

Breaking News in Inflammation

By **Susan Elliott-Smith**

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Oral inflammation is a problem associated with a growing number of diseases throughout the body. Research experts share the latest information on periodontal disease, its associations and how to present an accurate oral health message to patients.

It sounds like science fiction, but in reality it is science fact: For every one of the cells that make up our body, there are 10 bacteria cells living in us or on us. Sometimes these bacteria co-exist harmlessly with us; sometimes not, said Steven Offenbacher, DDS, PhD, MMs. In the oral cavity, some bacteria grow in a micro-community of biofilm, or plaque, described as a tough, "coral reef" structure of micro-organisms that can be difficult to remove and thrive in the oxygen-poor environment of the mouth.^{1,2}

As the plaque builds up – due to a lack of good home care, infrequent dental cleanings and sometimes a genetic predisposition to do so – the body begins an assault on it known as inflammation.

Signs of severe inflammation that the dental hygienist might see during an exam include redness of the gingiva, ulceration of the pocket epithelium and bleeding on probing – classic symptoms of gingivitis. In some cases, dental hygiene debridement and regular home oral hygiene care can return the gingival tissues to a state of health. However, for some individuals the inflammatory process continues and expands, the collagen of the periodontal ligament breaks down and bone resorption occurs, resulting in periodontitis.³

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These are inflammation basics dental hygienists learn in the first few days of their education. The question is: What's new? Is there any breaking news in inflammation?

"The breaking news in inflammation is that it is an all-pervasive host response that is intimately linked to a number of very common conditions that afflict individuals," said Ray Williams, DMD. These afflictions include diabetes mellitus, cardiovascular disease (CVD) and adverse pregnancy outcomes, to name a few. What is the link between the body's bacterial battle in the mouth and distant locations in the body?

"When you have certain bacteria in your mouth, your body reacts with inflammation," said Ira B. Lamster, DDS, MMSc. "As a result of that inflammation, cells release molecules that affect local tissue and may go beyond the gingiva and affect other cells, tissues and organs in the body," he continued, adding that these molecules have been shown to affect blood vessels that supply the heart, brain and other organs.

"Patients may hear it but have to appreciate that oral disease is an inflammatory response that provides bacterial

exposure to the whole body," Offenbacher stated. "In other words, this is a disease that leaks throughout the body."

The Process of Inflammation

What dental hygienists understand and need to know about inflammation depends somewhat on when they completed their dental hygiene education and the degree to which they have remained abreast of the evidence in this area, according to Karen B. Williams, RDH, MS, PhD.

"The one thing we talk about a lot is plaque, but there is also the degree to which the immune system can manage the microbial insult," she commented.

In the last five years, the role of inflammation in many diseases has become readily apparent. Diseases once associated with other factors – such as atherosclerosis, Alzheimer's, diabetes – are now thought of as inflammatory diseases, according to Ray Williams.

"We used to talk about atherosclerosis as a lipid or cholesterol and fat disease. Now we talk about it as an inflammatory disease," he commented. "Inflammation has come to the forefront of many systemic conditions, and we realize that unraveling the mysteries of the inflammatory response and its resolution may offer phenomenal clues on how to prevent not just oral disease, but other diseases," Ray Williams continued.

Inflammation is a complex reaction, according to Lamster. "This discussion is how a localized inflammation can affect other parts of the body," he commented. "There are 300 to 400 different species of microorganisms in the oral cavity," and the body's inflammatory response to these organisms is usually protective but can have detrimental effects.

Ray Williams explained that inflammation is a normal protective response of the host that is a necessary part of protecting us against bacteria and other insults, "but inflammation, in its zeal to do a good job, also leads to mediators, enzymes and lipids that ultimately can have a destructive component to the oral tissue," he continued. "We have always thought of inflammation as being a result of some form of injury. In the case of the mouth, that injury is most often that accumulation of bacterial plaque on the teeth and the gingiva that then elicits the host's inflammatory response."

In short, we are our own worst enemies in the bacterial fight. "For years now, our focus has been on the etiologic role of the bacteria," said Ray Williams. "Now we realize that bacteria in the mouth elicit a host immuno-inflammatory response. Although the response is protective and appropriate, in its exuberance, it actually leads to destruction of the tissues around teeth."

Genetic, microbial, immunological and environmental factors influence both the risk and progression of infection. The American Academy of Periodontology says that perhaps one-third of Americans may be genetically susceptible – making them up to six times more likely to develop periodontal disease.²

Diseases such as diabetes can enhance the effects of inflammatory response. Critical links between periodontal disease and the development of type 2 diabetes, as well as the development and progression of its complications, were reported in June in the first-ever symposium presented by dentists to diabetes experts at the American Diabetes Association's Annual Scientific Sessions' 68th event. One of the many complications of diabetes is a greater risk for periodontal disease. Patients with oral inflammation face greater difficulty controlling blood glucose levels. Intensive periodontitis treatment significantly reduces levels of A1C, a measure of glucose control over the prior two to three months. These links between oral and systemic health may start even before clinical diabetes begins, the diabetes association reported in a post-meeting news release.

In women who are pregnant, premenstrual or are taking oral contraceptives, changing hormone levels can cause oral inflammation flare-ups.² Other medications that disrupt the mouth's bacterial ecosystem, including antihistamines, antidepressants, cancer drugs, steroids and especially those that cause xerostomia, can also make the gingival tissue more susceptible to infection.²

It is important for the dental hygienist to understand that half the variability in the severity of periodontal disease is caused by genetic differences, and the genetic basis of inflammatory response plays a key role, Offenbacher said. Conditions such as diabetes or smoking can make the disease even worse, especially if the genetic predisposition is present.

"We now know that bacterial infections work to modify the host's local tissue metabolism. We used to think that bacteria just caused an inflammatory response, and that we just had to eliminate or reduce the infection to reduce the inflammation," stated Offenbacher. "But we now understand that the bacteria cause a change in the local tissue metabolism (by epigenetic mechanisms) that can produce stable changes in the local tissue metabolism that favor the re-emergence of the bacterial biofilm."

He explained that this is caused by changing the structure of the host's chromatin and DNA by a process called epigenetic modification. This suggests, according to Offenbacher, that while eliminating the bacteria may reduce inflammation, the infection has placed an "epigenetic footprint" on these tissues that can persist even after the bacteria are removed, resulting in a sustained alteration in tissue metabolism that makes it easier for the biofilm to re-establish. For example, the periodontal tissues will release more glucose after being epigenetically modified, and that glucose will enhance the colonization and growth of many biofilm bacteria.

The Oral-Systemic Link

"The first associations between periodontal disease and other diseases focused on four categories," Lamster explained.

"Certain cardiovascular/cerebrovascular diseases, adverse obstetrical outcomes, diabetes and respiratory diseases. There is fairly robust literature on each of these topics."

There are newer associations being made between oral inflammation and cancer, end-stage renal disease and even, according to a recent cover story in the *Journal of the American Dental Association*, dementia.

"What this has led to is the concept that oral health is a very good general measure of overall health," said Lamster. "The cause-and-effect relationships are not as well defined. In other

words, you can ask the question: If I treat periodontal disease, will I avoid a heart attack or stroke? The answer is not that simple. These are complex diseases. Periodontal disease in all likelihood contributes to these diseases, but is by no means the only risk factor."

Karen Williams agreed, cautioning dental hygienists not to attribute causality for patients, such as because they have periodontal disease, they will have a heart attack in the future.

"Just because periodontal inflammation has been shown to be a risk factor for other systemic diseases doesn't mean that periodontal disease causes other problems," she said. "There is a body of evidence out there in the literature that shows that periodontal inflammation is a risk factor. Most of those findings are derived from observational designed studies. They are not experimental and thus don't definitively establish a causal link."

Instead she encourages professionals to understand the periodontal inflammatory process' connection to patient's systemic health.

"[Dental hygienists should] understand that bacteremias and endotoxemias, associated with oral organisms, can occur in individuals with periodontitis," she continued.

Once these periodontal pathogens enter the bloodstream, they can contribute to atheroma formation.

"I think that's the link that dental hygienists need to understand," she continued, that periodontal pathogens can contribute to atheroma formation and atherosclerosis. "It's not that the periodontal disease will cause a heart problem, per se, it's the fact that those organisms, once they enter the bloodstream, can stimulate endothelial cells, and that gets the whole systemic inflammatory process going."

On the flip side, treating periodontal inflammation can improve endothelial function that theoretically reduces systemic risk and periodontal pathogens and can attempt to reduce the microbial load, according to Karen Williams.

"Having said that, it doesn't mean if you have periodontal disease and you treat it, that you'll cure systemic diseases either," she continued. "The whole issue of causality needs to be considered practically. We don't have evidence of causality either way – that periodontal disease causes these systemic factors or that treating periodontal disease will prevent those factors."

Most of the studies done to date, Karen Williams pointed out, are observational, meaning researchers examine disease outcomes – cardiovascular, pregnancy, diabetes, etc. The researchers observe these outcomes in populations that already have them or don't have them and draw comparisons.

"So there's no manipulation of an independent variable, which is one of the requirements for establishing causality," she stated, adding that there are several criteria for establishing causality. "We can say there is a correlation," Karen Williams continued. "There is a relationship between these. We don't know specifically what that relationship is at this point. There is quite a bit of research going on right now to elucidate what the actual relationship is. It could be something as simple as some underlying factor in the human being that makes them predisposed to systemic and periodontal diseases. It's very much a hot topic."

One of the newest areas of research concerns resolvins, naturally occurring serum proteins that can shut down the inflammatory response.⁴

"The resolvins can act locally at the periodontal lesion level to stop leukocyte recruitment and basically promote resolution of the periodontal lesion," Karen Williams explained. She cau-

tions that these studies have only been conducted using animals, specifically in rabbits with periodontal disease.

"As is so often true with new information, just because it shows promise in animals does not necessarily mean that it will show promise in humans. It's something to keep our eye on," she said.

Treatment Options for Now

"Research is still very much in the early stages in terms of saying which treatment options provide the best systemic outcomes. I don't think we know that yet," commented Karen Williams, who mentioned large, multi-state clinical trials that will illuminate treatment options.

"We know how to treat periodontal disease," she said, placing quality, traditional individualized care, with appropriate follow-up, at the top of the list, followed by scaling and root planing and surgery when indicated. "Those things we know reduce periodontal inflammation," she continued.

Offenbacher agreed, noting that there are few randomized clinical trials that have been published regarding new information on research in treatment options.

He continued, explaining that early data suggest that the potential for the systemic benefits of periodontal therapy may exist, and that the potential benefits of prevention are possibly even greater.

"Treating gum conditions to reduce oral disease is reason enough. It is safe and improves oral health – which is very important – and these treatments may also have systemic health benefits. We just don't know for sure, yet," Offenbacher stated.

The aspect that is frequently neglected, Karen Williams observed, is effectively engaging the patient in self care. "The dental hygiene model has always been: We'll tell you what to do and we'll show you how to do it. Then, by default, you will suddenly become enthused and do as they have been instructed. It doesn't work that way," she explained. This lecturing approach continues to be the preferred model despite the fact it has not proven to be a successful tool in changing patient behavior.

Instead, Karen Williams endorses a strategy called brief motivational interviewing, an approach not many dental hygiene programs are teaching right now. "I do know that, more and more, you are seeing information about it. It requires training to do well. Basically...the clinician serves as a counselor," she said. "Motivational interviewing allows the individual to find their own solutions to their own problems with directed guidance by the hygienist. When you help people articulate the reasons they do or don't engage in oral health behaviors, then they can see the argument they have in their head very objectively. It's amazing and has been shown to be effective in motivating individuals to engage in other health-related behaviors. They say, 'I didn't even know I thought that.' "

The process has been shown to help a variety of health-related outcomes, from losing weight to quitting smoking. "It should be effective with oral health behaviors and thus reduce inflammation. Theoretically, this may have potential for reducing periodontal associated risk for the many systemic complications," Karen Williams continued. "Karen Williams continued.

Lamster endorsed the dental hygienist's critical role in treatment. "Dental hygienists really understand prevention," he stated. "And now, they really need to understand that inflammation is a systemic process."

While telling patients these facts, Lamster advised, the dental team also needs to take action. When treating a patient with cardiovascular disease, for example, the dental team should question if the patient's health is stable and if that patient can tolerate dental treatment. For the patient with respiratory disease, for whom aspiration is of great concern, the use of a rubber dam is very important.

"In particular, the relationship between periodontal and respiratory disease is very direct," he said.

"The best thing you can do for a patient of childbearing years is advise them, if they are considering becoming pregnant, that it is important for them to be concerned about their oral health," Lamster said, adding that treatment studies of pregnant women have yielded conflicting results. It is important for the patient to share with the dentist and dental hygienist if they are taking fertility drugs or making plans to become pregnant. Achieving ideal oral health prior to pregnancy is a sound strategy.

Offenbacher supported maintaining a focus on prevention and reducing infection. Studies that support the links between better dental management and lower medical care costs are in progress and should help assist the dental team's effort in decision making.

"Some studies show that treating [the disease] reduces the systemic inflammatory response. Those studies are encouraging," Offenbacher said, adding that some clinical studies shows benefits to treating pocket depths of more than 4 mm, reducing bleeding scores and establishing of treatment intervals that minimize inflammation that occurs between visits.

"The inflamed periodontal tissues create a surface area about the size of the palm of your hand," Offenbacher said. "If you had an infection that size outside of your mouth that you could see, you would be treating it." He noted that a recent study (currently in press) showed that approximately 40 percent of patients enrolled in a cardiovascular trial who were made aware of periodontal disease sought dental care. "It's a promising sign," he commented.

Ray Williams also wanted to see the focus on minimizing inflammation as part of overall prevention and treatment. "It's not enough to minimize bacterial build-up, but we've got to keep on eye on inflammation," he commented. While plaque accumulation, plaque control and home care are important, they're just part of the picture.

"In addition to making sure that our patients achieve the best home care that they can, we also want to make sure that whatever patients are doing leads to minimal inflammatory response," he commented. This would include regular visits to the dentist and hygienist. In addition, he would like the dental team to approach gingivitis not as a simple, reversible problem, but one that represents a source of inflammation for the entire body.

"Now we appreciate that gingivitis represents oral inflammation that can be very harmful to the rest of the body," Ray Williams stated.

Offenbacher recommended that dental hygienists make patients aware of the oral health-systemic associations, cautioning against overstating the evidence on associations or the systemic benefits of treatment.

"If you have a patient in the chair who has a lot of inflammation, a lot of bleeding on probing, it is prudent to advise the patient that inflammation compromises the entire body," Offenbacher commented. "We can't say we can reverse this. Treating periodontal disease seems safe. Anything that improves oral health has a positive impact on overall health."

Offenbacher also stressed the importance of increased visits a patient needs to maintain their oral health.

"The point is that gum disease is chronic – low-grade but persistent. We may see inflammation, but not enough to cause bone loss. We need to think about supportive therapy intervals and the optimum treatment needed to protect the patient from infection and inflammation – not just periodontal disease progression," Offenbacher said. He also encouraged dental teams to think in a new way about treatment; that it is not always about protecting a patient from attachment, bone or tooth loss.

"I am more inclined to look at a hopeless, periodontally diseased tooth as a potential chronic source of infection and inflammation," he said, adding that removing a tooth or providing more definitive care sometimes is the best option to protecting overall oral health.

The focus returns to individual treatment. What does each individual need to improve their oral and overall health outcomes?

"Because periodontal disease is an endemic infection, I think first and foremost is dental hygienists need to understand that treating periodontal inflammation or treating the periodontal lesion needs to be targeted to the individual," stated Karen Williams.

Beyond performing prophylaxis or scaling and root planing, the dental hygienist needs to think of periodontal disease as a modifiable risk factor for systemic diseases. In other words, changing the patient's oral health will have an impact on their overall health.

Whatever tools dental hygienists have on hand to communicate the associations of systemic disease to oral inflammation, those tools must be tailored to the patient, said Offenbacher.

Karen Williams agreed, adding that visual aids work well. While photos of disease may educate the patient as to what conditions the dental hygienist is looking for, the intraoral camera shows the patient what is actually occurring inside their own mouth.

"The one thing that surprises me is how few dental hygienists will have a glucometer in their office," Karen Williams said. She offered as an example, the patient who has rampant periodontal disease and a lot of inflammation, "that is out of kilter with the amount of plaque on the teeth." This should raise a red flag for hypoglycemia, pre-diabetes or undiagnosed diabetes. A simple screening would reveal for the dental hygienist and the patient that a trip to the primary care physician is needed for a diagnosis. Williams' support of dental office screenings is one taken up by a Chicago-area dentist determined to train dental teams to offer the simple, in-office blood test (see box on this page).

An Oral Health Message

"Floss or Die!" declared a popular bumper sticker. While this message is "over the top," Lamster observed that other communications promoted by many oral health manufacturers have a more accurate, positive content.

"They are delivering the right message. Oral health is about more than keeping teeth," Lamster said. At present, the messages passed along through the consumer channel – via television, print media and the Internet – are fairly good, he noted.

Offenbacher observed that there is definitely a trend toward a holistic approach to having a healthy mouth. "Many of the television commercials and oral product advertisements talk about or suggest it without over-promising," he said. "It is going to

A Grassroots Approach

A Chicago-area dentist expands his oral health services to include screenings for overall health situations.

When a patient visits the physician's office, he or she is typically screened for a variety of issues through blood tests. While many patients are diligent about regular physicals and periodic screening under their primary care physician, others are less so. Ronald Schefdore, DMD, the first dentist to receive a Clinical Laboratory Improvement Amendments (CLIA) license, is working to discover health issues in patients who have less-than-perfect attendance at their physician's office.

Schefdore administers blood tests to patients with periodontal disease because disease frequently shows up in the gums before any other place in the body. His goal is to encourage other dental teams to perform simple blood tests and help them secure the tools to do so.

Because the government would not allow any other dentist to get a CLIA license after issuing one to Schefdore, he turned to Biosafe Labs in Chicago to create an FDA-approved finger-stick test that dentists and hygienists can use. It is accompanied by a patient consent form, is lab accurate and requires just a drop of blood. Biosafe Labs assumes the responsibility for sending a professional report to both the patient and the dental office that details the patient's cholesterol, C-reactive protein and glucose levels.

"Periodontal disease elevates those three chemistries, so it falls well within the scope of dentistry to test for these things and offer a safety net for the physician," said Schefdore. He noted that over-the-counter tests purchased at local pharmacies might not be covered by malpractice carriers. Dentists should check with insurance carriers for liability issues before administering any test.

Type 2 diabetes is exploding in the U.S., and the dentist and the dental hygienist are in the perfect position to screen patients, explained Schefdore, who cited a CNN story that reported an extra 3 million cases of the disease emerged in the U.S. in the past two years.

"We have the ability for the first time in dentistry to actually improve the health of the United States. We would be the first place that people would be going for their overall health...People who [go to the dentist] think they're healthy. [When] they go to the physician, [typically] they are sick and it's already too late." Schefdore commented.

"Bloody gums are a problem. It's a sign of periodontal disease, and it needs to be treated. If you washed your hands and they were bloody, everybody would be concerned," he continued.

Schefdore, who travels the country giving a four-hour presentation on the research and connections of high C-reactive protein, cholesterol and glucose readings because of periodontal disease, compares a dentist to "being an oral physician." The presentation also includes his own findings and treatment recommendations.

"We can really [use screening procedures] to shine in the profession – especially dental hygienists. It's an exciting time to be in the profession," Schefdore concluded.

take some time for us to see an actual therapeutic claim." The current target of the oral health care message remains antibacterial, antiplaque and anti-inflammatory.

Ray Williams supported the current consumer message. "I think that our corporate partners have also tuned in to inflammation, and that we are seeing education of the consumer now by the oral care companies about the importance of inflammation. It is not only good for oral health but also overall health. It's a very helpful strategy," he continued, commenting that any straightforward description of inflammation and its effect on the system is important.

At this point in time, what also has importance are the messages coming from groups such as the World Health Organization that enforce healthy lifestyles, said Lamster. Messages regarding weight control through diet and exercise, smoking cessation, and the importance of personal hygiene have a positive impact on patients and open the door for dentists and dental hygienists to have more in-depth conversations with patients about lifestyle choices.

"These are messages that are relevant to patients with cardiovascular disease, or those who have diabetes mellitus or have periodontal disease. It's an opportunity for dentists and dental hygienists to deliver this message. It goes well beyond what effect it will have in terms of managing periodontal disease," said Lamster.

"I think the message is getting through, but change occurs very slowly," Lamster observed. "You measure change in terms of years or even decades, as opposed to weeks or months. You can deliver the message on television...but it has to be emphasized in the dental office by dentists and dental hygienists seeing patients every day. I believe that dental hygienists have a major responsibility in this regard."

Lamster noted that primary health care can be provided in the dental office. Well-patient visits are more likely to be scheduled on a regular basis in the dentist's office than in the physician's. In addition, the patient spends more time with the dental hygienist who, from the patient's view, is less threatening.

"A dental hygiene visit tends to be very relaxed," Lamster said, contrasting this with a visit with a physician or a dentist. Consider the "white-coat hypertension" experienced by many nervous patients. "Blood pressure goes up, and the patient may simply not be listening. It is important to deliver this message when the patient is interested and calm," he continued.

Conclusions

As the population ages and becomes more medically complex, patients seen in the dental office will have more chronic diseases and will rely on numerous medications to control these disorders, commented Lamster. "It is very important that the education of dentists and dental hygienists be focused on health care, and not just oral health care," he said.

Offenbacher observed that many physicians want to connect with their patient's dental team. In 2007, he participated in a three-day, cross-disciplinary conference to examine the potential connection between periodontal disease and systemic health. The Scottsdale Project, an 18-member panel that also included Karen Williams as moderator, reviewed the link between dental health, oral flora and systemic illness, and published a group report later that same year. Health professionals

with expertise in periodontology, endocrinology/diabetology, cardiology, cerebrovascular medicine and epidemiology were represented. This expert panel deliberated over expert testimony, held intense discussions of the evidence gathered from a systematic review of over 118 articles, and debated the strength of the evidence to support the experts' answers to eight focused questions. The resulting recommendation was for developing guidelines to assist dental and medical providers in identifying patients at risk for periodontal disease, diabetes and CVD.

The panel concluded that ultimately, broad change in clinical practice will depend on reform in health care policy and professional education, both of which are influenced by the various organizations that represent physicians, dentists, nurses, dental hygienists, diabetes educators, physician assistants, dieticians and other allied health care disciplines, in addition to the insurance industry.⁵

This continual evaluation of the next step to take in communicating systemic associations is a positive move, concluded Ray Williams. "I am delighted that dentistry has turned its attention to inflammation because it is very apparent that the role of inflammation is central to what we as dentists and dental hygienists are trying to prevent and treat."

Karen Williams viewed the current understanding of systemic disease as an open door for new opportunities for the dental hygienist as an educator and counselor.

"Dental hygienists have an opportunity to utilize the education they have gotten in a way they haven't been able to before," she said. If dental hygienists stay abreast of research, they may be able to contribute to good overall health outcomes in the future. She added that professionals must be diligent in reading literature and attending continuing education programs.

She concluded: "As a collaborative member of the dental team, [dental hygienists] can provide a lot of leadership in this area."

How do we educate dentists and dental hygienists in the future? How do we link them to others in the health care field? These are questions posed by Lamster.

"The takeaway message is that oral-systemic associations have raised ancillary yet very important questions that relate to the future of the profession," he concluded. "We would be irresponsible if we didn't change the way we educate dentists and dental hygienists. The idea is to convey a message that will improve oral health and general health."

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