

An Overview: Introduction to the RCDSO Symposium - Oral Health: A Window to Systemic Disease



This PEAK article is a special membership service from RCDSO. The goal of PEAK (Practice Enhancement and Knowledge) is to provide Ontario dentists with key articles on a wide range of clinical and non-clinical topics from dental literature around the world.

PLEASE KEEP FOR FUTURE REFERENCE.

An Overview: Introduction to the RCDSO Symposium Oral Health: A Window to Systemic Disease



MICHAEL GLOGAUER, D.D.S., PH.D Assistant Professor, CIHR Group in Matrix Dynamics, University of Toronto



CHRISTOPHER A. MCCULLOCH, D.D.S., FR.C.D. (C.), PH.D. Professor and Director, CIHR Group in Matrix Dynamics, University of Toronto

Do Periodontal Infections Increase Risk of Systemic Diseases?

With the support and encouragement of the RCDSO, a group of dentists, physicians, epidemiologists, health-care policy experts, researchers, students and educators met in Toronto, in early February 2005, to consider this question.

The issue of whether periodontal infections, particularly periodontitis, can increase risk of myocardial infarction, stroke and preterm births has been on the dental profession's radar screen for at least a decade. But new developments in the story, as well as the decision by a number of manufacturers of dental products to promote this possible connection for marketing purposes (e.g. Floss or Die!!!), has raised the stakes and interest levels for both the public and dentists alike.

Increased public awareness of the impact of dental disease on overall health is, of course, a welcome change. Many patients, and maybe some practitioners, tend to separate the mouth from the rest of the body, and consider oral health separate from human health. While such views among dentists were relatively common 30 years ago, current research and trends in dental education have promoted the idea that dentists are, in reality, human health-care specialists with a focus on oral disease and wellness. Indeed as dentists, if we are to maintain appropriate standards of care, we must be up-to-date with the latest scientific advances in our field, and be willing and able to critically evaluate these advances, and implement them into our practices when appropriate.

But how strong must be the evidence before we implement change? And when is it

Diseases and Medical Conditions that May Be Associated with Untreated Periodontal Infections

Myocardial Infarction

Stroke

TABLE 1

Diabetes

Pneumonia

Preterm Births

appropriate to implement change in practice protocols? For example, if repeated clinical studies with strong research designs show clear-cut differences of risk of myocardial infarction between groups with and without periodontitis, at what point are these differences considered clinically significant? Should we be advocating prevention of periodontal diseases not just to improve oral health, but for the global well-being of the individual?

A common theme that emerged from the symposium is that there are wide variations of outcomes between the multiple clinical research centres that are focusing on these questions (Table 1). Studies of risks of myocardial infarction in individuals with and

without periodontitis using cross-sectional experimental designs have provided rather different estimates in reports from research centres in North Carolina¹ compared to, for example Seattle, Washington² and Finland³. It is not known why these differences exist but a crucial question is: Are these data on increased risk of

systemic disease real, reproducible and potentially important in the way that we manage oral disease?

A Little History

The idea that infections in one part of the body could impact the function and the health of other organs and tissues was a particularly popular notion in the late 1800's, and traces of the original thinking on this are mentioned by Greek philosopher/scientists around 500 BCE. Canada's own Sir William Osler (circa 1900), a world-famous medical scientist, was an important proponent of systemic spread of infection, and he encouraged his medical students to carefully evaluate the mouth as part of a routine health examination.

The recognition that tooth-borne films of bacteria were critical for the development of caries and periodontal diseases, and the emergence of the dental profession as a separate profession from medicine, gradually led to new ways of thinking. First, caries and periodontal diseases came to be regarded as specifically oral problems, and therefore, the sole responsibility of the dental profession. Second, there was no solid evidence that periodontal diseases could produce significant infections in remote tissues. Accordingly, by the 1940s, the idea of systemic spread of periodontal diseases had disappeared from teaching and research programs.

A Change of Heart

Researchers are by nature, a curious lot and also like to stay employed. In the early 1980s, the original ideas of focal infections and the spread of systemic disease from the mouth sparked the idea that maybe these theories should be tested using more powerful and modernized research methods than were available in the early 1900s. Consequently, as a result of the efforts of a group of researchers funded by the American National Institutes of Health (NIH) and other international agencies, cross-sectional data from large populations were interpreted to show increased risk of myocardial infarction and stroke in patients with existing periodontal infections compared to healthy controls⁴. There were also a series of studies that examined a relationship between preterm births in women with more periodontal inflammation and attachment loss⁵. In some reports, treatment of periodontal infections was associated with reduced pre-term births and with improved diabetic control. Clearly, there were some sort of links between periodontal inflammation and systemic diseases, but it is not a completely clear picture.

Controversies

Because of the interest among researchers and the dental profession in general, there have been a very large number of studies conducted to test the validity of the relationships, for example, between periodontal destruction and prevalence of myocardial infarction and stroke. While some research centres in the USA, South America and Germany have shown increased risks for stroke of up to four-fold⁶, other research groups can find no relationship⁷. Consequently we might question whether confounding variables such as smoking, which increases risk of both periodontal diseases and myocardial infarction, might be clouding the data.

Pathobiological mechanisms

Evidence obtained over the past decade clearly identifies inflammation as a critical mediating factor in the development of cardiovascular diseases⁸. Further, it has been proposed that preterm labour is induced by infection or inflammation at a distant site⁹ from the uterus which leads to the release of prostaglandins (pro-inflammatory molecules) that cause inappropriately timed uterine contractions. Notably, periodontal diseases are inflammatory diseases in which prostaglandins and other inflammatory mediators are greatly elevated¹⁰. Indeed, C-reactive protein is increased in individuals with periodontal infections and is also an important risk factor for myocardial infarction¹¹. These types of associations have led to the simplistic model that inflammatory mediators from periodontal infections may impact on other, remote organs and tissues; or that systemic spread of periodontal pathogens may settle out on blood vessel walls and there promote atheroma formation. While there is some evidence from animal models and clinical research to support both of these mechanisms, they are, at this stage, largely hypothesis.

However, it is also possible that a pre-existing, hyperinflammatory phenotype, may predispose a person to both periodontal diseases and inflammation-mediated vascular disease¹². To more definitively link periodontal infections and systemic inflammation as a cause or as an exacerbating factor for the progression of cardiovascular diseases will require a lot more fundamental and clinical research.

The data are more solid from well-designed clinical studies indicating that periodontal diseases may have a significant impact on the maintenance and ongoing treatment of diabetic patients. Several studies have shown that diabetic patients with periodontal disease are able to maintain lower blood glucose levels more easily¹³ and with lower doses of insulin once their periodontal disease has been treated effectively. These types of findings have significant long-term health benefits for these patients: prevention of the onset of diabetic complications including blindness and kidney failure not only affects a patient's quality of life, and also have a significant benefit for our already overtaxed healthcare system. While the evidence is strong for the benefits of treating oral diseases in diabetics, as

dentists we continue to see diabetic patients who struggle with their glycemic control and present with chronic periodontal diseases.

Do These Findings Impact Our Practices?

We are not at the point where we can definitively say to out patients: "Treat your periodontal infection and this will prevent a future heart attack." However, there are certainly a large number of cross-sectional and cohort studies that suggest there may be a link between oral health and systemic diseases¹⁴. Consequently, it may be prudent for dentists to inform their patients of these possible links in a responsible manner, clearly outlining that while the evidence is accumulating, the nature of the data is circumstantial.

Although the linkages between vascular diseases such as stroke and myocardial infarction with oral diseases are still in the testing ground, there are a number of systemic diseases in which there is more clearly a benefit to eliminating or controlling periodontal diseases. Aspiration of oral bacterial pathogens has been linked to pneumonia in the institutionalized elderly^{15,16}. Further, patients with blood dyscrasias and white blood cell defects benefit by more frequent periodontal maintenance through the reduction of oral bacterial loads¹⁷ and the subsequent infections which often follow in these immunocompromised individuals.

Future Research Is Needed

There is currently recognition within the research community that some sort of interactions exist between oral diseases and systemic health. But the specific nature of these interactions and the complex connections between periodontal inflammation and inflammatory disorders in the vasculature, remain hidden due to the underlying similar pathobiology that exists between many of these diseases. As a result more powerful and better designed multi-centre studies (some of which are currently ongoing) are required to clarify these links. While it may take many years for these studies to be completed, it now seems more certain that optimizing oral health has significant benefits for patients suffering from some systemic diseases such as diabetes.

It would seem prudent that we advise our patients and the health-care community that oral health can have a significant impact on overall health and well-being. Physicians need to be reminded that, just because they are not involved in the clinical management of oral disease, does not mean that the mouth is unimportant in the overall health of their patients. It may be worthwhile to remind them of Sir William Osler and, in the research world, what goes around, comes around.

References

- 1. Beck J, Garcia R, Heiss G, Vokonas PS, Offenbacher S. Periodontal disease and cardiovascular disease. J Periodontol. 1996; 67 (10 Suppl):1123-1137.
- Hujoel PP, Drangsholt M, Spiekerman C, DeRouen TA. Periodontal disease and coronary heart disease risk. JAMA. 2000: 284:1406-1410.
- 3. Mattila KJ, Asikainen S, Wolf J, Jousimies-Somer H, Valtonen V, Nieminen M. Age, dental infections, and coronary heart disease. J Dent Res. 2000: 79:756-760.
- 4. Chun YH, Chun KR, Olguin D, Wang HL. Biological foundation for periodontitis as a potential risk factor for atherosclerosis. J Periodontal Res. 2005; 40:87-95.
- 5. Jeffcoat MK, Geurs NC, Reddy MS, Goldenberg RL, Hauth JC. Current evidence regarding periodontal disease as a risk factor in preterm birth. Ann Periodontol. 2001; 6:183-188.
- 6. Grau AJ, Becher H, Ziegler CM, Lichy C, Buggle F, Kaiser C, Lutz R, Bultmann S, Preusch M, Dorfer CE. Periodontal disease as a risk factor for ischemic stroke. Stroke. 2004; 35:496-501.
- 7. Tuominen R, Reunanen A, Paunio M, Paunio I, Aromaa A. Oral health indicators poorly predict coronary heart disease deaths. J Dent Res. 2003; 82:713-718.
- 8. Sattar N, McCarey DW, Capell H, McInnes IB. Explaining how "high-grade" systemic inflammation accelerates vascular risk in rheumatoid arthritis. Circulation. 2003; 108:2957-2963.
- 9. Damare SM, Wells S, Offenbacher S. Eicosanoids in periodontal diseases: potential for systemic involvement. Adv Exp Med Biol. 1997; 433:23-35.
- 10. Heasman PA, Lauffart BL, Preshaw PM. Crevicular fluid prostaglandin E2 levels in periodontitis-resistant and periodontitis-susceptible adults. J Clin Periodontol. 1998; 25:1003-1007.
- 11. Pai JK, Pischon T, Ma J, Manson JE, Hankinson SE, Joshipura K, Curhan GC, Rifai N, Cannuscio CC, Stampfer MJ, Rimm EB. Inflammatory markers and the risk of coronary heart disease in men and women. N Engl J Med. 2004; 351:2599-2610.
- 12. D'Aiuto F, Parkar M, Brett PM, Ready D, Tonetti MS. Gene polymorphisms in pro-inflammatory cytokines are associated with systemic inflammation in patients with severe periodontal infections. Cytokine. 2004; 28:29-34.
- 13. Kiran M, Arpak N, Unsal E, Erdogan MF. The effect of improved periodontal health on metabolic control in type 2 diabetes mellitus. J Clin Periodontol. 2005; 32:266-272.
- 14. Elter JR, Champagne CM, Offenbacher S, Beck JD. Relationship of periodontal disease and tooth loss to prevalence of coronary heart disease. J Periodontol. 2004; 75:782-790.
- 15. Limeback H. Implications of oral infections on systemic diseases in the institutionalized elderly with a special focus on pneumonia. Ann Periodontol. 1998; 3:262-275.
- 16. Scannapieco FA, Bush RB, Paju S. Associations between periodontal disease and risk for nosocomial bacterial pneumonia and chronic obstructive pulmonary disease. A systematic review. Ann Periodontol. 2003; 8:54-69.
- 17. Goultschin J, Attal U, Goldstein M, Boyan BD, Schwartz Z. The relationship between peripheral levels of leukocytes and neutrophils and periodontal disease status in a patient with congenital neutropenia. J Periodontol. 2000; 71:1499-1505.

Acknowledgements

Chris McCulloch is Professor and Director of the Canadian Institutes of Health Research Group in Matrix Dynamics, University of Toronto. Michael Glogauer is Assistant Professor, Canadian Institutes of Health Research Group in Matrix Dynamics, University of Toronto and is a Clinician Scientist of the CIHR.

