugs, such as trihexyphenidyl hydrochloride or biperiden (Akineton), are partially effective agents for dystonia, but even these drugs work in only a minority of patients. It is critical to start at a low dose and increase the dose very slowly to try to minimize the adverse effects such as dry mouth, blurred vision, urinary retention, confusion, and memory loss.

GABA-ergic Therapy

Baclofen (Lioresal) is a GABA-ergic agent which is used in spasm. The starting dose is 10 mg at bedtime. Increase the dose by 10 mg each week to a maximum of 30 mg three or four times daily. The best data for baclofen is not for oral medications but for intrathecal injections of baclofen delivered with an implantable pump.[43,44] Main side effects include drowsiness, confusion, dizzi-

ness, and weakness. Finally, a recent report suggests tiagabine (Gabitril), a GABA-reuptake inhibitor which is used as an adjunctive anticonvulsant treatment of partial seizures, can be helpful in bruxism reduction.[45] The doses for tiagabine used to suppress nocturnal bruxism at bedtime (4 mg to 8 mg) are lower than those used to treat seizures."

Benzodiazepines Therapy

Benzodiazepines can be effective for suppression of focal, segmental, and generalized dystonia.[46] They bind to a specific benzodiazepine receptor on GABA-receptor complex, thereby increasing GABA affinity for its receptor. No study has found a significant difference between the various benzodiazepines and clonazepam (Klonopin), which has been widely used in movement disorders. The starting dose for clonazepam is 0.25 mg at bedtime and gradually increasing the dosage to a maximum of 1 mg four times daily. The main side effects include drowsiness, confusion, trouble concentrating, and dizziness.

Botulinum Toxin

Step 3 in the process of treatment for oral motor disorders involves the selected use of the toxin produced by the anaerobic bacterium clostridium botulinum. This injectable drug is able to block motor nerve conduction and, once injected, it suppresses muscle activity for a time period ranging from eight weeks to 16 weeks with botulinum toxin type-A. Any clinician who has used this medication will testify to its powerful and dramatic effect in some cases. Unfortunately, this treatment is only palliative. The vast majority of the reports described in this paper relate to botulinum toxin type-A (Botox) unless specified otherwise. When unit doses are provided, they refer to units of Botox, a product manufactured by Allegan since this is the primary product available and used in North America. The clear contraindications to the use of botulinum toxin are known allergy to the drug; infection or inflammation at the proposed injection site(s); pregnancy and/or women who are lactating; and an inability of a patient to cooperate, or high levels of fearfulness toward the method. The final caveat is that while botulinum toxin injections sound simple and safe, there are complications. In this regard, it is should be reserved for patients with an unequivocal diagnoses. The specific applications and indications for botulinum toxins are presented below.

The final caveat is that while botulinum toxin injections sound simple and safe, there are complications.

Oromandibular Dystonia (With Recurrent Jaw Opening Motion)

Oromandibular dystonia is a focal dystonia affecting the trigeminal and oral-perioral musculature. It is considered present when repeated, often asynchronous, spasms of muscles of these muscles are present. Treatment with botulinum toxin has been found helpful and there are many variations of oromandibular dystonia, but one common one is involuntary jaw opening dystonia. One complication of jaw opening dystonia is that the temporomandibular joint can become physically locked in the wide open position so that even after the dystonic contraction stops, the jaw will not easily close. Several authors have described the use of botulinum toxin injections into the lateral pterygoid muscle when a patient exhibits focal dystonia which results in jaw opening.[47-49] While the above authors have focused on injecting the lateral pterygoid muscles, sometimes the submandibular muscles e.g., anterior digastric and platysma, can play a role in jaw opening activity and here again there are several reports in the literature that report on botulinum injection of these muscles.[50,51]

Hyperactivity of the Tongue

The tongue is often strongly active in tardive and spontaneous dyskinesia, some types of oromandibular dystonia, and can be involved as a manifestation of the motor effects seen in cerebral palsy. Botulinum toxin injections into the genioglossus and the intrinsic tongue muscles has been used to treat this motor problem with limited success.[52-55]

Injections Tips

Botulinum toxin is a safe therapy when administered in the appropriate doses by an experienced clinical specialist. A recent review discussed the dosage and injection sites for the commonly injected jaw muscles.[56] To become proficient with this method, it is recommended that the clinician spend some time in the anatomy laboratory injecting more than one cadaver with a colored dye and then dissecting the dye-injected cadavers to know if the injection was placed correctly. While for some, deep muscles, e.g., lateral pterygoid, it is advisable to use electromyographic localization method to ensure proper placement of the needle. Most times, this additional methodology is not required

in most patients since many of the primary target muscle (e.g., masseter, temporalis, anterior digastric, genioglossus, orbicularis oris, muscles of facial expression, levator tensor palate and the intrinsic tongue muscles) can be easily palpated or clear injection landmarks identified. For some of the injection targets, e.g., parotid, lacrimal and submandibular salivary glands, EMG will not help prove one is in the correct place, although it would help one to know one is in an incorrect location.

Side Effects From Botulinum Injection

Side effects can be divided into site of injection side effects and medication-related side effects. With regard to site of injection side effects, the needles being used for most injections are small (between 27- to 30-gauge needles), and if the skin is cleaned properly, then the chance of local hematoma, infection or persistent pain in the injection site is very, very low. Regarding medication-related side effects, they are generally few, transitory and well tolerated by patients if they occur. The most common medication-related side effect is adjacent muscle weakness, e.g., an inadvertent weakening of the muscles of facial expression or swallowing when this is not desired. For patients who have had injections into the lateral pterygoid or palatal muscles, slurred speech with palatal weakness is a distinct possibility as well. In general, these "inadvertent weakness" complications due to local diffusion of the drug can and does occur.

Moreover, this complication is technique and dose-dependent.[57-59] A second side effect with botulinum toxin injections of the masticatory muscle is an alteration in the character of the saliva of patients who have not had direct salivary gland injections. While this is an uncommon problem, some patients report that their saliva is diminished and thicker, i.e. ropy saliva, and is more likely for higher doses and for injections around the parotid or submandibular gland. Obviously, sometimes this effect is desired if there is a substantial sialorrhea problem.

In most cases, the previously mentioned complications are usually less problematic than the untreated original motor disorder and will not generally stop the patient from seeking additional injections. However, if the injections are being used to primarily treat pain secondary to contraction, then these complications might be more bothersome. Fortunately, persistent, more significant complications are distinctly rare. For example, systemic complications are uncommon and although several studies have reported a flu-like syndrome, particularly after the first injection, such symptoms have also been reported following a placebo injection. Finally, some patients develop antibodies to the toxin. It is unclear exactly what factors predispose to development of antibodies, but some studies suggest that risk is increased by higher and more frequent injections and for this reason, injections are not done more often than once every 12 weeks.

The most common medication-related side effect is adjacent muscle weakness.

Summary Recommendations

The prognosis of patients with tardive dyskinesia or tardive dystonia is poor if the disorder persists after withdrawal of the medication. At best, the movements can be suppressed with motor-suppressive medications but often the medications produce only a small change. The same can be said for the prognosis of spontaneous dyskinesia and dystonia, but if the disorders are reasonably localized, botulinum toxins can be quite helpful. A better prognosis is offered for the drug induced dystonic EPS reactions. In these cases, recognition and communication about the suspicion of a drug-induced EPS back to the prescribing clinician is the first step. Withdrawal from the medication or reduction of the medication is logical. There are several medications that can be used to help the patients manage this disorder, and when indicated, careful and cautious use of botulinum toxin in resistant cases is appropriate. ■■■■

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Robert E. Horseman, DDS

A Crowning Moment … Not So Much

I was flat on my back. I mean, really flat, not leaned back — **flat**. Only a few minutes before I had been admiring the view out the window, a verdant arboretum complete with a burbling fountain and chirping birds with visitation rights. Periodontists need this sort of environment to compensate for spending 10 years on their education instead of being high school dropouts extorting $40 million per year for making forgettable movies or hitting assorted balls with a variety of sticks.

Now, because I had been relieved of my glasses, the view was less distinct and definitely less soothing. Staring down at me right out of Central Casting, were three slightly out-of-focus figures garbed in the familiar accoutrements recognized by anybody who spends a lot of TV time absorbed in the drama of hospital operating rooms.

It had taken me 86 years to get here. It was a destination delayed by an amalgamation of good genes, ignorance, and dumb fool luck. But now the jig was up. The failure of the root canal treatment as a result of a cracked root after 35 years rendered my upper-right second bicuspid hors de combat. After an initial period of resentment over the betrayal of a tooth upon which I had lavished so much care and money since my 11th year, resignation set in. Goodbye, O loyal and faithful servant; hello, **IMPLANT**!

There is an opinion shared by many patients that if a dentist is to be considered an authority on any given procedure, he should have undergone that procedure himself. A reasonable expectation, I suppose, but one that brain surgeons and I do not share.

That's why I no longer do full dentures. I never understood how anybody could suc-

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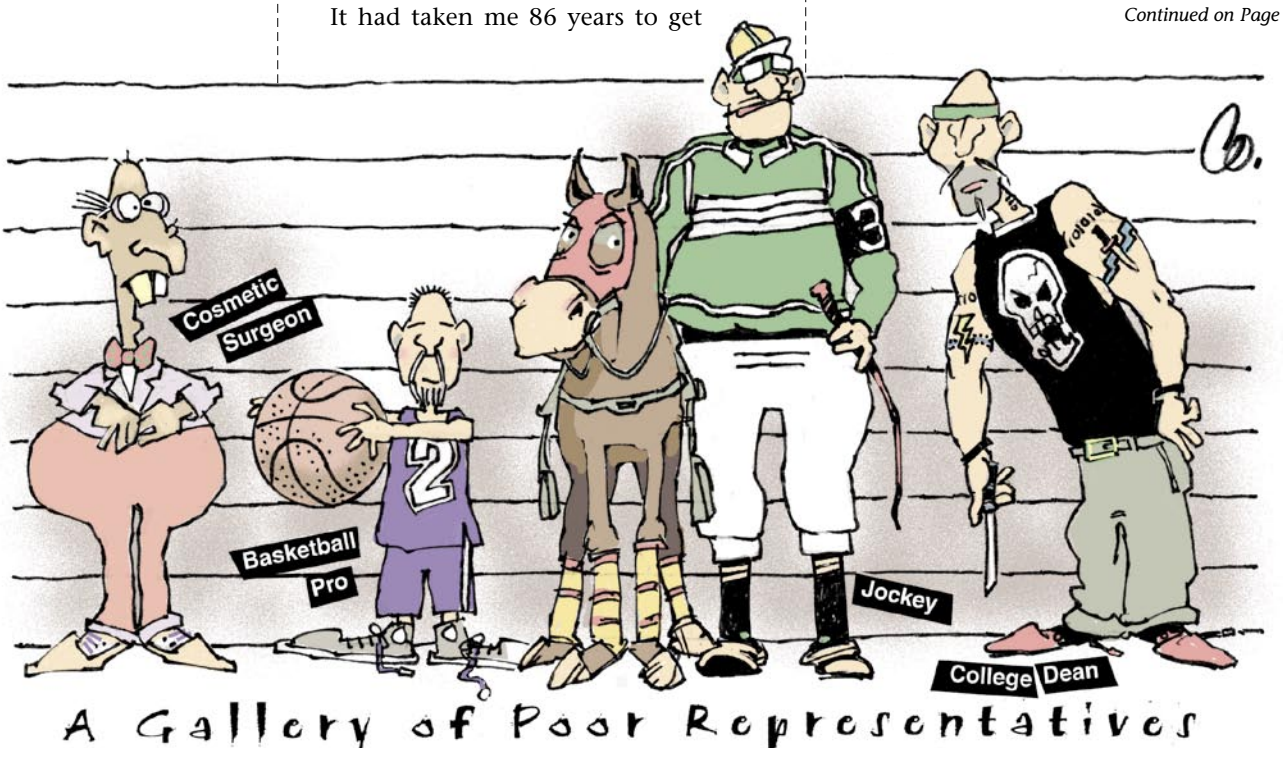

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cessfully negotiate any meal that didn't consist solely of mashed potatoes, custard, and tofu while equipped with upper and lower dentures. Certainly not with mine. There is not enough Fixodent in the world to entice me to give up my natural teeth to become more simpatico with edentulous patients.

Just a relatively few years ago, a bridge would have been my choice. Anybody can have a bridge if a couple of stable abutments are present and they don't mind the necessary reduction for the abutment crowns. Early implants were a pretty iffy proposition as researchers found their way through blades, screwed-in castings, vitreous carbon, and anything else that held promise. Happily, titanium won. Titanium sounds expensive, like platinum and uranium, therefore, superior with a certain cachet of snob appeal.

A relatively simple procedure, explained Dr. Tom Gaffaney, the perio guy down the hall who is doing the job. I'll be the judge of that. Even if my vision was obscured by green-clad elbows and latex gloves, there was nothing wrong with my ears. Drilling the hole for the titanium cylinder, although painless, sounded something akin to reducing ice cubes to crushed ice in a slow-speed blender. Bone is an excellent conductor of sound, especially when it has only four inches to travel from drill to ear.

There is not enough Fixodent in the world to entice me to give up my natural teeth to become more simpatico with edentulous patients.

At that point, things became a little vague. But before I had completed counting the holes in the acoustical tile ceiling, binocular-eyed Gaffaney and his team of efficient assistants were giving me detailed instructions for postoperative care: Motrin, Perioguard, amoxicillin, and the office phone number. From the patient's viewpoint, it was almost a nonevent and, best of all, that stupid "no pain, no gain" mantra was not applicable.

"And I'll have my new crown in what, a couple of weeks?" I asked, knowing better.

"Try three months."

This is the only thing wrong with implants if you are a go-go person who wants things done right now. You want your teeth whitened in one hour; lose 20 pounds over the weekend. Sorry, folks, but you can bet the periodontists would like nothing better than to make the whole deal a one-visit appointment. Then they could do implants for VIP movie people at about one mil a pop, and the eight-hour stint in the 9-by-10 operatory wouldn't look so bad.

A dentist with a missing bicuspid is a poor representative of the profession, like an ugly cosmetic surgeon or a really obese Jenny Craig rep. So, in the interim, if any of my people want to know firsthand about the joys of wearing a one-tooth flipper, they've come to the right place. I won't lie. ■■■

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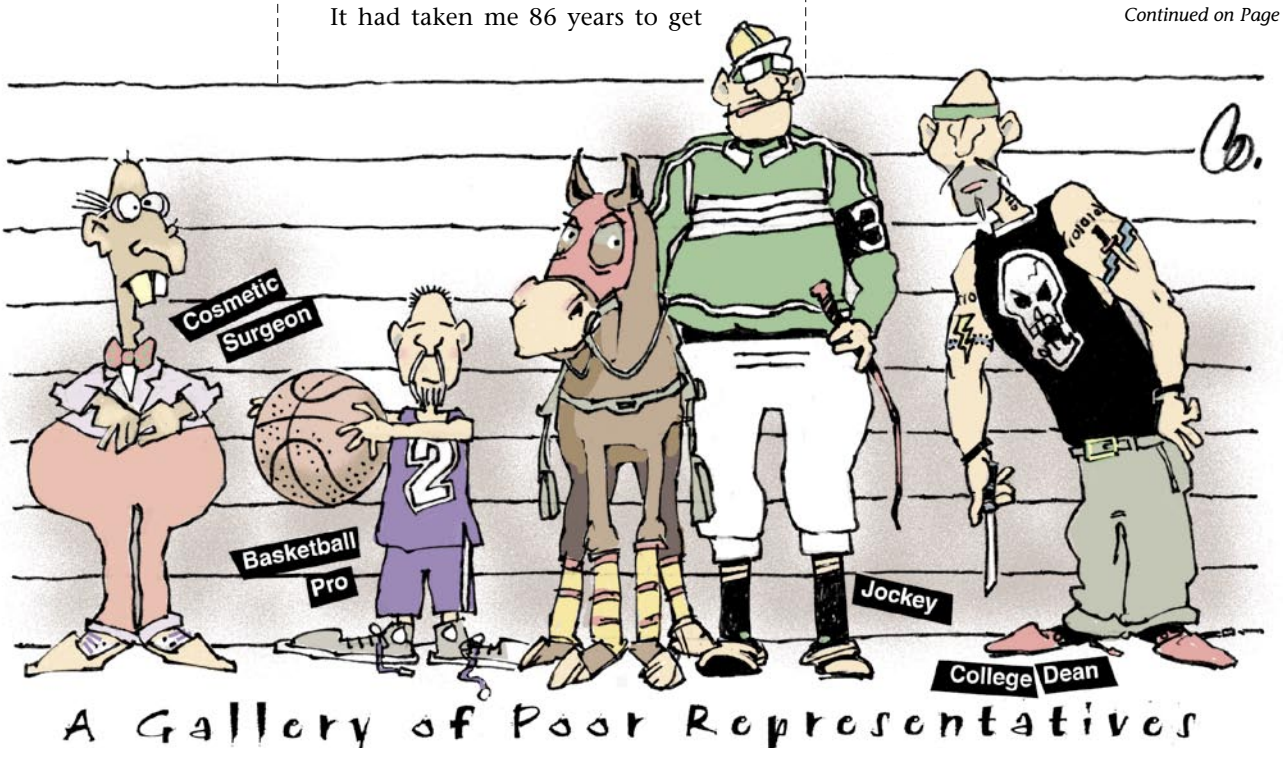

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