

Oral Health—Systemic Health: What Is the True Connection?

In recent years, the dental and medical literature as well as the mainstream media have featured a number of articles that highlight links between oral health and general health. Some of these articles have been emblazoned with dramatic headlines while others have been more responsible in cautiously pointing out emerging evidence of possible connections between oral conditions and systemic conditions.

At present there seems to be some debate in the dental profession, allied professions and among the public about the level of evidence surrounding these connections. Do oral conditions cause systemic conditions, or vice versa? What messages should individual dentists and dental organizations be broadcasting about the oral health—systemic health connection?

To take stock of the current state of understanding of the oral—systemic link, JCDA convened a panel of Canadian subject experts to reflect upon various aspects of this important topic. Drs. Howard Tenenbaum, George Sándor and Chris McCulloch of the University of Toronto and Dr. Debora Matthews of Dalhousie University all agreed to participate in this discussion.

The Panel



Howard Tenenbaum,
DDS, PhD, Dip Perio,
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Debora Matthews,
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George Sándor,
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Christopher McCulloch,
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JCDA first turned to Dr. Howard Tenenbaum, who has recently done a lot of work on the oral—systemic connection both for the Ontario Dental Association and the Royal College of Dental Surgeons of Ontario.

JCDA: Dr. Tenenbaum, in your opinion what are the most important factors to consider when reflecting on the oral health—systemic health connection?

Dr. Howard Tenenbaum (HT): Certainly there are the articles in the scientific literature to consider, those that highlight the potential links between overall health and oral conditions in general and with periodontal disease in particular. While this focus on disease is important, I believe we must also look at the fact that there is evidence to show that the tissues of the oral cavity can act as a biological model for how tissues in any part of the body behave. If we wish to study cellular physiology at any level, from

simple cell culture experiments right down to the most intricate cell signalling, we can use periodontal tissues, gingival tissues, bone or ligament to model these other systems.

For example, it might be easier to obtain samples of periodontal tissue rather than cardiac tissue to study basic biological processes. We know that we can learn things from these studies of oral tissues that are applicable to other systems in the body.

JCDA: Are you thinking of the mouth as being a “window to the body” in this respect?

HT: The mouth can of course reflect the presence of other diseases. However, from my own perspective as a scientist, I still believe that the most important aspect of this “window” connection is at the level of basic cell biology where the mouth tissues present a model for studying other conditions. If we find something in the laboratory that might have a beneficial action

on any particular type of cell or tissue, we must ask if that same beneficial action can be replicated in the cells or tissues of another body system.

I believe that health researchers focusing on different body systems are simply at different points in a continuum, and when we talk about the oral and systemic connection, we have to think of physiology as well as disease.

JCDA: So you feel that there should be a greater emphasis placed on physiology rather than disease?

HT: We have to avoid a trap — one that I think we may have fallen into recently — where the profession might be trying to increase the public perception of the importance of oral health by showing that it has an impact on systemic health. It's almost as if we feel pressure to justify the importance of dental treatment by highlighting its impact on cardiac disease, for example.

I reject this approach and contend that oral health is simply a component of health and should not be thought of as being somehow separate from the health of the rest of the body. As a result of an oral condition, a person may be in pain, feeling poorly or not eating properly, and these problems are manifestations of poor overall health. A person is simply not well systemically if they are not well orally. This is not to minimize the putative or proven connections between oral inflammatory disease and systemic disease, mind you.

Dr. Tenenbaum mentions the connections between oral inflammatory disease and systemic conditions — but what is the strength of the evidence underpinning this relationship? JCDA asked Dr. Debora Matthews, a leader in evidence-based dentistry at Dalhousie University, to help summarize the current understanding.



Dr. Howard Tenenbaum

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JCDA: Dr. Matthews, according to the latest research, what are the main systemic conditions that have been linked to periodontal conditions?

Dr. Debora Matthews (DM): The most significant is diabetes, but more recently we've been looking at cardiovascular disease, in particular myocardial infarct and stroke, respiratory diseases and pre-term, low-birth-weight babies.

With respect to diabetes and periodontal disease, several well-designed studies have demonstrated a bidirectional relationship between the 2 conditions. There is good basic scientific research as well as good clinical and survey research linking these 2 diseases. Randomized clinical trials have shown that people with diabetes are 2.5 to 4 times more likely to develop periodontal disease than non-diabetics. These trials also show that treating periodontal disease can stabilize the glucose status in diabetic patients.

JCDA: So diabetes seems to have the strongest evidence of a bidirectional relationship with periodontal disease. What about the other systemic conditions?

DM: There appears to be a relationship, but not necessarily in both directions, between the presence of untreated periodontal disease and the risk for having a heart attack or a stroke, and similarly for respiratory diseases and for pre-term, low-birth-weight babies.

I would classify the evidence for myocardial infarct as moderately strong. There have been 3 recent systematic reviews, the strongest of which found that there was a small increased risk of coronary heart disease over and above the traditional risk factors such as hyperlipidemia, obesity or smoking. This risk was particularly increased in people under the age of 65. The strongest systematic review focused on prospective studies — which always provide the best evidence — and it found close to a 20% increase in risk of fatal heart attack in the presence of periodontal disease.

As for the studies examining the relationship between periodontal disease and stroke, the evidence is somewhat mixed. I would call it a strong but small association. The same applies for respiratory diseases and pre-term, low-birth-



Dr. Debora Matthews

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weight babies. More systematic reviews that include prospective studies must be done to definitively determine the relationship of periodontal disease with both of these systemic conditions.

JCDA: What are some of the challenges in trying to establish the strength of these relationships?

DM: We have to consider causality, but it's always difficult to tell which condition comes first. In other words, is the damaged immune system in a diabetic making periodontal disease worse or is periodontal disease in fact impairing the glucose control of a diabetic? To effectively answer such questions, a study must ideally establish temporality, specificity and a dose response gradient. The challenge is that all chronic diseases are multifactorial, which makes it extremely difficult to account for all risk factors — such as genetics, socioeconomic status and environmental influences — for diseases being linked with periodontal conditions.

The concept of the mouth as a window to the body arose in the initial discussion with Dr. Tenenbaum. Can the mouth be used as a "diagnostic" window to the body? JCDA approached Dr. George Sándor, a doubly qualified dentist and physician, to shed some light on what can be ascertained about systemic health by looking into a patient's mouth.

JCDA: Dr. Sándor, when you look into a patient's mouth, what does it tell you about the general health of a patient?

Dr. George Sándor (GS): It actually starts well before an examination of the mouth, because as practitioners we need to be excellent observers and excellent listeners. Observing can begin as your patient shuffles into your operatory and you may suspect that he has Parkinson's disease or if he drags one foot behind the other, you may consider a history of hemiplegia and stroke. Listening

can begin by taking a detailed medical history of your patient.

Then as we examine the mouth, we might notice that the teeth look very shiny, that the layer of enamel on the occlusal surfaces of the mandibular molars or the lingual surfaces of the maxillary anterior teeth

are thinned, and we might suspect that the patient has gastroesophageal reflux disease or GERD. Yet GERD is a mere symptom of other conditions, such as obstructive sleep apnea. Perhaps one hasn't made that link before, but GERD is a very important comorbidity of obstructive sleep apnea.

So dentists need to look for valuable hints to recognize potential systemic problems in a patient. These are all clues that a talented practitioner will recognize and piece together.

JCDA: Are there any systemic conditions for which oral conditions are the precursor or may be the early signs?

GS: Dentists may become aware of systemic conditions in a patient well before a physician, primarily because we see patients on a regular basis and have the opportunity to update a patient's health history. The serial follow-up nature of dentistry places us in an ideal observational position to be able to suggest to people that there could be something else systemically wrong with them.

Certainly with inflammatory bowel disease, the cobblestone changes in the buccal mucosa can precede the development of other symptoms and so it is possible that one could notice this and then find out later that the patient in fact has Crohn's disease.

JCDA: Are there interesting avenues of research being conducted that highlight the mouth as a diagnostic window to the body?

GS: Karyotyping or scraping the buccal musoca was previously used when we were thinking of the Barr body. Sophisticated advances now allow researchers to use salivary gland biopsies in the labial salivary glands as a way to follow people who have such conditions as Sjögren's syndrome, to try to characterize and prognosticate their disease. This is also true in those patients who are treated for leukemia with a bone marrow transplant and may over time develop a condition called graft-versus-host disease.



Dr. Christopher McCulloch

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Returning to Dr. Tenenbaum's thoughts on the intrinsic link between oral and general health, JCDA talked with Dr. Chris McCulloch, a leading researcher in the field of cell biology, to learn about his experiences straddling the boundary between "oral health" and "systemic health" research.

JCDA: Dr. McCulloch, how did you become involved in research on fundamental problems in cell structure and function?

Dr. Chris McCulloch (CMc): I was always interested in biology going back to high school and biological aspects of dentistry were also of some interest. My periodontology training program at Columbia University in New York was also very biologically and experimentally oriented. That program reinforced my interest in exploring fundamental questions in biology and how they might relate to dentistry. Some of my teachers at the time were involved in research linking the idea that gingival crevicular fluid enzymes might reflect the behaviour of neutrophils. If we could measure neutrophil enzymes, we could use this as a way of looking at how circulating neutrophils might contribute to periodontal breakdown, not just in terms of fundamental problems but also clinically.

Several years later I started my own lab and, in collaboration with Jaro Sodek and Chris Overall at the University of Toronto, I really started to appreciate how systemic factors, particularly neutrophil-derived enzymes that are found in the periodontium, might have a significant impact in terms of periodontal health. This was very much a 2-way street, as it wasn't just systemic health that was impacting the health of the periodontium. Perhaps the health of a person's mouth could impact their overall health.

JCDA: How did your research evolve from an oral health focus to examining more basic problems in cell biology?

CMc: I decided to concentrate my research on fundamental aspects of the behaviour of certain cells that are common to the periodontium, but which are also found in heart muscle. I became more interested in cardiac physiology, so I started to focus on how connective

tissue cells in heart muscle, called fibroblasts, contribute to heart failure. In heart failure, if you have some idea of what the cells are doing in terms of their structure and function in, for example, the development of fibrosis after a heart attack, then you are likely to have a better idea about how to treat it.

I then became quite involved with the Ontario Heart and Stroke Foundation, obtaining funding and delivering lectures on the relationship between oral disease and systemic disease and the importance of the connective tissue matrix and connective tissue cells in heart failure.

JCDA: Do you consider yourself an oral health researcher or a basic science researcher?

CMc: The biology of the periodontium is part of the biology of all human beings. There should be no disconnect here. While medicine and dentistry may have separate historical traditions, biologically they focus on common issues. In terms of my research, what is happening in certain cells in the mouth or the heart is not dissimilar because they're all part of the same functional organism.

When I collaborate with other researchers in cell and molecular biology, they are primarily concerned about whether or not I can contribute to their research program and if there are sufficient common research interests between us to make progress. I have never encountered criticism about my training and background as a dentist. So any perceived barriers between general health and oral health research are, to me, quite artificial.

JCDA asked the panellists for their thoughts on the specific messages that individual practitioners and the dental profession should convey about the oral health-systemic health relationship.

JCDA: In your opinion, what messages should individual dentists provide to patients about the oral health-systemic health connection?

DM: In terms of specific advice for people with diabetes, we should advise these patients to visit the dentist regularly for routine assessments of their periodontal condition. Periodontal therapy should be part of an overall therapy regimen, because we know that diabetics who have good periodontal maintenance have more stable blood sugar levels than those who don't.

CMc: When a patient shows interest, I will discuss recent data indicating that poorly controlled periodontitis may be part of a more generalized inflammatory syndrome that affects many tissues, in addition to the periodontium. In other words, if you have increased inflammation in your mouth, you may have increased inflammation elsewhere in your body, such as atheromas. These inflammatory lesions may be causally linked.

GS: It is the responsibility of not just individual dentists but of dental organizations to promote the knowledge and role of the mouth in terms of ideal and optimum health. Because all health care professionals are in a preventive business, we have to prevent disease at all levels, not just in the mouth but disease that may be noticed in the mouths and then occurring elsewhere.

JCDA: How can our dental organizations advocate for greater understanding of the importance of oral health to general health?

GS: I think that organized dentistry must promote the view that conditions in the mouth do not occur in isolation from conditions elsewhere in the body and that systemic and oral diseases aren't just related, they are inextricably linked.

DM: Other health professionals are beginning to connect the mouth back to the body, which is something that we, as dental professionals and dentists, have known all along — that oral health is not separate from general health. Dentistry has the right message, and that is prevention. We do this well. We have our patients come in on a regular recall basis

to help catch diseases early. I think prevention is a message that other health care professionals could take to heart.

CMc: Our organizations must continue to put research on the agenda and make sure that it stays on the agenda. Research needs to be a focus in our organizations' print and e-journals on a routine basis, to ensure that research is placed front and centre. The profession should also organize symposia, venues in which colleagues can feel comfortable critiquing existing methods or raising issues about diagnostic and treatment approaches where we may not be doing particularly well. We need to remember that a profession that does not renew itself scientifically or does not generate its own stable of investigators can move from being a profession to being a trade.

GS: We must urge funding agencies, such as the CIHR, to assess dental research in a more global manner, because what occurs in the mouth has an effect on the musculoskeletal system, the cardiovascular system, the respiratory system and the digestive system. Oral health research should not be viewed in isolation from other areas of health research because these links are absolutely essential.

To bring the panel discussion to a close, JCDA asked Dr. Tenenbaum to help summarize the panellists' thoughts on the oral-systemic connection.

HT: When we consider all of the ideas that were discussed here, it is clear to me that the true oral health-systemic health connection is that oral and systemic health are inseparable. We can try to justify the delivery of dental treatment for periodontitis on the basis of literature linking this disease to other systemic diseases. However, we need to remember that maintenance or achievement of optimal oral health is a goal unto itself. As such, dental treatment to achieve oral health requires no additional justification!

Moreover, when one looks at the biological research related to dental physiology, we have become more knowledgeable about the physiological and pathophysiological mechanisms governing other cells and tissues of the body. This knowledge can only lead to greater insights regarding other tissues and organ systems



Dr. George Sándor

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— once considered disparate — but from a biological perspective, evidently not so disparate from oral cells and tissues. This knowledge base can only lead to improvements in the understanding and treatment of diseases, not only in the mouth, but elsewhere.

It is this physiological and pathophysiological continuum that connects tissues in the oral cavity to other remote organ systems in both health and disease that has also been defined and recognized with increasing clarity. This concept presages a more biological approach being taken by dentists regarding diagnosis and management of oral diseases. I think our discussion also shed some light on the contribution of the dental sciences and clinical dentistry to the overall health and well-being of Canadians that should not be underestimated. ✦

PANEL MEMBERS

Dr. Tenenbaum is associate dean of diagnostic and biological sciences and professor of periodontology at the faculty of dentistry at the University of Toronto. His major area of research involves bone metabolism, using in vitro model systems to address questions of bone cell function and differentiation. A secondary

research focus involves the study of temporomandibular joint dysfunction and facial pain.

Dr. Matthews is head of the division of periodontics at Dalhousie University. Some of her current research interests include an oral health assessment for seniors in Nova Scotia. She is a leader in evidence-based dentistry and teaches several courses at Dalhousie in this discipline.

Dr. Sándor is professor and clinical director, graduate program in oral and maxillofacial surgery and anesthesia, University of Toronto and Mount Sinai Hospital; coordinator of pediatric oral and maxillofacial surgery at The Hospital for Sick Children and Bloorview Kids Rehab, Toronto, Ontario; and docent in oral and maxillofacial surgery at the University of Oulu, Oulu, Finland. His areas of research include bone regeneration and tissue engineering; hyperbaric oxygen; congenital deformities, growth and development; and pediatric dental implantology.

Dr. McCulloch is director of the Canadian Institutes of Health Research Group in Matrix Dynamics and a professor in the faculty of dentistry at the University of Toronto. He was recently named Canada Research Chair in Matrix Dynamics. His research focuses on the regulation of connective tissue cells and the signalling mechanisms that control their metabolism. To read more about Dr. McCulloch's research, please consult "Integrating Dentists into the Biomedical Mainstream." *Alumni Today*, Vol. 25(1), Winter 2007, pp. 20-22.

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