

Acetaminophen toxicity

Controlling biofilm

Endodontic sealers

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Negotiating
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Office Lease



OF THE CALIFORNIA DENTAL ASSOCIATION

Journal

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Stormy Weather

JACK F. CONLEY, DDS

In spring of this year, the most serious concern of many practitioners was whether the long, hot summer would bring rolling blackouts. Most colleagues we talked with who were in areas that might expect power emergencies had planned alternatives that would enable them to satisfactorily cope with the loss of power while they provided dental care. By mid-summer, much of the anxiety surrounding the California power crisis had been temporarily avoided by much milder than usual temperatures.

But in another arena, the socio-political temperatures surrounding the safety of dental amalgam were sizzling. We cannot recall another time when the California Dental Association has been sitting at the center of a virtual quagmire of related matters. As this is written, there are three issues that have become almost inextricable. They are:

The Proposition 65 saga, on which CDA legal staff have been diligently working for some time to resolve on behalf of California dentists;

Lawsuits filed in Los Angeles and San Francisco in June by consumer groups claiming, among other things, that CDA has misled the public about alleged dangers of mercury in amalgam fillings; and

Legislative activity (SB 26) seeking to eliminate funding for the Dental Board of California and thus terminate the activity of the current membership of the Board.

By the time this column is read, we hope there will have been some positive resolution of these intertwined matters. Until then, CDA leaders and staff will be at the front and center of an undesirable storm at the very time they are undertaking efforts to implement a new knowledge-based governance model that has resulted from the applied strategic

planning process in place for more than a year and a half.

Those who have been closely following comments here, or the news and comments in the CDA Update in recent months, will probably agree that there have been allegations, charges, and assertions from outside the profession that simply have no merit. Starting with the Proposition 65 case and continuing with the suits that have been filed (but, as of late July, not served on CDA), representatives and legal advisors of the consumer interest groups central to the anti-amalgam campaign appear to ignore scientific evidence that amalgam poses no health risks, in favor of an agenda that accuses the American Dental Association, CDA, and the Dental Board of California of covering up the truth about mercury in amalgam and misleading the public.

While some progress has been made in the efforts to resolve the Proposition 65 issue, it appears that CDA's efforts on behalf of dentists in that matter have been used against the association in the suits seeking to ban mercury from the dental office. And, the consumer legal adviser negatively links the association to supporting the thus far unsuccessful efforts of the Dental Board to adopt a Dental Materials Fact Sheet acceptable to their cause.

The Dental Board matter in total is far more complex and involves many more issues than just the safety of dental amalgam. Yet, in late July, the public assaults by consumer groups on the Board's effectiveness were focused on the failure of the Board to approve a Dental Materials Fact sheet that would be acceptable to these groups. In a letter from the attorney representing "Consumers for Dental Choice" to the president of the Board attacking the Board's efforts to develop an acceptable

Fact Sheet, CDA was also pulled into the complaint and accused of “double self-interest”: “The CDA’s economic self-interest is to protect the revenues of the ADA’s ‘Seal of Acceptance’ program,” and “The CDA’s institutional self-interest is to protect dentists from tort scrutiny for failing to warn their patients of the risks of these fillings.”

At the time of this writing, the possibility of the Board being able to develop a fact sheet acceptable to their key detractors before legislative activity determining its fate concluded seemed unlikely. The public goal for the consumer groups is a fact sheet that is easy to read and will facilitate a practical discussion between dentists and patients on the comparative merits and demerits of restorative materials used in dentistry. The real agenda of the consumer groups would seem to be a document that would set forth “facts” that support the anti-amalgam agenda rather than the scientific facts that the dental world, and in this case the Board and their independent consultant on the matter, know to be the truth. It seems that the consumers and their legal advisers will not accept anything less than a document that will fly in the face of current scientific knowledge. The other part of the strategy being employed by the public groups in this three-eye storm might be to keep public pressure on the Board and on organized dentistry until they extract a large monetary settlement from the profession that is to their satisfaction. If that were to occur, we might see the storm over amalgam subside for a few years. Based upon the fury out there now, that seems unlikely.

At the same time that this storm was raging, ADA released data from a year 2000 public opinion survey conducted by an independent survey firm in which

dentists are identified as the leading source of patient information on oral health issues (44 percent). The next-most-used source was consumer magazines (10 percent). If we relate this information to our existing controversy, it would seem that we are headed for a situation where dentists might continue to be the leading and trusted source of information on restorative materials, but the quality of information received by the public could be determined and approved by consumer groups and other agencies rather than by dentistry. Even if the concerns are well-intended, it is another case of third-party interference, this time into the science of dentistry.

In response to the significant amount of concerning information released by these consumer advocates, the CDA Board of Trustees was asked in August to approve a short-term Proactive Public Awareness Strategy to educate the public about these visible dental issues. The strategy includes training spokespeople, issuing news releases, running radio spots in the top five state markets, and buying print advertising. The intent is to reinforce CDA’s reputation as the trusted source to the public on dental issues. It is hoped that this educational campaign will move public emotion in this storm away from concerns fostered by the unsupported claims and charges by those groups and individuals with motives that are, at best, questionable. Public sentiment should be based upon the facts, and only the facts.

The Biofilm Problem and a Few Simple Solutions

GEORGE K. MERIJOHN, DDS

AUTHOR

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The May 2001 *Journal of the California Dental Association* cover story, “The Biofilm Problem,” provided a valuable look at the ubiquitous nature of biofilm. I commend the authors, Dr. Wenyuan Shi, Dr. Casey Chen, and Ms. Elinor deLancey Pulcini, for their in-depth analysis of the subject, covering aspects such as biofilm formation, complexity, worldwide presence, and pervasiveness in clinical dentistry. Dr. Shi and Ms. Pulcini both recognized that the quality of dental water is critical in terms of patient contamination risk.

Although this understanding of the nature of biofilm is very important, dentistry still has not developed foolproof methods to fully protect at-risk patients from the disease-transmission potential associated with dental unit waterlines.

As pointed out in his excellent introduction to the CDA Journal issue, John W. Beierle, PhD, indicated that a number of patients are at high risk for disease transmission from a buildup of human pathogenic bacteria in dental unit waterlines. This group includes patients who are very young; very old; infirm; undergoing chemotherapy or radiation therapy; or immunosuppressed

from HIV infection, AIDS, organ transplants, and other conditions.

This is a large and increasing segment of our population, yet we cannot always identify these at-risk patients before dental treatment. Some dental patients have at-risk conditions not yet diagnosed. It is impossible, therefore, to know with certainty which patients are most susceptible to disease transmission from dental unit waterlines.

Likewise, it is impossible always to determine in advance of treatment which dental patients are capable of transmitting diseases. As a result, the dental profession adopted the universal precaution protocol for infection control: Every patient is assumed to be capable of transmitting diseases in the dental office and therefore identical infection control precautions are taken with all patients regardless of their health history. An obvious solution to the dental unit waterline dilemma is to establish a “universal precaution” protocol and assume that every patient is at significant risk of disease transmission from waterlines. Therefore, all patients would receive only sterile irrigant for every dental procedure. That means, of course, that every irrigation device -- including all dental drills, three-

way syringes, and ultrasonic scalers -- must deliver sterile output irrigant to the patient. Unfortunately, this capability is lacking in the vast majority of equipment systems used in clinical dentistry today.

The waterline preventive measures currently practiced in the majority of dental offices fall short of the ideal goal. Flushing dental unit waterlines might lower the bioburden mass, but it does not eliminate human pathogens. Furthermore, from a microbiological standpoint, dental unit waterline disinfection can cause overpopulation of potentially pathogenic organisms that are not susceptible to the disinfectant. And, although special "micro" filters are available to attach to waterlines, they still allow human pathogens to pass through to the patient.

Hopeless situation? Not at all! Looking at the problem from a different perspective offers practical, cost-effective, time-efficient, and surprisingly simple solutions. The article "Prevention of Bacterial Endocarditis: Recommendations" (Journal of the American Dental Association, Vol. 128, August 1997, and Journal of the American Medical Association 1997, 277:1794-1801) cited the following dental procedures as high risk for producing bacteremia:

- Dental extractions;
- Periodontal therapy (surgery, scaling and root planning, probing, recall maintenance, subgingival placement of antibiotic fibers/strips);
- Prophylactic cleaning of teeth or implants where bleeding is anticipated;
- Endodontic surgeries that require the incision of or reflection of gingival or mucosa;
- Dental implant placement and replantation of avulsed teeth;
- Initial placement of orthodontic bands (not brackets);

These are the highest risk dental procedures in terms of disease

transmission from contaminated dental unit waterlines because they either cause or are associated with bleeding and therefore are considered invasive by nature. They are by far the most important procedures for which to deliver sterile output irrigant. If clinicians first focused on making these procedures safe, patients and dentistry alike would benefit greatly.

There is no question that there are "gray-zone" situations and procedures in general dentistry for which it may be difficult to plan. For instance, the gum may bleed if the high-speed drill nicks it during tooth preparation. However, it is best for patients' welfare and the profession not to suffer the institutional paralysis that comes with trying to define a solution for every clinical situation before instituting important change. The dental profession should immediately implement solutions for the already published and clearly defined at-risk procedures, and then consider other situations thereafter.

The solutions offered here for consideration are remarkably easy. A typical dental practice can implement them in a matter of days. Our private practice has had these protocols in place for more than five years. These solutions are clinically effective and are time- and cost-efficient (see report by G. K. Merijohn, DDS, published in CDA Update: Vol. 9, No.6, June 17, 1997).

Clinicians performing any of the high-risk dental procedures listed above should address three critical decision-making criteria:

Will a Dental Drill Be Used During the Procedure?

If so, the drilling system should be designed to pass sterile irrigant through sterile tubing and exit a sterile handpiece. The traditional dental high-speed handpiece with its waterline is incapable of meeting these criteria. However, drilling systems that deliver sterile output

irrigant are readily available and not prohibitively expensive. For clinicians who only occasionally perform invasive procedures with a dental drill, portable dental units are available that cost from \$2,500 to \$4,500 and can be moved from one operatory to another. The irrigant costs approximately \$2 per single-use disposable bag (250 ml of sterile IV saline solution).

The drilling speed may be a little slow for routinely cutting hard metal alloy restorations; but for surgical procedures (including sectioning restored teeth), these systems work very well. In fact, slower drills are better for surgical procedures: They cause much less trauma to the bone than the high-speed drills commonly used in dental surgery.

Will Irrigation Be Needed During the Procedure?

Examples of irrigation include flushing in a gingival sulcus, flushing under a tissue flap, and flushing an open wound (e.g., a gingivectomy or extraction site). Although many clinicians rely on the readily available three-way air-water syringe attached to the dental unit waterline for irrigation, there are safer and better ways to irrigate wounds and/or bleeding areas.

To eliminate waterline contamination risks, the clinician can simply do the following:

- Pour sterile water (\$1.50 per 250ml multi-use bottle) into a disposable cup or sterilized container, if preferred;
- From the cup, fill a new 10 cc disposable syringe (\$0.11-\$0.50 per unit) that was pre-sterilized in the sterilizer;
- Irrigate the site.

For clinicians who are only rinsing the mouth where there are no open wounds, such as after a recall maintenance procedure, using a disposable syringe and disposable cup filled with common tap water is acceptable. On average, water taken directly from the tap is of better

microbiologic quality than water delivered from the three-way syringe and dental unit waterline.

Will an Ultrasonic Scaler Be Used?

If so, there is no way to completely eliminate the dental unit waterline contamination problem. For more than 20 years, dentistry, especially dental hygiene, has placed a great deal of faith in ultrasonic instrumentation that, to date, validated well-controlled clinical research does not support:

- **Lack of evidence proving superior results.** There are no published, properly controlled clinical studies that demonstrate statistically significant superiority over hand scalers and curettes with respect to: preventing periodontal attachment loss, maintaining periodontal attachment levels, and/or preventing tooth loss in humans; and preventing occupationally related repetitive-stress injuries such as carpal tunnel syndrome.
- **Demonstrated occupational health hazard.** The aerosol spray associated with using ultrasonic scalers in a typical treatment room setting (dental hygienist performing treatment without a dental assistant operating an independent high-speed evacuation line) exposes the dental hygienist to unacceptable disease transmission risks. See these references:

Journal of the American Dental Association, Vol. 129, September 1998: Aerosol and splatter contamination from the operative site during ultrasonic scaling.

Journal of Periodontology, Vol. 69, No. 4, April 1998: Blood contamination of the aerosols produced by in vivo use of ultrasonic scalers.

Journal of Periodontology, Vol. 75, No. 5, May 1999: Aerosol and splatter production by focused spray and standard ultrasonic inserts.

- **Potential Patient Health Hazard.**

The American Dental Association Council on Scientific Affairs published a report in the November 1999 *Journal of the American Dental Association* titled "Dental Unit Waterlines: Approaching the Year 2000." The article stated, "The use of instruments such as the ultrasonic scaler, which potentially could force organisms into breaks in the gingiva, may raise the possibility of introducing microorganisms into the bloodstream."

- **Relatively high cost.** The cost for purchasing and maintaining ultrasonic scaler units and tips is substantially more for the dental practice than the cost associated with utilizing the finest hand instruments.

In 1993, the CDC introduced universal precaution recommendations for infection control practices in dentistry. It recommended that patients always receive sterile output irrigant during any dental surgery. The use of sterile output irrigant for invasive, at-risk procedures has long been the unquestioned standard of care in medicine. The ADA has not adopted this CDC recommendation as a regulatory guideline for routinely performed invasive, at-risk dental procedures.

A Call to Action

With or without regulations requiring dental clinicians to provide specific safeguards, such as sterile output irrigation, patients deserve the safest possible measure of care during invasive, at-risk dental procedures. Dentists -- including all periodontists and all endodontists performing surgery -- who use conventional dental unit waterlines and high-speed drills while performing the invasive, at-risk procedures indicated above could take a leadership position and proactively improve their treatment delivery systems to provide patients with sterile output irrigant.

By taking the initiative, these

clinicians would help provide needed support for dentistry's waterline improvement efforts. In addition, voluntarily acting to improve public safety would further enhance public and media opinion about the progress being made by the dental profession.

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Dental Research Can Be Easy to Access

BY DEBRA BELT

Just about everyone knows the scenario. In the few extra minutes left on your lunch break, you decide to do a quick Internet search. After conducting a general search on a topic of interest you get 7,000 hits. Or zero hits. Or you find a great site and it asks you to log in and "register" (i.e., fork over a Visa card number). Or you have to download software to be able to access the site. By the time the software is half loaded, the next patient is in the chair, and time is up.

The Internet can be a fabulous tool or a source of frustration. In helping make the World Wide Web more wonderful than worrisome, here are some easily accessible sites recommended by dental professionals. Especially useful are the journals listed in bold face. Their sites offer free full text of articles and provide a search mode for quick searches on specific topics.

<http://www.cda.org/>

Just a reminder that the site of your professional organization may easily yield that esoteric piece of information about infection control regulations or any other topic ranging from dental amalgam to current legislation. The Journal of the California Dental Association from January 1998 through the present and the CDA Update from January 1996 through the present are also available here. (Adobe Acrobat 3.0 is needed to view some older issues of the Update, and a link to download the software is provided.) Additional resource for the public including details on dental health topics such as fluoride, preventive care, baby bottle tooth decay, and care for seniors. Several reports are also in Spanish.

<http://www.ada.org/>

Includes a discussion forum for members, Washington weekly update, regulatory issues, current ADA News and free full text of Journal of the American Dental Association articles from 1998 through the present. Material for the

public includes oral health topics, news and media.

<http://www.nature.com/bdj/index.html>

Direct link to the British Dental Journal, which offers content search and free full text of articles dating back to 1997. Also includes information on topics such as evidence-based dentistry.

http://www.cda-adc.ca/public/frames/eng_index.html

Site of the Canadian Dental Association and its Journal offering free full text of articles dating back to 1998. We did not detect a way to search articles, but journal indexes are listed by month. Looking for specific info on this site may take a little more time.

<http://www.ihs.ox.ac.uk/cebd/dentlink.htm>

Centre for Evidence Based Dentistry is associated with the Institute of Health Sciences in Oxford. This a great site for a plethora of dental links including dental associations around the world, association and dental schools as well as information on amalgam, implants, fluoride, cancer and evidence-based dentistry. Links to specialty journals include British Journal of Orthodontics, International Endodontic Journal, and Journal of Oral Rehabilitation.

<http://www.toothfairy.org>

For a lighthearted break, check out the home page of the tooth fairy. Written by an RDH, this site has tooth fairy FAQ (i.e. Q: How much money does the tooth fairy give for a baby tooth? A: One whole dollar. Baby teeth are precious even if they are tiny.), oral hygiene tips, tooth fairy tales, the brush-along song, and several links to other dental sites such as Virtual Periodontology.

<http://www.fdi.org.uk/about/index.htm>

Home page of FDI World Dental Federation. Links to FDI World Dental Press for books and to the International Dental Journal where abstracts of articles from 2000 can be viewed. This site also hosts the "ultimate dental events calendar" and details about the activities of the FDI, which cover every aspect of dentistry and take place all over the world.

<http://www.harcourt-international.com>

Link to Journal of Cranio-Maxillofacial Surgery and British Journal of Oral & Maxillofacial Surgery (Go to Journals, search keyword dental) This site also allows perusal of health science and medical titles specific to dentistry.

<http://www.nohic.nidcr.nih.gov/>

National Oral Health Information Clearinghouse is a resource for special care patients includes an oral health database and special care publications.

<http://www.nas.edu/>

Site of the National Academies, "Advisers to the nation on science, engineering and medicine," includes subject index on biology, chemistry and environmental issues. Access to periodicals including Proceedings of the National Academy of Sciences, Issues in Science and Technology and Beyond Discovery: The Path from Research to Human Benefit. Search mode and free full text of current and archive articles.

<http://www.nature.com>

Site of Nature Publishing Company is highly interesting, but takes a little bit of time to navigate. It provides links to a vast array of journals on genetics, molecular cell biology, biotechnology, and immunology. Visitors can view current journals, but archive searches require opening an account. This site also provides links to specialist journals such as the British Journal of Pharmacology and Encyclopedia of Life Sciences (registration required).

Dental Vaccine Shows Preclinical Success

Researchers at the Forsyth Institute have discovered a potentially important antigen for a vaccine against dental caries.

The antigen, reported in the July issue of *Infection and Immunity*, gives rise to greater immune response than do many previously tested antigens and strengthens an already powerful case for embarking on clinical trials for a caries vaccine.

The ultimate goal of the research team, led by Martin Taubman, DDS, PhD, and Daniel Smith, PhD, is to find a way to prevent tooth decay throughout life by administering an anti-caries vaccine to children aged 12 to 24 months.

"Despite the great advances in caries research over the past few decades, dental decay remains the major infectious disease that affects children worldwide," according to Dominick P. DePaola, DDS, PhD, president and CEO of the Forsyth Institute. "A vaccine for caries would be extraordinarily exciting because it could free tens of millions of children from the ravages of dental disease."

The newly reported antigen is the key component in a new formulation of a mucosal vaccine that can be squirted into the nose, rather than injected or swallowed like some other vaccines. This vaccine and others developed at Forsyth have proved effective in preclinical trials.

The researchers have previously received approval to enter clinical trials and are currently seeking support or partners to produce the vaccine.

Acupuncture Can Control Gag Reflex

British dental researchers found success in controlling patients' gag reflex using ear acupuncture, allowing treatment of patients whose reflex reaction has kept them from visiting the dentist, according to study results published in the June 9 issue of the *British Dental Journal*.

For the study, 10 people agreed to try ear acupuncture to control gagging during a dental treatment. Four of the patients had severe gag reflexes that made treat-

Study Says Laser Decreases Surface Cavities

Lasers used as an enamel and dentin "conditioner" in place of acid etching can provide additional protection against carious attack, according to a study in the *American Journal of Dentistry*, February 2001.

Researchers at the University of Granada in Spain and the University of Texas found that laser treatment showed a 56 percent decrease in coronal outer primary surface caries lesion mean depth, compared to acid etching.

The article notes that previous studies have shown that etched enamel margins followed by bonding and composite placement inhibits progression of secondary caries at the restoration interface. The researchers say that it may be possible that laser treatment affects lesion progression to a greater degree than acid-etched conditioning.

According to the authors, the exact mechanism of caries prevention with laser irradiation was not addressed in their study. They speculate that acid resistance might be caused by a reduction of enamel permeability and solubility.

They conclude that further studies are necessary to establish a definitive mechanism of caries resistance for laser-irradiated surfaces.

ment impossible while the other six had reflex reactions severe enough to make treatment possible only under sedation.

Acupuncture needles were inserted into a specific "anti-gagging" point on each ear, adjusted briefly, and left in place during the dental procedure. Procedures ranged from tooth extraction to tongue biopsy.

With the help of ear acupuncture, all of the patients got through their dental procedures successfully, the researchers report. The acupuncture completely controlled the gag reflex in eight of the cases and partially controlled the reflex in the other two cases. The acupuncture procedure added just two to three minutes to the patients' chair time.

How the acupuncture quells the gag reflex is unclear, according to the researchers. They said the needle stimulation may block certain nerve pathways. One of the main nerves involved in swallowing also supplies the part of the ear where the anti-gagging acupuncture point is located.

They also note that further research is needed to determine whether acupuncture's benefit could stem in part from

the so-called "placebo effect," where the power of suggestion helps the patient psychologically overcome a problem.

Scientists Identify New Gene Tied to Oral Cancer

A newly identified gene appears to play a key role in the development of oral cancer, according to scientists at the University of Alabama's Comprehensive Cancer Center.

The new oncogene, GKLF, shows only a limited expression in normal cells but is over-expressed in virtually all cancers of the oral cavity and 70 percent of breast carcinomas, the scientists said. Further research confirms the expression of GKLF is unique to cancers of the oral cavity and breast and not a general growth pattern in all types of cancer.

Working with a mouse model at the Cancer Center's Transgenic Animal Facility, the scientists were also able to identify the cancer-causing role of the oncogene.

"When we caused the mice to over-express GKLF, their skin underwent increased cell proliferation, developed early changes of malignancy and finally overt cancer," says Dr. Michael J. Ruppert, who

leads the team of researchers responsible for the discovery. "This animal model confirms the ability of GKLF to induce both early and overt cancer."

"Increased expression of specific oncogenes in tumor cells can result from genetic alterations of the oncogene or of the mechanisms that regulate its expression," Rupert says. "This new oncogene will be a therapeutic target for drug discovery and other treatment strategies."

After Drug Use Ends, Cocaine Craving Gets Stronger Over Time

Using an animal model of drug craving in laboratory rats, researchers at the Intramural Research Program of the National Institute on Drug Abuse have found that craving for cocaine seems to increase, rather than decrease, in the days and months after drug use has stopped.

"This phenomenon helps explain why addiction is a chronic, relapsing disease," says Institute Director Dr. Alan I. Leshner. "Craving is a powerful force for cocaine addicts to resist, and the finding that it persists long after last drug use must be considered in tailoring treatment programs."

The research team, which included Drs. Jeff Grimm, Bruce Hope, Roy Wise, and Yavin Shaham, published its findings in the July 12, 2001, issue of *Nature*.

In the study, the scientists found that sensitivity to drug-associated environmental cues that often accompany drug craving, and relapse increased over a 60-day withdrawal period. Cocaine craving was inferred from the behavior of rats trained to press a lever to receive intravenous cocaine injections. Once the animals had learned to associate the lever-pressing with receiving cocaine, they were tested under conditions where they could continue to press the lever, but no longer received cocaine.

In humans, drug-associated environmental cues often stimulate cocaine craving and accompany relapse to drug-using behavior. The NIDA investigators wrote

in their report to *Nature* that "The data from this study suggest that an individual is most vulnerable to relapse to cocaine use well beyond the acute drug withdrawal phase."

Quitting Smoking Harder for Women Than For Men

A review of numerous research studies focusing on smoking cessation has concluded that while women may suffer greater relative risks of smoking-related diseases than do men, they tend to have less success than men in quitting smoking.

Dr. Kenneth A. Perkins from the University of Pittsburgh School of Medicine conducted the review and offers several reasons for this disparity in a paper published in the May 2001 issue of *CNS Drugs*.

These research-based findings include:

- Nicotine replacement therapy may not be as effective for women.
- Women smokers are more fearful than men of gaining weight if they quit.
- Medications to aid smoking cessation are not recommended for pregnant women.
- A woman's menstrual cycle affects tobacco withdrawal symptoms, and responses to antismoking drugs may vary by cycle phase.
- Husbands may provide less effective support to women who are trying to quit smoking than wives give to husbands.

"According to the recent report on women and smoking by the surgeon general, 3 million women have died from smoking-related diseases since 1980. Currently, women suffer 39 percent of all smoking-related deaths," says Dr. Alan I. Leshner, director of the National Institute of Drug Abuse. "Given the greater relative risk of women to incur smoking-related diseases, it is clear that we must find better approaches to help women break their nicotine addiction."

Perkins says that one of the intriguing observations that emerged from his review is that some forms of nicotine replacement therapy may not be as effective in women as in men. In some of the studies he reviewed, women had less treatment success using nicotine gum or nicotine patches than did men.

In contrast, other stop-smoking medications may more effective in women than in men. Because negative mood is more likely to precipitate smoking relapse in women than in men, Perkins suggests that use of antidepressant medications for smoking cessation could be more effective in women than men.

Perkins concludes that developing smoking cessation interventions that address the gender-specific concerns of women smokers could increase the success rate among women who are trying to stop smoking.

Federation Changes Name to Special Care Dentistry

The Federation of Special Care Organizations in Dentistry has reorganized and changed its name. Now called Special Care Dentistry, the organization comprises the membership and resources of three former Federation subgroups: the American Association of Hospital Dentists, the Academy of Dentistry for Persons with Disabilities, and the American Society for Geriatric Dentistry.

According to SCD officials, the reorganization will bring "a renewed focus to and address the significant oral health disparities between people with special needs compared to other the members of the population."

Dr. Ray A. Lyons, SCD president, says Special Care Dentistry's new name reflects the board's desire to create a new image for the organization.

10 Steps to Negotiating the Dental Office Lease

BARRY H. JOSSELSOHN, A PROFESSIONAL LAW CORPORATION, AND A. LEE MADDOX, DDS,
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ABSTRACT The dentist's office lease is one of the most critical legal agreements the dentist will sign in his or her professional career. Understanding the numerous economic and non-economic points of a lease is integral to the success of one's practice. This article discusses 10 key points that will ensure a fair and equitable lease agreement.

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The dentist's office lease is one of the most critical legal agreements the dentist will sign in his or her professional career. Unlike associateship relationships, which can be terminated, or partnerships/corporations with other dentists, which can be dissolved, the dentist's office lease cannot be ended unilaterally by the tenant or breached with impunity without the dentist's incurring substantial legal risk, liability, and economic fallout. Accordingly, the dentist's understanding the numerous economic and non-economic points during the course of negotiations with the landlord and the dentist's attorney's perusal of the dental lease are integral factors to the success of the dentist's practice. Considering the following 10

key points will ensure a fair and equitable lease agreement and business relationship with a landlord for years to come.

Negotiability

The proposed lease submitted to the dentist is simply the landlord's first offer of the terms of the contemplated relationship. Many dentists believe that because the lease offered to them is in writing or in a pre-printed form, it is not subject to modification or revision. Some dentists are wrongfully informed by their leasing agents that their proposed lease has been signed by all of the other tenants without revision (the incorrect implication being that the lease must be fair; otherwise, tenants would not have signed it). Nothing is further from the truth. All office leases are drafted in favor of the landlord; the

only issue is whether the lease has been drafted slightly one-sided, moderately one-sided, or extremely and unilaterally one-sided in favor of the landlord. Lease provisions favoring the landlord, however, will not be prominently noted nor highlighted in the document. Instead, the dentist's lease will be prepared by the landlord's attorney or landlord's real estate association to favor either their client or their constituents, respectively, and not to accentuate those lease provisions that have been intentionally drafted in favor of the landlord rather than the dentist tenant. Any agreement can be negotiated. An analysis of the lease and negotiations of the terms with the landlord need not be an acrimonious nor hostile event, but simply a first step in communicating to the landlord the dentist's desire to have the landlord-tenant relationship be fair and equitable. Recommendation: The dentist should always consult with a real estate attorney specializing in dental office leases before signing any long-term leases.

Option to Renew the Lease

An option to renew is a wonderful tool to provide the dentist with flexibility. At the end of the lease term, the tenant has the "option" to remain in the premises by notifying the landlord of the dentist's intent to stay. Or, to the contrary, if the dentist determines that it makes more sense to relocate to new premises, he or she reserves the right to leave without having previously entered into a longer-term lease. Options to renew, therefore, give one the security of a possible long-term lease without having to make a commitment to a long-term lease. Most options to renew are for periods from three to five years. The value of one's option to renew, however, can be severely limited by the landlord in the following ways:

1. Many leases allow only the original tenant to exercise the option to renew, not any buyer of the dental practice. This limitation will not be conspicuously disclosed in the document. Instead, most leases innocuously state that the option

to renew is "personal" or "unique" to the original "tenant" of the lease. If the proposed purchaser of one's dental practice is not able to exercise the previously negotiated option to renew, this could adversely affect the value of the practice, especially if there are only a few years left on the dentist's current lease. The risk that the current landlord might not renew the lease to the prospective buyer or that the lease may be renewed albeit at a substantially higher rental rate is significant and should be avoided.

2. The determination of fair market rent can also be fraught with risk. A careful perusal of the rental rate formula found in many options to renew reveals what appears to be an equitable definition of the fair market rental of the premises based upon current rents being charged for comparable space in similarly situated properties. However, the dentist must examine more closely many of these formulas. Some will state that the rental rate shall be the greater of fair market rental or the last year's rental rate. The result: In an escalating rental real estate market, fair market value shall provide the landlord with great upside potential. In a falling rental real estate market, if true fair market rents are below the last year's rental rate paid by the dentist, the lease mandates that the rental rate paid by the dentist during the option period shall still be the last year's rental rate (even though such rental rate could be far in excess of the lower fair market rental rate).

Assignment or Subletting of the Lease

The assignment or subletting of the dental lease to a prospective purchaser is critical to the later sale of the dentist's practice. Very few practices are sold to buyers who intend to move the practice to another location. Moving can cause substantial patient attrition as well as substantial costs in building out a new office. Therefore, the dentist's ability to assign or sublet his or her lease freely and without unreasonable restraint to the buyer is crucial. The landlord can limit the

dentist's ability to assign or sublet the lease in the following ways:

1. If the lease states that the landlord's consent "may be arbitrarily withheld," "withheld at the landlord's sole discretion," or words similar in effect, the landlord can unilaterally withhold consent at the time that the dentist requests the lease to be transferred to his or her buyer. No buyer of a dental practice will consummate a sale without a long-term lease securing the investment the buyer has just made. Moreover, sophisticated dental lenders will not lend money to purchase the practice without the lease term (with an option to renew) being equal in length to the term of the practice purchase loan. Instead, the lease should state that the landlord's consent "shall not be unreasonably withheld."

2. An increasing number of dental office leases provide that 100 percent of the rental income (received by the dentist subletting the premises) in excess of the rent obligation due under the lease (by the subletting dentist) must be paid to the landlord. The dentist should try to delete such obligation or negotiate a lesser percentage than 100 percent. Most importantly, the description of the "consideration" to be paid to the landlord should be limited to only sublease rental income and not any consideration for goodwill, covenant not to compete, or leasehold improvements received by the dentist when selling his or her practice. Otherwise, the landlord may legitimately claim a right to part or all of the practice sale proceeds received by the seller from the buyer of the dental practice.

3. The "recapture clause" gives a landlord the right to "take back" the premises even if the dentist has followed the protocol of first seeking the landlord's approval of the proposed buyer of the practice prior to transferring the lease. Such a recapture clause innocuously states that the landlord can consent to the assignment or, in the alternative, assign the lease to itself in lieu of the proposed buyer. Such recapture clause is placed in

leases and is exercised by landlords in escalating real estate markets or in those situations in which the landlord is not able to withhold its consent to the proposed buyer. Such a “recapture clause” must be stricken from the lease document.

4. Rent increases and repayment of tenant improvement allowances can be costly hidden surprises. When a dentist assigns his or her lease to a new buyer, the buyer has purchased the dental practice in contemplation of paying rent under the lease according to the selling dentist’s rent schedule negotiated at the time when the selling dentist signed such document. More and more leases have language in the documents stating that “as a condition for the landlord’s consent to any assignment,” the landlord may raise the rent or be repaid by the selling dentist all of the money which the landlord spent for the leasehold improvements in building out the seller’s dental office. Such provisions are unacceptable and should be removed from the agreement.

5. All leases provide that the selling dentist’s assignment of the lease to another dentist will not release the seller from any liability if such buyer later defaults under the lease. The language that provides that the selling dentist shall remain liable should be deleted, especially since the landlord will have previously approved the buyer as a bona fide and qualified party to assume the seller’s lease.

Exclusivity

In some shopping centers or other facilities that are not solely dental- or medical-related, being the only general dentist or specialist in that building or shopping center can enhance the value of the dental practice and the attractiveness of the office lease. Many landlords will initially object to any efforts by the dentist to restrict their freedom to lease to any prospective tenants; however, the dentist’s limiting the scope of the exclusivity can mitigate the landlord’s reluctance to provide such exclusion. For example, the request for exclusivity as a general

dentist would not adversely affect the landlord’s ability to lease to orthodontists, endodontists, periodontists, oral surgeons, or other specialists that could complement the general practice.

Relocation Clause

Many leases grant the landlord the right to relocate the dentist from existing office space to other premises within the building or center. Such clause permits the landlord to achieve higher occupancy by providing space to potential tenants who would otherwise not be able to secure needed square footage or a desired location but for the landlord’s right to move the tenant. If location is critical to the success of the dentist’s practice (for example, visibility to the public or existing patients), the dentist should delete the relocation clause from the document. At the very least, irrespective of the significance of the dentist’s office premises’ location, the landlord’s right to relocate the dentist should be subject to the following conditions:

1. The cost to rebuild the new premises to the condition of the dentist’s former practice should be borne entirely by the landlord.

2. The new premises should be substantially the same in size, dimension, configuration, decor, and nature as the dentist’s original office.

3. The landlord should not have more than one right to relocate the dentist during the lease term (including options to renew).

4. All of the costs incurred because of the relocation (new stationery, business cards, directory advertising, etc.) should be paid by the landlord.

Partial or Total Destruction of the Premises

This provision in the office lease is the most ignored and least understood by dentists and their legal counsel. Those California dentists who have survived the havoc earthquakes have wreaked on the state’s economy and their practices can

attest to the relevance and impact of this clause. Damage and destruction clauses are significant for the following reasons: They identify the rights and obligations of the landlord and the dentist if the premises (or the building or shopping center in which the premises are located) are damaged by an “act of God” such as fire, flood, or earthquake. Such clauses allocate responsibility to the landlord or the dentist for repairs to be made to the premises, determine the right, if any, to terminate the lease, and dictate whether the dentist is responsible to continue to pay rent during the period when the premises are not available for occupancy.

The dentist can protect him- or herself in the following ways:

1. By specifying a period within which the landlord must complete the restoration of the premises with the dentist beyond when the dentist may have the right to terminate the lease. Because dental office leases uniformly state that the landlord’s obligation is to make repairs “as soon as reasonably possible” or to use “due diligence,” such language does not give the dentist sufficient protection if the repairs cannot be made within a short period regardless of the landlord’s good faith efforts. If the dentist is unable to practice dentistry within, for example, six months from the date that the office was unusable, patients will find new practitioners to satisfy their imminent or urgent dental needs.

2. By making certain that the rent obligation will abate if the dentist is unable to use the premises during the time that it has been damaged. Rather than a rent reduction in proportion to the amount of square footage that has been destroyed or rendered untenable, there should be a rent abatement based upon the percentage of lost production in the practice. If the dentist is unable to practice dentistry or generate any substantial revenue, the diminution in value of the premises is absolute and the dentist should have no rent obligation (regardless

of the availability of part of the premises for dentistry).

3. By deleting language in the lease regarding rent abatement being a function of the landlord's "rental interruption insurance" paying such deficiency. The dentist's obligation not to pay rent should in no way be determined by the landlord's procuring such an insurance policy or the insurance company's election to pay such rental interruption proceeds to the landlord.

Right to Terminate

A properly drafted dental lease should recognize the frailty of health care professionals and the substantial likelihood of a long-term disability at some point in their careers. Accordingly, the lease should address the dentist's right to terminate in the event of his or her death or long-term disability (whether partial or total). Such right to terminate exercisable instead by the landlord is not appropriate and should not be included in the lease. The dentist's right to terminate the lease, however, would be exercised only in limited circumstances. As previously noted, the value of a dental practice is integrally tied to the dentist's ability to assign the underlying lease to another buyer. The practice's value would be substantially compromised if the buyer were not able to take over the existing lease. When then would it make sense to terminate one's lease? It would certainly make sense to terminate the lease in a situation where the practice is a startup, and the disabled or deceased dentist does not have a "viable" practice to sell, but merely a dental practice location with equipment, leasehold improvements, and some patients' charts and records. It would also make sense to terminate the lease in situations in which a selling dentist's health history or cause of death (HIV, substance abuse) could dramatically affect the salability of the practice.

Pass-Through of Expenses

The dentist and his or her dental real estate attorney must thoroughly understand and precisely define the total rent obligation for the entire term of the lease. Few leases provide for only a basic monthly rent obligation. Instead, leases more commonly provide for a "minimum rent" to be paid to the landlord with a pass-through of "operating costs or expenses" associated with the operation and management of the building or shopping center in which the practice is located. The lease will provide that the dentist pays a percentage or "pro-rata share" of such operating costs. Such pro-rata share is generally determined by a fraction equal to the total square footage of the office divided by the total square footage of the building or shopping center in which the practice is situated. However, the dentist needs to be aware of the following nuances.

1. Leases vary among passing through all of the operating costs to the tenants, all of the operating costs in excess of the costs incurred in a certain "base year," and none of the operating costs. For example, if operating costs of one's building were \$100,000 per year in calendar year 2000 and \$110,000 in calendar year 2001, note the substantial difference in the dentist's responsibility for costs if based on 10 percent of the total square footage in the building. In the first scenario, the dentist would be responsible for 10 percent of all the operating expenses (\$100,000). In the second scenario, the dentist would be responsible for only 10 percent of the increase in operating expenses (\$10,000).

2. When the "pro-rata share" or fraction is computed for determining one's liability for operating costs, the dentist needs to peruse how the denominator of the fraction is defined. Some leases provide that the denominator is the "total square footage then currently occupied and leased up" rather than "the total leasable square footage." Obviously, this subtle distinction can create economic trauma to the practice if the dentist is located in a building or shopping center with substantial vacancy.

For example, if the dentist's building has total "leasable" square footage of 20,000 square feet, and the dental office is 2,000 square feet, the dentist is then responsible for 10 percent of the operating expenses. However, if the building has substantial vacancy and only 8,000 square feet of the 20,000 square foot building is "then currently occupied and leased up," the dentist's responsibility for the operating expense has increased from 10 percent to 25 percent because the denominator of the fraction has been reduced. Again, these nuances in legal drafting of documents are not highlighted or pointed out to tenants prior to their executing their lease agreements.

3. Nearly all dental office leases have all or some portion of the operating costs shifted to the dentist-tenant. There are very few leases that provide that the landlord is solely responsible to pay for the building's operating expenses such as repairs, insurance, and property taxes.

Hold-Over Rental Clause

Leases provide for precipitous increases in rent when the dentist's lease has terminated, and the dentist has neither exercised the option to renew nor vacated the space. In such a situation, the landlord may permit the dentist to remain in the premises albeit at a substantially increased rental rate (usually 150 percent to 200 percent of the rent at time of conclusion of the lease term). While dentists often believe that they would not fail to exercise their option to renew or would vacate the premises in a timely manner if they chose not to remain, the stark reality is that sometimes their moves do not occur as punctually as anticipated. Architects and general contractors for the dentist's new space can be delayed in completing the project. Tenants can forget to exercise their option. They may endeavor in good faith to negotiate a new lease without success only to find these onerous rental rate provisions applicable to them. Recommendation: The application of such a penalty rate should be negotiated to occur only after a certain

period of time (for example, 30 to 60 days) after the lease terminates; or there should be a substantially reduced penalty provision (125 percent) if there is no “grace period” of time before its being enforced.

Indemnification

All well-drafted leases provide that the tenant “indemnify, defend, and hold harmless” the landlord from any losses or damages that the landlord suffers because of the negligent acts or omissions committed by the tenant. Such an indemnification provision has nothing to do with the rendering of dental services. Instead, it is an acknowledgment that if a patient or employee becomes injured on the premises through no fault of the landlord, there is great probability that the landlord will be named as a defendant in any litigation. Until such time that the landlord can be dismissed from the lawsuit or judged not responsible for the injury suffered by another party, the landlord will be incurring legal fees and court costs to defend itself. This provision addresses reimbursing the landlord for its out-of-pocket costs. Recommendation: A reciprocal provision should be sought to protect the dentist in the event that patients, staff, or third parties are injured on the premises or in the building due to the negligence of the landlord or its failure to abide by the terms of the lease. Most importantly, office leases also provide that the tenant waive any rights it may have against the landlord for the landlord’s breach or default of the terms of the lease. Such a provision should be stricken in its entirety from the document.

Conclusion

Most dental office leases do not require extended negotiations between the landlord and the tenant’s dental real estate attorney. Adversarial, acrimonious, or divisive communications between the parties in consummating a lease are the exception.

Very few leases are truly non-negotiable. Leases are never offered to

a dentist on a “take it or leave it” basis (even if real estate agents or other parties involved may present the lease in this way or intimate this position by the landlord).

Instead, rational and meaningful explanations made by the dentist and his or her dental real estate attorney to the landlord will confirm the seriousness with which the dentist is entering into this relationship and the thoroughness with which the dentist reviews contractual obligations. The dentist’s securing and obtaining a good lease protects the dentist and the practice during the time that the dentist owns it, plays a substantial role in the financial success of the practice during the dentist’s career, and enhances the practice’s value and the dentist’s ability to sell when he or she wishes to relocate or retire.

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A Comparison of the Effect of Three Endodontic Sealers on Adherence of Mouse Peritoneal Macrophages

AHMAD SADEGHEIN, DDS, MS; BEHNAM BOLHARI, DDS, MS; AND A. SARAFNEJAD, PhD

ABSTRACT Leakage of sealer from root canals to periapical tissues during root canal obturation may occur. This study was designed to evaluate the possible effect of three root canal sealers (zinc oxide-eugenol, Grossman, and AH 26) on adherence of mouse macrophages. Macrophages were obtained from the peritoneal cavity of BALB/c mice and suspended in RPMI-1640 medium. Adherence capacity assays were carried out in Eppendorf tubes. Each sealer was tested four times after mixing (immediately, 12 hours, 24 hours and 48 hours after) and for three period of incubation (10, 20, and 30 minutes) with suspended cells. Cells were counted under the light microscope, and the adherence index was determined. Zinc oxide-eugenol and Grossman sealers killed all macrophages, and the adherence index was considered less than 1 for these sealers. AH 26 reduced the adherence index in all different periods after mixing and incubation times. But in sealer that had mixed 48 hours before the experiment and with 10 minutes of incubation, the adherence index was increased slightly, but the difference was not statistically significant ($P < 0.05$).

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$$\text{Adherence index} = 100 - \frac{\text{Nonadherent macrophage/ml}}{\text{Initial macrophage/ml}} \times 100$$

FIGURE 1. The calculation formula for the adherence index.

One of the major reason for endodontic failure is incomplete obturation of the root canal. Usually, gutta percha cones and a sealer are used to obturate the root canal. A sealer should have at least some of the ideal characteristic as listed by Grossman; however, at this time there are no sealers that have all the ideal characteristics.¹

Root canal filling materials should be confined within the root canal system. However, leakage of the sealer from the root canal system to the periapical tissue during obturation may occur, which could affect treatment prognosis.^{1,2}

It has been demonstrated that inflamed periapical tissue contains a variety of immunocompetent cells, with macrophages predominating.^{3,4} Macrophages are implicated in bone resorption⁵ and play an essential role in the pathogenesis of human periapical pathosis.⁶ They have a main role in healing by phagocytosis and debridement of wound areas.⁷ It is well-known that adherence is the first step in the phagocytic process of inflammatory macrophages.^{7,8} Therefore, each material that can affect the adherence of macrophages will affect the phagocytosis.

This study was designed to evaluate possible effects of three root canal sealers -- zinc oxide-eugenol (Kemdent Works, Purton, Swindon, Wiltshire), Grossman (Roth International Ltd., Chicago) and AH 26 (Dentrey Division Dentsply Ltd. Weybridge, Surrey, England) -- on macrophage adherence and, consequently, on repair.

Materials and Methods

Peritoneal macrophages were elicited from BALB/c mice aged 6 to 12 weeks. Each mouse was injected intraperitoneally with 5 ml of sterile thyoglycolate. Animals were sacrificed after two days, and the peritoneal cavity was washed with 10 ml of cold normal saline. After a two-minute massage, the cell exudate was removed with a syringe and centrifuged for five minutes at 250 x g at 4 degrees Celsius. Then, cells resuspended in RPMI-1640 medium were counted, adjusted in the same medium at 2-4 x 10⁶ macrophage / ml, and immediately tested. Eighty-five percent to 95 percent of these cells were macrophages by morphological criteria in Giemsa staining techniques. Viability as determined by trypan blue exclusion was always greater than 95 percent. The quantification of substrate adherence capacity was carried out according to the technique described by De la Fuente and colleagues,⁹ with minor modification. Sealers were placed in Eppendorf tubes at a certain height (5 mm) on the wall and on the floor of the tubes. Each sealer was tested four times after being mixing and placed in the tubes (immediately, 12 hours, 24 hours, and 48 hours after). After these periods, cell suspension was added to the tubes. In the control group, cell suspension was added to empty tubes. Adherence assays were performed at 10, 20 and 30 minutes of incubation at 37 degrees Celsius in a humidified atmosphere of 5 percent CO₂ to provide a maximum adherence index.¹⁰ After these times, nonadherent cell aliquots of 10 µl from each sample were taken, and the number of nonadherent macrophage/ml was counted in Neubauer

chambers. The adherence index was calculated according to the equation in FIGURE 1. The data were the evaluated statistically with the student's t-test. A value of P>0.05 was considered statistically significant.

Results

Results showed that zinc oxide-eugenol and Grossman sealers killed all macrophages in all tests situations, and the adherence index was considered less than 1 for these sealers. AH 26 reduced the adherence index in all different mixing and incubation periods, with the exception of 10 minute incubation in sealer that had been mixed 48 hours before the test. In that situation, the adherence index was increased slightly but this difference was not statistically significant (P<0.05) (FIGURES 2 THROUGH 5).

The difference in the adherence index in groups immediately and 12 hours after mixing was significant in 20- and 30-minute periods of incubation, and the difference in groups 24 hours after mixing was significant only in 30-minute periods of incubation (P>0.05).

Discussion

Gutta percha and sealer are essential for a successful root canal obturation. However, any sealer may extrude into periapical tissue, which could affect the healing process.^{1,2,11} Macrophages play an important role in the immune response of the host to noxious stimuli, as well as in the reparative process as a scavenger.^{7,12} At the level of periapical tissues, macrophages, with phagocytosis and antigen presentation, have a central role in repair

LEGEND FOR FIGURES 2-5

Control Sealer

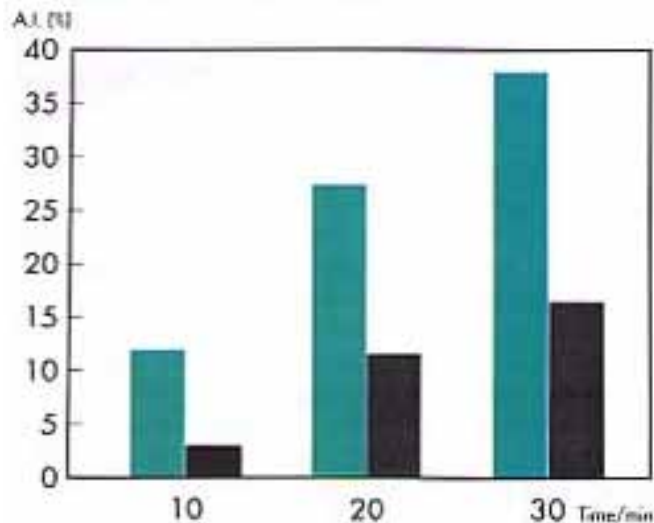


FIGURE 2. The adherence index results of the AH sealer immediately after mixing.

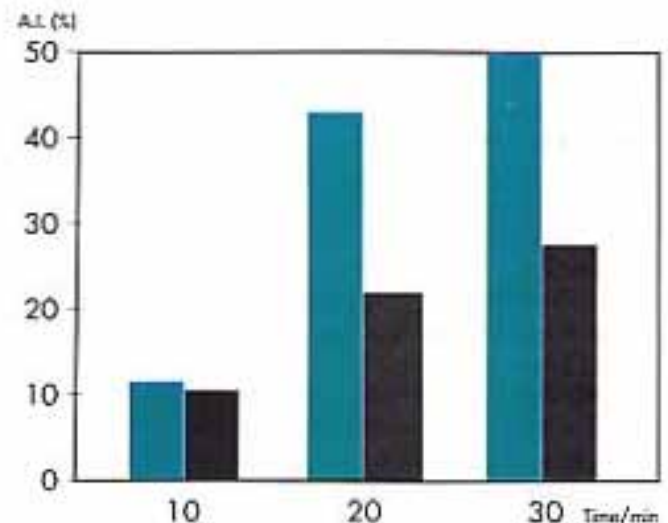


FIGURE 3. The adherence index results of the AH sealer 12 hours after mixing.

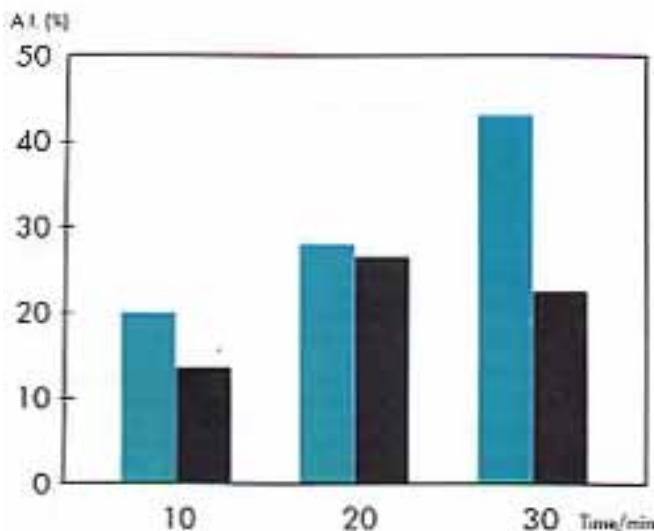


FIGURE 4. The adherence index results of the AH sealer 24 hours after mixing.

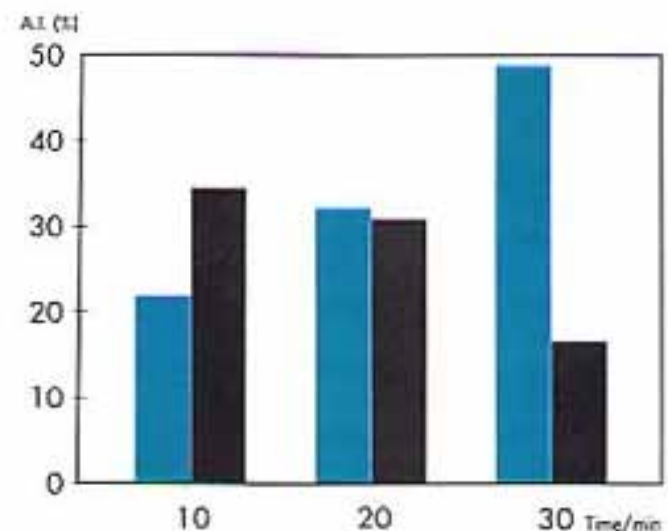


FIGURE 5. The adherence index results of the AH sealer 48 hours after mixing.

of chronic apical periodontitis.^{3,6,13} It is well-known that adherence is the first step in the phagocytic process of inflammatory macrophages.^{7,8} Therefore, each material that might affect the adherence of macrophages will affect phagocytosis and perhaps repair and inflammatory responses in periapical tissues.

Macrophages with adherence capacity were needed for this study. These cells

should be obtained from either an animal or human source. Since a lot of human blood is needed for human macrophages, animal models were used for this study. According to previous studies, the peritoneal cavity of mice is a good source of macrophages,¹⁴⁻¹⁸ and mouse macrophages have similar characteristics to human macrophages.¹² Intraperitoneal injection of thyoglycolate was used for

eliciting macrophages, per a technique by Valizadeh and colleagues.¹⁹ Substrate adherence capacity assays were carried out in Eppendorf tubes because the phagocytic cell adherence to a smooth plastic surface is comparable to that of animal tissues.^{9,20} For this experiment, three root canal sealers were selected (zinc oxide-eugenol, Grossman and AH 26). Zinc oxide-eugenol is the base of most sealers; Grossman

sealer is a zinc oxide-eugenol-based sealer with the most ideal characteristics; and AH 26 is a conventional root canal sealer with an epoxy resin base.

To evaluate macrophage adherence, the cell must be contacted only with sealer. For this reason, Eppendorf tubes were coated with sealer, and cell suspension was added to them. Therefore, these cells were surrounded with sealer. Results showed that zinc oxide-eugenol and Grossman sealers were very toxic to peritoneal macrophages. Some authors believe that the toxicity of these sealers is related to eugenol.²¹⁻²⁵ Becker and colleagues stated that eugenol is released from zinc oxide-eugenol up to one year after mixing.²⁶ Some authors, however, believe that the toxicity of zinc oxide eugenol results from zinc ions. Maseki and colleagues²⁷ observed the toxic effect of Zn²⁺ ions that decrease the ruffling borders of cell surfaces. AH 26 results showed that this sealer had less toxic effect than zinc oxide-eugenol and Grossman sealers on macrophages. However, a gradual increase in the number of dead cells after a 30-minutes incubation period could indicate that the gradual release of formaldehyde in the presence of moisture has a toxic effect on these cells. AH 26 decreased the adherence index in all tests, with the exception of 10 minutes incubation in sealer that had mixed 48 hours before the test. In that case there, was a slight increase of adherence index, which might be related to sealer projection after setting.

In this test, the wall of Eppendorf tubes were coated with sealer, and cell suspension was placed on the center of the coated walls; but in vivo there is no such condition, and apical extrusion of these sealers during root canal therapy could modify macrophage functions by modulating reparative mechanisms. Results indicate that peritoneal macrophages are very sensitive cells when they come into contact with the sealers used in this study. Because AH 26 didn't kill all the cells, it can be concluded that

AH 26 is the least-toxic sealer tested on macrophages.

REFERENCES

1. Ingle J, Bakland L, Endodontics, 4th ed. William & Wilkins, Baltimore, 1994.
2. Cohen S, Burns R, Pathways of the Pulp, 7th ed. Mosby, St Louis, 1998.
3. Weine FS, Endodontic Therapy, 5th ed. Mosby, St Louis, 1995.
4. Stern MH, Dreizen S, et al, Isolation and characterization of inflammatory cells from the human periapical granuloma. *J Dent Res* 61:1408-12, 1982.
5. Horton JE, Oppenheim JJ, et al, Macrophage-lymphocyte synergy in the production of osteoclasts activating factor. *J Immunol* 113:1278-87, 1974.
6. Torabinejad M, Eby WC, Naidorf JJ, Inflammatory and immunological aspects of the pathogenesis of human periapical lesions. *J Endod* 11(11):479-88, 1985.
7. Trowbridge HO, Inflammation, 5th ed. Quintessence, Chicago, 1997.
8. Male D, Champion B, Cooke A, Advanced Immunology, 2nd ed. JB Lippincott, Philadelphia, 1989.
9. De la Fuente M, Del Rio M, et al, Modulation of phagocytic function in murine peritoneal macrophages by bombesin, gastrin-releasing peptide and neuromedin C. *Immunology* 73(2):205-11, 1991.
10. Segura JJ, Guerrero JM, et al, Vasoactive intestinal peptide (VIP) inhibits substrate adherence capacity of rat peritoneal macrophages by a mechanism that involves cAMP. *Cell Adhes Commun* 1(3):210-21, 1993.
11. Seltzer S, Endodontology: Biologic Considerations in Endodontic Procedure, 2nd ed. Lee & Febiger, 1988.
12. Lewis CE, Mc Gee J, The Natural Immune System: The Macrophage, 1st ed. Oxford University Press, New York, 1992.
13. Segura JJ, Jimenez Rubio, Gomez Millan, Macrophage, 1st ed. Quintessence, Chicago, 1996.
14. Jimenez-Rubio A, Segura JJ, et al, In vitro study of the effect of sodium hypochlorite and glutaraldehyde on substrate adherence capacity of macrophages. *J Endod* 23(9):562-4, 1997.
15. Jimenez-Rubio A and Segura JJ, The effect of the bleaching agent sodium perborate on macrophage adhesion in vitro: implications in external cervical root resorption. *J Endod* 24(4):229-32, 1998.
16. Segura JJ, Calvo JR, et al, EDTA inhibits in vitro substrate adherence capacity of macrophages: endodontic implications. *J Endod* 23(4):205-8, 1997.
17. Segura JJ, Llamas R, et al, Calcium hydroxide inhibits substrate adherence capacity of macrophages. *J Endod* 23(7):444-7, 1997.
18. Segura JJ, Jimenez-Rubio AJ, et al, Effect in vitro of Tifell (formocresol-eugenol) on macrophage adhesion. *Int Endod J* 31(2):112-6, 1998.
19. Valizadeh M, Effect of Itraconazole & ketoconazole on major lyschmania in cell culture. Hygiene faculty of Tehran University, Thesis, 1992.
20. Noga SJ, Norman SJ, Weiner RS, Method in laboratory investigation: Isolation of guinea pigs monocytes and Kurloff cells. Characterization on monocyte subsets by morphology, cytochemistry and adherence. *Lab Invest* 51:244-52, 1984.
21. Biggs JT, Kamink EJ, Osetek EM, Rat macrophage response to implanted sealer cements. *J Endod* 11(1):30-6, 1985.
22. Arenholt-Bindslev D, Horsted-Bindslev P, A simple model for evaluating relative toxicity of root canal filling materials in cultures of human oral fibroblasts. *Endod Dent Traumatol* 5(5):219-26, 1989.
23. Briseno BM and Willershausen B, Root canal sealer cytotoxicity on human gingival fibroblasts: 2. Silicone- and resin-based sealers. *J Endod* 17(11):537-40, 1991.
24. Gerosa R, Borin M, et al, In vitro evaluation of the cytotoxicity of pure eugenol. *J Endod* 22(10):532-4, 1996.
25. Catanzaro Guimares SA and Percinoto C, Effect of some endodontic materials on the influx of macrophages and multinucleated giant cell development in experimental granulomas. *J Endod* 10(3):101-4, 1984.
26. Becker RM, Hume WR, Wolinsky LE, Release of eugenol from mixtures of ZOE in vitro. *J Pedod* 8(1):71-7, 1983.
27. Maseki T, Nakata K, et al, Lack of correlation between the amount of eugenol release from zinc oxide eugenol sealer and cytotoxicity of the sealer. *J Endod* 17(2):76-9, 1991.

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Controlling Biofilm and Microbial Contamination in Dental Unit Waterlines

THOMAS K. LEE, DDS; EMILE J. WAKED, DDS; LAWRENCE E. WOLINSKY, PhD, DMD; RONALD S. MITO, DDS; AND RICHARD E. DANIELSON, PhD

ABSTRACT Despite the fact that the ADA had set the goal of less than 200 colony-forming units per milliliter of unfiltered output water from dental unit waterlines to be achieved voluntarily by the year 2000, there is much confusion and resistance within the profession with regard to waterlines. Many in the profession are still wondering what the most effective means are to predictably achieve the goal. It is a well-established fact that bacterial biofilm can readily form within dental unit waterlines and degrade the microbial quality of the water in dental units regardless of the water source. These biofilms are primarily formed by various microcolonies of bacteria that attach to surfaces over time within the waterlines. An increasing number of medically compromised and immunocompromised patients being treated in dental offices and increased public awareness have brought about renewed interest in this issue. There are generally four categories of products that are available to address this issue: independent water systems, sterile water delivery systems, filtration, and chemical treatment protocols. A recent study at the University of California at Los Angeles demonstrates that the Ultra chemical treatment protocol can be an effective means of controlling biofilm in dental unit waterlines.

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Since Blake first described the microbial contamination of dental unit waterlines in 1963,¹ there have been numerous studies that affirmed his findings and explored ways to control the contamination. It is now well-established that the microbial quality of the water in dental unit waterlines can easily be compromised regardless of the water source due to the presence of biofilm.²⁻⁴ These biofilm are primarily formed by various microcolonies of bacteria and fungi that attach to the inner surfaces of dental unit waterlines over time, usually after no more than a few weeks at room temperature. Colonization of bacteria within the waterlines can occur through fluid retraction from the operating field through high-speed handpieces and air-water syringe lines when anti-retraction valves fail to work properly. However, even with properly working anti-retraction valves and sterile water as its source water, biofilm can eventually establish itself if no preventive



FIGURE 1. Scanning electron micrograph of new tubing in a dental unit waterline at 120x magnification.



FIGURE 2. SEM of new tubing in a waterline at 2,500x magnification.



FIGURE 3. SEM of biofilm buildup in a dental unit waterline at 120x magnification.

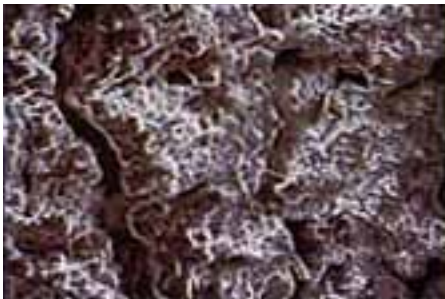


FIGURE 4. SEM of biofilm buildup in a waterline at 2,500x magnification.

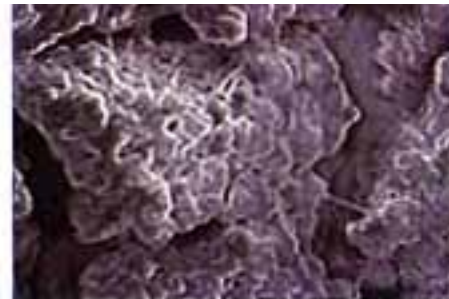


FIGURE 5. SEM of biofilm buildup at 4,500x magnification.



FIGURE 6. An open dental unit box showing numerous plastic tubes.

and disinfection measures are taken. In fact, as long as there is water present for a few weeks, biofilm will form in all dental unit waterlines even if no patients have been treated with a particular dental unit (**FIGURES 1 THROUGH 5**).

A quick review of biofilm and resulting bacterial contamination in general would be beneficial for a better understanding of its significance in dentistry. Biofilm and its bacteria are everywhere in nature, as long as there is a stagnant body of water or moisture. The representation of biofilm dentists are most readily familiar with is the dental plaque present in everyone's mouth. The slimy dark green stuff seen growing on any chronically wet surface is also biofilm. As such, biofilm formation in general is not unique to dentistry and is a major problem that has been dealt with in many other industries, such as the food and beverage industries. Another good example of biofilm hazard is public water fountains in parks and public buildings

since water can also stagnate in them for long periods.

The topic of biofilm and resulting microbial contamination in dental unit waterlines did not gain widespread attention from the dental profession until recently. The increasing number of medically compromised and immunocompromised patients treated in dental offices and increased public awareness have created a renewed interest in this issue.⁵ The main concern in dentistry is that contaminated water from biofilm-laden dental unit waterlines may be ingested by patients, may contact open wounds, or may be aerosolized and inhaled by patients and care providers during routine dental visits.⁵ Although no scientific evidence to date has demonstrated any direct detrimental health effects from biofilm-contaminated-water exposure to patients or practitioners, there is indirect evidence that points to the need for improved water quality in

dental offices.⁵⁻⁷ Most health professionals would also agree that it is inconsistent with currently practiced infection control protocols to routinely introduce large amounts of microorganisms per milliliter into patients' mouths when so much effort is made to disinfect and sterilize various dental instruments and equipment. There is a misconception among most dental professionals that the quality of the water going into the dental unit waterline is the same quality coming out the other end. This is simply not the case.

In dentistry, the stagnant water problem is exponentially compounded by the nature of dental unit waterlines. The extensive use of long, thin plastic waterlines within a dental operatory results in an extremely high surface-to-volume ratio within the tubing. In other words, there is a very large inner surface area for the small volume of water that passes through dental unit waterlines, leading to extremely high surface area

contact for the water in the system (**FIGURE 6**). Most dental procedures use relatively small amounts of water throughout the day, even during an active treatment day. Thus, only small amounts of water move through the tubing at any given time, contributing to easy formation of biofilm and ample time for the resulting microbial contamination of the water. Water sitting in such an environment for extended periods, e.g., overnight and weekends, at room temperature when the dental units are not in use would easily be a breeding ground for microbial proliferation and the resultant biofilm.⁵

In addition, friction near the tubing surface significantly slows down the movement of proximal water until the water flow at the surface is minimal. This hydrodynamic phenomenon, known as laminar flow, is another reason for the proliferation of the biofilm in dental unit waterlines since this phenomenon ensures prolonged contact time between the tubing inner surface and the proximal water.^{5,8} Another contributing factor to consider is that the polyurethane and polyvinyl chloride materials primarily used for waterline tubing also happen to be good substrates for biofilm formation because of their texture, as compared with the texture of metal piping, for example. The above-mentioned conditions add up to an ideal environment for biofilm formation within dental unit waterlines. Once a biofilm is established within a waterline, it quickly develops three-dimensional matrices that are quite resistant to most disinfecting efforts, and its inner layers are often able to survive germicidal assault. The biofilm is self-sustainable and does not require any further microbial contamination for future proliferation, and the water output from that unit becomes highly contaminated with bacteria that continuously proliferate and detach from the established biofilm.^{3,4}

The American Dental Association, through its Council on Scientific Affairs and Board of Trustees, in 1995 recommended that the research and dental manufacturing communities develop

methods to control and eliminate biofilm in dental unit waterlines. The ADA set a goal of less than 200 cfu/ml in unfiltered output water from dental unit waterlines for all dental procedures by the year 2000.⁹ The ADA's goal is more stringent than the drinking water standard, which is less than 500 cfu/ml; and the American Public Health Association along with the Organization for Safety and Asepsis Procedures have issued statements supporting the ADA goal.^{10,11}

The ADA and the Centers for Disease Control and Prevention guidelines recommend flushing waterlines for several minutes to remove suspended bacteria before the first patient of the day is treated, and for 20 to 30 seconds between patients to remove material that may have been retracted during treatments.^{5,12,13} Such flushing may minimize the risk of colonization and cross infection; however, its effects are only temporary. It is now well-established that flushing alone fails to eliminate or prevent bacterial colonization.^{3,14}

In recent years, the Food and Drug Administration has approved various products intended to improve the microbial quality of dental unit water.⁵ These products generally fall into four categories: independent water systems, sterile water delivery systems, filtration, and chemical treatment protocols.

An independent water system is disconnected from the municipal (tap) water source and draws fluid from a reservoir bottle holding the practitioners' choice of water or treatment solution. Most major dental unit suppliers now offer retrofitting for older dental units for this option, and it is not too costly. The major advantage of this design is that the practitioner's independent water source of choice and various chemical treatments for the dental unit waterlines can be used. While regular flushing with a disinfectant solution is easy and practical with this system, the system can also be used to dry the internal surfaces of the waterlines by purging the system of the solution until

the system is void of the water. Although waterlines are less susceptible to biofilm formation while when they are kept dry overnight, there is no literature to support that dental unit waterlines left dry overnight achieve biofilm control. It is also noteworthy that sterile water put into an ordinary independent water system would not maintain its sterility as it goes through the dental unit waterlines.

Sterile water delivery systems, required for surgical procedures, are expensive to purchase and operate, and are often less convenient to use than other available delivery systems in the general dentistry setting. For the sterile water delivery system to be effective, it must be kept independent of the dental unit waterlines and the waterlines must be either replaced or sterilized after each use. Although well-suited for many surgical procedures, sterile water delivery systems are neither practical nor necessary for most general dentistry procedures.

Filtration involves the use of 0.2 m m membrane filters. Although this method can be effective in filtering out most of the potentially harmful bacterial organisms, location of the filter within the waterlines and its maintenance are critical to its success since the filters have no effect on pre- or post-filter biofilm formation itself. Of particular concern is that the dental unit waterline segment beyond the filter remains vulnerable to colonization over time. Hence, the distance between the filter and the high-speed handpiece or the air-water syringe must be minimized or eliminated because the biofilm can easily establish itself in such a location and essentially render the filter ineffective. Filters can be expensive and often require shortened replacement intervals as the biofilm colonies potentially get worse at the pre-filter location and clog up the waterlines at the filter point. Also, high levels of bacterial endotoxins that cannot be filtered with the 0.2 m m membrane filters have been found in contaminated dental unit



FIGURE 7. SEM of dental unit waterline tubing after biofilm build-up and subsequent treatment by Ultra at 120x magnification.



FIGURE 8. SEM of dental unit waterline tubing after biofilm build-up and subsequent treatment by Ultra at 2,500x magnification.

waterlines when filtration methods are exclusively used for a long time.

Finally, chemical treatment protocols, depending on the nature of various germicidal agents, may be used intermittently as a “shock” treatment or continuously introduced into waterlines in small quantities.¹⁵⁻¹⁷ This protocol requires having an independent reservoir system from which the solution of choice can be originated. Bleach (sodium hypochlorite) along with various proprietary chemicals, such as Bio-2000 (chlorohexidine, glycerin and alcohol-based), Dentacide (iodine-based), Bioclear (citric acid-based) and Ultra (alkaline peroxide-based) are some of the examples of chemical treatment protocols on the market for dental practitioners’ use.

Some dental equipment manufacturers recommend weekly cleaning by flushing the units with a 10 percent bleach solution for 10 minutes. This approach has been supported by various studies and the ADA, with the understanding that details of the protocol must be adhered to for its clinical efficacy.^{15,16} However, bleach may have unintended corrosive effects on various parts of dental equipment and introduces the risk of patient exposure to harmful chemicals, such as trihalomethanes (suspected human carcinogen), in systems using continuous bacteriostatic chlorination.⁸

Another issue to keep in mind for various chemical treatments, especially the ones that are used continuously in

small amounts, is the potential bacterial resistance in the long run and their interactions with other dental materials used in the clinical setting such as bonding agents. Attempts to simply kill the bacteria within biofilm is also ineffective because disinfectants or germicidal agents often fail to penetrate the complex matrix of the biofilm, resulting in viable bacteria within the matrix that can get dislodged and immediately re-contaminate the water or eventually contribute to bacterial resistance. Literature review indicates that biofilm and resulting bacterial contamination within dental unit waterlines are best managed when biofilm itself is somehow physically removed. In fact, that is how dentists best deal with the other form of biofilm well known to dentistry -- dental plaque. Dental plaque is mechanically removed by brushing, flossing, and scaling and root planning. Although it is impractical to brush the insides of the dental unit waterlines where the biofilm reside, a chemical treatment that will physically remove the biofilm would be ideal.

Only one product in the marketplace, Ultra (formerly marketed as Ultrakleen, Sterilex, Baltimore, MD), has received ADA’s Seal of Approval in controlling biofilm. Ultra achieves the ADA-set goal of less than 200 cfu/ml by physically removing the biofilm within the waterlines. This physical removal of the biofilm prevents or minimizes bacterial contamination of the dental unit

waterlines. According to preliminary results of a recent study at UCLA (supported by a gift from A-dec, Inc.), the alkaline peroxide product Ultra was effective at physically removing the established biofilm (**FIGURES 7 AND 8**). Microbial evaluations as in various heterotrophic plate counts indicated that this alkaline peroxide product is effective at maintaining the water supply under the ADA goal of 200 CFU/ml when used weekly, as directed by the manufacturer.

TABLES 1 AND 2 represent preliminary data from the study.

The following are some of the results of the study:

- Flushing of the waterline before and after patient treatments failed to achieve the ADA goal.
- Bleach protocol achieved the ADA goal 54 percent of the time.
- Ultra achieved the ADA goal 100 percent of the time at one week after treatment.

When the recommended protocol is followed using Ultra, a water supply meeting the ADA set goal of less than 200 cfu/ml can be achieved, as long as the source water itself meets the ADA standard. Weekly treatments with this alkaline peroxide system (the manufacturer’s recommended protocol) will consistently achieve the water quality that is needed to satisfy the ADA goal of less than 200 cfu/ml. A-dec’s internal experiments have also indicated that Ultra is noncorrosive to various A-dec components within dental unit waterlines (personal communication with A-dec, Inc.).

Biofilm and the microbial contamination of dental unit waterlines are real issues that require real solutions in an everyday clinical setting. There are many ways to approach this problem as was reviewed in this article. It is recommended that each dental practitioner evaluate the clinical setting he or she is in and implement appropriate protocols to achieve the goal of delivering water that meets the ADA goal.

TABLE 1. Treatment and Sampling Frequencies.

	Treatment	Sampling
Group A	Flushing method/control	Weekly/ No Chemical Tx
Group B	Sodium hypochlorite(Bleach)	1day post Tx
Group C	Alkaline peroxide (Ultra)	1 day post Tx
Group D	Alkaline peroxide (Ultra)	8 days post Tx
Group E	Alkaline peroxide (Ultra)	15 days post Tx
Group F	Alkaline peroxide (Ultra)	22 days post Tx

TABLE 2. Colony Counts for Control and Treatment Groups

Group	Mean (log CFU)	SE (log CFU)	t-Statistic	p-value	Geometric Mean (CFU)
A	4.348	0.243	–	0.000	22284.351
B	2.207	0.423	4.392	0.000	161.065
C	-1.212	0.429	11.280	0.000	0.061
D	-0.224	0.475	8.568	0.000	0.597
E	1.314	0.622	4.544	0.000	20.606
F	1.062	0.630	4.870	0.000	11.535

Note: The t-statistics and p-values above are for comparisons of a particular group to Group A.

REFERENCES

- Blake GC, The incidence and control of bacterial infection in dental spray reservoirs. *Br Dent J* 115:413-6, 1963.
- Williams HN, Baer ML, Kelley JJ, Contribution of the dental unit water supply. *J Am Dent Assoc* 126(9):1255-60, 1995.
- Mayo JA, Oertling KM, Andrieu SC, Bacterial biofilm: a source of contamination in dental air-water syringes. *Clin Prev Dent* 12:13-20, 1990.
- Whitehouse RL, Peters E, et al, Influence of biofilm on microbial contamination in dental unit water. *J Dent* 19:290-5, 1991.
- ADA Council on Scientific Affairs, Dental unit waterlines: Approaching the year 2000. *J Am Dent Assoc* 130:1653-64, 1999.
- Mills SE, The dental unit waterline controversy: Defusing the myths, defining the solutions. *J Am Dent Assoc* 131:1427-41, 2000.
- Pankhurst CL, Johnson NW, Woods RG, Microbial contamination of dental unit waterlines: the scientific argument. *Int Dent J* 48(4):359-66, 1998.
- Costerton JW, Overview of microbial biofilms. *J Ind Microbiol* 15:137-40, 1995.
- ADA Council on Scientific Affairs and ADA Council on Dental Practice, Infection control for the dental office and dental laboratory. *J Am Dent Assoc* 127:672-80, 1996.
- Bednarsh H, Bond W, presiders, Dental unit water: how good is good; how bad is bad? Symposium presented at: American Public Health Association Annual Session, Indianapolis, Nov 10, 1997.
- Organization for Safety and Asepsis Procedures, Position paper on dental unit waterlines. OSAP, Annapolis, Md, 1997.
- Centers for Disease Control and Prevention, Recommended infection-control practices for dentistry, 1993. *Morb Mortal Wkly Rep* 41(RR-8):1-12, 1993.
- American Dental Association, Dentist's desk reference: Materials, instruments and equipment, 2nd ed. ADA, Chicago, 1983, p 16.
- Williams JF, Johnston AM, et al, Microbial contamination of dental unit waterlines: prevalence, intensity and microbiological characteristics. *J Am Dent Assoc* 124:59-65, 1993.
- Fayle SA, Pollard MA, Decontamination of dental unit water systems: a review of current recommendations. *Br Dent J* 181:369-72, 1996.
- Williams HN, Kelley J, et al, Assessing microbial contamination in clean water dental units and compliance with disinfection protocol. *J Am Dent Assoc* 125:1205-10, 1994.
- Meiller TF, DePaola LG, et al, Dental unit waterlines: biofilms, disinfection and recurrence. *J Am Dent Assoc* 130:65-72, 1999.

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Acute Acetaminophen Toxicity: Report of a Case

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ABSTRACT A case of acetaminophen overdose in a patient presenting with a mandible fracture is presented to illustrate the clinical scenario, pathophysiology, and treatment of acute toxicity with this commonly used over-the-counter medication.

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Acetaminophen (N-acetyl-p-aminophenol) is an over-the-counter analgesic and antipyretic agent that has gained tremendous popularity in the past three decades due to its presumed safety and low toxicity, especially when compared to the gastrointestinal side effects of aspirin and other NSAIDs. It is the most widely used and recommended nonprescription analgesic and antipyretic medication in the United States.¹ The drug was first discovered at Johns Hopkins University in 1877, but it was not marketed in the United States until 1950, replacing phenacetin. The association between the excessive use of phenacetin and the development of renal failure is well-documented.² In the United Kingdom, overdose is commonly seen in young adults.³ The first reported case of acute acetaminophen-induced hepatic necrosis after massive overdose was reported in 1966.⁴ Acetaminophen hepatotoxicity is

well-recognized^{5,6} and is observed with ingestion of massive doses as a result of accidental ingestion or attempted suicide. In the previous decade, it was reported to be the No. 1 cause of acute hepatic necrosis and a major method of attempted suicide in the United Kingdom.⁷ Currently, acetaminophen is implicated in 15 percent to 30 percent of deliberate self-poisoning in the United Kingdom.⁸

For adults, the recommended daily dosage is not to exceed 4 grams. The minimum acute toxic dose (minimum single dose required to produce toxic effects) is 5 to 15 grams (10 to 30 500 mg tablets). The acute lethal dose (minimum single dose required to cause death) ranges from 13 to 25 grams.⁶ Almost 50 percent of adults develop fatal liver damage at an oral dose of 250 mg/kg (17.5 g in a 70 kg adult) and 100 percent at 350 mg/kg (24.5 g in a 70 kg adult).⁹ Chronic hepatic enzyme microsomal induction, as in chronic alcoholism or barbiturate use, and concomitant ingestion of

TABLE 1. Commonly Encountered Acetaminophen-Containing Preparations

Anexia:	Hydrocodone/acetaminophen
Capital with codeine:	Codeine/acetaminophen
Darvocet:	Propoxyphene/acetaminophen
Fioricet with Codeine:	Codeine/caffeine/acetaminophen
Lorcet:	Hydrocodone/acetaminophen
Lortab:	Hydrocodone/acetaminophen
Percocet:	Oxycodone/acetaminophen
Tylenol #3:	Codeine/acetaminophen
Tylox:	Oxycodone/acetaminophen
Vicodin:	Hydrocodone/acetaminophen
Wygesic:	Propoxyphene/acetaminophen
Zydene:	Hydrocodone/acetaminophen

acetaminophen can cause severe hepatic damage at oral doses of less than 10 grams.¹⁰⁻¹³

Case Report

A 64-year-old male was referred to the Oral and Maxillofacial Surgery Department at the Atlanta Veterans Affairs Medical Center. His chief complaint was pain in his lower jaw. He reported being assaulted 11 days prior to admission. Past medical history was remarkable for splenectomy secondary to previous abdominal trauma, prostate cancer, cigarette smoking, and alcoholism. The patient stated that he was not taking any medications and was homeless.

Physical examination revealed right facial pain along the inferior border of the mandible with opening and closing. The patient also had tenderness to palpation in his left preauricular region and decreased sensation in his right chin and lip. Abdominal examination was positive for tenderness to palpation in the right upper quadrant. Radiographic evaluation revealed a right mandibular body and left subcondylar fractures. Admission labs were significant for elevated LDH (2116 u/l) (normal: 71-207u/l), AST (SGOT) (233 u/l) (normal: 4-140 u/l), and total bilirubin (1.7 mg/

dl) (normal: 0.3-1.4 mg/dl), which are consistent with nonspecific parenchymal liver damage. The patient was admitted for evaluation of elevated liver enzymes and treatment of mandibular fractures. Subsequent hepatitis serology was negative.

During the second hospital day, upon further questioning, the patient admitted to consuming 36 tablets of 500 mg acetaminophen (18 grams) with acute ethanol ingestion in a period of two days prior to admission. On the third hospital day, the following values were obtained: LDH 129 u/l, AST (SGOT) 115 u/l, total bilirubin 0.5 mg/dl, which are consistent with recovery from the prior hepatic insult.

Discussion

In recent years, acetaminophen has gained wide acceptance as an over-the-counter medicine and in prescription-combination medications for the treatment of pain and fever. It is also found in many commonly available cold medications, sleep aids, and allergy-relief medicines. Prescription use of acetaminophen is usually found in combination with other pharmaceuticals for the treatment of pain (TABLE 1). Many patients take medications containing acetaminophen on a daily basis. It is not

uncommon for patients to be unaware of the potential complications their over-the-counter medications may pose when combined with prescription medications. This lack of awareness can result in significant morbidity and mortality in otherwise healthy patients and especially in those who have compromised hepatic function.

The initial presentation of acute lethal acetaminophen overdose can be asymptomatic or may present with mild gastrointestinal irritation including nausea and vomiting. The latter presentation is more commonly observed in children. Twenty-four to 48 hours after ingestion, a latent period is observed characterized by a false sense of well-being. Signs of progressive hepatic encephalopathy (disturbances in consciousness, hyperreflexia, asterixis, and, rarely, seizures) may develop three to four days after ingestion. Liver dysfunction may manifest itself in a variety of clinical symptoms. However, jaundice, fetor hepaticus, and hepatic encephalopathy are usual. Centrilobar hepatic necrosis may extend to involve the entire lobule. In some cases, there is evidence of concurrent renal and myocardial damage.¹⁴ Death from hepatic failure occurs four to 18 days after ingestion. Patients with suspected acute acetaminophen overdose should be rapidly referred to the emergency department for prompt medical attention including plasma acetaminophen levels, liver function tests, induced emesis, and subsequent administration of activated charcoal and/or N-acetyl-L cysteine. Induced emesis and N-acetyl-L cysteine are most effective if provided within four to six hours and 10 hours after ingestion respectively.⁶ Patients should be closely monitored several days after ingestion for development of symptoms of hepatic encephalopathy. In patients who recover, liver function tests progressively return to normal several days after ingestion.

About 5 percent of acetaminophen

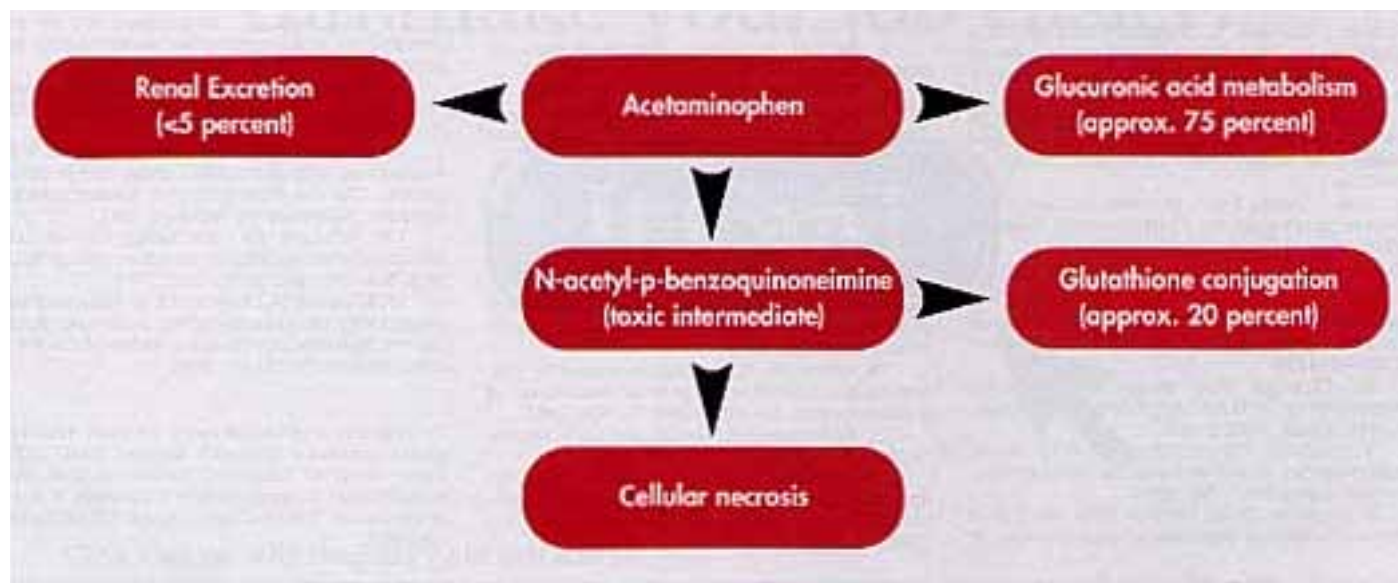


FIGURE 1. Overview of acetaminophen metabolism.

is excreted unchanged by the kidneys. The glucuronic sulfate pathway of the liver metabolizes the greater fraction of the drug. A smaller portion is metabolized by the hepatic microsomal oxidase system into a toxic metabolite, N-acetyl-p-benzoquinoneimine, that is rapidly conjugated by glutathione. In toxic overdose, depletion of hepatic glutathione leads to the accumulation of N-acetyl-p-benzoquinoneimine, which mediates hepatic necrosis due to electrophilic attack of nearby structures in hepatocytes. N-acetyl-L cysteine is used as an antidote since it is a precursor of glutathione and therefore facilitates the conjugation of the toxic intermediate (FIGURE 1).⁶

Dentists and other health care professionals frequently manage patients with pain. A careful history and a high index of suspicion are essential to reduce the significant morbidity and mortality associated with excessive acetaminophen ingestion.

Questions that are designed to identify patients with compromised liver function should be a routine part of the patient evaluation. Patients should be alerted to the fact that acetaminophen

(Tylenol) can be harmful and that it only takes eight extra-strength tablets to reach the maximum daily dose. Patients with compromised liver function as in chronic alcoholism have a decreased ability to clear acetaminophen and are more prone to toxic injury. Conversely, acute alcohol ingestion in an otherwise healthy individual will actually induce the hepatic microsomal oxidase system and increase the removal of the toxic ingredient from plasma. In this case report, the patient neglected to report self-medication with acetaminophen despite initial questioning during the history and physical. Markedly elevated liver function tests led to the discovery of acetaminophen-induced hepatotoxicity. Fortunately, the patient recovered successfully; and no residual hepatic damage was observed. However, the literature is replete with cases of hepatic necrosis after acute acetaminophen overdose.¹⁵⁻¹

REFERENCES

- Rose SR, Subtleties of managing acetaminophen poisoning. *Am J Hosp Pharm* 51:3065-8, 1994.
- Katzung BG, Basic and Clinical Pharmacology, 5th ed. Appleton and Lange, Norwalk, Conn, 1992, p 505.
- Dubose TD Jr, Molony DA, et al, Nephrotoxicity of non-steroidal anti-inflammatory drugs. *Lancet* 344:515-8, 1994.
- Davidson DGD, Eastham WN, Acute liver necrosis following overdose of paracetamol. *Br Med J* 2:497-9, 1966.
- Black M, Acetaminophen hepatotoxicity. *Gastroenterology* 78:382-92, 1980.
- Ellenhorn MJ, Schonwald S, et al, *Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning*, 2nd ed. Williams and Wilkins, Baltimore, 1997, pp 180-95.
- Henry J, Volans G, Analgesics: II -- Paracetamol. *Br Med J* 289:907-8, 1984.
- Loeb DS, Ahlquist DA, Talley NJ, Management of gastroduodenopathy associated with the use of non-steroidal anti-inflammatory drugs. *Mayo Clin Proc* 67:354-64, 1992.
- Prescott LF, Critchley JAJH, The treatment of acetaminophen poisoning. *Ann Rev Pharmacol Toxicol* 23:87-101, 1983.
- Pirotte JM, Apparent potentiation by phenobarbital of hepatotoxicity from small doses of acetaminophen. *Ann Intern Med* 101:403, 1984.
- Fleckenstein JL, Nyquil and acute hepatic necrosis. *N Eng J Med* 313:48, 1985.
- Licht H, Seeff LB, Zimmerman HJ, Apparent potentiation of acetaminophen hepatotoxicity by alcohol. *Ann Intern Med* 92:511, 1980.
- McClain CJ, Kromhout JP, et al, Potentiation of acetaminophen hepatotoxicity by alcohol. *J Am Med Assoc* 244:251-3, 1980.
- Kumar V, Cotran RS, Robbins SL, *Basic Pathology*, 5th ed. Saunders, Philadelphia, 1992, pp 229.
- Johnson MW, Friedman PA, Mitch WE, Alcoholism, nonprescription drugs and hepatotoxicity. The risk from unknown acetaminophen ingestion. *J Gastroenterol* 76:530-3, 1981.
- Schiodt FV, Rochling FA, et al, Acetaminophen toxicity in an urban county hospital. *New Eng J Med* 337:1112-7, 1997.
- Johnston SC, Pelletier LL Jr, Enhanced hepatotoxicity of acetaminophen in the alcoholic patient. Two case reports and a review of the literature. *Medicine* 76:185-91, 1997.

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Shedding Light on Amalgam

Did a pleasant thought pass through your mind today? Did something tickle your risibility to the point of causing the corners of your mouth to rise ever so slightly? If so, then you just don't get it, do you? The world is going to hell in a handbasket, environmentally speaking, and you need to pay attention.

Environmentalists are determined to convince us that if we are not part of the solution, we are part of the problem. Fortunately, we have an on-the-ball governmental agency working overtime to discover new threats to our way of life. Combining forces with concerned citizens who see global warming and pollution of air, water, food and dirt proliferating faster than boy bands, the U.S. Environmental Protection Agency has just issued another warning.

Michael Osborne, chief of the Indoor Environment Management Branch of the EPA, recently revealed that candles can now be blamed for Earth's pollution. The pollution from a burning candle can exceed standards the agency sets for air quality, he says. This announcement immediately caused Valerie Cooper, executive director, of the National Candle Association to burst into spontaneous combustion. It's not the lit candle that contributes to the high level of particulates, she explains, but the result of candles smoldering.

These two entities, the EPA and the NCA, have sensibly arrived at a tentative compromise, suggesting that candlewicks be trimmed to a quarter inch, the house be ventilated, and all lit candles be kept out of drafts, much as you would an older person. Please try to keep that in mind at your next birthday party or when rolling blackouts prompt your area to fire up all the candles it can lay hands on.

Would that our remaining pollution problems could be coped with so easily. Specifically, we refer to the ongoing amalgam wars. The skirmishes seem to be heating up with the enthusiastic support of trial lawyers asking themselves, "WWJD?" referring, of course, to Johnny Cochran.

All right, all those who believe that mercury is a toxic substance raise your hands. Right -- 100 percent. Now, all those who believe that it is a major threat to personal health when incorporated in silver amalgam fillings, a show of hands please. Ah, not so many, but when combined with the hesitant hands of those not so certain one way or the other, a group to be reckoned with.

One particularly disturbed lady on television recently declared that "silver" fillings (a misnomer she hates) contain 50 percent mercury, and a conspiracy was afoot fomented by dentists and their organizations to keep consumers from realizing this.

Robert E.
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Aside from the fact that amalgam is esthetically on a par with homemade soap, it seems to be a scientifically proven fact that mercury vapor is released every time the owner of amalgam-filled teeth chews. Chews what? Mashed potatoes or beef jerky? You would think the quantity of the vapors released might depend on the texture of the food and the forces of mastication.

Never mind, mercury vapor belongs in lamps, not in your mouth is the reasoning here. One mouth = X amount of vapor, possibly an infinitesimal amount, but most adults have any number of amalgams accumulated since childhood. A conservative estimate puts the total number at slightly more than 875,642,416,924 as of last Thursday. These are primarily Class 1s and 2s with a sprinkling of Class 5s. A gentleman in Biloxi, Miss., is said to have a Class 4 placed by his dentist in 1904.

Let us imagine that around 6 p.m., beginning on the East Coast, all these mouths start chewing their dinners. The release of mercury vapor suddenly becomes less of a personal problem and more of a national one as the cumulative toxicity exhaled exacerbates our air pollution beyond tolerable levels. The toxic air, despite the normal flow of wind from West to East, proceeds westerly like the "wave" at sporting events, passing through time zones like Grant through Richmond.

Three meals a day plus snacks, 150 million amalgam-enhanced jaws chomping away -- the portents are mind boggling! We are fortunate that there are those who care enough to press for solutions to this problem. So far, considerably more heat than light has evolved.

Shall dentists immediately start to work excavating old amalgams, thereby releasing even more mercury vapor in the process? An undeniably profitable, but potentially unethical, idea. Should the proposal be based on toxicity fears or sweetened with the promise of enhanced esthetics? Shall amalgam be declared a controlled substance, the use of which invites a stretch in a federal pen? What about the International Amalgam Cartel? It's not going to be too happy explaining the ban to its stockholders. Shall a law putting a \$50 cap on lawyers' fees be enacted ASAP to discourage the frenzy that is sure to erupt when mercury poisoning becomes the most popular litigation since sexual harassment?

These are some of the profound questions that face us today. In the interests of fair play, may we recommend arbitration with the EPA and the National Candle Association offering their input on this smoldering dilemma?