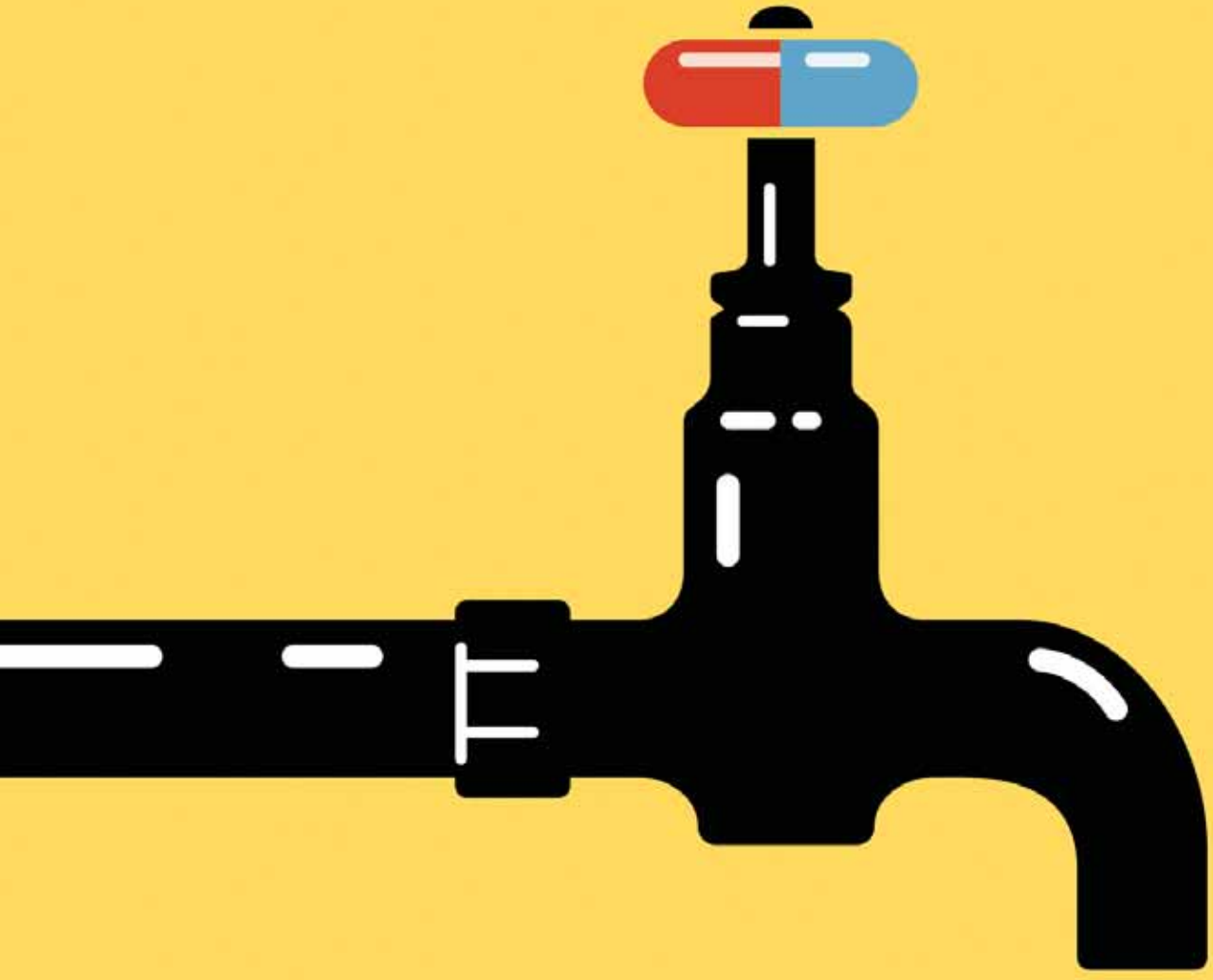
Journal
CALIFORNIA DENTAL ASSOCIATION
November 2015

Evidence-Based Pharmacology for Chronic Pain

Prevention Is Better

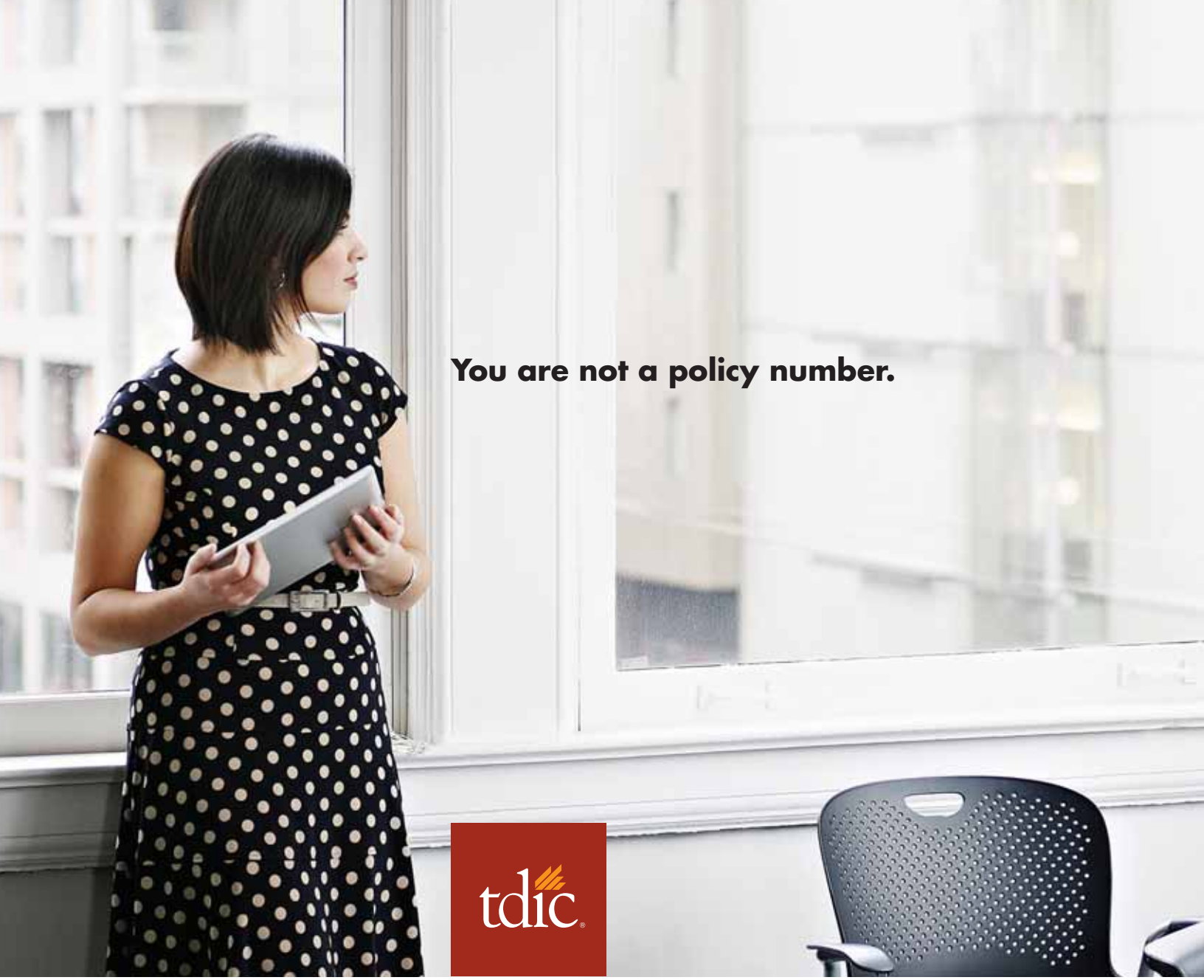
Supplements and Alternative Therapies

Prescription Opioid Abuse



PAIN CONTROL AND PREVENTION

Peter L. Jacobsen
PhD, DDS



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CDA JOURNAL, VOL 43, N°11

CURES

Kerry K. Carney, DDS, CDE

Have you had the call from a person who wants a prescription for pain meds before coming in for an examination and treatment? It usually occurs after normal business hours. Sometimes it is a patient new to your practice. Sometimes it is someone pretending to be a patient of record. The alarm bells in your head go off when you offer to see the person but some commitment or encumbrance prevents him or her from coming in to be evaluated and having any treatment rendered. All the caller wants is a prescription to relieve the pain until an appointment and treatment are possible.

In three decades of practice, I have seen a number of variations of this scenario, but my feeling has always been the same: I feel like someone figures I am an easy mark. Someone is trying to pull something over on me. Someone wants to leverage my compassion and obtain a prescription opioid under the guise of needing pain relief. But recently, my perception has changed. It is not all about me and my need to avoid being exploited. It is about an epidemic in prescription drug abuse.

One of the most rewarding aspects of being a dentist is the ability to alleviate pain through intervention. To take those patients who could not sleep or function due to dental pain and, through ministering, bring them back to pain-free oral health. That is a gift of gratification to the dentist as well as a gift of relief to the patient.

However, efforts to bring every patient to a pain-free state have helped bring us to the present epidemic of prescription opioid abuse.

Efforts to bring every patient to a pain-free state have helped bring us to the present epidemic of prescription opioid abuse.

In the last two decades, pain has been promoted as the fifth vital sign.[1] Health status assessments commonly incorporate the findings of the four traditional vital signs: blood pressure, heart rate, temperature and respiratory rate. Pain assessment was adopted as the fifth vital sign by many soon after the turn of this century. The hypothesis was if pain were assessed like a vital sign it could be measured and treated appropriately. Self-evaluation of pain based on a subjective numeric (1-10) scale or on an iconic (smiley face to frowny face) scale has been used to "measure" this fifth vital sign.

If a requirement for health is freedom from pain, then in the past, patients in pain may have been undermedicated.

Recent criticisms of this treatment philosophy point out that unlike the other vital signs, pain cannot be measured objectively. Also, pain is a sign or symptom of an ailment. Treating the pain level with analgesics does not address the cause of the pain.

Concomitant with this trend to consider pain as a vital sign, prescriptions for opioid analgesics skyrocketed. Opioid-related overdose and overdose-related deaths assumed epidemic proportions. There are an estimated 44 prescription opioid-related deaths a day.[2] This is a staggering statistic.

Hydrocodone prescriptions have surpassed prescriptions written for drugs designed to treat common chronic conditions (e.g., simvastatin). The startling fact is the U.S. population consumes "80 percent of the world's opioid supply and 99 percent of the world's hydrocodone supply."[3]

In the first 15 years of this century, the number of prescription opioid-related deaths has quadrupled. Dentists prescribe 8 percent of all prescriptions for opioids. After primary care physicians and internists, dentists are the most frequent prescribers of opioids. However, dentists hold the dubious honor of being "the main prescribers of opioids for patients aged 10 to 19."[3]

These figures should make every dentist reevaluate how they prescribe opioids. In addition to changing our prescription behavior, we need to think about what roles we can play in the face of this epidemic of prescription drug abuse.

We can reevaluate our analgesic preferences based on evidence of effectiveness and modify our prescriptions accordingly. We can educate our patients about proper medication use and appropriate disposal. One of the primary reasons for prescription opioid abuse is the ease of access. Excess medication is frequently available in the home medicine cabinet.

Many communities have drug disposal days when medication can be dropped off for disposal at specified locations (such as police or fire stations). Passing this information along to our patients with the prescription might help reduce medication hoarding.

Prescription drug monitoring programs (PDMP) are in operation in 49 states. These programs are designed to assist in the reduction of pharmaceutical drug diversion without affecting legitimate medical practice and patient care.

In California, our PDMP is the Controlled Substance Utilization Review and Evaluation System, known as CURES. All prescribers will be required to register with CURES by July 1, 2016. When such a database is well-

implemented, a dentist could easily check on a patient's prescription medication history before making decisions about the appropriate therapeutic steps to take.

The goal is to reduce abuse by reducing the easy access to prescriptions from various numbers of physicians and dentists. Checking and documenting the patient's prescription history regularly could be the best protections for both the patient and the dentist should something untoward occur. As always, the devil will be in the details. If CURES is quick and easy to use, it can have a significant impact.

There are many factors that have contributed to the current state of affairs. Along with the increased number of prescriptions written and dispensed, there has been a remarkable increase in aggressive marketing by pharmaceutical companies and an increased acceptability to use medications for different purposes.[4]

The dentist's role in this epidemic is not insignificant. When we write a prescription for a pain medication, we sometimes use the abbreviation "PRN Pain." The Latin term is pro re nata (as the situation demands or as needed). Our intention is to direct the patient to take the medication as the situation demands to relieve pain. However, the time has come to write ourselves an effective prescription; the situation demands that we collaborate with physicians, pharmacists and government agencies to take action to stem this epidemic of prescription drug abuse. ■

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CDA JOURNAL, VOL 43, N°11

Dentistry for the Ages Series — A Gross Omission

After examining countless radiographs of patients in their 80s and 90s with nonrestorable carious lesions, calcified pulpal canals, no evidence of periapical pathology and, most important, no symptoms, it would seem that minimally traumatic treatment plans (palliative care) should be the standard of care.

The scholarly, academic articles submitted relating to access to care, costs of care, demographic considerations, etc., were informative and well-researched. More practical, wet-fingered approaches to the care of the aged would have been much appreciated.

The surgical challenges of removing teeth in older patients, with the above noted findings, and the consequent pain, swelling, bruising, risks, etc., should be cause for reconsideration. There are numerous strategies that avoid the trauma and provide satisfactory long-term results. Often, older patients' primary concerns relate to cosmetics … so important to self-image and confidence.

I would love to hear from readers regarding your experiences.

DAN E. RUDIN, DDS
Redondo Beach

Dear Dr. Rudin,

Thank you for your feedback on the *Journal*'s two issues on Dentistry for the Ages and sharing some of the clinical challenges you have faced when delivering care to frail older adults. We completely agree with your comments regarding the need for palliative care for older adults at the end of life. July's issue (Part 1) was designed to set the scene for some of the issues that arise when caring for older adults, while August's issue (Part 2) was intended to deliver the more practical, clinical approaches you requested.

For example, the Seattle Care Pathway (pages 429-437) outlined an evidence-based approach to appropriate treatment planning and delivery based upon an older adult's functional status. Alternative

treatments for root caries that could be delivered in a palliative care setting were discussed on pages 439-445, including the use of silver diamine fluoride, partial caries removal and glass ionomer restorations. As you indicated, the care of older adults encompasses a range of clinical presentation, from healthy older adults requiring comprehensive care to frail elders needing palliative care. Therefore, links to additional online courses and case studies of complex geriatric patients were presented on page 459 for clinicians interested in continuing education on this topic.

DICK GREGORY, DDS
SUSAN HYDE, DDS, MPH, PHD, FACD
San Francisco

Professionalism at the Crossroads

Over the last couple of years, I, like most dentists, have been exposed to situations where patients have complained about dentists who, by providing a single treatment option of his or her choice, dramatically upselling and other actions focusing on increasing office productivity, have made those patients mistrust our profession. I am uneasy about responding to these patients. I do not wish to denigrate other dentists, but I have trouble defending them. I usually say something like, "Let me take a look and I will give you my opinion," just ignoring my level of discomfort.

I guess we should recognize that, like it or not, we are a profession, and patients, consciously or otherwise, expect us to act professionally, however they define it. Coincidentally, next year will be the 150th anniversary of the ADA Code of Ethics. It seems like a good time to recognize that the public is aware, at some level, that dentists have an ethical foundation.

Interestingly, the ADA has recently completed a consumer survey related to the ADA Code of Ethics. When made aware of the content of the ADA Code and told that ADA members agree to abide by the Code, nearly 70 percent of consumers indicated that they would be more likely or much more likely to choose an ADA member dentist the next time they are looking for a dentist.

Perhaps it is time for our profession to refocus on what it means to be a dental professional. Maybe, with some effort on the part of organized dentistry, we can even use this information to help members feel that organized dentistry is helping them compete in the dental marketplace.

GARY HERMAN, DDS
Los Angeles

The *Journal* welcomes letters

We reserve the right to edit all communications. Letters should discuss an item published in the Journal within the past two months or matters of general interest to our readership. Letters must be no more than 500 words and cite no more than five references. No illustrations will be accepted. Letters should be submitted at editorialmanager.com/jcaldentassoc. By sending the letter, the author certifies that neither the letter nor one with substantially similar content under the writer's authorship has been published or is being considered for publication elsewhere, and the author acknowledges and agrees that the letter and all rights with regard to the letter become the property of CDA.

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The New Autonomy

David W. Chambers, EdM, MBA, PhD

Privacy protection, informed consent, blocking public health initiatives and moral hazard arguments (why should I pay into a pool for benefits I need less than others do?) have pushed "right to autonomy" into the center of public attention.

On national television recently, gang members in Florida who specialized in robbing high-end homes bragged that they used Google Earth to plan their break-ins. They were five times referred to as "the alleged robbers" and they pleaded "not guilty." That is a level of sophistication in separating the glory of a national TV spot from its consequences every lawyer would admire.

The average American surrenders massive amounts of personal information at the click of a mouse, but opposes collecting any data that could possibly be used unfavorably. Government resources are to be targeted to the most efficient use, but profiling is illegal. Quarantines, mandatory vaccinations and evacuation orders in the face of forest fires are resisted even by those who find them perfectly reasonable.

The proper term in philosophy is "respect for autonomy," not "right to autonomy." The origin is two Greek words "auto" and "nomi," meaning "self" and "rule." The value runs deep in America, with its strong Anglo-Saxon and Germanic heritage. The Magna Carta was not a guarantee of benefits to the common person. It was a protection for the minor nobility from arbitrary laws imposed by the king, who, after all, was French, not English.

In the 1820s, debates in England's Parliament veered toward high-tone public character assassination. Broughton said Channing was an "ass," but that gave Channing no right to take offense. It was as though inflammatory comments were safe when placed in "scare quotes" — if you know what I mean. A cub parliamentary reporter named Charles Dickens ridiculed this nonsense in his first novel, giving us the term "Pickwickian." It means wishing to be taken seriously only by those who agree and to be immune from judgment from those who do not agree. Social media posts are flagrantly Pickwickian. In fact, much on social media is just cheap self-promotion, sometimes even complete with a Pickwickian legal disclaimer at the end.

Perhaps dentists only have a Pickwickian right to respect for their autonomy. Informed consent is mutual agreement between professional and patient — double autonomy. This exits when it is accepted that patients can judge dentists, when dentists must stand behind every implication of their positions. Perhaps with the best of intentions, dentists have officially muddled this notion. Claims about "putting the patients' interests first" are meant to advertise a higher calling and justify unquestioned trust through selective messaging. Of course, such slogans are not expected to be taken literally. Saying so and then reserving any escape clause seems to be wanting to have it both ways and to undermine respect for autonomy. ■

The nub:

1. You cannot protect what you are willing to give away.

2. Anything a dentist says is an irreversible procedure.

3. Wanting only to be heard "in a favorable light" is asking too much.

David W. Chambers, EdM, MBA, PhD, is professor of dental education at the University of the Pacific, Arthur A. Dugoni School of Dentistry, San Francisco, and editor of the *Journal of the American College of Dentists*.

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Higher Risk of Tooth Loss Among Smokers

A new study recently confirmed that regular smokers have a significantly increased risk of tooth loss. According to research published in the Journal of Dental Research, the association between smoking and the incidence of tooth loss was stronger in men than women and stronger in younger versus older individuals. In a large cohort study, the authors aimed to investigate the association between cigarette smoking and smoking cessation and the prevalence and incidence of tooth loss.

The researchers found female smokers were 2.5 times more likely to lose their teeth than nonsmokers were while male smokers were up to 3.6 times more likely. The findings were independent of other risk factors, such as diabetes, and are based on data from 23,376 participants in three different age groups.

"Most teeth are lost as a result of either caries or chronic periodontitis. We know that smoking is a strong risk factor for periodontitis, so that may go a long way toward explaining the higher rate of tooth loss in smokers," explained lead author Thomas Dietrich, a professor from the University of Birmingham, in a news release.

The researchers also reported that smoking cessation was consistently associated with a reduction in tooth loss risk, with the risk of tooth loss approaching that of never smokers after approximately 10 to 20 years of cessation.

For more information, see the study in the Journal of Dental Research, October 2015, vol. 94, no. 10, pp. 1369-1375.

Silica Nanoparticles May Help Repair Damaged Teeth

A new study from the University of Birmingham shows how submicron silica particles can be prepared to deliver important compounds into damaged teeth through tubules in the dentine. The research shows how the development of coated silica nanoparticles could be used in restorative treatment of sensitive teeth and preventing the onset of tooth decay.

"The dentine of our teeth have numerous microscopic holes, which are the entrances to tubules that run through to the nerve," said Damien Walmsley, from the School of Dentistry at the University of Birmingham. "When your outer enamel is breached, the exposure of these tubules is really noticeable. If you drink something cold, you can feel the sensitivity in your teeth because these tubules run directly through to the nerve and the soft tissue of the tooth.

"Our plan was to use target those same tubules with a multifunctional agent that can help repair and restore the tooth, while protecting it against further infection that could penetrate the pulp and cause irreversible damage."

The aim of restorative agents is to increase the mineral content of both the enamel and dentine, with the particles acting like seeds for further growth that would close the tubules. Previous attempts have used compounds of calcium fluoride, combinations of carbonate-hydroxyapatite nanocrystals and bioactive glass, but all have seen limited success, as they are liable to aggregate on delivery to the tubules, according to the news release. This prevents them from being able to enter the opening, which is only 1 to 4 microns in width.

However, in the new study, the research team turned to submicron silica particles that had been prepared with a surface coating to reduce the chance of aggregation.

"We tested a number of different options to see which would allow for the highest level particle penetration into the tubules, and identified a hydrophobic surface coating that provides real hope for the development of an effective agent."

For more, see the study in the Journal of Dentistry, published online Aug. 7, 2015.

Oral Infection a Potential Risk Factor for Alzheimer's

In a recent review of more than 200 articles examining the suggested link between infections of the mouth and Alzheimer's disease (AD), authors address the "plausible etiology of late-onset AD being an oral infection."

Inflammation of the brain is a characteristic feature of AD, and in recent years, scientists have been searching for potential root causes — many looking to "peripheral infections," particularly those that originate in the oral cavity.

According to the authors, it is well established that many bacteria in the mouth, particularly in people with gum disease, find their way into the host bloodstream. If those bacteria pass the blood brain barrier, any number of them could be implicated in the Alzheimer's enigma, said Ingar Olsen, DDS, a professor at the University of Oslo, in a news release.

"I was amazed that so much of the research to date has been focused on a couple of groups of bacteria, namely spirochetes and *Porphyromonas gingivalis*, when there are well over 900 different bacteria in the oral cavity," said Olsen after reviewing the research. "Even oral *Candida* and herpes virus could possibly cause the inflammation in the brain that we see in Alzheimer's patients."

According to the review, herpes simplex virus is present in more than 70 percent of the population over 50 years of age, persists latently in the peripheral nervous system and is periodically reactivated in the brain. In addition, *Candida*, which is found in the mouths of half the world's population, can become treacherous and lead to infection if it enters the bloodstream.

Of *Candida*, the authors stated that "with a growing population of elderly, severe systemic fungal infections have increased dramatically in this age group during the last 30 years. Oral yeasts can be found in periodontal pockets, in root canals, on the mucosae and underneath dentures (denture stomatitis) (140-142). … Fungal molecules including proteins and polysaccharides [(1,3)-ß-glucan] were detected in peripheral blood serum, and fungal proteins and DNA were demonstrated by PCR in brain tissue of AD patients."

For more details, see the review published in the *Journal of Oral Microbiology*, 2015, 7:29143.

Teeth Samples Accurate in Predicting Age

Forensic biomedical scientists recently developed a test to predict the age of individuals on the basis of blood or teeth samples. According to the authors, age estimation from DNA methylation markers has seen an exponential growth of interest, however, the current published assays "can still be improved by lowering the number of markers in the assay and by providing more accurate models to predict chronological age."

For this study, researchers selected four age-associated genes (ASPA, PDE4C, ELOVL2 and EDARADD) and determined CpG methylation levels from 206 blood samples of both deceased and living individuals (between ages 0 and 91). In addition, 29 teeth from different individuals (between ages 19 and 70) were analyzed using the same set of markers. The authors were able to determine the age of individuals with a margin of error of 3.75 years for blood samples and 4.86 years for teeth.

"The behavior of our organs and tissues depends on which of our genes are activated. As we grow older, some genes are switched on, while others are switched off. This process is partly regulated by methylation, whereby methyl groups are added to our DNA. In specific locations, genes with high methylation levels are deactivated," said Bram Bekaert, a professor from the KU Leuven Forensic Biomedical Sciences Unit, in a news release.

For more, see the study in the journal *Epigenetics*, published online Aug. 17, 2015.

CDA JOURNAL, VOL 43, N°11

New Research Explains Origin of Enamel

In a recent issue of the journal *Nature*, researchers combine data from paleontology and genomics to discover the origin of enamel. According to the authors, enamel originated in the skin and colonized the teeth much later.

"Enamel, the hardest vertebrate tissue, covers the teeth of almost all sarcopterygians (lobe-finned bony fishes and tetrapods) as well as the scales and dermal bones of many fossil lobe-fins," the authors wrote. Enamel is the hardest substance produced by the body, composed almost entirely of the mineral apatite (calcium phosphate) deposited on a substrate of three unique enamel matrix proteins.

While humans only have teeth in the mouth, certain fish, such as sharks, also have small tooth-like scales, called "dermal denticles," on the outer surface of the body. In many fossil bony fish, and a few archaic living ones, such as the gar (*Lepisosteus*) from North America, the scales are covered with an enamel-like tissue called "ganoine."

The recent study investigated the genome of *Lepisosteus*, which was sequenced by the Broad Institute, and found that it contains genes for two of the three enamel matrix proteins: the first to be identified from a ray-finned bony fish. Furthermore, these genes are expressed in the skin, strongly suggesting that ganoine is a form of enamel.

To determine where enamel originated (mouth, skin or both at once), the researchers studied two fossil fish, *Psarolepis* from China and *Andreolepis* from Sweden. They found that in *Psarolepis*, the scales and the denticles of the face are covered with enamel, but there is no enamel on the teeth; in *Andreolepis*, only the scales carry enamel.

"*Psarolepis* and *Andreolepis* are among the earliest bony fishes, so we believe that their lack of tooth enamel is primitive and not a specialization. It seems that enamel originated in the skin, where we call it ganoine, and only colonized the teeth at a later point," explained one author, Per Ahlberg, a professor at Uppsala University.

For more, see the study in the journal *Nature*, published online Sept. 23, 2015.

Mouth Rinse Could Help Predict Recurrence of HPV-Related Oropharyngeal Cancers

Oropharyngeal cancer patients who were found to have detectable traces of human papillomavirus type 16 (HPV16) in their saliva following cancer treatment are at an increased risk for recurrence, according to a study led by researchers at the Johns Hopkins Bloomberg School of Public Health.

In a small study, 7 percent (five of 67) of oropharyngeal cancer patients who had HPV16 DNA in their oral rinse at the time of diagnosis were later found to still have traces of HPV16 DNA in their oral rinse following treatment. Of these, all developed a local recurrence of the cancer. The finding could lead to new follow-up protocols for oropharyngeal cancer patients, according to the researchers.

"It's a very small number so we have to be somewhat cautious," said Gypsyamber D'Souza, PhD, an associate professor in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health, in a news release. "The fact that all of the patients with persistent HPV16 DNA in their rinses after treatment later had recurrence meant that this may have the potential to become an effective prognostic tool."

The team of researchers tracked 124 patients who had been diagnosed with oropharyngeal cancer, collecting oral rinses from patients at the time of diagnosis and again following treatment, at nine, 12, 18 and 24 months after diagnosis. In this study, the authors report that disease recurrence was diagnosed roughly seven months after the detection of HPV16 DNA in the oral rinse. Presence of HPV16 DNA in oral rinses may allow for the detection of cancer recurrence before any other clinical signs or symptoms, which enables earlier treatment options.

For more, see the study published online in the journal *JAMA Oncology*, July 30, 2015.

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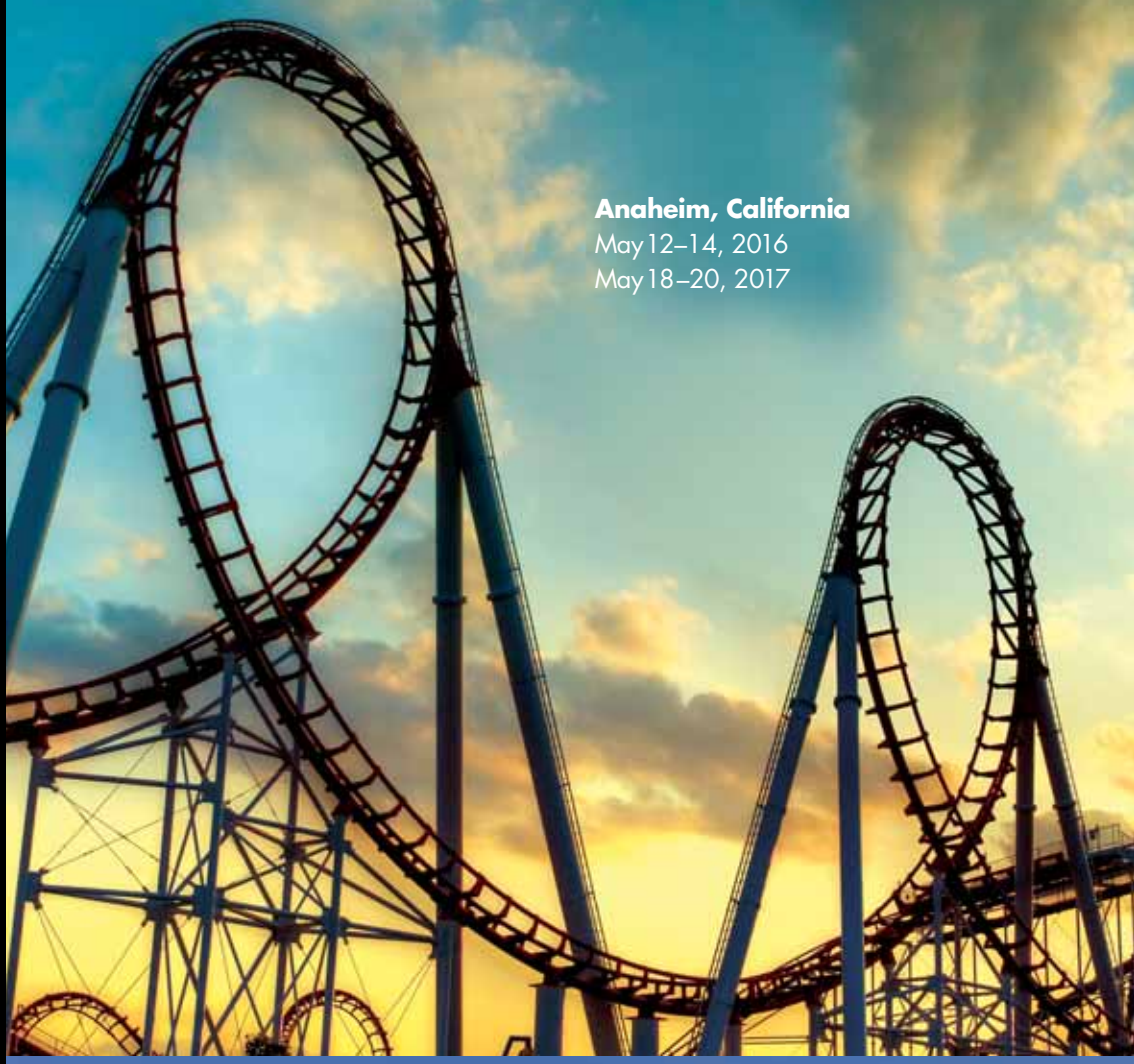

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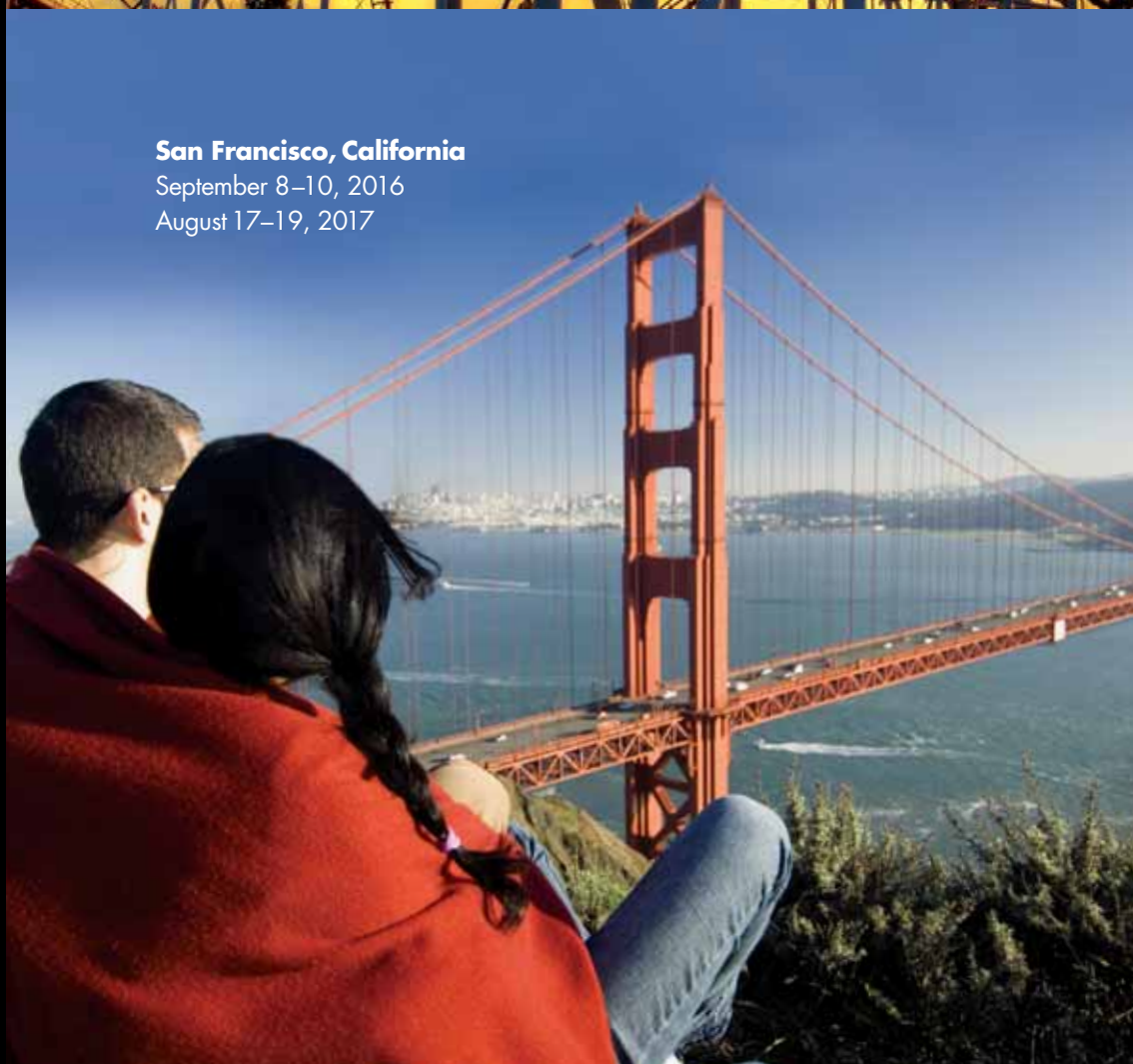

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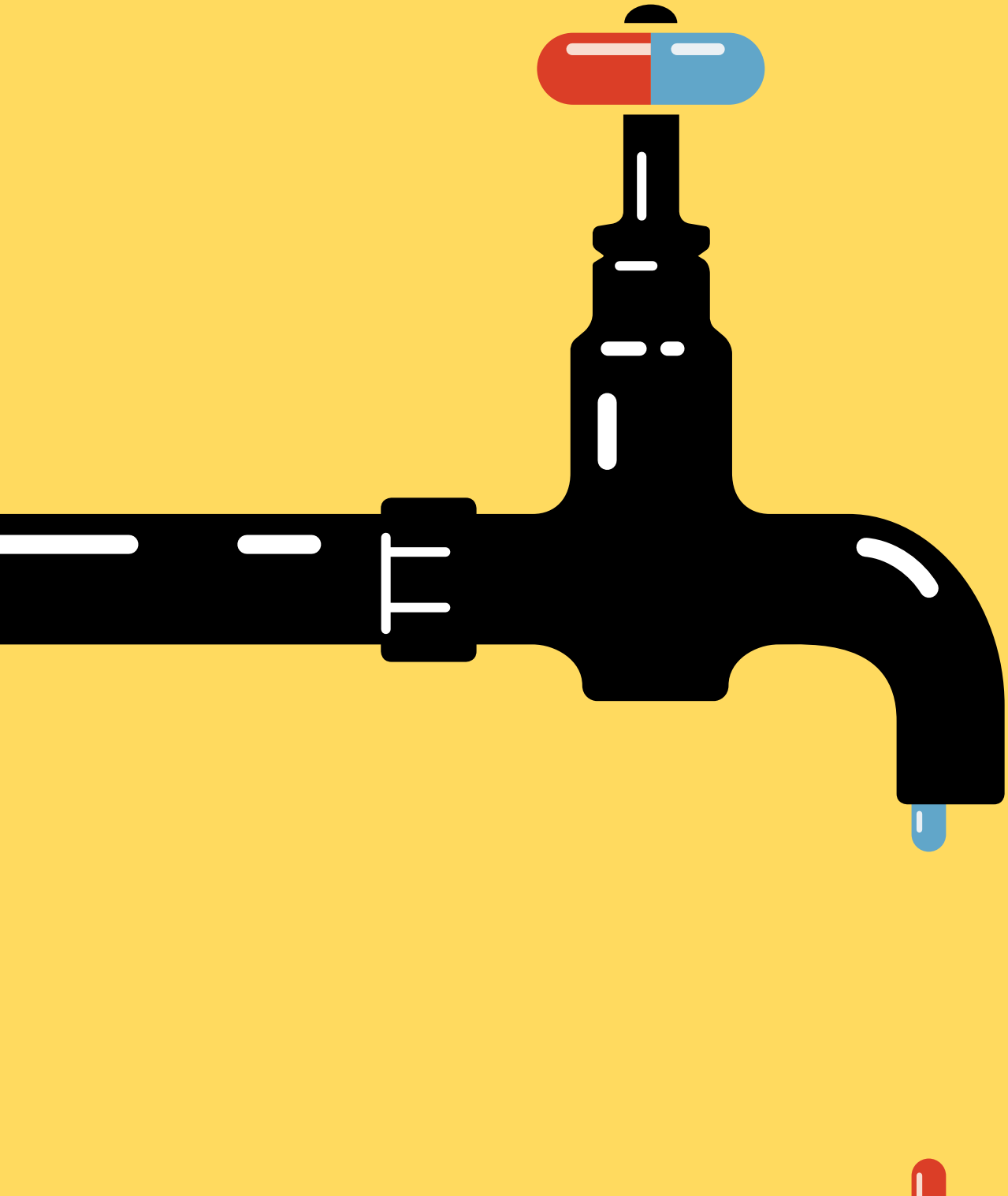

CDA JOURNAL, VOL 43, N°11

Pain Control and Prevention

Peter L. Jacobsen, PhD, DDS

GUEST EDITOR

Peter L. Jacobsen, PhD, DDS, lectures extensively on dental pharmacology as well as over-the-counter dental drugs and products. Dr. Jacobsen directed the Oral Medicine Clinic at the University of the Pacific, Arthur A. Dugoni School of Dentistry for more than 25 years. He is a diplomate of the American Board of Oral Medicine and past chairperson of the Council on Dental Therapeutics of the ADA. He is the author of *The Little Dental Drug Booklet*, a succinct handout and reference on commonly prescribed dental medications. *Conflict of Interest Disclosure: None reported.*

The three Ps of pain control are psychological, physiological and pharmacological. Those three approaches span the range of treatments we have to manage patients with pain. Actually, the first P of pain control should be for prevention — stopping the pain before it starts, and we can do that, too.

Good oral health care focuses on minimizing the risk of pain, adequately informing the patient of potential problems, preventing problems and encouraging the patient to seek treatment as soon as problems arise. Timely and appropriate treatment means less pain overall.

This edition of the *Journal* addresses pain control and its many facets. In addition, it also includes timely information relative to pain control medication regulation and abuse. Both are important considerations dentists and pharmacist are increasingly required to keep in mind.

Glenn Clark, DDS, MS provides insights and guidelines on the management of chronic pain. I think you will come to appreciate the complexity of chronic pain and the many quagmires that exist in its management. This is especially true if you're not well educated in the area of chronic pain.

Raymond A. Dionne, DDS, PhD, and Sharon M. Gordon, DDS, MPH, PhD, elucidate the stepwise approach and range of over-the-counter medications available for the responsible and effective management of acute oral pain, including preemptive pain control, preventing it before it starts. We will all come to appreciate the many over-the-counter medications that are underutilized and underappreciated, but can provide equal and sometimes more effective acute pain control than the opioids, with a lot less liability and side effects.

Philip J. Gregory, PharmD, MS, provides an interesting perspective relative to natural products and

modalities for the management of pain. Many of our patients are asking for such treatment approaches. Natural products, combined with appropriate psychological encouragement, can be very effective.

Nevertheless, pain control isn't simple; pain control gone wrong is a national problem. Actually it is an epidemic. There is an epidemic of pain medication abuse and addiction and dentistry is part of it. We are part of it mostly out of ignorance, but if we focus our attention and practice good dentistry, we can become part of the solution. Tony J. Park, PharmD, JD, and Doreen Pon, PharmD, BCOP, BCPS, both pharmacists, provide us information on the epidemic of abuse and the new laws and systems in place to address the changes necessary to get medicine and dentistry back on the track of good health care and good pain control and, at the same time, reduce the risk, temptation and opportunity for narcotic abuse.

I am convinced you will find this issue interesting. The information and paradigms you learn, you will use multiple times, every day in dental practice. Though much of it will be a refresher or a confirmation that you are already doing the right thing, I also suspect that you will be able to glean some tidbits of new information that improve your pain control skills and protect your patients and their families from the very real problem of narcotic abuse. ■

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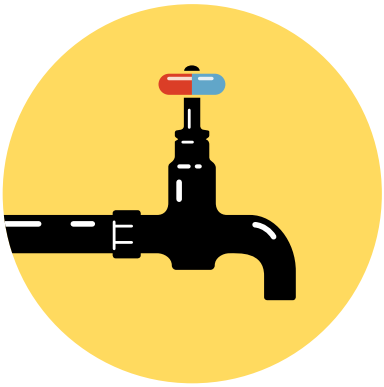

Evidence-Based Pharmacologic Approaches for Chronic Orofacial Pain

Glenn Clark, DDS, MS

ABSTRACT For neuropathic pain, the three medications to use are gabapentinoids, tricyclic antidepressants and serotonin norepinephrine reuptake inhibitors plus topical anesthetics. Beta-blockers, tricyclic antidepressants and anti-epileptic drugs are effective preventive medications for daily migraine headaches. The three FDA-approved drugs for fibromyalgia, pregabalin, duloxetine and milnacipran, are not robust. For osteoarthritis, nonsteroidal anti-inflammatories have good efficacy, and when gastritis contraindicates them, corticosteroid injections are helpful.

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This article provides an overview of medications that have reasonable evidence and can be used to help manage a variety of chronic, painful orofacial diseases. As a way of comparing these medications in this article, we have attempted to find the associated numbers needed to treat (NNT) for a single patient to achieve a 50 percent reduction in his or her symptoms. While most diseases are acute and resolve with time, there is a wide variety of chronic diseases that manifest with pain in the orofacial region that are not cured and thus clearly benefit from pharmacologic therapy. Some of the diseases this article addresses and a short description of each are presented in **TABLE 1**. The diseases listed in this table are not a complete list of all chronic conditions in the orofacial region and we do not cover cancer pain, burning mouth syndrome, trigeminal neuralgia or masticatory muscle spasm, bruxism or dystonia for example. Moreover, because this article focuses on pharmacologic therapies, this does not imply that medications are the only form or even the best form of treatment, just one that needs to be considered in an attempt to help a patient. Specifically excluded from this article because of limited time and space were platelet-rich plasma injections, hyaluronic acid injections, adipose derived stromal cell therapy, botulinum toxin for pain/spasm, marijuana and opioids for cancer and the anticonvulsant

TABLE 1

Disease	Description
Neuropathic pain/ persistent dentoalveolar pain	Neuropathic pain (NPP) is a chronic pain resulting from injury to the nervous system. The injury can be to the central nervous system (brain and spinal cord) or the peripheral nervous system (nerves outside the brain and spinal cord). Persistent dentoalveolar pain (PDAP) is when there is persistent (chronic) continuous pain symptoms located in the dentoalveolar region and cannot be explained within the context of other diseases or disorders.
Chronic daily headache/chronic migraine	Chronic daily headache (CDH) is a descriptive term that includes disorders with headaches on more days than not and affects 4 percent of the general population. Chronic migraine (CM) is one of the most common forms of the CDH and occurs with the transformation of the episodic migraine to chronic migraine.
Fibromyalgia/ myofascial pain	Fibromyalgia is a chronic disorder characterized by widespread musculoskeletal pain, fatigue and tenderness in localized areas. Myofascial pain refers to pain caused by muscular irritation. The large upper back muscles are prone to developing myofascial pain that radiates from sensitive points, called trigger points, throughout muscle tissue. Muscular irritation and upper back pain is due to muscle weakness and repetitive motions.
Osteoarthritis/ rheumatoid arthritis/ juvenile idiopathic arthritis	Osteoarthritis is a degeneration of joint cartilage and the underlying bone, most common from middle age onward. It causes pain and stiffness, especially in the hip, knee and thumb joints. Rheumatoid arthritis is a chronic progressive disease causing inflammation in the joints and resulting in painful deformity and immobility, especially in the fingers, wrists, feet and ankles. Juvenile idiopathic arthritis, also known as juvenile rheumatoid arthritis, is the most common form of arthritis in children and adolescents.

medications used for trigeminal neuralgia. Finally, while not advocating opioids for chronic orofacial pain (chronic headache, arthritis, fibromyalgia) and orofacial neuropathic pain (NPP) conditions, we do discuss what is known about opioids for these problems (TABLE 1).

Topicals, Serotonin Norepinephrine Reuptake Inhibitors, Gabapentinoids, Tricyclic Antidepressants and Opioids for Neuropathic Pain

Topical Medicines for Chronic Orofacial Pain

It has been 15 years since the first article that discussed topical orofacial pain medications was published in the *Journal of the American Dental Association*.[1] Since then, several research studies, case reports and review papers have been published.[2-6] An excellent new review of the literature on topical treatments for chronic pain suggested that this modality has some distinct advantages, such as lower side effects, fewer drug-drug interactions and improved patient tolerance.[7] This nonsystematic review made a suggestion on how to select and utilize topical agents for a patient's neuropathic pain, but this form of therapy is often not used for chronic neuropathic pain because topical pain suppressive medications have been shown to be less effective than other pharmacologic methods in rigorous research studies.[8] A 2015 review examined efficacy by performing a careful calculation of the NNT to achieve a 50 percent pain relief level for a multitude of neuropathic pain medications. By calculating the NNT, it is possible to compare medications that were not directly compared inside a randomized clinical trial. Specifically, this study reported an NNT of 10.6 for high-concentration capsaicin patches, which is quite poor. Unfortunately, this study did not determine the NNT for lidocaine patches and, based on this, these authors gave only a weak recommendation for use and proposed these topical agents could be a second-line therapy along with tramadol (a weak opioid) for peripheral neuropathic pain. The two most common topical agents used in an orofacial pain clinic include nonsteroidal anti-inflammatory medications for arthritic disease, such as ketoprofen gel and diclofenac gel, and topical anesthetics, such as benzocaine and lidocaine, for neuropathic pain and other topical agents such as capsaicin or a mixture of anesthetic and an anticonvulsant agent. These agents are usually mixed into a skin-penetrating vehicle (Lipoderm or pluronic lecithin organogel) or if used intraorally, into a methylcellulose paste (orobase) that allows transmucosal absorption of the medication. In a 2014 systematic review of the literature, the efficacy of topical medications as a treatment for neuropathic pain was examined.[9] The authors included randomized, double-blind studies where 5% topical lidocaine with placebo or another active treatment was used on chronic NPP patients (postherpetic neuralgia, trigeminal neuralgia and postsurgical or posttraumatic neuralgia). The authors included 12 studies where lidocaine was compared with a placebo or an active control. The results of this analysis found all studies had a high risk of bias and there was no clear evidence of an effect of topical lidocaine for NPP, although individual studies reviewed indicated that it was effective for relief of pain. In contrast, a 2003 study reported on the efficacy of 5% lidocaine patches in the

treatment of focal peripheral neuropathic pain syndromes using a randomized, double-blind, placebo-controlled study design.[10] This study revealed that, as an add-on therapy, the 5% lidocaine patch was clearly effective in reducing ongoing pain and allodynia. The authors calculated the NNT for lidocaine in this study to be 4.4. Unfortunately, none of the above cited studies or reviews specifically looked at the use of topical anesthetics for focal orofacial neuropathic pain and specifically for persistent dentoalveolar pain. This is an important distinction because using topical medications on more readily absorbent mucosal tissues might make a large difference in efficacy of the topicals used intraorally versus using them on skin. A 2008 case study showed that topical medications versus systemic medications can have a substantial effect and thus might be considered as a first-line therapy for some chronic neuropathic oral pain patients.[11] While the study provides only a low level of evidence because it is a retrospective chart review of 39 patients treated for orofacial neuropathic pain, it showed that the pain was significantly reduced, even in those who had received only topical medications.

Nocebo-Responsive Patients

The next logical question is: Who would benefit from a topical medication only approach? Many patients would prefer a topical medication if it works well for its safety and convenience, but this question also raises the issue of the nocebo-responsive patient. Placebo analgesia makes individuals experience relief of their pain simply by virtue of the anticipation of a benefit. Placebos mimic the action of active treatments and promote the endogenous release of opioids. In contrast, the nocebo response is when a verbal suggestion of negative outcomes results in the amplification of pain. Anxiety is thought to positively influence the strength of nocebo response in those predisposed to it.[12] Often, patients cannot take systemic medications because of side effects, and in the nocebo-responsive patient, these side effects occur in very low doses. A systematic review recently examined to what degree adverse medication reactions can be blamed on the nocebo response versus the medication itself.[13] Specifically, this study examined randomized controlled trials with a parallel design of any drug therapy compared with pharmacological placebo in patients with fibromyalgia and diabetic peripheral neuropathy. The authors concluded that nocebo effects substantially accounted for adverse events in the reviewed drug trials. Identifying nocebo-responsive patients is actually easy, as they will readily tell you, if asked, that they get all of the adverse effects of medications and firmly wish to avoid systemic medications. It is a curiosity that this same patient will often take nutraceuticals and use topical medications.

Gabapentinoids and Serotonin Norepinephrine Reuptake Inhibitors Used to Treat Chronic Continuous NPP

The systematic review and meta-analysis by Finnerup and colleagues in 2015 on pharmacologic treatments of neuropathic pain examined various per os (PO) medications in addition to the topical medications we described earlier.[8] Specifically, this review calculated the NNT to achieve 50 percent pain relief level in one patient for several types of medications. The study found that for serotonin norepinephrine reuptake inhibitors (SNRIs), duloxetine and venlafaxine, the NNT was 6.4. For the gabapentinoids, pregabalin and gabapentin,the NNT was found to be 7.2 to 7.7. For tricyclic antidepressants (TCAs), the NNT was 3.6, which is clearly lower, but the authors of this review did not consider TCAs a first-line therapy. Another study that examined pregabalin and gabapentin in matched patients with peripheral neuropathic pain was reported in 2010.[14] Specifically, this study performed a cost-consequences analysis in a nested case-control design in patients with refractory chronic peripheral neuropathic pain. The study examined data from two 12-week-long, observational, prospective studies in primary medical care involving 44 patients treated with gabapentin (cases) and 88 patients treated with pregabalin (controls) who were matched for age and sex. They concluded that the pregabalin appeared to be associated with greater reduction in mean weekly intensity of pain, but there were no significant differences in cost compared to gabapentin. As a result of these data, the authors suggested that there was strong evidence for these three medication classes and they should be considered first-line treatments in neuropathic pain.

Tricyclic Antidepressants for Neuropathic Pain

In contrast to the review recommendations by Finnerup and colleagues,[8] who judged TCAs more or less equivalent to gabapentinoids and SNRI class medications, a different systematic review looked at nortriptyline, a TCA class medication, as a treatment for neuropathic pain. This review found nortriptyline to be clearly better than placebo but the authors could not recommend it as a highly efficacious medication.[15] This study included only randomized, double-blind studies of at least two weeks' duration comparing nortriptyline with placebo or another active treatment for chronic neuropathic pain. The authors included six studies treating 310 participants (mean or median age 49 to 64 years) with various neuropathic pain

TABLE 2

Evidence-Based Neuropathic Pain Treatments	Numbers Needed to Treat
Gabapentinoids	7.2 to 7.7
Tricyclic antidepressants	3.6
Serotonin norepinephrine reuptake inhibitors	6.4
Topical anesthetics	4.4
Opioids (strong and weak)	4.3

conditions. Based on their analysis, the authors found little evidence to support the use of nortriptyline to treat the neuropathic pain conditions and suggested it was not a first-line treatment. These authors suggested that other medicines, such as duloxetine and pregabalin, had stronger evidence than nortriptyline. Unfortunately, none of the articles cited above on PO medications for neuropathic pain have specifically evaluated trigeminal neuropathic pains, such as persistent dentoalveolar pain, and these medications are essentially used off label when treating this or other trigeminal manifestations of neuropathic pain.

Opioids for Neuropathic Pain in the Orofacial Region

There is very little quality scientific literature that examines the use of opioids for neuropathic orofacial pain disorders, but there is adequate literature on neuropathic pain in other regions of the body. For example, a 2014 systematic review examined the efficacy of oxycodone for neuropathic pain in adults.[16] The review identified three qualified studies with 254 participants who had either painful diabetic neuropathy or postherpetic neuralgia. Controlled release oxycodone (oxycodone CR) was dispensed in all three studies, with doses titrated up to a maximum of between 60 and 120 mg daily compared to a placebo medication. The authors concluded that all studies had one or more sources of potential major bias and while greater pain intensity reduction and better patient satisfaction was seen with oxycodone, the evidence was considered third-tier evidence. At least one adverse event was experienced by 86 percent of participants taking oxycodone CR compared to 63 percent taking placebo. The authors reported that the NNT for an additional harmful effect (number needed to harm, NNH) was 4.3. They concluded that no convincing, unbiased evidence suggests that oxycodone (as oxycodone CR) is of value in treating people with painful diabetic neuropathy or postherpetic neuralgia. Another study examined the use of morphine in combination with nortriptyline for neuropathic pain.[17] This study was a randomized, double-blind, crossover trial that included patients with neuropathic pain. Patients were randomized to one of three groups to receive either oral nortriptyline, morphine or their combination. During each of three six-week periods, doses were titrated toward maximal tolerated dose (MTD). Fifty-two patients were enrolled and 39 completed at least two of the three treatment periods. The results showed that the combination of both medications was better than each one individually. However, combination treatment also resulted in moderate-to-severe constipation and dry mouth. The authors concluded that there was a superior efficacy of a nortriptyline-morphine combination over either monotherapy, with constipation, dry mouth and somnolence as the most frequent adverse effects. Finally, the systematic review and meta-analysis by Finnerup and colleagues on neuropathic pain medications did comment on opioids.[8] Specifically, they reviewed the evidence on efficacy and side effects of opioids when used for NPP and concluded that while the NNTs were moderately low for both strong opioids and tramadol (a weaker opioid), they offered only a weak recommendation for use of both tramadol (second-line therapy) and strong opioids (third-line therapy). It should be noted that in 2014 the FDA issued a ruling that tramadol would be an FDA Schedule IV drug and described it as a centrally acting opioid analgesic.[18] Prior to 2014, tramadol was not an FDA scheduled drug (**TABLE 2**).

Preventive Agents and Rescue Medications for Chronic Daily Headaches

Naproxen and Episodic Migraine

For many patients with episodic migraine, the triptan-class medications (sumatriptan, zolmitriptan, rizatriptan, naratriptan, eletriptan, almotriptan and frovatriptan) are a great solution to aborting their disabling migraine headaches. Unfortunately, this class of medications has an FDA prescription limitation of eight tablets a month maximum, which most insurance companies follow. If the patient's headaches are infrequent (fewer than eight times per month), the patient will have an adequate supply of medication. Another approach is needed for those cases where the headaches are more than eight times per month. In 2014, a study compared doses of sumatriptan plus naproxen in combination versus naproxen alone for the treatment of episodic migraine.[19] The study described a two-center, double-blind, randomized, parallel-group study. Subjects were equally randomized to one of two groups to receive daily treatment. Group one received 85 mg sumatriptan plus 500 mg naproxen sodium and group two received 500 mg of naproxen sodium only for one month followed by two months of the same medications used for episodic acute treatment. The results of the study

showed no significant group difference with regard to the number of migraine headache days. However, more subjects in the naproxen only group prematurely withdrew from the study more often because of lack of efficacy. The authors concluded that there were subsets of patients who can use naproxen sodium alone and have a significant reduction in migraine headache days. Until recently, conventional wisdom suggested that any patient with possible medication overuse headaches needed to stop all analgesics, including NSAIDs. This idea was examined in a 2012 study that looked at the evidence basis of using NSAIDs and other complementary treatments for episodic migraine prevention in adults.[20] Specifically, this report conducted a systematic review of published studies from June 1999 to May 2009 that focused on nontraditional therapies, NSAIDs and other complementary therapies. Based on the studies reviewed, the authors suggested that *Petasites* (butterbur) was effective for migraine prevention and that several NSAIDs were helpful as well, including ibuprofen, ketoprofen, naproxen and naproxen sodium.

Effectiveness of Preventive Medications for Chronic Migraine

When abortive medications (triptans and analgesics) are not adequate, most clinicians consider adding a preventive medication to suppress the headache. There are several types of preventive medications used for chronic migraine, including beta blockers, TCAs and anticonvulsants, which are also known as anti-epileptic drugs (AEDs). Of these, the one that is not FDA approved for migraine prophylaxis is amitriptyline. In a 2001 meta-analysis type study, all types of antidepressants and their efficacy on chronic migraine were examined.[21] This study found 19 individual studies that included tricyclic antidepressant class drugs and 12 of them used amitriptyline. The authors concluded that patients treated with antidepressants were twice as likely to improve as those treated with placebo, and that the overall NNT was 3.2 for TCAs. A 2014 study examined the efficacy and mechanism of anticonvulsant drugs in migraine.[22] Efficacy has been demonstrated in randomized, placebo-controlled trials for topiramate and valproic acid, including divalproex sodium. In the case of topiramate, efficacy has been demonstrated for chronic migraine and even medication overuse headache, questioning the established concept of medication withdrawal. Unfortunately, anticonvulsants often produce more side effects and sometimes adverse events that require treatment cessation. In 2013, a systematic review was published that examined valproate (valproic acid or sodium valproate or a combination of the two) for the prophylaxis of episodic migraine.[23] This review assessed the efficacy and tolerability of these medications on prevention of migraine attacks in adult patients with episodic migraine. The authors included only prospective, controlled trials of valproate taken regularly to prevent the occurrence of migraine attacks, to improve migraine-related quality of life or both. Ten papers were included in the analysis and of these, two trials showed that sodium valproate reduced headache frequency by approximately four headaches per 28 days as compared to placebo. Another four trials showed that divalproex sodium more than doubled the proportion of responders relative to placebo and one study of sodium valproate (34 participants) versus placebo supported the latter findings. There was no significant difference in the proportion of responders divalproex sodium versus propranolol (one trial). Pooled analysis of data from two clinical trials demonstrated a slight but significant advantage for topiramate 50 mg over valproate 400 mg. The authors concluded that valproate is effective in reducing headache frequency, is reasonably well-tolerated in adult patients with episodic migraine and had an NNT between 3.0 and 4.0. With regard to propranolol, a 2003 systematic review examined 20 studies that evaluated medications for migraine prevention in adolescents and children younger than age 18.[24] Unfortunately only one study examined propranolol and allowed the NNT to be calculated. This review claimed that propranolol was quite effective for headache prevention and reported an NNT of 1.5 to produce a two-thirds reduction in headache frequency. A different systematic review published in 2013 examined the efficacy of topiramate for the prophylaxis of episodic migraine in adults.[25] Twenty papers describing 17 unique trials met the inclusion criteria for this review. Analysis of data from nine trials showed that topiramate reduced headache frequency by about 1.2 attacks per 28 days as compared to placebo. Meta-analysis of those studies where different doses were used showed that 200 mg is no more effective than 100 mg in reducing headache frequency and it had an NNT of 4.0. When topiramate was compared to

Analysis of data from nine trials showed that topiramate reduced headache frequency by about 1.2 attacks per 28 days as compared to placebo.

TABLE 3

Evidence-Based Chronic Daily Headache Treatments	Numbers Needed to Treat
Long-acting nonsteroidal anti-inflammatory drugs (naproxen)	Not available
Beta-blocker (propranolol)*	1.5
Tricyclic antidepressants (amitriptyline)	3.2
Anti-epileptic drugs (valproate)	3.0 to 4.0
Anti-epileptic drugs (topiramate)	4.0
N-methyl-D-aspartate blocker (memantine)	Not available
Opioids	Not available

*Data based on propranolol use in children and adolescents only.

either a TCA class drug (amitriptyline) or a beta blocker (propranolol), no significant difference was found in efficacy. There was a slight significant advantage of topiramate over valproate noted in two studies on reducing headache frequency. It is interesting to note that behavioral therapy (relaxation) improved migraine-specific quality of life significantly more than topiramate. Adverse events were not uncommon when using topiramate but they were usually mild and of a nonserious nature. The authors concluded that topiramate in a 100 mg/day dosage is effective in reducing headache frequency and reasonably well-tolerated in adult patients with episodic migraine.

NMDA Receptor Blocking Agents for Chronic Migraines

There are many chronic migraine sufferers who are resistant to both the usual and customary abortive and preventive class medications. A 2014 study examined if memantine was a logical and appropriate medication for the treatment of primary migraine and other primary headaches.[26] Memantine is a known N-methyl-D-aspartate receptor blocking agent (NMDA), and while it has primarily been used to reduce the progressive loss of memory in Alzheimer's, it has some "off-label" evidence that it can suppress migraine pain via its NMDA-suppressive effects. The authors of this study included less rigorous studies (retrospective case reports) and two prospective clinical trials. From these data they concluded that memantine (10-20 mg daily) may be a useful treatment option for the prevention of primary headache disorders used as either a monotherapy or adjunctive therapy for the refractory chronic migraine patients.

Do Chronic Migraine Patients Take Their Medications as Prescribed?

When suggesting that a patient take a medication daily, the biggest barrier to efficacy is often medication adherence. A 2014 study described how well chronic migraine patients adhered to their prescribed medication protocol.[27] The study looked at prescriptions from Truven MarketScan Databases, a U.S. claim database, and focused on patients older than18 years of age who were diagnosed with chronic migraine and had been prescribed one of the commonly used migraine preventive agents (antidepressants, beta blockers or anticonvulsants). Medication usage was calculated and a cutoff of ≥ 80 percent was used to classify adherence. The authors found 8,688 patients met the inclusion/exclusion criteria and adherence ranged between 26 percent and 29 percent at six months and between 17 percent and 20 percent at 12 months. They found that adherence was similar except for amitriptyline, nortriptyline, gabapentin and divalproex, which had significantly lower odds of adherence when compared to topiramate.

Opioids for Chronic Daily Headache/ Chronic Migraine

Almost universally, headache specialists do not recommend opioid therapy for management of severe headache, except as a rescue medication when the headache is deemed an emergency. In 2015, there was a report on the use of various medications for the management of headache emergencies.[28] The authors of this report, which was based on 9,362 emergency room visits for headache, showed that 18 percent of the time a prescription for either an opioid or barbiturate was given. For most patients, headaches are not emergencies and in 2010, a task force of the European Federation of Neurologic Societies stated that simple analgesics and nonsteroidal anti-inflammatory drugs are the recommended treatment for episodic tension-type headaches (TTH) and that triptans, muscle relaxants and opioids should not be used[29] (**TABLE 3**).

Chronic Myofascial Pain/Fibromyalgia Medications

Efficacy of Medications to Treat Fibromyalgia

There are several off-label medications that are used to help patients who have widespread myofascial pain and/or fibromyalgia. The FDA approved pregabalin for the treatment of fibromyalgia in 2007 and within two years, two SNRIs, duloxetine hydrochloride and milnacipran hydrochloride, were also approved. Not approved but still commonly used in fibromyalgia are the TCA class drugs, amitriptyline and nortriptyline. A 2015 review examined the use of various medications used for fibromyalgia.[30] The authors of this study

examined U.S. commercial insurance claim data from 2007 to 2009 and performed comparative effectiveness of amitriptyline, duloxetine, gabapentin and pregabalin on health care utilization in patients with fibromyalgia. With this data, the study identified fibromyalgia patients who were prescribed amitriptyline, duloxetine and gabapentin. These data were compared with fibromyalgia patients who were prescribed pregabalin. The number of outpatient visits, prescriptions and hospitalization decreased slightly after initiating one of the study drugs, but the number of emergency department visits increased after treatment initiation. Duloxetine was associated with a small but significant decrease in outpatient visits, number of other prescribed drugs, hospitalizations and emergency department visits compared to pregabalin users. Little differences in health care utilization rates were noted among amitriptyline and gabapentin users compared to pregabalin. This study suggested that fibromyalgia patients still had high health care utilization before and after initiation of amitriptyline, duloxetine, gabapentin or pregabalin, but that duloxetine users had less health care utilization than pregabalin users. A 2012 study examined the role of TCAs and SNRIs in the treatment of fibromyalgia.[31] Only studies with a randomized controlled trial design that tested the efficacy of various antidepressants were included. Thirty-five studies, which included 3,528 patients, were included in the meta-analysis. The authors reported that 42 percent of these patients treated with SNRIs versus 32 percent of patients treated with placebo reported a 30 percent pain reduction. They calculated the NNT of this medication class as 10. For tricyclic medications, the authors reported that 48.3 percent of patients treated with TCAs versus 27.8 percent of patients treated with placebo reported a 30 percent pain reduction. They calculated the NNT of this medication class as 4.9. This study concluded that amitriptyline and the SNRIs duloxetine and milnacipran are first-line options for the treatment of fibromyalgia patients. However, they also conclude that a moderate number of patients drop out of therapy because of intolerable adverse effects or they experience only a small relief of symptoms, which does not outweigh the adverse effects. Finally, a 2010 responder analysis study design examined the efficacy of pregabalin used for fibromyalgia.[32] This analysis obtained individual patient data from four randomized double-blind trials (2,757 patients) of pregabalin in fibromyalgia lasting eight to 14 weeks. From these data an improvement response was calculated as well as the NNT for pregabalin 300 mg, 450 mg and 600 mg daily compared with placebo. The derived data showed that the maximum response occurred at four to six weeks and was unchanged after this. The NNTs for a greater/equal to 50 percent improvement in pain intensity after 12 weeks was 22 for pregabalin 300 mg, 16 for pregabalin 450 mg and 13 for pregabalin 600 mg daily. The authors concluded that pregabalin helped with pain reduction compared to placebo in fibromyalgia and to a lesser degree with sleep disturbance. Unfortunately, the NNTs were quite high.

Effective Dose and Cost-Benefit of Pregabalin for Fibromyalgia

With all medications that suppress nerve activity there are issues with side effects and even adverse events which must be balanced against the therapeutic benefit of the medication. This is true for the TCAs, gabapentinoids and the SNRIs medications commonly used for fibromyalgia. If the patient takes too little of the medication because of side effects, it will not be effective and its cost will not be justified. Since pregabalin's approval for fibromyalgia in 2007, multiple studies have examined its efficacy. In 2013, a systematic review of the literature examined what an effective daily dose would be as well as the cost-effectiveness of pregabalin in the treatment of fibromyalgia.[33] This study identified four reports that allowed cost of therapy to be calculated and all four were randomized controlled trials with placebo controls. The study concluded that pregabalin (150 mg/day) did not have significant efficacy in comparison to placebo, but generic pregabalin in the treatment doses of 450 mg/day or 600 mg/day is highly cost-effective.

Behavioral Methods Versus Medication in Fibromyalgia Treatment

Because some fibromyalgia patients will not tolerate medications with moderate side effects, in 2014 the role of cognitive behavioral therapy (CBT) versus medications (pregabalin, duloxetine and milnacipran) was examined in a review.[34] This study looked at the relative economic effect (cost benefit) of patients in a randomized study comparing CBT (n = 57), medications (n = 56) or usual medical care (n = 55). The costs of health care use were estimated from patient self-reports, and the authors reported that total costs per patient in the CBT group were significantly lower than those in patients receiving either medications or usual medical care. The authors also concluded that the CBT group was best in all of the comparisons performed assessing quality of life and pain levels. This finding was also supported by a 2014 systematic review-style study that examined the treatment efficacy of nonpharmacologic versus pharmacologic treatment for fibromyalgia.[35] Outcomes examined in the review included pain, sleep disturbance, fatigue, affective

TABLE 4

Evidence-Based Fibromyalgia/Myofascial Pain Treatments	Numbers Needed to Treat
Gabapentinoids (pregabalin)	13
Tricyclic antidepressants (amitriptyline)	4.9
Serotonin norepinephrine reuptake inhibitors (duloxetine)	10.0
Cognitive behavior therapy	Not available
Opioid therapy	Not available

symptoms (depression/anxiety), functional deficit and cognitive impairment. The authors included 21 pharmacologic studies and found that only amitriptyline demonstrated a significant effect on as many as three core fibromyalgia symptoms, but it exhibited many adverse effects including tachyphylaxis. There were 64 studies that examined nonpharmacologic approaches to fibromyalgia and they were generally of poorer quality. Nevertheless, significant positive effects were shown on several symptom domains. These therapies included repetitive transcranial magnetic stimulation (rTMS), balneotherapy exercise, cognitive behavior therapy and massage. The authors speculated that few of the medications commonly used for fibromyalgia will demonstrate significant relief across multiple fibromyalgia symptom domains and additional research combining medications with nonpharmacologic treatment methods are now needed.

Opioids for Fibromyalgia

Like headaches, most rheumatologists do not recommend strong opioid therapy for the management of fibromyalgia, although there is some evidence that a weak opioid such as tramadol has a role to play. A survey was conducted in 2015 on the use of opioids in fibromyalgia patients after hysterectomy surgery.[36] In this study researchers identified and studied 208 adult patients undergoing hysterectomy. The pre- and postsurgery data collected included a fibromyalgia survey, pain severity survey and miscellaneous psychological function questionnaires as well as preoperative opioid use. The authors found that patients with higher preoperative fibromyalgia survey scores were significantly more likely to exhibit increased postoperative opioid consumption. The speculation is that with higher fibromyalgia, the release of endogenous opioids may have altered the patient tolerance to exogenous opioids. In 2015, a study examined the value of long-term opioids for management of fibromyalgia.[37] Specifically, this study was a 12-month observational study that included 1,700 adult patients with fibromyalgia. Several questionnaires were collected on these patients to capture information on their medication usage. The patients were then divided into three groups: those taking opioids (concurrent use of tramadol was permitted), those taking tramadol (but no opioids) and those not taking opioids or tramadol. The patients' pain levels were assessed periodically using the Brief Pain Inventory, Fibromyalgia Impact Questionnaire, Patient Health Questionnaire, Insomnia Severity Index, Sheehan Disability Scale and the 7-item Generalized Anxiety Disorder Scale. The results of the study showed that both the nonopioid cohort and the tramadol-only cohort demonstrated significantly greater reductions in multiple pain and disability measures. The authors concluded that those in the opioid cohort showed less improvement in pain-related interference with daily living, functioning, depression and insomnia. They concluded that there was little support for the long-term use of opioid medications in patients with fibromyalgia. Finally, in 2014 the British Pain Society published a guidelines paper on the treatment of fibromyalgia.[38] This paper described in detail the potential pitfalls in the use of long-term opioids and provided the rationale as to why these medications are not recommended for fibromyalgia (**TABLE 4**).

Anti-inflammatory, Anticytokine and Opioid Medications for Arthritis

NSAIDs for Temporomandibular Osteoarthritis

A 2012 systematic review of randomized controlled trials examined which interventions worked best for the management of temporomandibular joint osteoarthritis.[39] The review focused on studies of adults older than age 18 and compared any form of nonsurgical or surgical therapy for temporomandibular osteoarthritis (TMJ OA). The review included three articles that qualified and, unfortunately, pooling of data for a meta-analysis was not possible. The findings derived from these three studies showed that diclofenac sodium given PO as compared with occlusal splints were equivalent in efficacy. Moreover, using a glucosamine supplement appeared to be just as effective as ibuprofen for the management of TMJ OA. This review suggests that clinicians currently have three methods of helping their TMJ arthritis patients, including NSAIDs, occlusal splints and glucosamine supplementation. Unfortunately, with only three studies that qualified for inclusion, it was not possible to compare and contrast the various NSAIDs available to select from when treating arthritis. A comparative review on the relative efficacy of NSAIDS was published in 2007 that analyzed data from the Oxford pain

group.[40] This group constructed a table for comparing analgesics commonly used for acute pain by calculating the NNT, which is the number of patients who need to receive the active drug for one to achieve at least 50 percent relief of pain compared with placebo over a four- to six-hour treatment period. The Oxford pain table shows that all NSAIDs have an NNT of 1.6 to 3.0 and in this table it is evident that NSAIDs are clearly more efficacious than acetaminophen for osteoarthritis. In agreement with this observation is a meta-analysis on the relative efficacy of NSAIDs versus acetaminophen in reducing osteoarthritis pain.[41] Of course, for the gastritis-susceptible patient, acetaminophen remains a good choice for relieving arthritis pain.

Temporomandibular Joint Corticosteroid Injections

It is becoming increasingly clear that temporomandibular joint (TMJ) injections with local anesthetic and corticosteroid can be an effective first-line modality for patients with limited mouth opening and for painful arthritis. In 2011, a case series based on 17 consecutive patients was published on the effectiveness of TMJ injections in patients with disc displacement without reduction (DDWOR).[42] The authors claimed that active mouth opening before injection ranged between 15 and 40 mm (average 29 mm) and it increased by 10 mm after injection. The authors concluded that TMJ injection with corticosteroid (20 mg of triamcinolone) and 1 cc of 2% lidocaine was recommended as an alternative first-line management modality for DDWOR. In 2012, another study examined the role of intraarticular (IA) corticosteroids for the TMJ arthritis.[43] The subjects in the study were 63 children (68 percent female) who were diagnosed with juvenile idiopathic arthritis (JIA) who received 5 to 10 mg triamcinolone hexacetonide as an intraarticular injection. Primary outcomes assessed in all subjects were the safety of the procedure and efficacy as determined by the change in maximal incisal opening (MIO). The authors reported that only one patient developed the steroid complication of hypopigmentation, and none developed degeneration or ankyloses and their maximum interincisal opening was increased from 40.8 ± 0.93 to 43.5 ± 0.90 mm. In support of these findings is a systematic review of the literature that examined intraarticular injections of corticosteroid for the treatment of knee osteoarthritis.[44] This review included 28 randomized controlled trials (single or double blind) and among other findings, compared IA corticosteroid against placebo and against other IA corticosteroids. The overall consistent finding of these studies was that IA corticosteroid was more effective than IA placebo for pain reduction. The authors showed that at one week postinjection this medication had an NNT of 3 to 4. This effect was short-lived, however, because at four to 24 weeks postinjection the authors found that the effect on pain and function was not of statistical or clinical importance. Comparisons of IA corticosteroids showed triamcinolone hexacetonide was superior to betamethasone for a number of patients reporting pain reduction up to four weeks postinjection. Comparisons between IA corticosteroid and joint lavage showed no differences in any of the efficacy or safety outcome measures.

Primary outcomes assessed in all subjects were the safety of the procedure and efficacy as determined by the change in maximal incisal opening (MIO).

Anticytokine Therapy for Rheumatoid Arthritis

A 2013 study described the issue of immune modulators and osteoarthritis.[45] The process of degrading the cartilage surface involves both wear and tear with resulting inflammation as well as the immune system. Research shows that T cells, B cells and macrophages all invade the degenerative joint and release cytokines, prostaglandin E2, metalloproteinases and chemokines as well as activate the complement system.[46] Of course, in rheumatoid arthritis (RA), which is an acknowledged autoimmune disease, anticytokine therapies have a clear role, but whether these medications should be used in osteoarthritis is not clear.[47] The cytokines that promote inflammation are specifically targeted by medications that cause neutralization of tumor necrosis factor-alpha (TNFα). In 2015 a study examined the role of antitumor necrosis factor (antiTNF) therapy for RA.[48] The first "biologic" class drug for RA, was a monoclonal antibody, infliximab, to human TNF. Since then multiple other biologic class drugs have been developed, although their use on patients with temporomandibular arthritis is largely restricted to patients with proven RA or JIA. In 2013, a study examined how effective the biologic class of immune modulators was in JIA patients.[49] This case series study examined both the less specific disease modifying arthritic drugs (DMARDs) and the more specific biologic class of immune modulators. The study included 154 cases in a rheumatology clinic and the

TABLE 5

Evidence-Based Osteoarthritis or RA/JIA Treatment	Numbers Needed to Treat
Nonsteroidal anti-inflammatory drugs	1.6 to 3.0
Corticosteroid injections	3.0 to 4.0
Biologics*	4.0
Opioids	Not available

*For rheumatoid arthritis.

eligible patients ranged in age from 16 to 24 years of age with average disease duration of eight years. The study reported that 29 percent of the patients were still on biologic therapies and had been for several years. Mild disease activity in the temporomandibular joint was detected in only 14 percent of these patients, suggesting this was an effective therapy that should be considered for use in the JIA population. A 2007 study examined the number needed to treat to a 50 percent response rate according to criteria put forth by the American College of Rheumatology for adalimumab, etanercept and infliximab when used on patients with RA.[50] There were three randomized controlled trials, one for each of the drugs included in the review. The calculated NNTs varied slightly depending on the method used but after adjustment the NNTs were adalimumab 4.0, etanercept 4.0 and infliximab in a double dosage 4.0. The authors concluded that these three anti-TNF therapies had equal efficacy for the treatment of RA.

Opioids for Arthritis

A 2015 systematic review examined the role that opioids might play in the management of osteoarthritis pain.[51] This review included 20 randomized controlled trials that examined a variety of strong (oxycodone, buprenorphine, hydromorphone, morphine, fentanyl and oxymorphone) and weak opioids (tramadol, tapentadol and codeine). The authors found that overall, opioids were superior to placebo in reducing pain intensity in most studies but were not superior to placebo in achieving a 50 percent pain reduction in two studies. Patients with opioids dropped out more frequently than those with placebo but there was no significant difference between opioids and placebo in the frequency of serious adverse events or deaths. The authors concluded that opioids were superior to placebo in terms of efficacy and inferior in terms of tolerability. They suggested that short-term opioid therapy may be considered in selected chronic OA pain patients but that it is not a first-line treatment option for chronic OA pain. An earlier systematic review from 2011 examined the value of opioid therapy for rheumatoid arthritis pain.[52] This review included 11 studies (672 participants) that examined the efficacy of single doses of various opioid and nonopioid analgesics. The authors reported that there were no differences between analgesic drug (opioid versus nonopioid) efficacy in these studies. One strong opioid investigated was controlled-release morphine sulphate in a single study with 20 participants. Six studies compared an opioid to placebo and were found superior to placebo but also engendered more adverse events (most commonly nausea, vomiting, dizziness and constipation). Interestingly, one study reviewed compared an opioid (codeine with paracetamol) to an NSAID (diclofenac) and found no difference in efficacy or safety between interventions. The authors thus concluded that there is limited evidence that weak oral opioids may be effective analgesics for some patients with RA, but adverse effects are common and may offset the benefits of this class of medications (**TABLE 5**).

Summary

Neuropathic Pain

When all of the above studies are taken into consideration, it appears that clinicians have at least three types of systemic medications, gabapentinoids, TCAs and SNRIs, to use as well as topical anesthetics to help patients manage their chronic continuous neuropathic pain. Unfortunately, the NNTs for all three of the systemic medications cannot be judged a robust treatment because they range from 3.6 to 7.7. If the NNT were 2.0 or below, this would be considered robust or very good. Nevertheless, it is important to have a three-medication option because sometimes the side effects of the above medications limit their usefulness. For some patients, opioids can be used infrequently for breakthrough pain. For those who do not want to take systemic pain suppressive medications for their pain, they may get adequate relief with topical anesthetics applied directly to the neuropathic pain site. For those who start with topical and do not get full or adequate relief, they can use one or more of the systemic medications in addition to topical anesthetics. What are needed now are NNT calculations for combinations of medications such as gabapentinoids and TCAs or gabapentinoids and topical anesthetic medications. Moreover, these studies need to be performed on patients who have a localized chronic continuous trigeminal nerve neuropathic pain disorder.

Chronic Daily Headache

For patients who have moderate- to very-frequent daily headaches, preventive medications are necessary and helpful. Clinicians have at least three types of systemic PO medications (beta-blockers, TCAs and AEDs) to use as well as an NMDA blocking agent to help patients

manage their chronic, continuous daily headaches and frequent migraines. The NNTs for these medications are moderately low (3.0 to 4.0) but are not judged as robust treatments. For the patient who does not want to take prescription medications, the evidence reviewed suggests that *Petasites* (butterbur) would be a first-line therapy along with 500 mg of naproxen sodium. Opioids are, and continue to be, used (almost 20 percent of the time) in the emergency room when patients with severe headache pain event seek emergency help, but in general, most experts feel opioids are not a logical treatment choice for either episodic or continuous headaches.

Fibromyalgia and Widespread Myofascial Pain

The data on pregabalin, duloxetine and milnacipran, the three medications approved by the FDA for fibromyalgia, suggest that they work better than placebo but are not robust in their efficacy and in fact are best judged as quite poor treatments (NNT > 10). Fibromyalgia and widespread myofascial pain treatment will continue to involve combining medications with nonpharmacologic treatment methods with the latter being the preferred method of treatment. Lower-strength opioid therapy (e.g., tramadol) is utilized with reasonable efficacy to help the most severe fibromyalgia-disabled patient.

Osteoarthritis, Rheumatoid Arthritis and Juvenile Idiopathic Arthritis

The available data on NSAIDs shows they are reasonably efficacious for osteoarthritis. The NNTs for NSAIDs, corticosteroid injections and the biologics range from 1.6 to 4.0 and therefore are judged as very good to fair. Acetaminophen remains a good choice for relieving arthritis pain for the gastritis-susceptible patient. Intraarticular TMJ injection with corticosteroid (20 mg of triamcinolone) and 1 cc of 2% lidocaine is an alternative first-line management modality for both disk displacement without reduction and for most types of acute TMJ arthritis. Finally, for the symptomatic rheumatoid arthritis and juvenile idiopathic arthritis patient, biologic therapies (antiTNF-alpha) have been shown to diminish RA- and JIA-related disease activity in the temporomandibular joint. Whether biologics should ever be used in adolescents or adults with severe osteoarthritis disease of the TMJ is unclear. Finally, lower strength opioid therapy (e.g., tramadol) is utilized with reasonable efficacy to help the most severe osteoarthritis-disabled patient. ■

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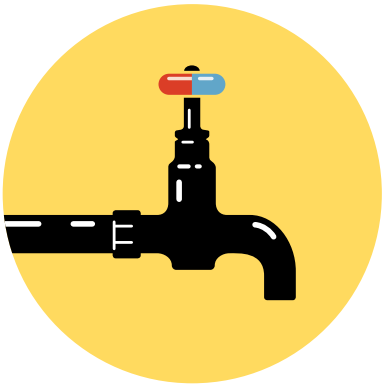
CDA JOURNAL, VOL 43, N°11



Changing Paradigms for Acute Dental Pain: Prevention Is Better Than PRN

Raymond A. Dionne, DDS, PhD, and Sharon M. Gordon, DDS, MPH, PhD

ABSTRACT The drugs available for the management of acute orofacial pain have changed very little since the introduction of ibuprofen into practice 40 years ago. Orally effective opioids, acetaminophen, aspirin and NSAIDs remain the mainstay of analgesic therapy. Increased recognition of the societal and personal impact of opioid diversion and abuse requires re-examination of the traditional approach of prescribing an opioid-containing analgesic combination to be administered by the patient "as needed" (PRN) starting postoperatively.

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Strategies for the management of pain from the orofacial region can be grouped into three general categories: blockade of perioperative pain to permit performance of a procedure that would otherwise be too noxious, control of acute pain following a surgical procedure that produces tissue injury and subsequent inflammation, and interventions for chronic pain. Local anesthetics are the mainstay of dentistry for controlling perioperative pain but opioids are also often used as part of sedation regimens to control acute procedural pain. Nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids are the drug classes primarily used to control acute postprocedural pain. A wide range of pharmacologic and nonpharmacological modalities is used for management of chronic temporomandibular disorders (see "Evidence-Based Pharmacologic Approaches for Chronic Orofacial Pain," page 643). The drugs and doses used for acute postprocedural pain have been well-characterized through thousands of controlled clinical trials, providing a robust evidentiary basis for therapeutic recommendations. Understanding of the pathophysiology of inflammation and the dynamic changes in pain processes following tissue injury has also been greatly informed by basic and clinical research findings. This article summarizes evidence from the scientific literature to provide a rationale for the

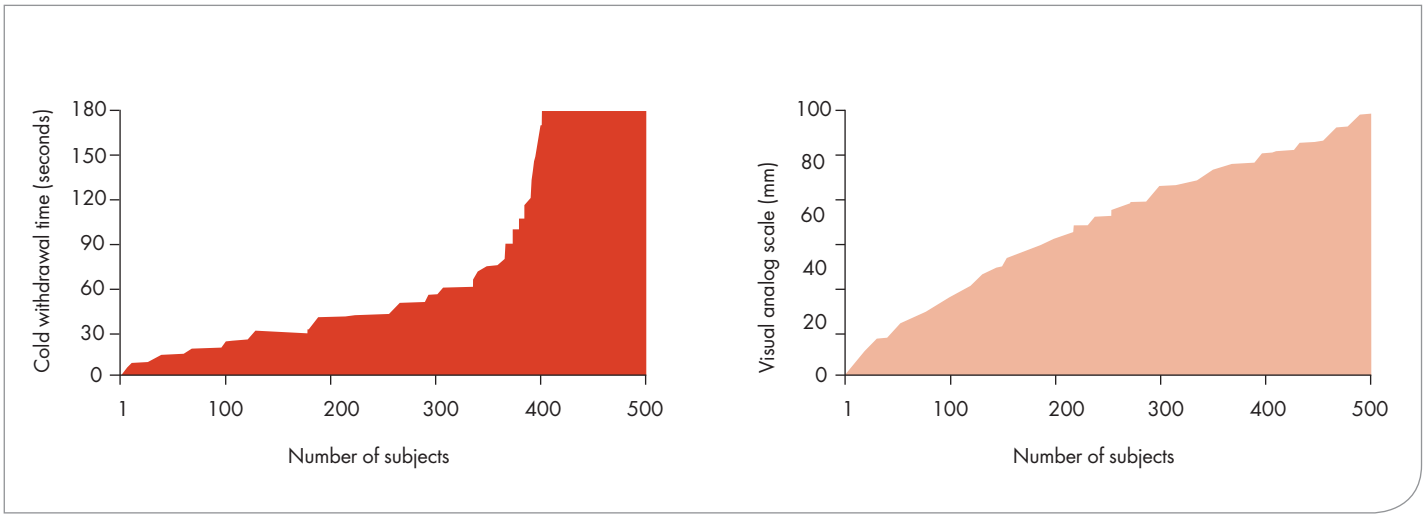

FIGURE 1. The wide variability in pain responses across the population is demonstrated by the range of responses to acute experimental pain. The graph on the left shows the amount of time before subjects withdrew their hands from ice water due to pain, ranging from a few seconds up to the maximal time allowed for this test (180 seconds). The graph on the right shows the rating of pain in response to a brief stimulus of 49 C applied to the forearm, ranging from very low ratings to the maximal anchored by the words "worst pain imaginable" (Adapted from Kim H et al. *J Pain* 2004; 5:377-384).

management of acute dental pain and prevention for improved efficacy and safety rather than continuation of traditional "take as needed" clinical practice.

Analgesic drugs — not acute pain — have become the problem. The widespread prevalence of pain is estimated to affect more than 116 million people in the U.S. with an estimated cost to society of between $560 and $635 billon annually.[1] Recognition of this large unmet need has led to more aggressive pharmacological management of pain and the introduction of pain as the fifth vital sign for medical care. However, the increased use of opioid analgesics for pain management has also contributed to increased misuse of analgesics that contributes significantly to problems of drug safety. More than 40,000 deaths are attributed annually to adverse drug reactions and overdoses, a greater number of deaths than those attributed to motor vehicle accidents or firearms.[2] Opioid drugs are major contributors to drug morbidity and mortality with more than 16,000 deaths associated with opioid analgesics prescribed for therapeutic indications.[3]

Approximately 11 percent of opioids prescribed annually in the U.S. are by dentists,[4] suggesting that a significant number of deaths each year are due to opioid drugs prescribed for dental indications. This is despite the fact that NSAIDs administered for acute pain are not only more effective than acetaminophen[5] or acetaminophen-opioid combinations,[6] but also have greater safety. Most acute dental pain is inflammatory in origin and NSAIDs are extremely effective for inhibiting inflammatory pathways, while opioids are devoid of anti-inflammatory activity and cause significant morbidity. These generalizations are supported by a large number of well-controlled clinical trials, indicating that the routine use of opioid-acetaminophen combinations rather than NSAIDs for dental pain is neither evidence based nor a logical clinical practice.

Wide variability in pain and analgesia demonstrates that "one size does not fit all" for managing acute pain. Patients differ widely in their inherent genetic makeup, and even that can be changed due to environmental influences. Physiologic processes exist that can augment or minimize the perception of noxious stimuli as painful. The release of beta-endorphins as part of endogenous analgesic processes can also decrease pain perception while stress responses due to anxiety can augment pain perception. Lastly, idiosyncratic differences between individuals, expectations based on experiences and sociocultural influences can also cause variable pain perception.

The wide range in pain responses is illustrated by a study[7] that exposed all individuals to the same stimuli (49 C applied to the skin of the forearm) that resulted in pain reports ranging from little or no pain to the worse pain imaginable (**FIGURE 1**). Similarly, the amount of pain reported following the removal of two partially impacted third molars by the same oral surgeon under carefully controlled conditions ranged from slight to severe pain.[8] A study of variability following general surgery in which patients self-administered morphine via patient-controlled analgesia resulted in a greater than fortyfold range in the amount of analgesic drugs that patients indicated was sufficient to adequately relieve their pain.[9] This wide range in pain report and analgesic drug use illustrates that it is nearly futile to predict how much pain an individual patient will experience following a procedure producing tissue injury. However, knowledge of the processes that are activated by tissue injury (neuronal conduction of a

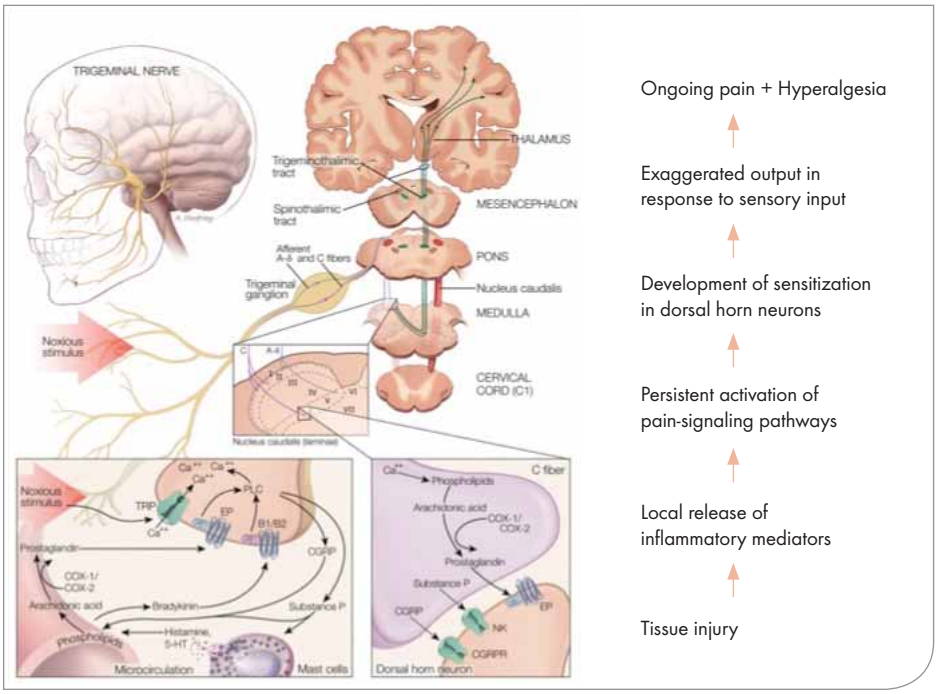

FIGURE 2. Sites for preventive interventions to minimize the development of acute pain. The lower left panel illustrates the formation of pro-inflammatory prostaglandins at the site of injury that activate and sensitize peripheral pain receptors to signal pain. The lower right panel illustrates the release of pro-nociceptive transmitters in dorsal horn neurons that can also result in sensitization due to cyclooxygenase (COX) mediated prostaglandin formation. Once these processes have been established, the exaggerated output is transmitted to the central nervous system to result in hyperalgesia (upper panel). NSAIDs act at the site of injury and in the dorsal horn to prevent the development of sensitization, local anesthetics can attenuate the pain signaling that contributes to the development of sensitization; opioids act in the CNS to modulate the intensity and reaction to painful inputs without attenuating the development of hyperalgesia (Adapted from Woodcock J, et al. *Nat Rev Drug Discov* 2007; 6:703-10).

nociceptive message, acute inflammation, development of peripheral and central sensitization) provides an informed basis for clinical interventions that can block or attenuate these processes. Clinical pain is also modulated by processes that the clinician cannot predict or control, e.g., augmentation of pain perception due to experiences and an exaggerated stress response, and require individualizing pain treatment based on the patient's history and responses to the analgesic drugs administered.

The PAIN Prevention Paradigm

The acronym PAIN signifies four evidence-based steps that a dentist can use to delay the onset of postoperative pain in the first few hours following a procedure producing tissue injury and minimize the intensity of pain over the two to three days when acute inflammation normally augments pain perception.

P = Prevention

Pain in the orofacial region can be prevented by attenuating the development of hyperalgesia due to the development of sensitization in pain-sensing neurons at the site of injury and in the central nervous system that can lead to increased pain for days after the initial tissue injury. Increased neuronal activity caused by damage or inflammation of the tooth pulp, temporomandibular joint or orofacial musculature induces changes in the peripheral nervous system that is described as peripheral sensitization.[10] Cells in oral tissues respond to tissue injury to produce pro-inflammatory mediators that act by binding to cellular receptors that in turn signal through second messengers. One group of pro-inflammatory mediators that is well-characterized for acute orofacial pain is derived from membrane phospholipids to generate arachidonic acid. Prostaglandin E_2 (PGE_2) is produced by conversion of arachidonic acid via the cyclooxygenase (COX) pathway and sensitizes nociceptive nerve endings, thereby potentiating the actions of other inflammatory mediators such as bradykinin (**FIGURE 2**). Sensitization of peripheral nociceptors is minimized in the absence of PGE_2 and pain sensations are thus attenuated. Therefore, NSAIDs that block prostaglandin synthesis or function following tissue injury in the mouth are effective for minimizing acute inflammatory pain.

A third process that influences the onset, intensity and duration of orofacial pain is the development of neuronal changes in the central nervous system that is induced by the barrage of neuronal input caused by injury and inflammation of peripheral tissues, described as central sensitization. If unchecked, this afferent neuronal barrage results in augmented responses that can last for days after the injury. Non-noxious sensory inputs will be perceived as painful and noxious inputs will be perceived as greater than normal. A common example is the exquisite pain that can occur after sunburn that results in pain for days after the exposure has ended and produces discomfort from otherwise innocuous stimuli.

The phenomena of peripheral and central sensitization are probably additive and contribute to both the intensity and duration of postoperative pain. Recognition of the clinical importance of the development of sensitization has led to attempts to block its development and thus minimize postoperative pain and decreases analgesic use during recovery. The ability to decrease analgesic use is particularly desirable in ambulatory dental outpatients

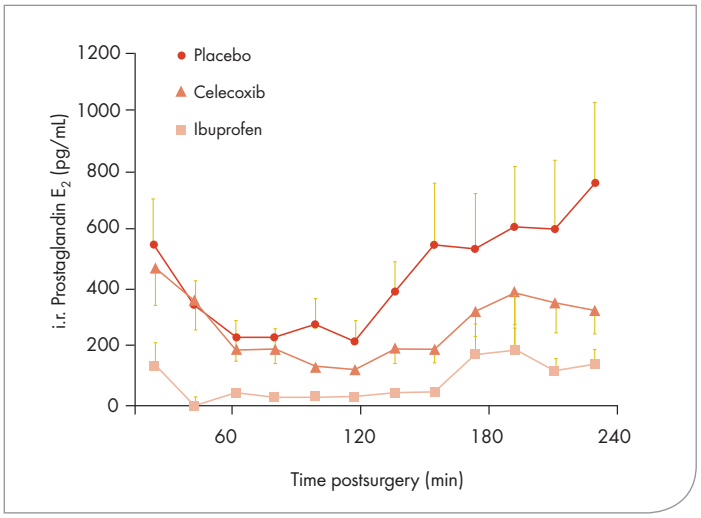

FIGURE 3A.

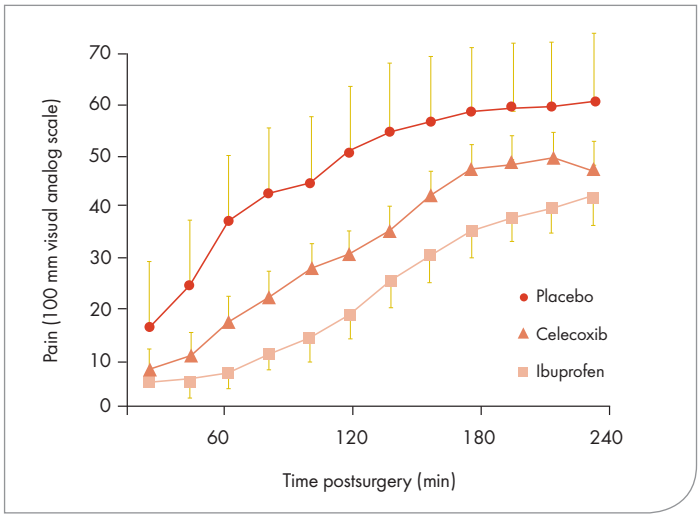

FIGURE 3B.

FIGURES 3. The relationship between peripheral levels of prostaglandin E_2 (PGE_2) and the onset of pain following tissue injury (the removal of impacted third molars). **3A** illustrates increased formation of PGE_2 over two to four hours postoperatively due to the actions of both constitutive COX-1 and inducible COX-2. Administration of the dual COX-1 and COX-2 inhibitor ibuprofen significantly suppresses PGE_2 to the limits of detectability. Administration of a selective COX-2 inhibitor celecoxib significantly suppresses PGE_2 formation at time points consistent with the expression of COX-2 at the site of injury. **3B** demonstrates significantly reduced pain following preventive administration of ibuprofen to a greater extent than pretreatment with celecoxib, likely due to the greater suppression of both COX-1 and COX-2. (Adapted from Khan AA et al. *Clin Pharmacol Therap* 2002; 72:44-49).

who are much more sensitive to the adverse effects of opioid drugs. Decreasing pain and adverse drug effects makes the postoperative period less unpleasant, enhances return to normal function, probably lowers apprehension about future clinical procedures and, thus, may contribute to less opioid use and misuse.

Translating these observations into the management of pain in the dental environment can be readily achieved with currently available drugs:

- The use of a long-acting local anesthetic for a dental procedure results in less pain over the first four to eight hours postoperatively in comparison to lidocaine with epinephrine[11,12] that subsequently results in less pain over the 48 hours after the procedure.[13,14] This demonstrates that suppression of acute pain in the immediate postoperative period attenuates the development of central sensitization, presumably by blocking the neuronal barrage into the central nervous system (CNS) that otherwise occurs as the local anesthetic dissipates.
- The administration of an NSAID before or immediately after a dental procedure results in less pain during the first four to eight hours postoperatively[15,16] by suppressing the release of prostaglandins and other inflammatory mediators that contribute to the sensitization of peripheral nociceptors.[17-20]
- The combination of NSAID pretreatment before pain onset and a long-acting local anesthetic additively reduces pain following oral surgery, as a model of acute dental pain, such that patients report little pain over the first six to seven hours postoperatively.[11]
- Preventive administration of NSAIDs results in less postoperative pain than traditional opioid-containing analgesic combinations[21] with fewer side effects[22] and no potential for opioid abuse or misuse.

A = *Anti-inflammatory drugs*

Administration of an NSAID in the preoperative period allows sufficient time for drug absorption during the procedure and the one to two hours of local anesthetic duration postoperatively. Preoperative administration of 400 mg of ibuprofen was demonstrated to increase time to the first request for postoperative analgesic medication by approximately two hours in comparison to placebo pretreatment.[15] A subsequent study demonstrated that preoperative administration of 800 mg of ibuprofen significantly lowered pain intensity over the first few hours after oral surgery as the effects of local anesthesia dissipated.[16] Administration of a second dose four hours after the initial dose extended this preventive analgesic effect to result in less pain than placebo, acetaminophen given pre- and postoperatively or acetaminophen plus 60 mg of codeine administered postoperatively. The ability to suppress pain onset and lower the intensity of postoperative pain up to eight hours is replicable[23,24] and extends to the use of other NSAIDs, such as flurbiprofen[25] and other dental conditions such as orthodontic pain.[26]

Comparison of ibuprofen administration prior to periodontal surgery versus administration immediately following surgery demonstrated that both groups experienced delayed onset of postoperative pain in comparison to placebo.[27] A similar study using naproxen[28] also could not differentiate

TABLE 1

Factors for Individualizing Analgesics to a Patient

Medical history	• Avoid opioid if any previous drug abuse or alcoholism. • Avoid opioid if history of nausea or vomiting from previous opioid administration. • Avoid acetaminophen if current or previous liver disease. • Avoid NSAID if history of ulcers, irritable bowel disease, renal disease or cardiovascular disease. • Avoid any drug in same class if previous history of allergy.
Family history	• Avoid opioid exposure if family history of drug abuse.
Body weight	• Consider greater analgesic dose if BMI > 30. • Consider lower analgesic dose if BMI < 18.
Clinical procedure	• Premedication with NSAID and use of long-acting local anesthetic indicated if surgical procedure makes severe postoperative pain likely. • Pre-existing infection may interfere with local anesthetic efficacy, carefully test for signs of anesthesia before initiating procedure.
Patient apprehension	• Patient self-report of "somewhat nervous" about the procedure, consider use of nitrous oxide to minimize intraoperative pain perception. • Patient self-report of "moderately nervous" about the procedure, consider use of enteral sedation with a benzodiazepine to minimize pain perception and recall. • Patient report of "very nervous" or "terrified" about procedure, consider use of parenteral sedation or general anesthesia.
Risk factors for drug abuse	• Avoid any opioid if patient identifies necessity or personal perception for oxycodone or hydrocodone containing combinations. • Avoid opioid if any history of drug rehabilitation or previous arrest related to drug-seeking behavior. • Avoid opioid if family history of drug abuse due to high heritability of abuse.

between pre- and immediate postoperative administration, suggesting that preoperative administration is not critical for suppressing pain onset. Subsequent recognition of the induction of a second form of cyclooxygenase (COX-2) in the postoperative period[29] suggests that blockade of prostanoids released during surgery by constitutive COX-1 is less important than suppression of COX-2 and prostanoid release during the postoperative period. Consistent with this observation is that both preoperative and postoperative administration of ibuprofen is equally effective at suppressing pain and prostaglandin E_2 levels at the extraction site.[17] These studies provide strong evidence that administration of ibuprofen and other NSAIDs prior to induction of COX-2 and subsequent release of pro-inflammatory prostanoids is a proven preventive strategy to suppress pain in the immediate postoperative period (**FIGURE 3**). Opioids do not have any acute anti-inflammatory effects and allow inflammation to be initiated in the immediate postoperative period, leading to acute pain and inflammation, as well as augmenting the pronociceptive effects of other mediators being released as part of the inflammatory process.

NSAIDs are one of the most widely used drug classes for dental pain and are generally more efficacious than aspirin, acetaminophen or combinations of these two drugs with an opioid,[30,22] presumably due to the inflammatory cause of most dental pain and the NSAIDs' prominent anti-inflammatory effects. When used as directed for over-the-counter dosing regimens, ibuprofen, ketoprofen and naproxen sodium are both safe and effective for most patients across a wide variety of dental pain conditions.[31,5] Limitations to orally administered NSAIDs for dental pain include slow onset when not given prior to pain onset, the inability to consistently relieve severe pain, and adverse gastrointestinal effects when given repeatedly, which limits the ability to increase doses beyond the recommended range. Selective COX-2 inhibitors, e.g., celecoxib, were developed to achieve the therapeutic effects of traditional NSAIDs with the toxic gastrointestinal effects but it is now realized that they have cardiovascular effects that increases the incidence of myocardial infarction and stroke when given chronically. These considerations indicate the need to carefully weigh the benefit-to-risk relationship of each drug and the specific patient being treated in order to individualize and optimize the therapeutic benefit for individual patients.

I = Individualize

Recognition of the enormous heterogeneity among individual patients and their responses to analgesic drugs suggests that translating to improved therapy requires abandoning the "one-size-fits-all" paradigm for pain management.[32,33] Not only does genetic variability among individuals contribute to the wide range of responses to pain and analgesia, tissue injury results in increased expression of pro-inflammatory mediators[18] that are also influenced by interindividual genetic variation.[20] The epigenetic influences of a lifetime also influence the dynamic responses between tissue injury, nociceptive signaling and eventual pain perception.[34] The likelihood that

each patient's analgesic needs will vary indicates a need to individualize the drugs and doses administered. Factors for individualizing analgesic therapy can be considered in advance and then adjusted to the responses of the patient in order to optimize therapeutic outcomes, both efficacy and safety (**TABLE 1**).

N = Narcotics (opioids)

While NSAIDs have proven very effective for dental pain, the inability to enhance analgesia with increasing dose has led to attempts at additive analgesia by combining ibuprofen with an orally effective opioid. Results to date have been equivocal in comparison to the analgesic effects of 400-600 mg of ibuprofen alone and due to the incidence of opioid-mediated side effects. The current published evidence indicates that either oxycodone or hydrocodone can provide additional pain relief at the expense of increased adverse effects when an NSAID alone does not provide adequate pain relief using the first three steps of the PAIN prevention paradigm.

Ibuprofen plus codeine: The combination of 400 mg of ibuprofen plus 20-60 mg of codeine in comparison to ibuprofen alone results in modest additive analgesia for one to two hours (**TABLE 2**). The genetic variability of codeine metabolism results in a wide range of blood levels that can result in effects ranging from no detectable analgesic effect to respiratory depression in children.[38] In the absence of a marketed fixed-dose combination of ibuprofen plus codeine and the potential for drug diversion and abuse if a separate prescription for codeine is provided, there does not appear to be a good rationale for combining codeine with ibuprofen for additive analgesia.

Ibuprofen plus oxycodone: Analgesic combinations containing oxycodone have generally been perceived to be more effective than codeine-containing combinations based on the ten- to twelvefold greater potency attributed to oral oxycodone in comparison to oral codeine.[39] But if the recommended dose of oxycodone in these combinations, (5 mg every six hours) is administered this should result in the same analgesia as 50-60 mg of codeine. The results of several clinical trials and two systematic reviews indicate that 5 mg of oxycodone produces analgesia that is additive to 400 mg of ibuprofen (**TABLE 2**). A 10 mg dose of oxycodone provides even greater additive analgesia but with a dose-related increase in side effects.[37,40]

In order to provide additive analgesia using 400-600 mg of ibuprofen prior to pain onset, and with continued preventive dosing every four to six hours, an additional dose of 5-10 mg oxycodone may provide additional therapeutic benefit but with a problematic incidence of opioid side effects in ambulatory patients, including drowsiness, nausea and vomiting. Acute inflammatory pain usually peaks at 48 hours following surgery and starts to decrease in intensity by 72 hours. Providing patients with a prescription for a limited supply of 400 mg ibuprofen plus 5 mg of oxycodone tablets (Combunox) permits individualized dosing of the opioid to provide additive analgesia but requires careful control of the drug supply to minimize diversion and misuse. Refills should only be considered under unusual circumstances, preferably only if the patient has been examined to verify the need for additional analgesic and to rule out complications such as infection or alveolar osteitis.

Ibuprofen plus hydrocodone: The combination of 200 mg ibuprofen plus 7.5 mg hydrocodone (Vicoprofen) produces an additive effect than either of the drugs alone at these doses, but there is no evidence that the level of analgesia provided is greater than 400-600 mg of ibuprofen alone. The therapeutic advantage of this combination is the ability to administer the hydrocodone in addition to preventive ibuprofen in patients who still report sufficient unrelieved pain to justify the adverse effects and abuse risk of this commonly abused opioid drug. Combining one tablet of the marketed fixed-dose combination with 200-400 mg ibuprofen would result in a combined dose of 400-600 mg of ibuprofen plus 7.5 mg hydrocodone. Only a limited number of tablets (N=10-12) should be prescribed without any refills and patients should be instructed on the appropriate use and storage of the drug to avoid diversion or misuse.

Translating the PAIN Prevention Paradigm to Clinical Practice

Clinical procedures that warrant postoperative analgesic use will likely produce less discomfort for the patient and a more predictable postoperative course by shifting from traditional acetaminophen- or aspirin-oral opioid combinations to a preventive strategy. Administration of 400-600 mg ibuprofen or a similar NSAID that the patient tolerates prior to the procedure or immediately afterward will result in delayed onset and less intensity of pain due to the suppression of inflammatory mediators released by tissue injury. Use of a long-acting local anesthetic should attenuate the development of hyperalgesia by blocking the afferent nociceptive barrage that results in greater pain that can persist for two to three days. Combining these two preventive strategies results in additive effects that can minimize pain following surgical procedures with minimal adverse effects. However, due to the wide individual variability that exists across the patient population, some individuals will still report pain that warrants intervention. In those cases, administration of an opioid-containing

TABLE 2

Selected Clinical Studies Evaluating the Additive Effects of Ibuprofen and an Oral Opioid for Postoperative Pain

Drug Combination	Indication/Outcome	Citation
Ibuprofen + Codeine		
400 mg ibuprofen + 60 mg codeine	Postoperative dental pain NS additive analgesia	Cooper et al., 1982[35]
400 mg ibuprofen + 60 mg codeine	Postoperative dental pain Additive analgesia Increased adverse events	Petersen et al., 1993[36]
400 mg ibuprofen + 20 mg codeine	Postoperative dental pain Additive analgesia No increased adverse events	McQuay et al., 1989[22]
Ibuprofen + Oxycodone		
400 mg ibuprofen + 2.5 mg oxycodone	Postoperative dental pain No additive analgesia	Dionne, 1993[37]
400 mg ibuprofen + 5 mg oxycodone	Postoperative dental pain No additive analgesia	Dionne, 1993[37]
400 mg ibuprofen + 5 mg oxycodone	Postoperative dental pain NS additive analgesia NS increase in adverse events Longer time to remedication	Derry et al. 2015[41]
400 mg ibuprofen + 5 mg oxycodone	Postoperative denal, abdominal or pelvic pain Additive analgesia Faster onset, longer pain relief Well-tolerated	Oldfield, Perry, 2006[42]
400 mg ibuprofen + 10 mg oxycodone	Postoperative dental pain Additive analgesia at one and two hours Increased adverse events	Dionne, 1993[37]
Ibuprofen + Hydrocodone		
400 mg ibuprofen + 5 mg hydrocodone	Periodontal surgery pain Additive analgesia	Betancourt et al., 2004[43]
400 mg ibuprofen + 15 mg hydrocodone	Abdominal analgesia Abdominal surgery pain	Sunshine et al., 1997[43]
200 mg ibuprofen + 7.5 mg hydrocodone	Abdominal or gynecologic surgery pain	Widemen GL et al., 1999[45]
400 mg ibuprofen + 15 mg hydrocodone	Additive analgesia	Widemen GL et al., 1999[45]

NS = nonsignificant statistically

NSAID combination such as oxycodone or hydrocodone without lowering the NSAID dose can result in additional relief for the two- to three-day postoperative period when pain is maximal. Only a limited amount of the opioid-combination should be prescribed and parents or a significant other should manage the dosing and frequency of administration. All unused opioid-containing drug supplies should be destroyed or returned to the pharmacy as the pain subsides. Any continued requests for opioids should be met with concern and require an exam to confirm the nature of the problem and to rule out complications such as infection that are not appropriately treated with an opioid. ■

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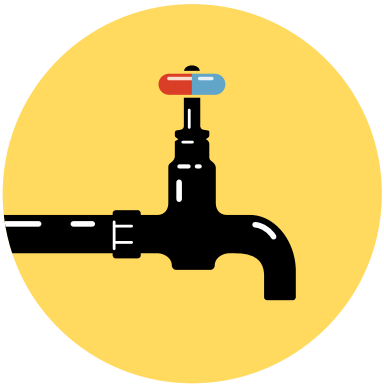
CDA JOURNAL, VOL 43, N°11



Dietary Supplements and Alternative Therapies for Pain Management

Philip J. Gregory, PharmD, MS

ABSTRACT The use of complementary and alternative medicines (CAM) continues to grow in North America. The most recent National Health Interview Survey found that in 2012, 33.2 percent of respondents reported usage of some form of CAM in the previous 12 months. A survey of adult patients in a U.S. dental school clinic found that 24 percent reported the use of herbal supplements. Dietary supplements and alternative therapies are often used for pain management.

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The use of complementary and alternative medicines (CAM) continues to grow in North America. Complementary medicine generally refers to nonmainstream practices that are used together with conventional medicine. Alternative medicine is typically a nonmainstream practice that is used in place of conventional medicine practices. Another term commonly used today is "integrative" medicine. This involves a conscientious and purposeful integration of complementary and conventional approaches to medicine in a coordinated way.

CAM and integrative therapies include a variety of therapeutic interventions, including herbals and other dietary supplements, energy medicine such as yoga and qigong, acupuncture, chiropractic, homeopathy and others.

The most recent National Health Interview Survey found that in 2012, 33.2 percent of respondents reported usage of some form of CAM in the previous 12 months. The most commonly used CAM therapies were nonvitamin, nonmineral dietary supplements. Approximately 18 percent of respondents reported use of a dietary supplement in the previous 12 months. About 11 percent of respondents reported use of yoga, tai chi and qigong. Other commonly reported CAM therapies were chiropractic (8.4 percent), meditation (8 percent), special diets (3 percent) and homeopathy (2.2 percent). Among dietary supplements specifically, the most common were fish oil (7.8 percent), glucosamine or

CDA JOURNAL, VOL 43, N°11

TABLE 1

Comparative Effectiveness of Dietary Supplements for Pain Management[7]

Supplement	Condition	Effective Rating*	Reported Side Effects**
Cayenne pepper	General pain	Likely effective	Skin irritation, burning sensation, redness
Camphor	General pain	Likely effective	Skin irritation
Glucosamine sulfate	Osteoarthritis pain	Likely effective	GI upset, headache
Arnica	Osteoarthritis	Possibly effective	Skin irritation, itchiness, rash
Cat's claw	Osteoarthritis pain	Possibly effective	Headache, dizziness, upset stomach
Devil's claw	Back pain, osteoarthritis	Possibly effective	GI upset, abdominal pain
Turmeric	Osteoarthritis	Possibly effective	GI upset, diarrhea
Willow bark	Back pain	Possibly effective	GI upset, itching, rash
Arnica	Myalgia, postsurgical pain	Insufficient evidence	Skin irritation, itchiness, rash
Bromelain	Osteoarthritis, knee pain	Insufficient evidence	GI upset, diarrhea, allergic reaction
Glucosamine hydrochloride	Osteoarthritis	Insufficient evidence	GI upset, headache
Willow bark	Osteoarthritis	Insufficient evidence	GI upset, itching, rash
Arnica	Wisdom tooth extraction	Possibly ineffective	Skin irritation, itchiness, rash
Bromelain	Myalgia	Possibly ineffective	GI upset, diarrhea, allergic reaction

*Effectiveness rating based on Natural Medicines' (www.naturalmedicines.com) evidence-based effectiveness ratings.
**Not a complete list.

chondroitin (2.6 percent), probiotics (1.6 percent) and melatonin (1.3 percent).[1]

A survey of adult patients in a U.S. dental school clinic found that 24 percent reported the use of herbal supplements. The most commonly reported supplements were green tea (39.5 percent), garlic (14.3 percent), echinacea (9.5 percent) and ginkgo (9 percent). It is important to note that this survey did not evaluate the use of nonherbal dietary supplements and did not specifically assess supplements for pain.[2]

In the U.S., dietary supplements are defined as any product or ingredient intended for ingestion that contains a dietary ingredient. A dietary ingredient is considered to be any vitamin, mineral, herb or botanical, or a concentrate, metabolite, extract or constituent of a dietary substance. Dietary supplements are regulated by the Dietary Supplement Health and Education Act (DSHEA) of 1994. DSHEA defines dietary supplements and sets criteria for what is permitted in the marketplace. The regulatory approach for dietary supplements is much different than for drugs. Whereas drugs go through an extensive premarket approval process, dietary supplements do not require premarket approval. Due to this difference in regulatory status, dietary supplement marketers are not legally permitted to make disease treatment claims. In other words, dietary supplement marketers cannot claim that their products treat particular diseases like arthritis or fibromyalgia. However, they can make "structure-function" claims. They can claim to affect some structure or function of the body (e.g., "promotes a healthy metabolism").

Dietary Supplements

Several dietary supplements are marketed for relieving pain (**TABLE 1**). Not surprisingly, common chronic pain syndromes are most frequently targeted, such as pain related to osteoarthritis or lower-back pain. Very few dietary supplements have been evaluated specifically for orofacial pain or dentistry-specific issues. Nonetheless, patients may be trying these supplements for a variety of pain-related issues including those that have never been studied. The following provides a brief overview of the evidence for select commonly used supplements for pain and/or inflammation.

Counterirritants

Cayenne pepper (*Capsicum frutescens*). The best-known counterirritant is capsaicin, the constituent isolated from cayenne pepper that makes the pepper hot. Topical capsaicin is thought to work by stimulating peripheral nociceptors in the skin. Over time, desensitization of the nervous tissue occurs, resulting in pain relief.[3]

Several clinical trials have evaluated topical capsaicin for musculoskeletal pain including symptoms of osteoarthritis. While most trials suggest benefit, this effect appears to be modest.[3] A meta-analysis found that topical capsaicin 0.025% cream reduced pain by 50 percent or more in 38 percent of patients compared to 25

percent of patients receiving placebo. This corresponds with a number needed to treat (NNT) of 8.1 for one additional patient to achieve this clinically significant response.[4]

For pain related to neuropathic conditions, topical capsaicin seems to be more effective. An analysis of studies using capsaicin 0.075% cream found that the NNT is 5.7 for one additional patient with neuropathic pain to have a clinically significant response.[4] A high-dose capsaicin patch containing 8% capsaicin (Qutenza) is available as a prescription drug and is approved specifically for postherpetic neuralgia pain. It's applied for just one hour in the prescriber's office with at least three months between applications. About 40 percent of patients respond and have about a 30 percent reduction in pain.[5]

Camphor *(Cinnamomum camphora).* Camphor is an essential oil extract from the plant *Cinnamomum camphora*. It is found in some single-ingredient camphor-containing products, but often is one component along with other ingredients, such as menthol or glucosamine.

Although camphor has been found to have counterirritant effects, clinical research is lacking. One clinical trial evaluated a topical product containing camphor, glucosamine and chondroitin in patients with osteoarthritis of the knee.[6] Although the product was found to modestly reduce pain compared to placebo, the study had serious methodological flaws.

Anti-inflammatory Agents

Many dietary supplements are promoted for relieving pain due to known or suspected anti-inflammatory effects.

Bromelain. Bromelain is a proteolytic enzyme isolated from the fruit and stems of the pineapple plant (*Ananas comosus*). Bromelain is thought to have anti-inflammatory effects through a variety of potential mechanisms. Bromelain seems to decrease pro-inflammatory prostaglandin synthesis. It might also reduce thromboxane and bradykinin synthesis. Bromelain might also affect inflammation by inhibiting leukocyte migration and activation.[7]

Clinical research has evaluated bromelain for a variety of uses including management of knee pain and pain related to osteoarthritis. In a preliminary, open-label and nonrandomized study, bromelain 200 mg or 400 mg reduced symptoms of acute knee pain by 41 percent and 59 percent, respectively.[8] However, in another clinical trial, bromelain 800 mg daily for 12 weeks did not significantly reduce knee pain related in moderate-to-severe osteoarthritis.[9]

> The best-known counterirritant is capsaicin, the constituent isolated from cayenne pepper that makes the pepper hot.

Cat's claw *(Uncaria guianensis).* Cat's claw is a woody vine native to tropical areas of South and Central America. Cat's claw is thought to reduce inflammation by inhibiting production of inflammatory prostaglandins and decreasing levels of tumor necrosis factor-alpha.[7]

In one clinical trial, a 100 mg daily freeze-dried extract of cat's claw reduced knee pain following physical activity in patients with osteoarthritis.[10] In another preliminary trial, cat's claw modestly reduced the number of painful joints compared to placebo in patients with rheumatoid arthritis.[11]

Devil's claw *(Harpagophytum procumbens).* Devil's claw is native to the Kalahari and Savannah desert regions of Africa. The tuber of the devil's claw plant is used to prepare extracts for use in dietary supplements. Iridoid glycoside constituents such as harpagoside seem to inhibit the cyclooxygenase (COX) and lipoxygenase inflammatory pathways.[7]

Several clinical trials have evaluated devil's claw for treating pain related to osteoarthritis. When used alone or in combination with anti-inflammatory drugs, devil's claw appears to decrease osteoarthritis pain and reduce the need for conventional drugs. Most studies have used devil's claw root standardized to contain 2% harpagoside and 3% total iridoid glycosides.[7,12]

Similarly, clinical research has found that devil's claw extract can significantly reduce lower-back pain. Some studies have found devil's claw to be comparable to the anti-inflammatory COX-2 inhibitor rofecoxib (Vioxx).[12-14]

Turmeric *(Curcuma longa).* Turmeric is a spice commonly used in Asian food. Its constituent, curcumin, is the yellow-colored component that gives curry its color. The curcumin constituent also seems to have anti-inflammatory effects through inhibition of COX-2, leukotrienes and other pro-inflammatory pathways.[7]

Several preliminary clinical trials have found a specific turmeric extract (Meriva) 500 mg twice daily significantly decreases pain compared to baseline in patients with osteoarthritis of the knee. This extract was standardized to provide 20% curcuminoids.[15,16]

Willow bark *(Salix alba).* Willow bark is primarily used as an analgesic or anti-inflammatory because it contains salicylates including salicin, which is ultimately metabolized to salicylic acid. Extracts of willow bark seem to inhibit the COX-2 enzyme and thereby reduce inflammation.[7]

Clinical research has had inconsistent findings. Some research shows that it significantly reduces lower-back pain when an extract is used providing 120-204 mg daily.[17,18] For osteoarthritis, some research suggests modest benefits for reducing

pain; however, some studies have found no benefit compared to placebo.[7,19,20]

Miscellaneous Agents

Several other supplements are used for pain with a variety of unique mechanisms that are dissimilar to most conventional medications used for pain management.

Glucosamine. Glucosamine is among the most commonly used dietary supplements. It is also one of the best studied. Glucosamine is an amino sugar that is a normal component of cartilage proteoglycans. It is also required for the production of glycoproteins and glycosaminoglycans, which are found in synovial fluid, cartilage, ligaments and mucus membranes. Glucosamine is thought to help reduce symptoms of osteoarthritis by stimulating metabolism of chondrocytes in articular cartilage and by inhibiting production of mediators of inflammation and cartilage breakdown.[7]

There has been a lot of controversy about whether glucosamine actually reduces symptoms of osteoarthritis. This is largely attributed to a well-publicized trial, the Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT), which found that glucosamine hydrochloride was no more effective than placebo for reducing pain in patients with osteoarthritis of the knee.[21]

Despite the negative findings from the GAIT study, the majority of evidence, when pooled and analyzed as part of a meta-analysis, shows that glucosamine significantly reduces pain related to osteoarthritis. However, the form of glucosamine and treatment duration are important factors. Studies evaluating the glucosamine sulfate salt form have consistently shown significant, but modest, reductions in pain related to osteoarthritis. Most of these studies have used a single, proprietary glucosamine sulfate product (DONA, Rottapharm/Madaus). Studies evaluating glucosamine hydrochloride preparations have found no significant benefit. Additionally, treatment of 24 weeks or longer seems to be important for showing beneficial effects. [22,23]

Many glucosamine products come as a combination product containing glucosamine plus chondroitin and often other ingredients as well. There is no reliable evidence that these combinations are more effective than glucosamine sulfate by itself.

Arnica (*Arnica montana*). Arnica is native to mountainous regions of Europe and North America. The plant is actually considered poisonous when taken orally. It can increase blood pressure, cardiac toxicity, gastroenteritis and muscle paralysis. Due to these safety concerns, most arnica products are meant for topical application only or are prepared as homeopathic dilutions containing little to no actual active ingredient.[7]

There has been a lot of controversy about whether glucosamine actually reduces symptoms of osteoarthritis.

Arnica has been studied in patients undergoing third molar extraction. Most studies have found that homeopathic arnica does not significantly decrease pain, swelling or wound infection.[24]

Arnica has also been studied for reducing postoperative pain following tonsillectomy, knee surgery and carpal tunnel surgery. Several studies found that arnica modestly reduced postoperative pain.[25-27] However, some studies found no benefit.[28,29]

In patients with osteoarthritis, arnica gel applied topically significantly reduced pain in patients with osteoarthritis of the hand or knee.[30,31] In patients with myalgia, findings have been mixed[7] (**TABLE 1**).

Drug-Supplement Interactions

Many dietary supplements have the potential to interact with other medications. These interactions can occur through mechanisms similar to conventional drugs — via pharmacodynamic (e.g., additive pharmacological effects) or pharmacokinetic interactions (e.g., inhibition of cytochrome P450 enzymes).

This biggest concern with dietary supplements used for pain management has to do with antiplatelet effects. Bromelain, cat's claw, devil's claw and turmeric have antiplatelet effects. Taking these supplements along with drugs with antiplatelet or anticoagulant effects (e.g., NSAIDs, aspirin, warfarin, clopidogrel, etc.) might increase the risk of bruising or bleeding.[7]

Supplement Quality

Numerous news reports have highlighted the quality problems suffered by the dietary supplement industry. Although DSHEA requires dietary supplement manufacturers to follow good manufacturing practices, implementation and enforcement of this requirement remains an issue. The biggest problem relates to dietary supplements containing what is actually stated on the ingredient label. Numerous reports have shown that many products contain too little or too much of an active ingredient. In some cases, products have been found to be contaminated with pesticides or heavy metals. In other cases, products have been found to be adulterated (intentionally or unintentionally) with prescription drugs.[40]

Several third-party quality-testing programs have emerged over recent years to help solve supplement quality problems. The

TABLE 2

Resources for Information About CAM Therapies

Name	Link
ConsumerLab	ConsumerLab.com
National Center for Complementary and Integrative Health	nccih.nih.gov
Natural Medicines	naturalmedicines.com
NSF International	nsf.org/services/by-industry/dietary-supplements
Office of Dietary Supplements	ods.od.nih.gov
USP Dietary Supplement Verification Program	usp.org/usp-verification-services/usp-verified-dietary-supplements

most rigorous programs are the USP Dietary Supplement Verification Program and NSF International certification program. These voluntary programs ensure that manufacturers follow good manufacturing practices and consistently produce products that contain what the label indicates. These products can be identified by a seal on the label. These are excellent programs, but relatively few products available on the market have participated in these programs.

ConsumerLab.com also tests dietary supplement products to determine if they contain what is stated on the label, among other things. Although not as rigorous or complete as the USP and NSF International programs, ConsumerLab.com verification can provide some confidence to the consumer that a product reliably contains what is on the label.

Alternative Modalities

Several alternative treatment modalities have the potential to play a role in pain management.

Hypnosis. Hypnotherapy or hypnosis is a modality that attempts to produce a state of consciousness in which the patient is highly responsive to suggestion. The use of hypnosis has been applied to many therapeutic endeavors including reducing pain, treating fear and anxiety and a long list of other applications. Clinical research suggests that hypnosis can help reduce pain related to lower-back pain, postoperative pain, cancer-related pain, temporomandibular disorders, dental procedure pain and other pain syndromes.[7,32,33]

Aromatherapy. The practice of aromatherapy involves using essential oils for therapeutic purposes. These oils are the volatile oils of aromatic plants such as eucalyptus, lavender, clove, rosemary and others. Typically, the oils are vaporized via heat, added to a hot bath or applied topically through massage. The vapors from essential oils are thought to bind to olfactory receptors to elicit a variety of pharmacological responses, including relaxing effects, anxiety reduction, pain reduction and others. Different oils are thought to have different effects. Clinical research on aromatherapy is sparse and inconsistent. No reliable evidence shows that aromatherapy is effective for pain management.[7,34]

Acupuncture. Traditional Chinese medicine utilizes acupuncture as a core treatment modality. Acupuncture practitioners insert needles into specific points on the body known as "meridians." The meridians correspond to certain functions or organs of the body. By stimulating certain points, certain effects may be elicited.[7]

One of the most common applications of acupuncture is pain. Several studies have evaluated acupuncture for back pain, labor pain, osteoarthritis pain, cancer-related pain, shoulder pain and pain related to temporomandibular joint disorder. In most instances, studies have found that acupuncture significantly helps reduce pain.[35-39] However, much of the research is preliminary and poor quality.

Conclusion

The use of alternative therapies continues to grow in the United States and many patients will continue to be interested in these approaches as alternatives to or in addition to conventional approaches.

In some cases, there is evidence to support the use of these approaches for some pain syndromes; however, evidence is often preliminary, of poor quality and inconsistent. Although there may be benefit for some patients, due to the lack of high-quality data, it is often difficult to determine who is most likely to benefit, the most effective dose to use and for how long therapy should continue. Additionally, in most cases, these therapies have modest effects on pain. It is unlikely that these interventions can replace conventional treatments for moderate-to-severe pain, however, they many be able to serve as adjunctive treatment.

In most cases, these approaches are not associated with serious side effects and can be used safely. However, as with any therapeutic intervention, patient-specific factors should be considered. For example, many anti-inflammatory supplements have the potential to modestly inhibit platelet aggregation and potentially interact with conventional antiplatelet or anticoagulant drugs. Patients and practitioners need to recognize that any therapeutic intervention may have real and significant physiological and/or pharmacological effects that could result in adverse consequences.

For any patient interested in these approaches, the best starting point is a conversation about personal goals for therapy and the reasons for seeking these treatments (**TABLE 2**). These conversations can often be eye opening for patients as

well as practitioners and may contribute to improved overall management of pain. ■

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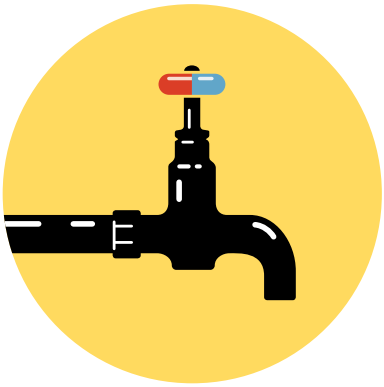
CDA JOURNAL, VOL 43, N°11



A New Paradigm for Providers: Dentists and Pharmacists

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On a typical Friday night at 6 p.m., a patient presents to a pharmacist in a metropolitan community pharmacy with a written prescription from a dentist for a hydrocodone/acetaminophen controlled substance. The patient appears to be in pain, as he cradles his cheek gingerly and contorts his face to try to find the one elusive facial expression that will mitigate his discomfort. The patient has never been to this particular pharmacy before, and in fact, lives close to an hour away by freeway. The pharmacist has a gut feeling that there is something suspicious about the patient and the prescription itself. The patient quickly becomes agitated and starts to verbally abuse the pharmacist and the entire pharmacy staff. The pharmacist desperately tries to contact the prescribing dentist to verify the authenticity of the prescription. Unfortunately, she has left for the weekend.

This scenario is played out in many community pharmacies across California. In days past, the pharmacist would likely accept the prescription at face value and dispense the medication accordingly, or at least make one attempt to contact the prescribing dentist, but then dispense the drug even if unsuccessful. In stark contrast, the pharmacist of today will likely refuse to fill this medication in the presence of one or more red flag indicators that suggest that the medication is being used for some other purpose than a legitimate one.

Legitimate Medical Purpose

California Health & Safety Code (HSC) § 11153(a) states that a "prescription for a controlled substance shall only be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his or her professional practice." And according to California Code of

Regulation (CCR) § 1761(b), "[e]ven after conferring with the prescriber, a pharmacist shall not compound or dispense a controlled substance prescription where the pharmacist knows or has objective reason to know that said prescription was not issued for a legitimate medical purpose." So the immediate question is: What is considered a "legitimate medical purpose"? An obvious example of an illegitimate medical purpose would be dentists prescribing tadalafil tablets (Cialis) for their patients. Generally speaking, dentists may prescribe controlled substances for conditions and diseases of the oral cavity, maxillofacial area and/or the adjacent and associated structures.[1] Legitimacy of medical purpose that turns on scope of practice is usually noncontroversial and can be easily delineated by pharmacists. Controversies are born from pharmacist-dentist interactions wherein there may be nothing wrong with the prescription itself, but the circumstances that led the patient to go to that particular dentist or pharmacy may preclude the pharmacist from dispensing a controlled substance because of the presence of one or more red flag indicators that are not resolvable by a reasonable explanation.

Red Flag Indicators

The California State Board of Pharmacy, through its precedential decision, "In the Matter of Accusation Against Pacifica Pharmacy; Thang Tran," provided a clear list of "red flags" that should "give the pharmacy/pharmacist an inkling of a potential problem, and thus invoke the Duty of Inquiry."

1. Irregularities on the face of the prescription.
2. Nervous patient demeanor.
3. Age or presentation of patient (e.g., young with chronic pain medications).
4. Multiple patients at the same address.
5. Cash payments.
6. Early refill requests.
7. Prescriptions for unusually high quantities.
8. Prescriptions for duplicative drugs.
9. Same prescribing patterns for multiple patients.
10. Initial prescriptions written for high-dose opiates (e.g., OxyContin 80 mg for first-time user).
11. Long distances traveled from patient's home to physician and/or pharmacy.
12. Inconsistent prescriber qualifications in relation to prescriptions prescribed.
13. Prescriptions with no logical connection to diagnosis or treatment.

From the perspective of the pharmacist, every controlled substance prescription written by dentists must be subjected to the test of whether any of the 13 red flag indicators exist. If so, then the pharmacist must conduct a follow-up reasonable inquiry that could require detective-like questioning to both prescriber and patient, to resolve the existence of any red flag. And herein lies the rub: most of these red flag indicators have little or nothing to do with the clinical presentation or pain management need of the patient — rather, there is heavy reliance on circumstantial evidence. Upon clear and convincing existence of any red flag indicator, an absence of a reasonable explanation for the existence equates to legal preclusion to the pharmacist from dispensing that controlled substance.

Application of a Red Flag Indicator

In the original example above, the red flag indicator is the one-hour freeway driving distance between the patient's home and the pharmacy. There is a legal presumption that the reason any patient would drive one full hour from his or her home to the dispensing pharmacy is because the patient is engaging in drug-seeking behavior, and no other closer pharmacy would accept that controlled substance prescription, or that the far-away pharmacy has a questionable reputation for being easy on drug abusers and drug diversioners. Regardless, if the pharmacist cannot obtain a reasonable explanation for why the patient drove so far to get his controlled substance prescription dispensed by this particular pharmacy, then the pharmacist may not, even after conferring with the prescribing dentist that the medication was dispensed for a legitimate pain need, dispense the controlled substance prescription. An example of a successful resolution of this distance problem is that the patient's place of employment is close to the pharmacy.

Use of the Controlled Substance Utilization Review and Evaluation System – CURES

Dentists and pharmacists alike will be required as of July 1, 2016, to register to be able to access the CURES database. HSC § 11165.1(a)(1)(A)(i) states that a "health care practitioner authorized to prescribe, order, administer, furnish or dispense Schedule II, Schedule III or Schedule IV controlled substances … shall, before July 1, 2016, … submit an application … to obtain approval to access information online regarding the controlled substance history of a patient that is stored on the Internet … contained in the CURES Prescription Drug Monitoring Program (PDMP)."

To register as a practitioner, go

to https://pmp.doj.ca.gov/pmpreg/Signup_input.action?at=12 and have at least the following information available for registration: state license number, specialty, degree and Drug Enforcement Administration number. If you need assistance, contact the Help Desk at 916.227.3843 or pmp_registration@doj.ca.gov. Once you submit the information online, follow the directions, which include printing document(s) and obtaining a notarized signature. Mail the documents to:

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The benefit of looking up CURES information for any patient before prescribing a controlled substance is the ability to see the patient's historical controlled substance prescribing and dispensing patterns that should pretty clearly suggest a high likelihood of drug-seeking behavior. A history containing multiple dentists and multiple pharmacies within a relatively short period should give a strong inkling of the possibility that the patient may be scamming the dentist for controlled substances.

Finally, as indicated in the CURES user agreement, "The Department of Justice (DOJ) limits access and dissemination of this information to licensed prescribers, licensed pharmacists, law enforcement personnel and regulatory board personnel strictly for patient care or official investigatory/regulatory purposes. The DOJ pursues regulatory and/or criminal sanctions for misuse of PDMP information. Logging into the PDMP system signifies you understand and agree to these terms." In other words, if a dentist decides against prescribing a controlled substance to her patient based upon information obtained in CURES, she absolutely may not share that information with the patient, regardless of the seemingly incriminating nature of that information. CURES information must not be confused with patient health information, for which the patient has absolute right to.

Conclusion

It is imperative to reinforce the cooperative and collaborative nature of the relationship between dentists and pharmacists. When pharmacists contact dentists soliciting additional clinical justification for a controlled substance, it is not for the sake of harassing the dentist (although it may certainly feel like it to the dentist sometimes). Rather, it is an attempt to resolve the existence of one or more red flag indicators that may suggest that the controlled substance is sought for a purpose other than a legitimate medical one. ■

REFERENCE

1. www.ada.org/en/advocacy/advocacy-issues/scope-of-practice.

THE AUTHOR, Tony Park, PharmD, JD, can be reached at tpark@capharmacylaw.com.

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MADERA: Building & practice. 6 Ops, 3000 sq. ft., Dentrix software, Dexis software, Pano. 2014 GR $850K. #CA289

MARIN COUNTY: Mill Valley 1,260 sq. ft. 3 Ops, 1 add'l Plumbed. Dentrix, Digital, Intra-Oral. #CA224

MARIN COUNTY: 3 Op practice w/views of Corte Madera Creek. 2014 GR $315K. Paperless charts, Schick, Eaglesoft. #CA286 IN ESCROW!

MILLBRAE: 1,500 sq. ft. leased office with 5 Ops, 1 add'l Plumbed, state-of-the-art equipment. 2014 GR $670K. #CA262

N. COAST: Endo Practice. 6 Ops, 5 Plumbed 3,300 sq. ft. Digital, Microscopes, EndoVision. #CA214

N. EAST BAY: SOLD Practice + Bldg. 7 Ops. 2,324 sq. ft. 12 GR $885K. #CA108

N. EAST OF SACRAMENTO: 2,500 sq. ft, 7 Ops with intra-oral, Digital X-ray, and Eaglesoft software. 2014 GR $1.5M. #CA268 IN ESCROW!

NORTHERN CALIFORNIA: Endo Practice. 3 Ops, 1 Plumbed, 1,200 sq. ft. 2 Microscopes, Digital. 2013 GR $319K+ #CA158

N. OF SACRAMENTO: 1,750 sq. ft. w/4 Ops. Intra-Oral, Digital, Pano, Laser, CAD-CAM, Dentrix. 2014 GR $1M. #CA260

N. OF SACRAMENTO: 1,324 sq. ft. office w/4 Ops, Dentrix, Pano. Owner worked 39 weeks in 2014. #CA267

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OAKLAND: NEW LISTING: Appx. 1,500 sq. ft. w/4 Ops, Dentrix software, Dexis Digital X-ray. 2014 GR $869K, adj. net $370K. #CA293

OROVILLE: 1,000 sq. ft., remodeled 2010. Dentrix & Dexis software, Digital Pan & X-rays, Laser, Intra-Oral. 2014 GR $512K. #CA287

OROVILLE: General Practice. 3 Ops, mostly new equipment & recently remodeled. Great satellite or startup practice. Owner retiring. #CA288

PINOLE: 4 Op Endo office w/Digital X-ray, Microscopes, and PBS Endo in approx. 1,200 sq. ft. 2014 GR $672K. #CA284

PLEASANTON: Facility Only, Former Endo Ofc, Good GP Startup. 2 Ops, 1 Plumbed & Partially Eq. 975 sq. ft. #CA195

SACRAMENTO: 7 equip Ops in 2,400 sq. ft., 1 add'l Op Plumbed. Pano, Softdent, Digital. 2014 GR $626K+. #CA250

SACRAMENTO: Practice and Condo. 1,300 sq. ft. office, 4 Ops. Eaglesoft. 2014 GR $650K. #CA261 IN ESCROW!

SACRAMENTO: 1,684 sq. ft., 6 Equip. stations in bay, 2 add'l Plumbed. 2014 GR $590K. #CA269

SACRAMENTO: Russian-speaking. 4 Ops, 1,500 sq. ft.. All new equipment, practice started recently. $1M over last 12 months. #CA290

SAN FRANCISCO: 780 sq. ft., 3 Ops (2 fully Equipped) near Union Square. 2013 GR of $854K, 55% overhead. #CA191

SAN FRANCISCO: Periodontal Practice & Condo Unit. 1,160 sq. ft. w/4 Op, 2014 GR $714K w/$363K Adj. Net. #CA274

SANTA ROSA: General Dentistry & Building. 3 Ops. 2013 GR $542K w/Adj. Net $182K. #CA200

SONOMA: Stand-alone 2,000 sq. ft. office w/4 Ops. Digital X-rays, Lasers, CAD/CAM. 2014 GR $675K on 3 day/week. #CA270

CENTRAL CALIFORNIA

CENTRAL COAST: General Dentistry. 6 Ops, 8 days Hygiene/wk. GR over $2M for last 3 yrs. Est. 30+ yrs. #CA208

FRESNO: General Dentistry Partnership. 2013 Partnership GR $4.7M. Selling Partner 2013 Net Inc $368K. #CA196

KINGS COUNTY: General Dentistry. 4 Ops, Pano, established for 50+ yrs. GR of $246K in 2014. #CA265

PASO ROBLES: Modern 4 op, 1,998 sq. ft. office with Digital X-ray, Softdent . 2014 GR $573K+. #CA275 IN ESCROW!

PORTERVILLE: General Dentistry, 6 Ops. 2014GR $555K, 7 year old equipment, retail center. #CA223

TULARE: 2,300 sq. ft. free-standing office w/5 Ops. 2014 GR $1.7M. 10 days Hygiene. Owner moving out of state. #CA273 IN ESCROW!

SOUTHERN CALIFORNIA

ANAHEIM HILLS: General Practice with 4 Ops, est. for 34 yrs. Dentrix, 6 days Hygiene per week. #CA279 IN ESCROW!

BANNING: General Practice. 6+ Ops. Paperless, Digital, EagleSoft. 8 Days Hyg/Week. 2014 GR $1.4MM+. #CA183 IN ESCROW!

BEVERLY HILLS: Small boutique practice, 2 Ops, 1 Equipped, Open Dental, Digital, 2014 GR $120K on 3 days/wk.. #CA215

BEVERLY HILLS: 5 Ops, EagleSoft, Digital, CEREC. Long-term staff, newer equipment. 2014 GR 1.07MM, Adj. Net of $406K. #CA210

CARSON: NEW LISTING! 3 Op General Practice. Paperless, EagleSoft, Digital, Pano. All equip. <3 yrs. old. 2014 GR $143K. #CA280

CYPRESS: General Practice, 5 Ops, 35 yrs. of Goodwill. 7 days Hygiene per week. $948K GR. #CA257 IN ESCROW!

GREATER LOS ANGELES: Perio Practice. 5 Ops, 34 Yrs. of Goodwill. Dentrix, Digital, Laser, great referral base. #CA173

HUNTINGTON BEACH: General Practice. 4 Ops, Digital, Pano. Nice Prof. bldg location. 2014 GR $534K. #CA277 IN ESCROW!

HUNTINGTON BEACH: 5 Ops, 28 yrs. of Goodwill, Digital, Pano, Laser, 12 days of hyg./wk. GR of $1.1MM+. #CA263

INLAND EMPIRE: NEW LISTING! Endo Practice. 4 Ops, 3 yr. new Equip., Digital, Cone Beam CT. 2014 GR $739K with low overhead. #CA281

INLAND EMPIRE: NEW LISTING! General Practice 7 Ops, Dentrix, Digital, Pano, 30 yrs. goodwill. 4½ days of Hygiene. #CA283

INLAND EMPIRE: NEW LISTING! General Dentistry, 4 Ops, Camera, Digital, Pano, 2014 GR $534K, Adj. Net 4196K. #CA285

LOS ANGELES: General Dentistry, 6 Ops, 5 Equipped, Est. 50+ yrs., SoftDent, Digital. 2014 GR $591K. #CA255

LOS ANGELES: Endo practice, 4 Ops, Cone Beam, 2014 GR of $360K on 21 hours/week. #CA259

N. ORANGE COUNTY: General Practice. 7 Ops, 6 Equipped, EagleSoft, Digital, Seller works 2 ½ days with GR of $542K. #CA248

ORANGE: General Dentistry. 4 Ops, Great location near Orange Circle. Est. 56 yrs. Digital. 2014 GR over $429K. #CA256

PALM DESERT: General Practice, 5 Ops, Est. for 32 yrs., 6 days of Hygiene/week/ GR of $824K and $339K Adj. Net. #CA245

PASADENA AREA: NEW LISTING! General Dentistry. 3 Ops, Dentrix, Dexis, CEREC, established for 50+ yrs. #CA283

PICO RIVERA: General Dentistry, 6 Ops, Est. in 1960. DentiSoft, Pano, 4½ days of Hygiene per week. 2014 GR of $690K. #CA258

S. ORANGE COUNTY: Pedo Practice with 4 Ops, 1 year new equipment, Digital, Pano/ $236K GR with room to grow. #CA222

SOUTH PASADENA: General Dentistry. 4 Ops, 3 Equipped, paperless, Digital, est. 37 yrs. 2014 GR $856K with $271K Adj. Net. #CA244

UPLAND: General Practice. 4 Ops, 3 Equipped. 25+ yrs. of Goodwill. 2014 GR of $221K with room to grow. #CA254 IN ESCROW!

VICTORVILLE: General Practice. 3 Ops, 3 Plumbed, 2,150 sq. ft. Est. 34 yrs., SoftDent. 2014 GR $273K. #CA149

WEST HOLLYWOOD: General Practice, 4 Ops, Intra-Oral Camera, Digital, Laser, 5 yr. old equip. 2014 GR of $613K . #CA212 IN ESCROW!

WHITTIER: General Dentistry. 4 Ops, 3 Equipped. Dentrix, Dexis. Est for 50+ yrs. on main street. 2014 GR $217K. #CA276

SAN DIEGO

CHULA VISTA: General Practice, est. 50+ yrs. 4 Ops, 3½ days of Hygiene, Dentrix. $493K GR in 2013. #CA109

COLLEGE AREA, SAN DIEGO: Very busy 6 Op General Practice with room to expand to 9 Ops. PPO, Dentrix, Digital. 2014 GR 1.7M. #CA231 IN ESCROW!

DOWNTOWN: Leasehold sale. Modern and chic downtown office in prime location. 3 Ops + room to expand. #CA232

ESCONDIDO: NEW LISTING! 4 Ops, 3 Chairs, Central Escondido, Doctor Retiring Excellent Opportunity to merge/ grow.#CA292

LA JOLLA: General Practice, 3 Ops, FFS and Delta Premier. 2014 GR of $559K. Owner retiring. #CA278

N. COUNTY INLAND: NEW LISTING! Highly regarded GP. FFS/PPO. 6 Ops. Free-standing building. #CA271 IN ESCROW!

S. BAY AREA, SAN DIEGO: General Dentistry, 3 Ops, 4 days hyg/wk. Retail center, Dentrix, Digital Pano, PPO & FFS. GR 2014 $524K. #CA206

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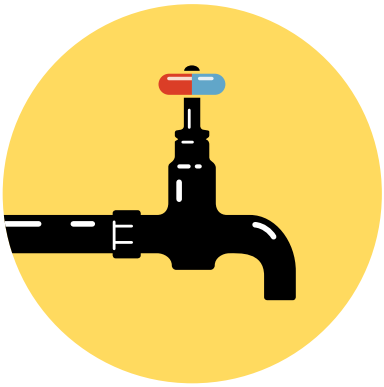

Combating an Epidemic of Prescription Opioid Abuse

Doreen Pon, PharmD, BCOP, BCPS; Kwaku Awuah; Danielle Curi; Ernest Okyere, PharmD; and Craig S. Stern, PharmD, MBA

ABSTRACT The past decade has witnessed an alarming increase in the number of deaths due to prescription opioids that has paralleled the rise in the number of opioid prescriptions dispensed. Prescription drug monitoring programs, abuse-deterrent formulations and proper disposal of opioids have been promoted to help combat the opioid epidemic. We discuss changes that dentists, the third most frequent prescribers of opioids, can implement to help reduce the risk of prescription opioid abuse in their communities.

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Conflict of Interest Disclosure: None reported.

The addiction and abuse potential of opioids is well-known, with tight regulations governing the prescribing and dispensing of these agents at the state and federal levels. In the late 1990s, however, greater focus began to be placed on the regular assessment and treatment of pain, with state medical boards loosening restrictions on the prescribing of opioids for chronic, noncancer pain. In 2001, the Joint Commission on the Accreditation of Health Care Organizations introduced new pain management standards, with recommendations to regularly assess and treat patients for pain by making "pain the fifth vital sign."[1] Coincidentally, around 2000, reports began to surface regarding adverse cardiovascular effects associated with selective cyclooxygenase-2 inhibitors (COX-2 inhibitors), which had been developed as safer alternatives to nonselective, nonsteroidal anti-inflammatory drugs (NSAIDs). In 2005, after reports of adverse cardiovascular effects associated with nonselective NSAIDs as well, the U.S. Food and Drug Administration (FDA) requested that warnings about adverse gastrointestinal and cardiovascular effects be added to all prescription NSAIDs. NSAIDs, along with acetaminophen and opioids, had been one of the most frequently utilized classes of drugs for the treatment of pain. Over the past decade, with fewer pharmacologic options perceived to be safe and effective for pain management, the use of opioids in the U.S. has significantly increased, with a similar increase in opioid-related overdoses and overdose-related deaths.[2] Easier access to prescription opioids, caused by increased prescribing, has undoubtedly contributed to the prescription opioid epidemic in the U.S. This article reviews the scope of and contributors to the current prescription opioid epidemic, and discusses various strategies that dentists can adopt to help combat the epidemic.

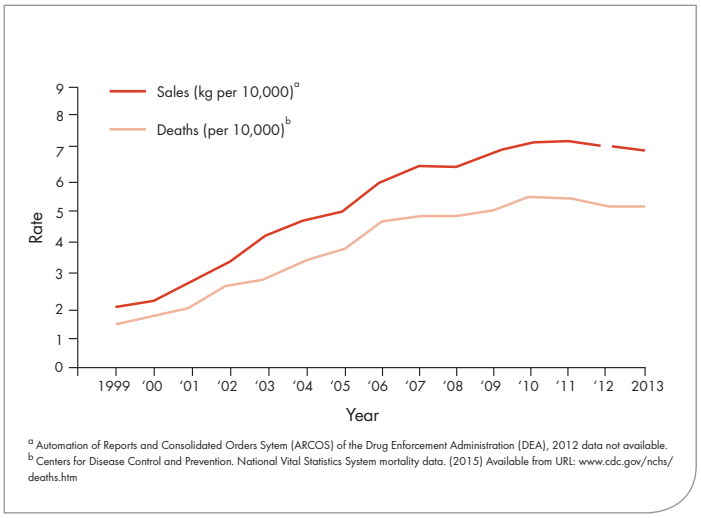

FIGURE 1. Rates of prescription opioid sales and deaths, 1999 to 2013.[5] Adapted from injury prevention and control: prescription drug overdose. Centers for Disease Control and Prevention website, www.cdc.gov/drugoverdose/data/index.html. Accessed May 2, 2015.

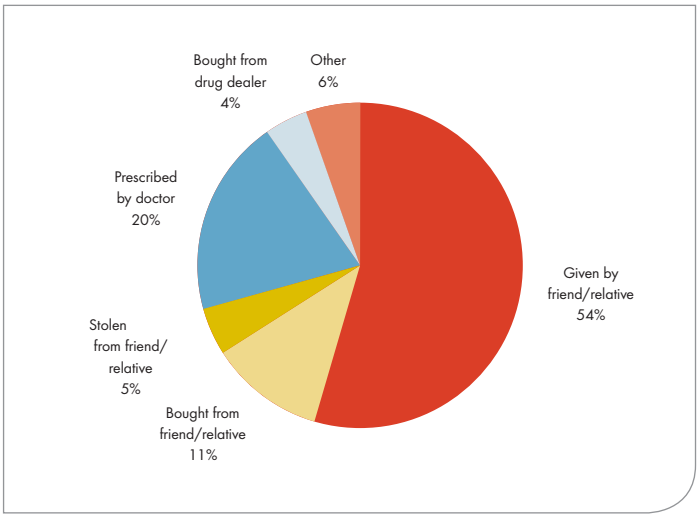

FIGURE 2. Source of prescription opioid used for nonmedical purpose.[14] Adapted from Jones CM, Paulozzi LJ, Mack KA. Sources of prescription opioid pain relievers by frequency of past-year nonmedical use: United States, 2008-2011. *JAMA Intern Med* 2014;174(5):802-3.

The Opioid Epidemic

Hydrocodone-containing products are the most frequently prescribed medication in the U.S., with 136.7 million prescriptions dispensed in 2011, bypassing chronic disease state medications, such as levothyroxine and simvastatin.[3] In fact, with just 4.6 percent of the world's population, the U.S. consumes 80 percent of the world's opioid supply and 99 percent of the world's hydrocodone supply.[4] Current data on annual opioid medication sales in the U.S. are estimated to equate to a quantity sufficient to supply every adult American with a 45-day supply of hydrocodone.[3] Between 1999 and 2013, the amount of prescription opioids dispensed in the U.S. and the number of deaths due to prescription opioids have both quadrupled, with more than 16,000 deaths attributed to opioids in 2013 (**FIGURE 1**).[5] Although the rate of opioid prescribing appears to be gradually leveling off, a significant decline in the rate of opioid prescribing has yet to be observed.

Dentists and the Opioid Epidemic

In a 2009 nationwide study of opioid prescribing patterns, dentists prescribed 8 percent of all prescriptions for opioids, just behind primary care physicians (28.8 percent) and internists (14.6 percent), and were the main prescribers of opioids for patients aged 10 to 19 (30.8 percent).[6] Dentists are also estimated to be frequent prescribers of immediate-release opioids, which tend to be more frequently abused than extended-release opioids.[7] It must therefore be considered that some of the opioids prescribed by dentists will end up being used for nonmedical purposes.

Dentists are uniquely positioned health care professionals in the community as they frequently come in contact with adolescents and young adults. The rates of current use of illicit drugs is highest among young adults aged 18 to 25 (19.6 percent) than any other age group.[4] Because adolescents and young adults may infrequently need to seek the care of other health care professionals, dentists may be the only health care professionals who will have the opportunity to screen many of the patients in this age group for potential substance abuse problems and help refer patients to available resources.

Acute Pain Versus Chronic Pain

Pain is often misleadingly classified as being either "acute" or "chronic" based on the duration of symptoms. While acute pain is usually thought of as a symptom of underlying tissue damage and activation of nociceptors caused by trauma or surgery that typically resolves as the injury heals, chronic pain may signal some sort of underlying disease pathology, as in the case of fibromyalgia or multiple sclerosis, or result from abnormal continued activation of nociceptors long after an injury has healed.[8] As such, pharmacologic interventions that may be useful for acute pain may have no effect in a patient with chronic pain and the management of a patient with chronic pain will usually require multiple modalities, with pharmacologic therapy playing a moderate adjunctive role.[8]

While there is evidence for the short-term use of opioids for the management of acute pain, the evidence for the long-term use of opioids for the management of chronic pain has come under scrutiny. A recent systematic review of the scientific literature found a lack of data regarding the effectiveness of long-term opioid use for chronic pain.[9] Despite widespread use of opioids for chronic pain, no controlled studies have evaluated the use of long-term opioids greater than one year for outcomes related to pain, function or quality of life.[9] On the other hand, evidence from

TABLE 1

Definitions to Describe Prescription Drug Misuse, Abuse and Related Events[13,28,29]

Misuse	Any intentional therapeutic use of a drug product in an inappropriate way.
Abuse	Any intentional, nontherapeutic use of drug product or substance, even once, for the purpose of achieving a desirable psychological or physiological effect.
Addiction	Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm and craving.
Aberrant Drug-Related Behavior	A behavior outside the boundaries of the agreed-on treatment plan which is established as early as possible in the doctor-patient relationship.
Physical Dependence	A state of adaptation manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug and/or administration of an antagonist.
Tolerance	A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more drug's effects over time.

Adapted from Savage SR, Joranson DE, Covington EC, Schnoll SH, Heit HA, Gilson AM. Definitions related to the medical use of opioids: Evolution towards universal agreement. *J Pain Symptom Manage* 2003;26(1):655-67. Smith SM, Dart RC, Katz NP, Paillard F, Adams EH, Comer SD, et al. Classification and definition of misuse, abuse, and related events in clinical trials: ACTTION systematic review and recommendations. *Pain* 2013;154(11):2287-96. Gourlay DL, Heit HA. Pain and addiction: managing risk through comprehensive care. *J Addict Dis* 2008;27(3):23-30.

observational studies appears to suggest that opioid therapy for chronic pain is associated with increased risk for overdose, abuse and dependence.[9] An observational study of patients receiving opioids for chronic noncancer pain found that, compared to patients taking no more than 20 mg of oral morphine equivalents per day, patients taking 50 mg to 99 mg per day had a 3.7-fold increase in overdose risk, and patients taking 100 mg or more per day had an 8.9-fold increase in overdose risk.[10] Various guidelines, therefore, recommend exercising extreme caution when prescribing greater than 90 mg to 200 mg of oral morphine equivalents per day for a patient, or consulting a pain management specialist for referral.[11,12]

Definitions Related to the Medical and Nonmedical Use of Opioids

Confusion is common among clinicians and patients regarding the terminology used to describe different patterns of nonmedical use of opioids (**TABLE 1**). For example, symptoms of physical dependence or tolerance to opioids are frequently mistaken for signs of opioid addiction. Many patients taking opioids on a chronic basis, whether for medical or nonmedical use, may exhibit symptoms of physical dependence, such as withdrawal symptoms upon abrupt discontinuation, or tolerance, such as requiring higher doses to achieve the same effects. However, these symptoms alone are not sufficient evidence of opioid addiction. A consensus definition developed by the American Pain Society, American Academy of Pain Medicine and the American Society of Addiction Medicine identifies four additional criteria for addiction: impaired control over drug use, compulsive use, continued use despite harm, or craving.[13] While opioid addiction implies ongoing nonmedical use of opioids, opioid abuse can include ongoing nonmedical use of opioids, as well as a one-time nonmedical use of an opioid. Opioid misuse, in contrast to opioid abuse, is defined as taking a prescription opioid for pain relief, but in a way not originally prescribed. For example, taking a higher dose or taking a dose more frequently than prescribed would be considered misuse. Taking an opioid that had been prescribed for dental pain when one has back pain would also be considered misuse.

Sources of Prescription Opioids Used for Nonmedical Purposes and the Role of Health Care Providers

Where do nonmedical users of prescription opioids obtain their opioids? Based on data from the National Survey on Drug Use and Health, an estimated 70 percent of nonmedical users obtained the opioids from friends or family members and only 20 percent reported obtaining the opioid through a legitimate doctor's prescription (**FIGURE 2**).[14] However, compared to those who reported the lowest frequency of opioid use (on to 29 days), those who reported the highest frequency of opioid use (200-365 days) were more likely to obtain opioids via prescription from a physician (17.9 percent versus 27.3 percent).[14] The sobering reality is that most prescription opioids that are being used for nonmedical purposes originated from legitimate prescriptions. Thus, efforts to combat the prescription opioid epidemic must target the diversion and sharing of legitimate prescriptions for opioids, as well as increased vigilance and screening for patterns of inappropriate opioid use before prescribing. Although most health care providers are well aware

of the potential dangers of prescription opioids, providers may not be as aware of the factors contributing the opioid abuse problem in the U.S. and recent policy changes to try to address the problem.

Prescription Opioid Hoarding

Given that the vast majority of nonmedical users of prescription opioids are obtaining them from friends or family members, there is a concern that most leftover opioid prescriptions end up in the medicine cabinet rather than being discarded. But why do patients have leftover prescription opioids in the first place?

Several studies have focused on trying to determine how many tablets of opioid medications patients actually use following painful procedures, compared to how many tablets they were prescribed. A 2006 survey of oral and maxillofacial surgeons in the U.S. revealed that 85 percent of the respondents almost always prescribed an opioid after third molar extractions and the average number of opioid tablets prescribed was 20 (range eight to 40).[15] However, the number of tablets patients actually consumed was not determined. To better characterize prescription opioid consumption following third molar extractions, Weiland et al. conducted a phone survey with 48 patients at 24 hours and seven days following surgery.[16] The median number of opioid tablets prescribed was 20 (range 10 to 40), and patients reported consuming a median of three tablets (range 0 to 10) at 24 hours, and a median of eight tablets (range 0 to 34) by day seven. None of the patients reported discarding their unused opioid tablets (median 12 tablets), and most reported storing the unused tablets in medicine cabinets.

A survey of adults in Utah confirmed that hoarding of leftover prescription opioids was common, with 72 percent of patients who had been prescribed an opioid reporting that they had leftover medication, and 71 percent of those patients reporting that they had kept the medication.[17]

Utilizing nonopioid analgesics and limiting the quantity of opioid medications prescribed after painful procedures may help to reduce the abuse and diversion of leftover prescription opioids. Additionally, all health care providers should educate patients on the hazards of hoarding and sharing leftover prescription opioids and counsel on recommended methods for disposal.

Disposing Leftover Prescription Opioids

The FDA recommends disposing of most medications by mixing with an unpalatable substance, such as used coffee grounds or kitty litter, placing in a sealed plastic bag and throwing in the household trash.[18] However, for certain controlled substances, such as the prescription opioids hydrocodone, oxycodone, hydromorphone, morphine and others, the FDA recommends that these controlled Schedule II medications be flushed down the toilet or sink to reduce the risk for overdose due to accidental ingestion.[18]

Alternatively, patients may turn in leftover prescription opioids to participating law enforcement agencies and pharmacies that are registered with the Drug Enforcement Agency to take back controlled substances.[19] In many communities, police stations have locked boxes for the collection of unneeded controlled substances. A few specially registered pharmacies may be able to accept leftover controlled substances for disposal. However, these registered and participating sites may be uncommon or difficult to find in the community.

The different recommended methods for disposing of different types of medications can cause confusion among patients and health care providers. Recently, AB 623 aimed at reducing prescription opioid-related deaths by reducing opportunities for inappropriate access was introduced in the California Legislature by Assemblymember Jim Wood, DDS (D-Healdsburg). One component of the bill proposed by Dr. Wood, a practicing dentist, would mandate that pharmacists counsel patients on the proper storage and disposal of opioids, thus helping to ensure that the majority of patients receiving prescription opioids are educated on how to safeguard the supply of prescription opioids in the community.

Abuse-Deterrent Formulations of Opioids

Abuse-deterrent formulations (ADFs) of opioids have been developed to prevent manipulation of the opioid formulations for the purpose of abuse. Some ADFs, such as hydrocodone extended-release (ER) and oxycodone ER, are formulated to resist physical alteration through chewing, crushing or dissolving, while other ADFs, such as morphine plus naltrexone and oxycodone plus naloxone, contain opioid antagonists that will block the euphoric effects of the opioid component when the formulation is manipulated through chewing, crushing or dissolving.[20]

Although ADFs may help to reduce abuse of the particular opioid formulation, they do not appear to be associated with decreased rates of opioid abuse and opioid-related deaths overall.[21,22] Unfortunately, as we have started to regain control over access to prescription opioids, more and more opioid abusers have begun turning to heroin as a cheap and readily accessible alternative. In one survey, although abuse of an ER formulation of oxycodone declined after it was changed to an ADF in 2010, reported use of heroin increased and 25-30 percent of respondents reported continued abuse of the oxycodone ADF.[23] Prescribers should therefore continue to exercise caution by limiting prescribing of ADFs of opioids.

Prescription Drug Monitoring Programs

Most states now have prescription drug monitoring programs (PDMPs), although the components of the programs are not all the same. It is hoped that accurately maintained PDMPs will help prescribers, pharmacists, law enforcement officials and regulatory boards to more effectively monitor and investigate

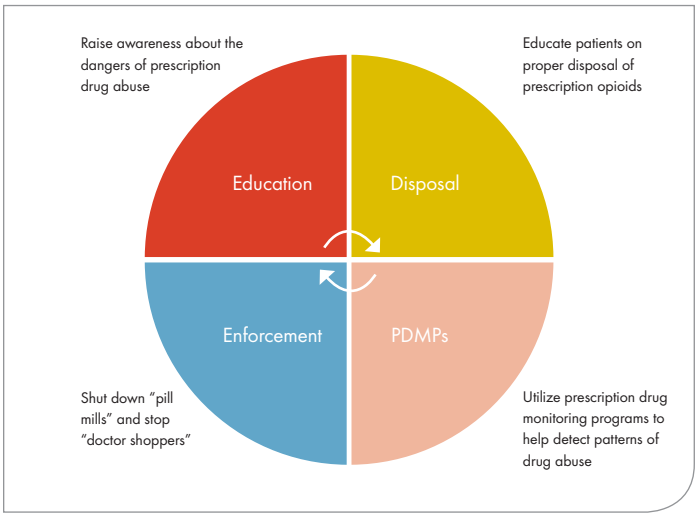

FIGURE 3. The prescription drug abuse plan.[30]
Adapted from Executive Office of the President of the United States. Epidemic: Responding to America's prescription drug abuse crisis, 2011. www.whitehouse.gov/sites/default/files/ondcp/policy-and-research/rx_abuse_plan.pdf.

TABLE 2

Reducing the Risk of Prescription Drug Abuse: Strategies for Health Care Professionals[7]

Screen for Substance Abuse	Inquire about alcohol, tobacco and drug use prior to prescribing opioids.
Minimize the Risk of Leftover Opioids	Prescribe the minimum quantity of opioid to manage acute pain. Educate patients to dispose of and never share leftover prescription opioids.
Prevent "Doctor-Shopping"	Use PDMPs to verify drug-use history. Be suspicious of patients who ask for specific drugs or report that their medication was lost or stolen.

Adapted from Denisco RC, Kenna GA, O'Neil MG, Kulich RJ, Moore PA, Kane WT, et al. Prevention of prescription opioid abuse: The role of the dentist. *J Am Dent Assoc* 2011;142(7):800-10.

patterns related to the prescribing, dispensing and use of controlled substances. California's PDMP is known as the Controlled Substance Utilization Review and Evaluation System (CURES) and is overseen by the California Department of Justice. Under CURES, information regarding prescriptions dispensed for Schedule II, III and IV substances must be electronically transmitted to CURES within seven days of dispensing.[24] While reporting of prescriptions to CURES is mandatory, checking the CURES database before prescribing or dispensing is currently not mandatory. However, health care providers involved in the prescribing or dispensing of controlled substances are encouraged to access the CURES Patient Activity Reports for patients under their direct care to assess for warning signs of inappropriate use of controlled substances, or "doctor shopping," a practice in which patients visit many different prescribers to obtain prescriptions. CURES appears to be an underutilized resource, with only an estimated 9.8 percent of the total number of licensed prescribers and pharmacists in California registered in 2014.[25] New legislation mandates that all California pharmacists and prescribers of controlled substances be registered with CURES by July 1, 2016, to facilitate ready access to records and help CURES realize its full potential.[24]

PDMPs have been implemented with the hope of helping to reduce the abuse and misuse of controlled substances, but without substantial evidence to demonstrate potential or actual benefits. Results have begun to trickle in from different states to suggest possible beneficial effects on the prescribing and dispensing of controlled substances after implementation of PDMPs. Florida's PDMP, implemented in 2011, was associated with a significant, 25 percent, decline in oxycodone-caused mortality, which was inversely related to the number of PDMP queries.[26] The investigators hypothesize that health care providers may have changed their prescribing habits for individual patients after querying the PDMP. Indeed, health care provider access to PDMP information has been shown to influence the prescribing habits of physicians treating patients presenting to the emergency department with painful conditions unrelated to acute injuries, with fewer or no opioids prescribed after reviewing PDMP data, compared to what was originally planned.[27]

Conclusions

The prescription opioid abuse problem has reached epidemic proportions in the U.S. A liberalized attitude toward prescribing of opioids that began over a decade ago has undoubtedly contributed to the problems we are experiencing now. Dentists, who are estimated to be responsible for 8 percent of all the prescriptions for opioids in the U.S. and the major prescribers of opioids among the 10-to-19-year-old age group, can play a major role in helping to combat the prescription opioid epidemic. Regaining control over access to prescription opioids will most likely require a multifaceted approach, including education, monitoring, proper disposal and enforcement, as no one intervention is likely to be successful on its own (**FIGURE 3**). Strategies that health care professionals should adopt to help reduce the risk for prescription drug abuse include screening patients for substance abuse prior to prescribing opioids, prescribing the minimum quantity of opioid to manage acute pain, educating patients to dispose of and never share leftover prescription opioids, and using PDMPs to verify drug-use histories and prevent "doctor shopping" (**TABLE 2**). However, as more programs are successfully implemented to control access to prescription opioids, health care professionals must also remain vocal advocates for their patients with legitimate needs for opioids, to ensure that the pendulum does not swing too far in the opposite direction, resulting in needless patient suffering. ■

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Drug Monitoring Programs Help Patients and Dentists

TDIC Risk Management Staff

Every day, dentists are called upon to relieve patients' pain. Sometimes that requires not only dental treatment, but also pharmaceutical assistance to manage pain while the patient heals. Opioid medications have been increasingly relied upon for pain relief, not only by dentists, but across the spectrum of health care delivery. In 2013, more than 137 million prescriptions of hydrocodone were dispensed in the U.S. Unfortunately, these drugs are also the most addictive and potentially deadly of prescription drugs. In the midst of intensified focus on opioid analgesics and rising abuse rates, public health agencies and government regulators are responding, and thoughtful and evidence-based prescribing is a necessity.

With such an important and prominent issue, The Dentists Insurance Company offers advice to dentists to protect both their patients and themselves from potential untoward consequences associated with pain management prescribing practices.

Risk management analysts suggest that when prescribing opioid analgesics, dentists prescribe only the required number of tablets and consider requests for refills cause for re-evaluating the patient's condition. Dental pain is most often acute pain associated with inflammation and in most instances should not require multiple prescription refills to manage. Analysts also note that prescription problems arise from inattention to the number of tablets and frequency of prescriptions provided, unfamiliarity with the drug or drug interactions and failing to maintain a current health history and record of the patient's current medications.

Further, analysts say common sense, prudence and accurate records are the most important things to keep in mind concerning prescriptions. Knowledge of the drugs prescribed and potential interactions or contraindications is essential, and the use of systems that demonstrate responsible prescription practices and contribute to full documentation are recommended.

The U.S. Drug Enforcement Administration estimates that seven million Americans abuse prescription medications, including opioid medications, prompting the recent reclassification of hydrocodone products, such as Vicodin and Norco, from Schedule III to Schedule II drugs.

Also developed as a tool to reverse this trend are state-run prescription drug monitoring programs (PDMPs). PDMPs have the capacity to collect and distribute controlled substance prescription information to authorized

users. Prescribers and pharmacists can access a patient's controlled substance prescription history prior to writing or dispensing a drug. This information can help prescribers and pharmacists identify patients exhibiting drug-seeking behaviors, as well as high-risk patients who could benefit from early intervention.

Analysts say dentists have multiple responsibilities when prescribing medication, and recognize the benefit of PDMPs for checking the patient's Schedule II history. This history provides additional information for decisions about abuse potential and whether to write a prescription for an opioid medication. From a liability standpoint, a dentist's risk increases if a patient suffers from abusing the drug and the dentist cannot prove diligence in checking the patient's history.

While PDMPs vary from state to state, 49 states have operational programs. The PDMP Center for Excellence reports 22 states, including Arizona, Minnesota, Nevada and North Dakota, have laws mandating that prescribers and, in some cases, dispensers use the PDMP in certain circumstances. Alaska, Hawaii, Illinois, New Jersey and Pennsylvania do not have mandatory enrollment, but do have PDMP databases.

In California, beginning July 1, 2016, all dentists who are authorized to prescribe, order, administer or dispense controlled substances are required to register for California's PDMP, known as the Controlled Substance Utilization Review and Evaluation System (CURES), administered by the state Department of Justice.

Analysts say systems such as CURES provide thorough documentation for dentists, and they can simply print the page with the patient's history and add it to the dental record. The following information is reported to CURES for each prescription dispensed:

- Patient's name, address, telephone number (if available), gender and date of birth.
- Prescriber's category of licensure, license number, National Provider Identifier (NPI) number and federal controlled substance registration number.
- National Drug Code (NDC) number of the controlled substance dispensed.
- Quantity of the controlled substance dispensed.
- ICD-9 (diagnosis) or ICD-10 code, if available.
- Number of refills ordered.
- Whether controlled substance was dispensed as a refill of a prescription or as a first-time request.
- Date of origin of the prescription.
- Date dispensing of the prescription is written.

Prescribers and pharmacists can access a patient's controlled substance prescription history prior to writing or dispensing a drug.

In states where PDMP use is not mandated, TDIC advises dentists to document, at minimum, the following prescription information in the patient's chart:

- Name and address of the patient.
- Date of transaction.
- Name, strength, quantity and nature of the controlled substances involved.
- Pathology and purpose for which the prescription is written.

Because PDMPs vary from state to state, guidelines for dispensing opioids exist in some states while other states are still developing guidelines. For instance, the Dental Board of California is currently working on guidelines to be released next year, while Pennsylvania guidelines on the use of opioids in dental practice were released in June.

The Pennsylvania guidelines state: "Opioid analgesics may be necessary for the relief of pain, but improper use of opioids poses a threat to the individual and to society. Providers have a responsibility to diagnose and treat pain using sound clinical judgment, and such treatment may include the prescribing of opioids. Providers also have a responsibility to minimize the potential for serious adverse effects, including the abuse and diversion of opioids." The Pennsylvania guidelines are available at www.padental.org/Images/OnlineDocs/ResourcesPrograms/Practice%20Management/opioid_dental_prescribing_guidelines3_13_15.pdf.

The following resources provide more information:

- Prescription Drug Monitoring Program Training and Technical Assistance at pdmpassist.org.
- Information on Drug Schedules I-V at dea.gov/druginfo/ds.shtml.
- More information on California's CURES program at oag.ca.gov/cures-pdmp.

Contact TDIC's Risk Management Advice Line at 800.733.0634.

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What to Expect When Cal/OSHA Comes Calling

CDA Practice Support

The following Q-and-A is an excerpt from the *Legal Reference Guide for California Dentists*, available on cda.org/practicesupport.

What triggers a Cal/OSHA inspection?

Cal/OSHA reviews all complaints and classifies each based on whether it presents an imminent hazard, is a serious complaint or is a nonserious complaint. Complaints from self-identified employees, employee representatives and government representatives are classified as formal complaints. All formal complaints trigger an on-site inspection. Nonformal complaints are those made by employees who do not identify themselves and by nonemployees. Nonformal serious complaints are investigated by telephone first, and may be followed by a letter or on-site inspection. Nonformal nonserious complaints are investigated by a letter to the employer in lieu of an on-site inspection. However, Cal/OSHA district managers have some discretion to conduct on-site investigations of these complaints. A complaint is invalid if the district manager determines it involves willful harassment of an employer. Cal/OSHA is not obliged to provide the employer with the identity of the complainant. Cal/OSHA also conducts "programmed inspections" when it is targeting an industry. For example, agriculture and the garment industry have been targets of programmed inspections. There is also a possibility that your practice will be inspected if a neighboring dental office has had frequent complaints and inspections.

I received a letter from the Division of Occupational Safety and Health regarding a complaint – what should I do?

Respond to Cal/OSHA's request for information to the extent possible. Provide photographs if they are useful. Once you have provided the information, do not expect Cal/OSHA to send you a notice that you have satisfactorily answered its inquiries. If Cal/OSHA finds your response unsatisfactory, an unannounced on-site inspection will occur. Cal/OSHA may choose to investigate some nonformal serious complaints by telephone or fax. It contacts employers first by telephone, then by faxed letter. The employer has five working days to respond; employers who do not respond are scheduled for an on-site inspection. Follow-up inspections may occur for some of the complaints handled through this process. You can find Cal/OSHA's policy and procedures for complaint evaluation and documentation online at www.dir.ca.gov/doshpol/p&pc-7.htm.

Do I have to provide the Cal/OSHA inspector access to my staff and office?

Always verify the identity of individuals to whom you allow access to your office. Cal/OSHA prefers to have your permission to conduct the inspection. An inspector may be willing to wait while you finish treating a patient, but will not wait beyond a reasonable time. If you are not present at the office when the inspector arrives, Cal/OSHA staff will attempt to contact you by telephone to gain permission. If the inspector cannot contact you, he or she will document the attempts to gain your permission and then will commence the inspection. If you refuse permission, the inspector will report back to the district manager, who will initiate the process for obtaining a warrant or taking other appropriate action.

What happens during a Cal/OSHA inspection?

Complaint-based inspections are unannounced. Cal/OSHA will request the presence of the employer or a representative for the inspection. You can accompany the inspector during the walk-through of the facility, but you may not be present during the inspector's interviews with staff. An employee or employee representative may also accompany the inspector during the walk-through. The inspection starts with an opening conference in which the inspector provides information on the purpose and scope of the inspection and how it will be conducted. The inspector reviews required written plans and then walks through the facility, taking photographs and speaking with staff as needed. At the end of the walk-through, the inspector meets with the employer for an exit conference. If violations were observed, the inspector may issue citations during the exit conference or provide the employer with a preliminary report, with citations to be issued at a closing conference that will be scheduled later. During the closing conference, Cal/OSHA staff review their findings, including the nature of the violations and how they can be abated, with the employer. Penalties are proposed and the employer is informed of the requirement to post a citation and other notices so employees may view them. Cal/OSHA informs the employer of the opportunity to hold an informal conference with the district manager to discuss the citation and penalties and of the separate opportunity to appeal. Cal/OSHA's inspection procedures are detailed in its policies and procedures manual, available at www.dir.ca.gov/samples/search/querypnp.htm.

I was cited by Cal/OSHA – what should I do? Do I need an attorney?

At the closing conference, Cal/OSHA staff will have reviewed their findings with you or your representative. You may choose to take one of these actions: 1. Correct the violations and pay

the proposed penalties. In this scenario, you effectively agree that there were violations and you will not appeal the citations. 2. Appeal the citations and proposed penalties. File an appeal with the Occupational Safety and Health Appeals Board within 15 working days of receiving citations. You can also request an informal conference with the district manager while you await your appeal hearing. An informal conference allows you to present evidence, offer explanations and clarify issues. After an informal conference, a district manager will determine if it is appropriate to withdraw or amend citations and revise penalties. An informal conference does not negate your right to a hearing before the Appeals Board, nor is it the same as the prehearing conference scheduled by the Appeals Board, although the scope is the same. You may request an informal conference any time before the day of the appeal hearing. Additional information on the appeals and hearing process and on informal conferences can be found in the Cal/OSHA policies and procedures manual at www.dir.ca.gov/samples/search/querypnp.htm. Whether you need or want an attorney depends on the nature and scope of the citations. A few nonserious violations may not warrant it, but seeking legal counsel is advisable for serious violations such as an injury to an employee or an alleged unsafe work environment.

I'd like to use the Cal/OSHA consultation service – is that a good idea?

Cal/OSHA offers a consultation service (800.963.9424), and a list of regional offices can be found at www.dir.ca.gov/dosh/consultation.html. Consultation staff can answer your questions via telephone and are available to conduct on-site assistance such as mock inspections. Consultation staff does not share information with Cal/OSHA enforcement staff about the businesses it assists. On-site consultations do not result in citations, but employers are expected to correct identified hazards in a timely manner.

What resources does CDA Practice Support provide to assist with compliance?

In addition to the previously mentioned CDA *Regulatory Compliance Manual* that contains sample written plans and necessary forms, you will find the following on cda.org/practicesupport:

- Cal/OSHA Training Requirements – checklist.
- Blood-Borne Pathogens Post Exposure Management Protocol – checklist, poster in poster set.
- Infection Control and Cal/OSHA – Q-and-A.
- Hepatitis B Vaccination: Requirement and Recommendations – article.

Regulatory Compliance appears monthly and features resources about laws and regulations that impact dental practices. Visit cda.org/practicesupport for more than 600 practice support resources, including practice management, employment practices, dental benefit plans and regulatory compliance.

Periscope offers synopses of current findings in dental research, technology and related fields

ORAL AND MAXILLOFACIAL PATHOLOGY

Distinct pathobiological behavior of oral mucosal melanoma

Tlholoe MM, Khammissa RAG, Bouckaert M, Altini M, Lemmer J, Feller L. Oral Mucosal Melanoma: Some Pathobiological Considerations and an Illustrative Report of a Case. *Head Neck Pathol* 2015; 9: 127-34.

Purpose: To illustrate the distinct differences between oral mucosal and cutaneous melanoma, the authors discuss the pathobiological aspects of the oral mucosal melanoma and present an illustrative case.

Background: Mucosal melanomas are somewhat rare, representing only 1.3 percent of all melanomas, and are accompanied by aggressive behavior and poor prognosis. They are distinct from cutaneous melanoma because they arise in areas not exposed to sun, have different cytogenetic changes and have different behavior and clinical course. Twenty-five percent of all mucosal melanomas arise in the oral mucosa. They may arise de novo, but approximately one-third arise from benign oral melanotic lesions. They are generally painless and grow rapidly and up to 36 percent will have cervical metastases and 85 percent will have distant metastases early in the course of the disease.

Discussion: Oral mucosal melanomas are usually painless, irregularly shaped, with variation in color from brown to blue to black, and are flat, nodular, plaque-like or a combination of these forms. Lesions excised when the malignant melanocytes proliferate within the epithelium (radial growth phase) prior to deep invasion have a relatively good prognosis. Once invasion into the submucosa into nodular aggregates occurs, there is a much less favorable clinical outcome. Once melanocytes undergo premalignant transformation, they may acquire additional cytogenetic changes, allowing them to acquire a malignant phenotype. Gain of function mutations or gene amplifications are much more common in oral mucosal melanomas than in their cutaneous counterparts. Conversely, some proto-oncogenes, such as BRAF, that are mutated in cutaneous melanoma are uncommon in the oral mucosal melanomas. These indicate differences in molecular tumorigenic pathways. The more aggressive nature and worse prognosis of oral melanomas, with a mean survival of two years, may be due to their painless and somewhat more hidden nature in addition to molecular differences.

Conclusions: Oral mucosal melanomas are especially aggressive malignancies that most often affect the palate and maxillary alveolar gingiva, are painless and grow quickly. They are often diagnosed late in the clinical course, commonly with loco-regional and distant metastases found. Early detection of this malignancy prior to invasion improves the chance for survival.

– David Cox, DDS, MBA

ORAL AND MAXILLOFACIAL SURGERY

Medication-related osteonecrosis of the jaw

Ruggiero SL, Dodson TB, et al. American Association of Oral and Maxillofacial Surgeons Position Paper on Medication-Related Osteonecrosis of the Jaw – 2014 Update. *J Oral Maxillofac Surg* 72:1938-1956, 2014. 2014 Oct;72(10):1938-56. doi: 10.1016/j.joms.2014.04.031. Epub 2014 May 5.

Purpose: Updated position paper from the national OMS society on the topic of medication-related osteonecrosis of the jaw (MRONJ).

Materials, methods and strength of evidence: Clinical experience, research and literature review used to update the risks, diagnosis, staging and management strategies of MRONJ.

Results: As the knowledge base and experience expands, it is critical to disseminate information about MRONJ to other relevant health care professionals and organizations, reflecting current data against historical practice.

Clinical relevance: Topics including dental implants, surgery, drug holidays, treatment recommendations and ongoing research are discussed.

– Steve Leighty, DDS

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ORAL AND MAXILLOFACIAL SURGERY

Prophylactic antibiotics in patients with prosthetic joints

Sollecito TP, Abt E, et al. The Use of Prophylactic Antibiotics Prior to Dental Procedures in Patients With Prosthetic Joints. *J Am Dent Assoc* 2015:146(1):11-16.

Purpose: Collaborative panel of experts disseminating evidence-based clinical practice guidelines on the use of prophylactic antibiotics in patients with prosthetic joints who are undergoing dental procedures.

Materials, methods and strength of evidence: Clarifies the 2012 panel of ADA and American Academy of Orthopaedic Surgeons findings, along with extensive literature review.

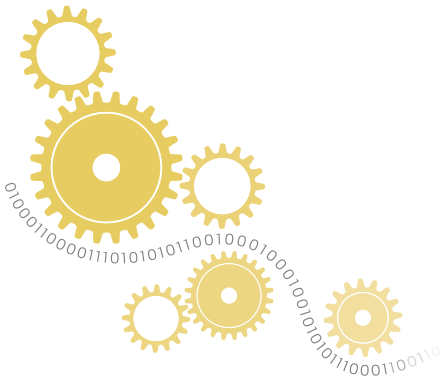
Results: In general, premedication is not recommended for joint replacement patients prior to dental procedures. Exceptions for higher-risk patients with special conditions are made.

Clinical relevance: In efforts toward best-practice and evidence-based dentistry, it is important to keep up with the "moving target" of prophylactic antibiotics use. Antibiotic resistance, allergies and adverse drug reactions are compelling reasons to avoid indiscriminate or cavalier use of antibiotics.

– Steve Leighty, DDS

Editor's note

Steve Leighty, DDS, an oral and maxillofacial surgeon practicing in Auburn and Roseville, Calif., passed away in mid-October. He served as an expert on the Periscope Editorial Board and as a reviewer for the Journal. *We are so grateful for his friendship and will miss him dearly.*



A look into the latest dental and general technology on the market

iPhone 6s (Apple)

Following the established schedule of a new iPhone every September, Apple has released the iPhone 6s. New with this latest generation iPhone is 3D Touch, whereby the phone is able to detect how hard the user presses on the screen and can respond dynamically depending upon the app being used. This is the smartphone-equivalent of a "right-click," allowing the user to preview the contents of an email message, queue up a music playlist, etc. The two cameras have also received significant upgrades, with the primary iSight camera now able to capture 12-megapixel still photos and 4k video (up to four times the resolution of 1080p HD video) while the front-facing FaceTime camera now captures selfies at 5 megapixels. In addition, Apple has introduced Live Photos, which capture the moments just before and after your picture and allow you to virtually "animate" your still photos with just the press of a finger. Boasting 2GB of RAM and a new A9 processor, the iPhone 6s is noticeably faster and more responsive than the iPhone 6, and significantly faster than any of the previous generations of iPhones. TouchID has also been improved for far quicker response times. Users get near-instantaneous unlocking of the device by simply placing their thumb over the sensor.

– Blaine Wasylkiw, CDA director of online services

Pocket (Read It Later Inc., Free)

Pocket for iOS allows users to save anything from a Web browser or other apps for viewing later on almost any device. Signing up with an email address or a Google account is required. Saving anything to Pocket is easy. From the web browser, users can save any site by using the "Share" button and selecting the Pocket icon. Videos, photos and links can be saved in the same manner. Saved items are stored for offline viewing later only on the device that saved the item. Many other apps have Pocket integration built in. For example, once connected to a Pocket account on the Twitter app, users can press on any link and have the option to send directly to Pocket. There are more than 1,500 applications with Pocket integration across multiple platforms including Mac, iOS, Android, Windows and Blackberry. Items can also be emailed from an authorized account to Pocket for storage. Viewing saved items in Pocket is also simple. On the iPhone, users can select from a listing of all their saved items with small picture previews. On the iPad, users can select from a panel grid of their saved items with slightly larger and more detailed previews. Unless stored directly on the device in which items were saved, viewing items requires an Internet connection to load the content.

– Hubert Chan, DDS

Number of Health Apps Hits 165,000

More than 165,000 mobile health apps are now available to consumers, according to a study from the IMS Institute for Healthcare Informatics. The IMS study found that the number of clinical trials utilizing health apps has more than doubled in the last two years, focusing on treatment and prevention of disease, and largely focused on the senior population, according to the study. Price isn't much of a factor as more than 90 percent of health apps are free. Several clinical organizations are tapping into their clinical resources to develop and promote patient-centered apps. Barriers remain to full adoption, however. This is a result of a "lack of scientific evidence, limited health care system integration, regulator and privacy unknowns and few provisions for reimbursement," according to the study.

– Blake Ellington, Tech Trends editor

Brushing App Has Impact on Oral Health

The Brush DJ app aims to motivate users to brush for the ADA-recommended two to three minutes. The app, which was featured in the December 2013 *Journal of the California Dental Association*, does this by playing music, taken either from the users' playlist or from the cloud. According to a new study published in the *British Dental Journal*, the app is helping change brushing habits. Specifically, of the 189 people who participated in the study, 70 percent reported that their teeth felt cleaner since using the app and 88 percent reported the app motivated them to brush their teeth for longer. Further, 92 percent would recommend the app to their friends and family. Four broad themes relating to how the app helped tooth brushing were reported: motivation, education, compliance and perceived benefits. Brush DJ launched in 2011. According to a news release, the app had been downloaded to more than 197,000 mobile devices by February 2015.

– Blake Ellington, Tech Trends editor

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LOS ANGELES COUNTY

CANOGA PARK (GP) - ***Price Reduced!!*** Turn-key practice w/ 2 equipped operatories, 1 x-ray room w/ chair in a 3 story medical dental building. Grossed approx. $147K in 2014. **Property ID #4237.**

CHATSWORTH (GP) – ***Price Reduced!!*** 5 equipped operatories. Grossed $918K in 2013. Projecting approx. $948K for 2014. Buyer's net of $398K. **Property ID #4537.**

Downey—GP with 47 years of goodwill. State of the art practice with 3 equipped ops in a 1,214 sq ft office. Easy Dental Software. Proj. $416K for 2015. Buyer's net of $154K. **Property ID #5080**

DUARTE—Turn-Key general practice in busy shopping center. 2 eq ops / 1 plumbd not eq. PPO/Cash/Denti-cal/Cap. **Property ID #5048.**

HUNTINGTON PARK (GP) - 30 years of goodwill located in strip shopping center. 3 equipped ops. Some Denti-cal. Buyer's Net of $104K. **Property ID #5054.**

LAWNDALE— Turn key general practice in a 2 story bldg with large signage. Has over 45 years of goodwill. Consists of 4 eq ops and 2 plumbed not eq. Has digital x-ray. Long term lease. Great opportunity. **Property #5051.**

LOS ANGELES (GP/Perio/Implants) - Beautiful practice. 5 equipped operatories w/ amazing views to the city. Buyer's net of $146K. In the Miracle Mile. **Property ID #4489.**

NORWALK— General practice w/ over 65 yrs of goodwill located in a well know community. 3 ops / 1 plmd not eq. NET $95K. **Property ID #5026.**

RESEDA – 3 equipped operatories (stand up dentistry). Grossed $281K for 2014 with monthly revenues of $22K. **Property ID#5017.**

TORRANCE (GP) 30 years of goodwill in a 3 story medical/dental bldg. 5 equipped operatories. Proj. approx. $325K for 2014. Net $103K. **Property ID #5036.**

WEST COVINA —Leasehold Improvement and Equipment Only! Brand new built out practice located in a new community near the Foothill Mountain. 7 ops / 1 plmbd not eq. **Great opportunity. Property ID #5077.**

WHITTIER - ***Price Reduced!!*** Leasehold Improvements & Equipment Only! Modern designed office in 4 story professional building. 5 eq ops. Has long term lease. **Property ID #5053.**

ORANGE COUNTY

ALISO VIEJO (Pedo) – 20 years of goodwill. 3 chairs in open bay 1 plumbed not equipped op. Buyer's net of $108K. **Property ID #5031.**

Irvine—Leasehold Improvement and Equipment Only! Pedo/Ortho/GP office w/2 eq ops & 3 chairs in Open Bay in Medical Bldg. **Property #5078.**

LAGUNA HILLS ***Price Reduced!!*** Modern designed GP. 15 years goodwill. 2 equipped ops. Private office plumbed. Buyer's net of $101K. **Property ID #5033.**

ORANGE- GP with over 40 yrs of gdwl located in a free standing bldg on a major Ave of Orange w/ plenty of heavy traffic. Net of $258K. **Property ID #5059.**

Rancho Sta Margarita—State of the Art practice located in a 2 story shopping plaza. Beautiful office with 7 eq ops. approx. 35-40 new patients/mo. Proj. approx. $811K for 2015. NET of $270K. **Property ID #5079.**

SAN JUAN CAPISTRANO (GP) - Well established Turn-key practice. 4 equipped operatories, 3 plumbed not equipped in 1,947 sq ft suite. Grossed ~$241K in 2014. **Property ID #5052.**

SANTA ANA - This GP is located in a 2 story strip mall with ample parking. Consists 4 eq ops. NO HMO. Proj. approx. $538K for 2015. **Property ID #5075.**

KERN, VENTURA,COUNTY & SAN LUIS OBISPO

BAKERSFIELD (GP) This office offers 18 yrs of goodwill. Consists of 6 eq ops, 1 plmbd not eq in a 1,800 sq ft suite. Proj. approx. $358K for 2015. Prop**erty ID #5060.**

SAN LUIS OBISPO COUNTY - Beautiful well established practice w / 6 equipped operatories in a 2,626 sq ft suite. Net $370K. **Property ID #5037.**

SIMI VALLEY (GP + Bldg for sale) Great opportunity to invest in a general practice and real estate. Established in 1964, 4 equipped operatories, 2 plumbed not equipped. Net $124K. **Property ID #5027.**

SAN DIEGO COUNTY

EL CENTRO (GP) – This practice is located in a single story building. Building is for sale. 5 equipped operatories. Projecting approx. $335K for 2015. Buyer's net of $86K. **Property ID #5023.**

Oceanside (GP) - Estab. In 1998 this practice is located in prof. med dent bldg. 5 ops computerized with digital laser x-ray. PPO/Cash/HMO. Projecting approx. $358K for 2015. **Property ID #5069.**

San Diego - GP located in a 3 story prof. bldg. 7 ops in a 2,980 sq ft suite. Proj. approx. $1.9M for 2015. NET $397K. **Property ID #5072.**

RIVERSIDE & SAN BERNARDINO COUNTY

APPLE VALLEY - 3 equipped operatories. Seller is working 4 days/wk and sees ~15-20 patients/mo. Monthly revenues of $44K. Net of $119K. **Property ID#5009.**

CHINO— Leasehold Improvement and Equipment + Condo. 4 chairs in open bay in single strip mall. This facility has been always at this location for 40 yrs. **Property ID #5076.**

CHINO HILLS - Leasehold Improvement and Equipment Only! 3 equipped ops 2 plumbed not equipped. New built out. Restaurants and Retails stores surround the practice. **Property ID #4501.**

INDIAN WELLS (GP) Modern designed practice with 4 equipped operatories in a 2,850 sq ft office. In shopping plaza. **Property ID #5041.**

MURRIETA - Well established general practice with 4 eq ops in a 2 story medical dental bldg. PPO & Cash only. BUYER'S NET OF $154K. **Property ID #5061.**

PALM DESERT—Well established practice in a free standing bldg. This modern designed practice consists of 5 eq ops in a 2,350 sq ft office. 100% patient referral. Insurance and Cash only. Does 8 days of hygiene. NET OF $361K. **Property ID #5058.**

PALM SPRINGS – General practice with 3 equipped ops located in a free standing bldg. Established in 2005. Suite is approx. 1,200. PPO/Cash /Denti-cal. Seller work 5 days/wk. Great opportunity. BUYER'S NET OF $175K. **Property ID #4487.**

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BAY AREA

AC-460 SAN FRANCISCO: Turn-Key Practice in great location Priced to Sell! 900 sf w/ 2 ops + 1 add'l. **$110k**

AC-335 SAN FRANCISCO: Two great practices for the price of one! **Now Only $475!**

AG-053 SAN FRANCISCO: 3,000 sf w/ 9 ops + 1 add'l. PRIME LOCATION! **REDUCED $400k**

BN-183 HAYWARD: ***Kick it up a notch by increasing the current very relaxed work schedule!*** 1,300 sf w/ 3 ops **$150k**

BN-279 CONTRA COSTA COUNTY: Excellent Merger Opportunity! 2-story. 1,350 sf w/ 3 ops +1 add'l **$60k**

BC-361 OAKLAND: Established for over 23+ years! 2,200 sf w/ 7 ops. **Now Only: $385k**

BC-381 PLEASANT HILL Facility: Open Floor Plan! 1,852 sf w/ 6 equipped ops! Move in Ready! **$80k**

BG-407 SAN LEANDRO: Prof bldg. Great signage! 1200 sf w/ 3 ops **$125k**

BN-426 BERKELEY: Step into this quality practice and you'll know you belong here! 1,384 sf w/ 3 ops. **$495k**

BC-432 PITTSBURG: Own this family-oriented Practice! 1,640 sf w/ 6 ops. **$350k**

BC-487 MARTINEZ Facility: Martinez/Pleasant Hill Border, Great for Specialist, 1750sf. 1op +5 add'l plumbed **$60k**

BN-452 CONCORD: Do not hesitate to act fast as this is a rare opportunity! 1,951 sf w/ 4sops. **$525k**

BN-463 FREMONT: Gross Revenues Exceeded $590k in 2014 on 4 day work week! 1,720sf w/ 3op + 4 add'l. **$485k**

CC-390 SOLANO COUNTY: Near Travis AFB! Highly visible location! 950 sf w/ 3 ops **Seller Motivated! REDUCED! $145k**

CC-456 SOLANO COUNTY: Highly visible location! 2,997 sf w/ 6 Dr ops + 2 Hyg ops +1 add'l **$850k**

CC-488 SANTA ROSA: State of the art office, wonderful views, great location w/ lots of potential 900sf w/ 3ops **250k**

CG-366 SONOMA CO.: Vibrant, growing community! 1,300+ sf w/ 4 ops. Over $760k in collections! **$420k**

CN-482 SANTA ROSA: Rare Opportunity in highly desirable area. 1050 sf w 3 ops **ONLY $150k**

DC-370 SAN JOSE: Facility Only. 1,600 sf w/ 3ops. Real Estate also available for purchase **$120k (Real Estate $1.5M)**

DC-476 DUBLIN: Shared Facility. Great for Specialist - Endo, Pedo or Ortho. 1100 sf w/ 2 ops+1 add'l **$125k**

DC-419 NEWARK Facility: Location, Location, Location! High Traffic Area, 1,400 sf w/ 4 ops **$120k**

DC-406 SAN JOSE: Amazing opportunity in Westgate Shopping Center. 6 ops + 80 mall hours per week **$400k**

DN-447 SUNNYVALE: Quality, family-oriented opportunity awaits your talent and skill. 1,200 sf w/ 3 ops + 1 add'l. **$395k**

DN-467 GILROY Facility: This traditionally styled practice is perfectly situated! 1,325 sf w/ 3 ops + 1 add'l. **$75k**

NORTHERN CALIFORNIA

EN-340 SACRAMENTO: Large HMO practice! 3,400 sf w/ 10 ops and Plumbed for 1 add'l **$950k**

EN-378 LINCOLN: quality practice with a wonderful patient base! 1,369 sf w/ 2 op + 3 add'l. **$170k**

EN-379 ROSEVILLE: An amazing opportunity in the location of your dreams! 1,040 sf w/ 3ops. **$295k**

EN-423 FOLSOM Oral Surgery Facility: 3,450 sf w/ 2 Lrg. Treatment Rooms. **Now Only $1 w/ Lease Assumption!**

EN-464 ROCKLIN Facility: Don't miss out on this remarkable opportunity! 2,150 sf w/ 4 ops. **$150k**

EN-475 ROSEVILLE Facility: Hesitate and you might miss out on this opportunity! 875 sf w/ 2 ops + 2 add'l. **$49.5k**

EG-479 FOLSOM: History is alive here with tributes to the past! 1,600 sf w/ 3ops. **$225k**

EN-484 FOLSOM Facility: Come live, practice and grow here! 1,934 sf w/ 4 Ops. **$150k**

FN-299 FERNDALE: Live and practice on the beautiful North Coast! 1,300 sf w/ 3 ops **$195k (Real Estate: $309k)**

FC-334 NORTHERN CA: Emphasis on prevention. 1,200 sf w/ 4 ops **$480k / Real Estate Also Available!**

FC-343 NORTHERN CA: Quality & location are the keys to success! 1,200 sf w/ 3 ops + 1 add'l & 1 hyg. Op. **$500k (Real Estate $375k)**

FC-415 FT. BRAGG: Excellent practice in peaceful, family -oriented community! 1,800 sf w/ 5 ops + 1 hyg. Op. **$425k**

GC-472 ORLAND: 1,000 sf w/ 2ops. Seller Retiring. **$160k**

GG-386 REDDING: Amazing Practice. Lease or Buy Real Estate! 2,860 sf w/ 4 ops. Plumbed for 2 add'l! **ONLY $285k**

GG-453 CHICO: 5,000 sf 7 ops Perfect for 1 or more dentists! **$395k**

GG-454 PARADISE: ~2,550 sf w 9 ops. 40 yrs goodwill! Amazing Opportunity! **$595k**

GN-201 CHICO: Beautiful practice, major thoroughfare, stellar reputation! 1,400 sf w/ 4 ops & room for another **$425k**

GN-244 OROVILLE: Must See! Gorgeous, Spacious. 2,500 sf w/5 ops! Collections over $450k in 2013. **Only $315k**

GN-258 REDDING: Pristine and attractive! Conveniently located! 2,100 sf w/ 3 ops + 2 add'l. **$300k**

GN-399 REDDING: Loyal patient base and relaxed workweek schedule. 1,440 sf w/3 ops. **$150k**

GN-418 REDDING: **Goodwill Galore!** Established for ~37 years. Seller is retiring! 3,200 sf w/6 ops +2 add'l. **$495k**

HG-298 REDDING FOOTHILLS: **HEALTH FORCES SALE!** Includes Cerec! 2,000 sf w/ 5 ops. **Practice $100k / Real Estate $250k**

HN-213 ALTURAS: Close to Oregon Border. FFS practice is 2,200 sf w/ 3ops +1 add'l **$115k**

HN-280 NORTHEASTERN CA: "Only Practice in Town" 900 sf w/ 2 ops **$110k**

SALES

NORTHERN CALIFORNIA CONTINUED

HN-290 PLACERVILLE: **Excellent Merger Op!** FFS. 1,400 sf w/ 4 ops **$210k**
HG-448 LAKE TAHOE AREA: **Call for Details!** Upscale Family Practice. 3400sf w 6 ops **$725k**

CENTRAL VALLEY

IG-367 MERCED: Newly Remodeled, Paperless. 1,550 sf w/4 ops **REDUCED! $325k**
IG-470 TRACY: Amazing opportunity. 1300 sf w/ 4 ops **$270k**
IN-345 MODESTO: Long-standing tradition of quality care. 3016 sf w/ 5ops + 1 add'l. **$495k**
IN-358 MODESTO: Practice nets over 50%! 1,200 sf, 3 ops+1 add'l. **REDUCED! $275k**
IN-397 FRESNO/MADERA: Focused on quality dental care & patient comfort! 2,000 sf w/5ops. **Seller Motivated: $440k**
IN-429 TRACY Facility: "Move-in ready" Hesitate and you might miss out! 2,488 sf, 5 ops **$245k/RE: $650k**
IN-474 STOCKTON: Too good to be true? Absolutely not! 1,600 sf w/ 3 ops. **$95k**
IC-468 SAN JOAQUIN VALLEY: High-End Restorative Practice! Don't miss out! 2,500 sf w/ 6ops. **$425k**
JC-349 FRESNO Facility: Motivated Seller retiring! Step right in and make yours! **Call for Details!**

SPECIALTY PRACTICES

I-9461 CENTRAL VALLEY Ortho: 1,650 sf w/5 chairs/bays & plumbed for 2 add'l **$180k**
DG-264 SAN JOSE Ortho: $300-400k in build-outs alone! 1800 sf w/ 5 chairs. **REDUCED! $195k**
CC-346 SO MARIN CO Perio: 1,142 sf w/ 3 ops. Meticulously maintained! **REDUCED! $199k**
BN-393 PINOLE Pedo: Popular Pedo Practice w 2,000 sf & 5 ops. **$1.2m**
CG-424 NAPA Prostho: Ready for Experienced, high-end Prosthodontist! One track to collect just under $1m **$725k**
CC-405 SOLANO CO. Endo: Endodontic Practice in a vibrant community! 1,250 sf w/ 4 ops. **$485k**
IC-267 CENTRAL VALLEY Ortho: beautifully landscaped. 1,728 sf w/ 6 chairs/bays + 1 add'l. **$225k / Real Estate Also Available!**
DC-459 SF PENINSULA (Perio): 50% Partnership Buy In! Call for Details! **$580k**
CG-481 S SONOMA CO (Ortho): 2070 sf w 7 chairs + 1 exam in Med/Prof Plaza **$295k**

ASK THE BROKER

Timothy G. Giroux, DDS is currently the Owner & Broker at **Western Practice Sales** and a member of the nationally recognized dental organization, ADS Transitions.

You may contact ***Dr Giroux*** ***at:*** **wps@succeed.net or 800.641.4179**

Corporate Dentistry is Here to Stay (Part 2)

Last month I gave three reasons why Corporate Dentistry is here to stay. While I do concur that Corporate Dentistry will continue to grow over the next several years, I believe that it will also reach a lower peak point than where most of the industry professionals think it will hit. Currently Corporate Dentistry comprises approximately 20% of the industry. Many think it may double in the next few years. Below are some reasons that I believe its growth will be self- limiting:

1.) While Corporate Dentistry has perfected the new forum of marketing through social media and the internet, I believe that patients will eventually sense that corporations exist to make a profit. While private practitioners obviously need to make a profit to stay in business, I still believe that most dentists realize that if patient concerns come first, the financial rewards will follow. Patients also want to know that the doctor giving them an injection with a three inch needle actually cares for them more than their own wallet. Compared to medicine, dentistry is still fairly affordable and properly educated patients are willing to pay a little extra for quality care with a practitioner they can trust. I think it is fairly safe to say that Corporate Dentistry trains their doctors to maximize their treatment plans. Eventually the general public will realize that fact. Of course there are private practitioners that are very adept at this also, but it is the rule for Corporate Dentistry.

2.) Corporate Dentistry sells itself to their associate dentists by telling them that the Corporation will take away most of the management headaches which allows them to simply practice dentistry. While some of that is true, it would cost less for a high producing dentist to hire a full time Human Resource/Office Manager to take away those headaches. The full time, hard working associates who start with Corporate Dentistry will hopefully come to understand that Corporate Dentistry exists because it takes approximately 40% of the profit out of the practice that would have normally been part of the take home pay for the owner/doctor. For example: Your typical $1 Million dollar practice should cash flow about $375K. Normally $700K of that practice is from dentist production and the rest is from hygiene. With bonuses, a doctor in Corporate would take home about 28% of his production of the $700K, or about $196K. Therefore, the same production in private practice would have yielded an extra $175K that would allow the doctor to hire that additional manager to take away his headaches and retain the remainder.

Therefore, it makes sense that Corporate Dentistry would only be attractive for dentists who do not want to work full time. Overhead costs in dentistry are high and will probably continue to grow, but dentists who work full time in their own busy practices will normally be more successful in their own well managed practices compared to Corporate.

Jon B. Noble, MBA

Mona Chang, DDS

John M. Cahill, MBA

Edmond P. Cahill, JD

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4085 SANTA ROSA GP & BUILDING

Practice and real estate offered for sale in well-established condominumized medical/dental complex conveniently located near Memorial Hospital. Tastefully decorated with a homey décor, practice occupies 1,200 sq. ft. ~ 3 fully equipped ops, private office, staff lounge, etc. Seller is retiring after almost 20 years but will assist for a smooth transition. Average Gross Receipts $256K with adj. net of approx $110K. Asking price $160K for the practice, and $270K for the real estate.

4010 SF GP

State-of-the-art, modern dental practice in gorgeous facility with recently upgraded reception, business and private office in approx. 3,200 sq. ft. office with 6 fully equipped ops. Located close to downtown. Assignable lease with options to renew. Equipment includes Inter-oral camera, laser, digital x-ray, air abrasive, Omnicam, Cerec, and implant system. 2014 Gross Receipts over $1.3 Million. 2015 on schedule for $1.6 Million. Asking $1.1 Million.

4083 SF ENDO

Seller is relocating out of area and offering a practice in prominent area close to downtown with excellent referral sources. Office space is approximately 1,950 square feet and is shared with another specialist. The practice has 3 fully equipped operatories. 2014 Gross Receipts $486K, 2015 on schedule for $498K. Owner willing to help for smooth transition.
Asking $290K.

4071 SAN MATEO GP

PENDING

Well-est. GP in single story professional dental building located on a heavily traveled main artery between downtown San Mateo and downtown Burlingame. 4 fully-equipped ops in modern office w/digital x-ray, inter-oral camera, laser & Cerec. Asking $459K.

4081 HAYWARD GP

PENDING

Seller retiring from successful GP with well-trained, seasoned staff. 4 fully-equipped ops. in seller owned building. Practice averages over $1M/year. All digital service. Asking price for practice only $732K. Building is also available for purchase.

4075 PETALUMA GP

SOLD

Established GP located in Petaluma in stunning 1,856 sq. ft. seller owned facility in class A, 10 year-old professional building. State-of-the-art office w/6 ops. 4 doctor-days & 4 hygiene days/wk. Avg. GR $640K. Asking $440K.

4069 SOUTH BAY PERIO

PENDING

Well established Perio practice in desirable South Bay location. Approx. 1,700 sq. ft. facility w/4 fully-equipped ops. in a professional dental building. 2014 GR $800K+. 3 doctor days per week. Practice sees 30-40 new pts. per month. Cone beam scanner & panoramic x-ray purchased recently. Seller willing to help in the transition. Asking $460K.

SOUTH SF SPACE FOR LEASE

Prominent dental building located in South San Francisco is looking for a general dentist and/ or specialist to start a practice or merge an existing practice into a 920-1000 square foot space. Owners of the building are open to discuss assisting in tenant improvement costs/ build out. Please inquire about this opportunity to begin your state-of the-art practice today! Please email vavalos@msn.com or call 650.867.5959.

UPCOMING:

SF DENTAL FACILITY

Facility only in the Sunset district, located on Ocean Avenue. 2 fully equipped ops with room for a 3rd op. Asking price $85K. Lease is transferable to Buyer.

SAN BRUNO GP

2014 Gross Receipts $279K. Convenient, spacious design, 4 op & private office. Asking $175K.

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Redwood City, CA 94061

Phone:
650.362.7004

Email:
dental@carrollandco.info

Website:
www.carrollandco.info

CA DRE #00777682

Practices Wanted

6093 CENTRAL MARIN COUNTY High quality practice available in hub of Marin County. Rock solid foundation. Consistent $700,000+ per year performer with strong Profits. 3-days of hygiene. Digital office.

6092 ROSEVILLE Great foundation. 2015 trending $350,000. 3-ops with 4th available. Convenient location on Douglas Boulevard. End cap suite in strip center with fantastic exposure.

6091 MODESTO 3-day per week practice collected $450,000 in 2014. Collections through July 23rd for 2015 were $256,000. 3-days of Hygiene. Great rent of $2,085 for 1,763 sq.ft. 5-op suite. Centrally located off Briggsmore Avenue. Hands-on Successor shall do very well here.

6089 MOUNT SHASTA Small town living renowned for mountain recreation, lakes & streams, fishing, golfing and abundant culture. Perfect escape from the Rat Race and corporate intrusion. On 3-day week revenues topped $800,000 in 2014. 2015 trending $850,000 with $450,000 in Profits.

6088 SANTA CRUZ Well established, lots of patients. Strong Hygiene Department with 6.5 days of hygiene per week. Collected $600,000 in 2014. 2015 trending $675,000+.

6087 LAKE TAHOE - NEVADA'S STATELINE Located adjacent to California's South Lake Tahoe. "Fee-for-Service" as practice is "Out-of-Network" with insurance companies. Collections last year topped $600,000 with Available Profits of $220,000. 3.5 days of hygiene per week. Escape California income taxes! Nevada State Board of Dental Examiners accepts the Western Boards.

6085 PERIO PRACTICE – SAN FRANCISCO BAY AREA 2014 collected $1.98 Million. Collections for first 7-months of 2015 totaled $1.29 Million has practice trending $2.2 Million. 7 Doctor days per week. Seller can work back. Beautiful 8-Op office.

6081 SANTA CLARA El Camino Real location. 2014 collected $687,000. 2015 is tracking $775,000 with Profits of $325,000. Management is on "cruise control." New Doc who is ambitious and extends hours shall push practice over the $1 Million bar very quickly. 5-ops in 1,700 sq.ft.

6080 SAN RAMON 8+ days of Hygiene per week. $450,000 invested in 6-Op office. Consistent $900,000+ per year performer. Attractive transition arrangements available.

6077 PERIO PRACTICE – SAN FRANCISCO'S NORTH BAY Highly regarded and located in desirable family area. On 3.5 day week, revenues were $1 Million in 2014 with profits of $400,000. Collections for first 7-months of 2015 topped $635,000. Beautiful facility with 4-Ops.

6071 CHICO Strength is 4-day Hygiene schedule. Retiring DDS focuses on restorative. Endo, OS, Perio & Pedo referred. 2014 collected $450,000. Beautiful 4-Op office. Full Price $150,000.

6070 VISALIA Strong foundation and well-positioned for ambitious successor. Strong Hygiene Department, beautiful facility, well equipped. Digital throughout. Not a Delta Premiere practice. Revenues trending $700,000 for 2015 on part-time schedule. Extend hours and be busier. Best location!

ANAHEIM HILLS Group member wanted. Hi identity. GP has space to share with Specialist. Pedo, Ortho or ?

ARROWHEAD Great mountain practice. Hi identity location. Conservative part-time owner with Associate grosses $4250,000. 3,000 patients. 4-ops. Digital x-rays. Practice $350K and RE $250K.

BAKERSFIELD AREA Small town. 4-op practice with building. Full Price $350,000 includes real estate. Renovations make property look new.

BAKERSFIELD Lady DDS grosses $800,000. Low overhead. Full Price $550,000.

CLAREMONT-UPLAND Gross $500,000+. Refers $250,000 in Ortho, OS, Endo. Hi identity. Seller can work back if acquired by Specialist.

DENTAL LOCATIONS Bell and Bell Gardens.

DENTURE PRACTICE Sees 30 denture patients per day. Perfect for Prosthodontist.

DIAMOND BAR Part-time practice. Grosses $400,000. Great opportunity. Full Price $360,000.

HAWTHORNE Located in strip center at busy intersection. 6-ops, 2 equipped in 1,600 sq.ft. suite. Full Price $95,000.

IRVINE Part-time practice is grossing $400,000. Beautiful office. Full price $360,000.

LAKE FOREST 7 ops across street from major employer in Orange County.

LOS ANGELES HMO practice doing $4.15 Million. $33,000 per month in cap checks. Includes real property.

MISSION HILLS Grossed $350,000, nets 50%. Senior DDS wants to work-back 2.5 days. Seller will finance.

REDLANDS Full price $35,000. 25-year phone number and fictitious business name. Great rehab opportunity which will grow with TLC.

REDLANDS Low overhead. 5- Ops. Should do $300-to-$400K first year with little marketing. Great Lease at $1.00 sq. ft. FP $250,000.

RIALTO Dental building on 2.3 acres. Land shall soon have $8,000/month in rental income.

RIVERSIDE Walmart Location.

SAN DIMAS HMO $8,000 month in cap checks. Hi Identity shopping center. Refers a lot. Specialist OK.

TORRANCE Grosses $300,000 with older DDS. 3-ops plumbed, 2 equipped. Beautiful A Class building. Full Price $250,000.

TUSTIN Free standing dental building with 5 ops. Full Price $1.4 Million.

TUSTIN Best Location in city Hi identity corner. Double your volume.

VICTORVILLE "Coming Up"

WEST LA Grosses $1.2 Million. Seeks Korean Lady DDS for specialty team. Plan to grow to $2 Million per year. Quality office. Full Price for 1/3 of goodwill $350,000.

YUCCA VALLEY Hi identity location. Small office. Used to do $500,000. Needs TLC. Full Price $150,000 includes building.

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