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Review of the Oral Disease-Systemic Disease Link. Part I: Heart Disease, Diabetes

Canadian Dental Hygienists Association Position Statements

Heart disease

Recent research indicates a low-to-moderate association between periodontal disease and heart disease and a moderate association between periodontal disease and stroke. In light of this, dental hygienists should educate clients at risk for these diseases about the potential risks and encourage oral disease prevention and treatment for this client population.

Diabetes

Recent research indicates mounting evidence of a probable bi-directional association between periodontal disease and diabetes. In light of this, periodontal prevention and treatment programs for persons with diabetes should be available, regardless of income level. In addition, dental hygienists should consider incorporating the following dental hygiene diagnosis and treatment issues into their practices; however, all clinical decisions should be based on the needs of the specific client:

- Educate clients with diabetes about the probable association between diabetes and periodontal disease and provide disease prevention and treatment services for individuals with diabetes.
- Increase interprofessional collaboration and communication between dental hygienists and other health professionals working with persons with diabetes. These new opportunities can focus on oral/general health assessments, leadership capacity, policy development, surveillance, program delivery, and evaluation.

Keywords: Diabetes mellitus; Heart diseases; Meta-analysis; Oral hygiene; Periodontal diseases; Review literature

CDHA Position Paper

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INTRODUCTION

THIS PAPER UPDATES THE 2004 CDHA POSITION PAPER entitled "Your Mouth – Portal to Your Body," on the links between oral health and general health.¹ The evidence from the 2004 paper, although preliminary, supports the conclusion that oral diseases may have an association with the occurrence and severity of diabetes mellitus and heart disease. In addition, the review found that oral hygiene treatment improved diabetic control of type 2 diabetes. Following the publication of the 2004 position paper, substantial new research on this topic has been published. The 2006 position paper updates the 2004 position paper with the growing body of research supporting a link between oral diseases and systemic diseases.

Periodontal disease may be the most prevalent chronic disease affecting children, adolescents, adults, and the elderly.² In addition, periodontal disease is an infectious disease that may be transmitted from one person to another. In the United States, there are recent national statistics indicating the prevalence of severe periodontal disease is 14% for adults aged 45 to 54 and 23% for those aged 65 to 74.³ Similar recent information for all of Canada is not available; however, 35 years ago, 15% of Canadians aged 19 years and over had periodontal pockets (Nutrition

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Canada National Survey).⁴ Many research studies define periodontal disease as periodontitis and gingivitis. Almost half of adults in the United States aged 35 to 44 have gingivitis.³ Similar proportions are believed to exist in Canada, although data are lacking.

METHODOLOGY

The methodological approach in this paper is a comprehensive review of systematic reviews, meta-analyses, and literature reviews on the connection between periodontal diseases and systemic diseases, specifically, preterm low birth weight, respiratory disease, diabetes, and heart disease. The research question was "What is the relationship between periodontal disease and the following four health issues: preterm low birth weight babies, diabetes mellitus, heart disease, and respiratory disease?" This question was used to develop the following search terms: periodontal disease, periodontal diseases, periodontitis, heart disease, heart diseases, cardiovascular disease, cardiovascular diseases, coronary heart disease, preterm birth, preterm births, low birth weight, low birth weights, pregnancy and pregnancy outcomes, diabetes mellitus, respiratory disease, respiratory diseases, chronic obstructive pulmonary

disease, pneumonia, lung disease, and respiratory tract infections.

The literature was limited to English language human studies in MedLine, the Cochrane controlled trials register, and Google Scholar. The search also included reference lists of published review papers to identify additional articles. The search cut-off date was March 2006 although one systematic review was included from September 2006. The search also included "gray" literature—information not reported in the scientific periodical literature—and web-sites known to contain publications on this topic. A recognized topic expert was consulted at a number of developmental stages followed by a consultation with the draft paper for CDHA members and other topic experts.

HEART DISEASE

Literature review

Cardiovascular disease (CVD), which includes coronary heart disease (CHD), atherosclerosis, coronary thrombosis, ischemic heart disease, and peripheral vascular disease, accounts for the death of more Canadians than any other disease. In 2003, it accounted for 33%⁵ of all deaths and costs the Canadian economy over \$18 billion a year.⁶ Of these deaths, 21% were due to cerebrovascular diseases.⁷

In the 2004 CDHA position paper, 15 of 17 studies reviewed supported an association between periodontal disease and cardiovascular disease.⁸ Several other reviews of the literature reach similar conclusions: in 2002, Hujuel reviewed periodontitis and CHD studies,⁹ Genco et al. reviewed periodontal and heart diseases,¹⁰ and Joshipura reviewed oral conditions and stroke and peripheral vascular disease.¹¹ In addition, Danesh in 1999 conducted a meta-analysis of the literature on this topic and concluded that persons with periodontal disease have a 21% risk of CVD.¹² In a review by Janket in 2003, only four studies identify some conflicting evidence showing that the relationship between periodontal disease and CVD is not strong.¹³

These reviews summarized a substantial amount of research, which indicates a possible association between periodontal disease and CVD. In addition, some researchers report that, due to the association between periodontal disease and cardiovascular disease, there is a need to refocus attention on primary and secondary oral disease prevention.¹⁴ However, these reviews cannot establish a causal relationship between periodontal disease and CVD, since they included primarily case control and cohort studies. Randomized controlled trials (RCTs) are the highest level of evidence and the only studies that can indicate a causal relationship.* A review by the Royal College of Dental Surgeons of Ontario questions whether confounding variables such as smoking, which increased risk of both heart disease and periodontal disease, might be influencing some of the outcomes of the research studies.¹⁵

One recently reported retrospective two-year study examines the impact of periodontal treatment on CVD. It investigated the effect of periodontal treatment on 144,225 health plan members (with medical and dental insurance plans) with one of three conditions: diabetes, coronary artery disease (CAD), and cerebrovascular disease. Costs per member per month showed that members with diabetes, CAD, and cerebrovascular disease who had periodontal treatment, as opposed to dental maintenance services, had lower medical costs. Although this study is not high-level research and has not undergone the rigors required for publication, it supports the need to conduct other treatment studies using RCTs.¹⁶

Although there is a need to conduct RCTs to determine a causal link between periodontal disease and heart disease, as well as to determine if periodontal treatment reduces the risk of CVD, there are several difficulties with conducting RCTs in this area. Heart disease develops over time and researchers cannot predict from the outset of a study if heart disease will develop. If the researchers randomly select 100 individuals and allocate them to a periodontal treatment or control group, it may be years before some of the people develop heart disease. Another complication is that asking people to forego periodontal treatment for long periods is unethical. Therefore, the RCTs need to focus on people who have developed heart disease, since a certain percentage of these people will experience a second cardiovascular event. A new National Institute of Dental and Craniofacial Research (NIDCR) pilot project uses this design.¹⁷ Individuals who have had one cardiovascular event will be allocated to treatment/no treatment groups to determine whether periodontal treatment has an impact on the development of further cardiovascular events.

Three biological mechanisms have been proposed to explain the association between periodontal disease and CVD (see figure 1).⁸

- Bacteria from the periodontal infection enter the blood and invade heart and blood vessel tissue causing harmful effects.
- The body responds to the periodontal infection with the production of inflammatory mediators that travel through the blood and cause harmful effects on the heart and blood vessels.
- Bacterial products such as lipopolysaccharides enter the blood and cause harmful effects on the heart and blood vessels.

The most recent evidence of this biological mechanism comes from a 2005 study showing that people with higher levels of bacteria in their mouths also tended to have thicker carotid arteries, an indicator of cardiovascular disease.¹⁸ In another recent 2005 systemic study, antibody response to periodontal bacteria was associated with coronary heart disease.¹⁹ It is interesting to note that in this study, the clinical signs of periodontal disease were not associated with CHD, but it was suggested that the quantity and quality of the immune response against oral bacteria provides a better measure of the association between periodontal disease and CHD. Other scientific evidence of

* A randomized controlled trial is an experiment where the investigator randomly assigns the subjects into groups to receive or not receive one or more interventions that are being compared.

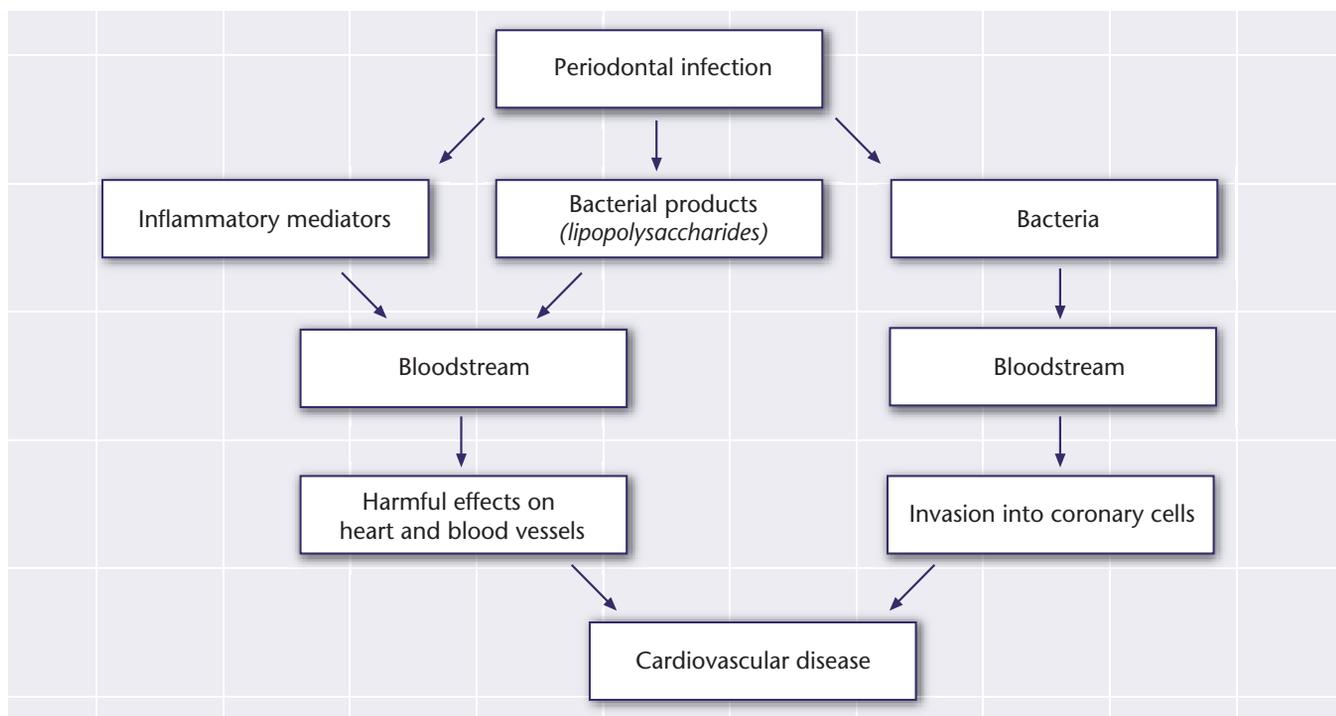


Figure 1. Proposed biological mechanism (association between periodontal disease and CVD)

these mechanisms comes from studies showing periodontal micro-organisms are found in the plaque build-up in the arteries.^{20,21} Also, recent findings show that the inflammatory mediators such as lipoprotein and triglycerides are significantly higher in subjects with periodontitis than in controls.²² In addition, increased levels of C-reactive protein were associated with periodontitis.²³ C-reactive protein is considered a biomarker for inflammation and is associated with elevated risk of heart disease.

Recently, researchers are suggesting there may also be a need for RCTs that explore the association between biological markers of periodontal disease and specific periodontal pathogens, instead of only clinical signs. This suggestion is supported by Janket et al.'s 2004 research showing that the more precise the dental health score, the stronger its associations with CHD and stroke.²⁴ Janket used a recently developed Asymptomatic Dental Score that used all dental factors expected to generate inflammatory mediators, such as dental caries, dentate status, and root remnants. This score was used along with the traditional Total Dental Index (TDI). Spahr et al.²⁵ in 2006 also supports this suggestion for studying biological markers as opposed to clinical signs. Their study showed that microbiological parameters, such as total periodontal pathogen burden, is of greater importance as a potential risk factor for CHD than the clinical parameter such as the Community Periodontal Index of Treatment Needs (CPITN).²⁵

RESULTS

The search retrieved two meta-analyses pertaining to this topic area. The first meta-analysis conducted in 2003 showed that individuals with periodontal infection had a higher summary relative risk (RR) of future cardiovascular

events (RR 1.19 95% CI, 1.08-1.32), with a slightly higher risk of 1.44 (95% CI, 1.20-1.73) for individuals ≤ 65 years of age. In addition, individuals with periodontal disease had a higher risk of future stroke (RR 2.85, 95% CI, 1.78-4.56).¹³ The authors conclude that periodontal disease is associated with a 19% increase in risk of future cardiovascular disease. This meta-analysis included nine cohort studies (eight prospective and one retrospective) (see reference list A). The author reports that confounding in some studies likely overestimated the risk by 12.9% and the use of client questionnaires to identify periodontal disease in other studies underestimated the risk by 29.7%. The balance of these two estimates indicates that the summary RR is probably underestimated. Periodontal disease was defined as gingivitis or periodontitis. The authors suggest that since CVD is multifactorial, all known means of prevention should be implemented, including oral hygiene maintenance.¹³

The second meta-analysis conducted in 2004 examined observational studies and found that periodontal infection increases the risk of cerebrovascular disease and coronary heart disease (CHD).⁽²⁵⁾ Subjects with periodontitis had an overall adjusted relative risk of CHD that was 1.15 times (95% CI: 1.06-1.25; $P=0.0001$) the risk for healthy subjects. Subjects with periodontitis had an overall adjusted relative risk of cerebrovascular disease of 1.13 (95% CI: 1.01-1.27; $P=0.032$). The meta-analysis included seven cohort studies and four cross-sectional and retrospective studies (see reference list B). The studies defined periodontal disease as gingivitis or periodontitis. The authors conclude that larger and better-controlled studies are needed to clarify the association between periodontal disease and CHD.

DISCUSSION

The methodology in both meta-analyses was very good, with a number of design strengths. Both clearly defined a quality criteria checklist for inclusion/exclusion of research and no publication bias was evident. Researchers in the 2003 meta-analysis took into account external validity, adequate follow-up, and also adjusted for confounders. They also gave extra points when it was possible to generalize to the whole population and when there was an extensive >10-year follow-up. However, current debate in research centres on the difficulties in adjusting for confounders. In addition, the 2004 meta-analysis found no heterogeneity when the overall relative risk was estimated from the seven individual studies. One of the drawbacks to the 2004 meta-analysis was that not all of the studies adjusted for established cardiovascular risk factors such as age, gender, cholesterol, weight, smoking, diabetes, and hypertension.

There are several other drawbacks to these meta-analyses. One drawback was that gingivitis and periodontitis studies were combined. It is reported that potential biological mechanisms may apply to periodontitis and not to gingivitis.²⁷ Studies on these two diseases, therefore, should be analyzed separately. Also, given that gingivitis is far more common than periodontitis, studies that separate these two diseases would provide more useful information on the need to screen and treat each disease. In addition, the meta-analyses did not include any randomized controlled trials, the gold standard in research.

The evidence from these two meta-analyses indicates that individuals with periodontal disease have a small-to-moderate increased risk of developing CVD and cerebrovascular disease and a moderate risk of developing a stroke. The summary relative risks reported in these two meta-analyses are consistent with the results from a number of other reviews conducted to date, which are mentioned in the literature section. Although the reported risk is small to moderate, the risk may have a moderate-to-high impact on public health, since almost half of the Canadian population may have gingivitis (which is included in some studies under the category of periodontal disease). Since cardiovascular disease is the number one cause of death in Canada and high costs are associated with treatment, there may also be a significant impact on the lives of Canadians and Canada's health care system. These meta-analyses provide preliminary support for preventing periodontal disease in individuals at risk for or suffering from CVD. The evidence is mounting. However, in the absence of treatment studies or RCTs, it is difficult to identify specific clinical practice changes.

DIABETES

Literature review

From 1999 to 2000 in Canada, there was a 5.1% prevalence of diabetes among adults.²⁸ One of the most striking health-related impacts of diabetes is that adults are twice as likely to die prematurely compared with adults without diabetes.²⁸ The prevalence of diabetes appears to be increasing over time and approximately 35% of adults are

unaware that they have the disease.²⁹ Diabetes takes an immense financial toll on Canadians, costing \$9 billion in health care, disability, work loss, and premature death.²⁹

There is a growing body of research indicating a bi-directional relationship between periodontal disease and diabetes.^{30,31} If clients have diabetes, they may be at greater risk of periodontal disease. And if clients have periodontal disease along with diabetes, the PD may be more severe than if they did not have diabetes. In addition, the treatment of periodontal disease is more difficult in a client with poorly controlled diabetes. Preliminary evidence from a double-blind randomized study confirms that periodontal therapy (scaling and root planing, plus metronidazole) leads to improvements in glucose control.³² Other research shows that improved glucose control can result from mechanical periodontal therapy combined with anti-microbial treatment.^{33,34} Poor glycemic control is recognized as a significant risk factor for complications related to diabetes, such as blindness, kidney failure, and heart and blood vessel disease.

The American Diabetes Association (ADA) acknowledges the link between periodontal disease and diabetes in their 2003 *Report on the Diagnosis and Classification of Diabetes Mellitus*: "periodontitis is often found in people with diabetes."³⁵ In 2000, the American Academy of Periodontology (AAP) took a strong public stand on this issue in their 1999 position paper³⁶ that acknowledges a bi-directional relationship between periodontal disease and diabetes. The AAP statement recommends that the oral health professional contact clients' physicians to inform them of any periodontal diseases, since periodontal infection may increase insulin resistance, lead to a worsening of the diabetic state, and increase the risk for diabetic complications. The position paper cites several studies, including controlled clinical trial evidence, to support the conclusion that mechanical therapy combined with systemic tetracycline antibiotics may improve glycemic control.

Although the exact biological mechanism of action has not been clearly established, there are several possible explanations. One of the proposed mechanisms to explain the bi-directional relationship between periodontal disease and diabetes is that they both stimulate the chronic release of proinflammatory cytokines that have a deleterious effect on periodontal tissues and interfere with insulin action. Bacteria and bacterial products also may produce insulin resistance and glucose intolerance.⁸ The periodontal infection provides a source of micro-organism products such as lipopolysaccharides, which may amplify the magnitude of the advanced glycation end (AGE) product-mediated cytokine upregulation. Some researchers propose that periodontitis may even predispose individuals to the development of type 2 diabetes.³⁷

RESULTS

A 2006 meta-analysis examined the extent and severity of periodontal diseases between diabetics and non-diabetics.³⁸ The meta-analysis was based on international studies including 18 comparative cross sectional studies,

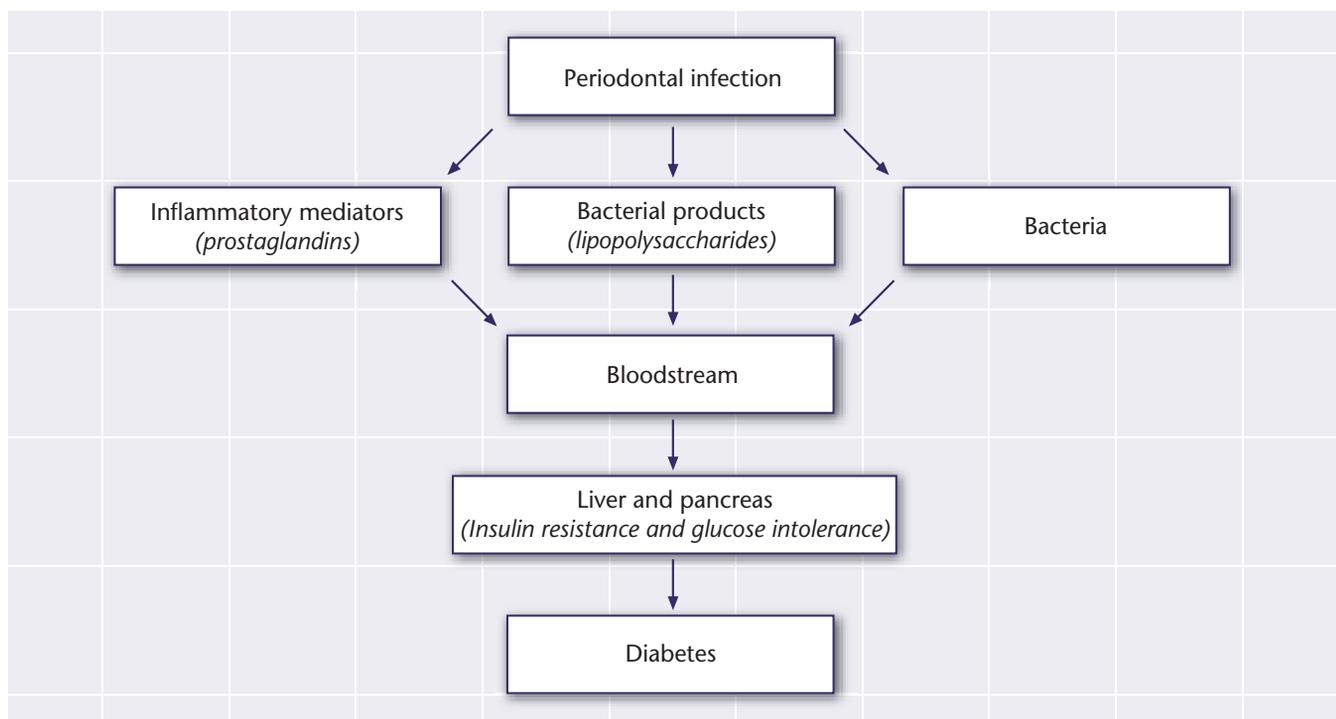


Figure 2. Proposed biological mechanisms (association between periodontal disease and diabetes)

3 prospective cohort studies, and baseline data from 2 clinical trials (see reference list C) comparing oral hygiene, gingival and periodontal status. The study shows the severity of periodontal disease was significantly higher in diabetics compared with non-diabetics but the extent of the disease was the same in both groups. The difference in the average of plaque index between diabetics and non-diabetics was statistically significant at 0.218 (95% CI, 0.098-0.330); the gingival index was 0.147 (95% CI, 0.012-0.281); probing pocket depth was 0.346 (95% CI, 0.194-0.498); clinical attachment loss, bleeding on probing, and the calculus index was not significant. The authors conclude that there is a need for educational campaigns and intensive intervention programs for diabetic clients with periodontal disease.

A 2004 review³⁹ examined 42 observational studies (see reference list D) and found that overall there was consistent evidence of greater prevalence, incidence, severity, extent, or progression of periodontal disease in individuals with diabetes. The evidence also supports a bi-directional relationship between periodontal disease and diabetes. In addition, a dose-response relationship provides some support for a cause-effect relationship. The review examined 25 observational studies and found that there is insufficient evidence to conclude there is an association between tooth loss, coronal or root caries, and diabetes. The 2004 review did not include any analysis of relative risk. The authors conclude that this evidence supports oral examinations and periodontal prevention and treatment for persons with diabetes.

DISCUSSION

The 2006 meta-analysis had some good design features, including pre-stated inclusion criteria. In addition, the author included international literature including studies from France, Turkey, Sweden, Finland, and the United States. This meta-analysis holds more strength than the meta-analyses in the heart disease section of this paper, since it included two randomized controlled trials.

These highlights may be considered along with the minor drawbacks to the analysis. The authors combined studies with different study populations, ages and sizes; and different diagnostic criteria for periodontal disease, resulting in a high degree of heterogeneity between studies. The author also included very dated studies, including two from the 1970s and four from the 1980s. Studies from these decades may vary greatly in their statistical analysis technique compared with more recent studies. Another drawback is the small difference in oral health status measures between the diabetic and the non-diabetic groups. Since there is growing international research on this topic, there is a need to develop international standards for the definition and diagnostic criteria for periodontal disease, which would allow more accurate pooling of original data. This would avoid the possibility of combining the odds ratios, relative risk and P values from two non-significant studies that may give significant results.

Substantial evidence from the 2006 systematic review and a review of the literature in 2004, which includes a large number of studies, supports an association between periodontal disease and diabetes. The relationship appears to be bi-directional and possibly a cause-effect relationship. That is, poor glycemic control may be a risk factor for periodontal disease and periodontal disease may have an

adverse effect on glycemic control. In addition to the outcomes of the research, several other issues may be considered when developing health policies for persons with diabetes. The prevalence of diabetes in the population may be increasing over time, and even small reductions in glycated hemoglobin (hemoglobin A1c) can result in dramatic reductions in some of the later complications of diabetes, including blindness, kidney disease, high blood pressure, and cardiovascular disease.⁴¹ In addition, periodontal disease can be prevented and treated. Therefore, periodontal therapy for the person with diabetes may have potentially great implications for public health; a call for periodontal prevention and treatment programs for persons with diabetes, regardless of income level, is warranted.

REFERENCES

- Lux J, Lavigne S. Your mouth – portal to your body: CDHA position paper on the links between oral health and general health. Part II. *Probe*. 2004;38(4):155-71.
- Canadian Dental Association. CDA position on association between periodontal disease and systemic disease [on-line]. Ottawa: CDA; February 2005 [cited 2006 Mar]. Available from: www.cda-adc.ca/_files/position_statements/periodontal_systemic_diseases.pdf.
- National Institute of Dental and Craniofacial Research. The burden of oral diseases [on-line]. [Cited 2006 Mar.] Available from: www.nidcr.nih.gov/AboutNIDCR/StrategicPlan/BurdenOralDiseases.htm.
- Bureau of Nutritional Sciences. Dental report [Nutrition Canada National survey]. Ottawa: The Bureau; 1977.
- Statistics Canada. Canadian life expectancy and death statistics 2003 [on-line]. Ottawa: Statistics Canada; 2004 [cited 2006 Aug]. Available from: <http://canadaonline.about.com/od/statistics/a/deathstats2003.htm>.
- Public Health Agency of Canada. Economic burden of illness in Canada on-line [on-line]. Ottawa: The Agency; 1998 (cited 2006 Aug 2006). Available from: http://ebic-femc.phac-aspc.gc.ca/home_e.php?Lang=e.
- Statistics Canada. Major causes of death [on-line]. Ottawa: Statistics Canada; 2006 [cited April 2006]. Available from: http://142.206.72.67/02/02b/02b_003_e.htm.
- Lux J, Lavigne S. Your mouth – portal to your body: CDHA position paper on the links between oral health and general health. Part I. *Probe*. 2004;38(3):115-34.
- Hujoel PP. Does chronic periodontitis cause coronary heart disease? A review of the literature. *J Am Dent Assoc*. 2002;133(Suppl):31S-36S.
- Genco R, Offenbacher S, Beck J. Periodontal disease and cardiovascular disease: epidemiology and possible mechanisms. *J Am Dent Assoc*. 2002;133(Suppl):14S-22S.
- Joshiyura K. The relationship between oral conditions and ischemic stroke and peripheral vascular disease. *J Am Dent Assoc*. 2002;133(Suppl):23S-30S.
- Danesh J. Coronary heart disease, *Helicobacter pylori*, dental disease, *Chlamydia pneumoniae*, and cytomegalovirus: meta-analyses of prospective studies. *Am Heart J*. 1999;138(5 Pt 2):S434-S437.
- Janket SJ, Baird AE, Chuang SK, Jones JA. Meta-analysis of periodontal disease and risk of coronary heart disease and stroke. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2003;95(3):559-69.
- Beck J, Offenbacher S. Potential public health implications of periodontal disease and cardiovascular disease relationships [on-line]. Presented at the National Center for Chronic Disease Prevention and Health Promotion conference "Public Health Implications of Chronic Periodontal Infections in Adults"; 2003 Apr 8-9; Atlanta, Georgia. Available from: www.cdc.gov/OralHealth/conferences/periodontal_infections.htm.
- Glogauer M., McCulloch CA. An overview: introduction to the RCDSO symposium – Oral health: a window to systemic disease. Toronto: Royal College of Dental Surgeons of Ontario; 2005.
- Albert DA, Papapanou P, Conicella ML, Sadowsky D, Aetna Dental. The effect of periodontal treatment on medical costs [on-line]. Abstract presented at ADEA/AADR/CADR meeting, Orlando, March 2006. Available from: http://iadr.confex.com/iadr/2006Orld/techprogram/abstract_74102.htm.
- National Institute of Dental and Craniofacial Research. Looking at the periodontal-systemic disease connection: The inside scoop [on-line]. [Cited Apr 2006.] Available from: www.nidcr.nih.gov/NewsAndReports/Media/InsideScoopPeriodontalDiseases.htm.
- Desvarieux M, Demmer R, Rundek T, Boden-Albala B, Jacobs D Jr, Sacco R, Papapanou P. Periodontal microbiota and carotid intima-media thickness: the oral infections and vascular disease epidemiology study (INVEST). *Circulation*. 2005;111(5):576-82.
- Beck JD, Eke P, Heiss G, Madianos P, Couper D, Lin D, Moss K, Elter J, Offenbacher S. Periodontal disease and coronary heart disease: a reappraisal of the exposure. *Circulation*. 2005;112(1):19-24.
- Chiu B. Multiple infections in carotid atherosclerotic plaques. *Am Heart J*. 1999;138(5 Pt 2):S534-S536.
- Joshiyura K, Hung H, Rimm E, Willett W, Ascherio A. Periodontal disease, tooth loss, and incidence of ischemic stroke. *Stroke*. 2003;34(1):47-52.
- Loesche W, Schork A, Terpenning MS, Chen Y, Kerr C, Dominguez BL. The relationship between dental disease and cerebrovascular accident in elderly United States veterans. *Ann Periodontol*. 1998;3(1):161-74.
- Wu T, Trevisan M, Genco RJ, Falkner KL, Dorn JP, Sempos CT. Examinations of the relation between periodontal health status and cardiovascular risk factors: serum total and high density lipoprotein cholesterol, C-reactive protein, and plasma fibrinogen. *Am J Epidemiol*. 2000;151(3):273-82.
- Janket SJ, Qvarnstrom M, MJ, et al. Predicting coronary heart disease utilizing dental health parameter. *Circulation*. 2004;109:1095-1100.
- Spahr A, Klein E, Khuseynova N, Boeckh C, Muche R, Kunze M, Rothenbacher D, Peshki G, Hoffmeister A, Koenig W. Periodontal infections and coronary heart disease: role of periodontal bacteria and importance of total pathogen burden in the Coronary Event and Periodontal Disease (CORODONT) study. *Arch Intern Med*. 2006;166(5):554-59.
- Khader YS, Albashaireh ZS, Alomari MA. Periodontal diseases and the risk of coronary heart and cerebrovascular diseases: a meta-analysis. *J Periodontol*. 2004;75(8):1046-53.
- Vettore MV. Periodontal disease and cardiovascular disease. *Evid Based Dent*. 2004;5(3):69.
- Public Health Agency of Canada. Diabetes facts and figures [on-line]. Ottawa: PHAC; 2006 [cited Apr 2006]. Available from: www.phac-aspc.gc.ca/ccdpc-cpcmc/diabetes-diabete/english/facts/index.html.
- Public Health Agency of Canada. Diabetes in Canada: national statistics and opportunities for improved surveillance, prevention, and control. Ottawa: PHAC; 2006 [cited Apr 2006]. Available from: <http://www.phac-aspc.gc.ca/publicat/dic-dac99/>.
- Grossi SG, Genco RJ. Periodontal disease and diabetes mellitus: a two-way relationship. *Ann Periodontol*. 1998;3(1):51-61.
- Taylor GW. Bidirectional interrelationships between diabetes and periodontal diseases: an epidemiologic perspective. *Ann Periodontol*. 2001;6(1):99-112.
- Tenenbaum H, Goldberg M. Point of Care Question 4 [patients with both diabetes and periodontal disease]. *J Can Dent Assoc*. 2006;72(1):38-39.
- Rodrigues DC, Taba M, Novaes AB, Souza SLS, Grisi MF. Effect of non-surgical periodontal therapy on glycemic control in patients with type 2 diabetes mellitus. *J Periodontol*. 2003;74(9):1361-67.
- Iwamoto Y, Nishimura F, Nakagawa M, Sugimoto H, Shikata K, Makino H, Fukuda T, Tsuji T, Iwamoto M, Murayama Y. The

- effect of antimicrobial periodontal treatment on circulating tumor necrosis factor-alpha and glycated hemoglobin level in patients with type 2 diabetes. *J Periodontol.* 2001;72(6):774-78.
35. American Diabetes Association. Expert Committee on the on the Diagnosis and Classification of Diabetes Mellitus. Report. *Diabetes Care.* 2003;26(Suppl 1):S5-S20.
36. Committee on Research, Science and Therapy. American Academy of Periodontology. Diabetes and periodontal diseases. *J Periodontol.* 2000;71(4):664-78.
37. Mealey BL, Rethman MP. Periodontal disease and diabetes mellitus. Bidirectional relationship. *Dent Today.* 2003;22(4):107-13.
38. Khader YS, Dauod AS, El-Qaderi SS, Alkafajei A, Batayha WQ. Periodontal status of diabetics compared with nondiabetics: a meta-analysis. *J Diabetes Complications.* 2005;20(1):59-68.
39. Taylor GW, Manz C, Borgnakke W. Diabetes, periodontal diseases, dental caries, and tooth loss: a review of the literature. *Compend Contin Educ Dent.* 2004;25(3):179-90.
40. Clark CM, Lee DA. Prevention and treatment of the complications in diabetes mellitus. *N Engl J Med.* 1995;332(18):1210-17.

REFERENCE LIST A

List of studies cited in: Janket SJ, Baird AE, Chuang SK, Jones JA. Meta-analysis of periodontal disease and risk of coronary heart disease and stroke. *Oral Surg Oral Med Oral Path Oral Radiol Endod.* 2003;95(5):559-69.

- Beck J, Garcia R, Heiss G, Vokonas PS, Offenbacher S. Periodontal disease and cardiovascular disease. *J Periodontol.* 1996;67(10 Suppl):1123-37.
- DeStefano F, Anda RF, Kahn HS, Williamson DF, Russell CM. Dental disease and risk of coronary heart disease and mortality [comments]. *Br Med J.* 1993;306:688-91.
- Genco R, Chadda S, Grossi S. Periodontal disease is a predictor of cardiovascular disease in a native American population. *J Dent Res.* 1997;76:408.
- Howell T, Ridker P, Ajani U. Periodontal disease and risks of subsequent cardiovascular in U.S. male physicians. *J Am Coll Cardiol.* 2001;37:445.

- Hujoel PP, Drangsholt M, Spiekerman C, DeRouen TA. Periodontal disease and coronary heart disease risk. *J Am Med Assoc.* 2000;284:1406-10.
- Joshiyura KJ, Rimm EB, Douglass CW, Trichopoulos D, Ascherio A, Willent WC. Poor oral health and coronary heart disease. *J Dent Res.* 1996;75:1631-6.
- Mattila KJ, Valtonen VV, Nieminen M, Huttunen JK. Dental infection and the risk of new coronary events: prospective study of patients with documented coronary artery disease. *Clin Infect Dis.* 1995;20:588-92.
- Morrison HI, Ellison LE, Taylor GW. Periodontal disease and risk of fatal coronary heart and cerebrovascular diseases. *J Cardiovasc Risk.* 1999;6:7-11.
- Wu T, Trevisan M, Genco Rea. Periodontal disease as a risk factor for CVD, CHD and stroke. *Circulation.* 1999;99:1109-25.

REFERENCE LIST B

List of studies cited in: Khader YS, Albashaireh ZS, Alomari MA. Periodontal diseases and the risk of coronary heart and cerebrovascular diseases: a meta-analysis. *J Periodontol.* 2004;75(8):1046-53.

Cohort studies

- Beck J, Garcia R, Heiss G, et al. Periodontal disease and cardiovascular disease. *J Periodontol.* 1996;67(Suppl.): 1123-37.
- De Stefano F, Anda RF, Kahn HS, et al. Dental disease and risk of coronary heart disease and mortality. *Br Med J* 1993;306:688-91.
- Howell T, Ridker P, Ajani U, et al. Periodontal disease and risks of subsequent cardiovascular in U.S. male physicians. *J Am Coll Cardiol.* 2001;37:445-50.
- Hujoel PP, Drangsholt M, Spiekerman C, et al. Periodontal disease and coronary heart disease risk. *J Am Med Assoc.* 2000;284:1406-10.
- Joshiyura KJ, Rimm EB, Douglass CW, et al. Poor oral health and coronary heart disease. *J Dent Res.* 1996;75:1631-6.
- Morrison HI, Ellison LE, Taylor GW. Periodontal disease and risk of fatal coronary heart and cerebrovascular diseases. *J Cardiovasc Risk.* 1999;6:7-11.

- Wu T, Trevisan M, Genco R, et al. Periodontal disease and risk of cerebrovascular disease: The first National Health and Nutrition Examination Survey and its follow-up study. *Arch Intern Med.* 2000;160:2749-55.

Cross-sectional and retrospective studies

- Arbes SJ, Slade GD, Beck JD. Association between extent of periodontal attachment loss and self-reported history of heart attack: An analysis of NHANES III data. *J Dent Res* 1999;78:1777-1782.
- Buhlin K, Gustafsson A, Hakansson J, et al. Oral health and cardiovascular disease in Sweden. *J. Clin Periodontol* 2002;29:254-259.
- Grau AJ, Buggle F, Ziegler C, et al. Association between acute cerebrovascular ischemia and chronic and recurrent infection. *Stroke* 1997;28:1724-1729.
- Loesche WJ, Schork A, Terpenning MS, et al. Assessing the relationship between dental disease and coronary heart disease in elderly U.S. veterans. *J Am Dent Assoc* 1998;129:301-311.

REFERENCE LIST C

List of studies in: Khader YS, Dauod AS, El-Qaderi SS, Alkafajei A, Batayha WZ. Periodontal status of diabetics compared with nondiabetics: a meta-analysis. *J Diabetes Complications.* 2006;20(1):59-68.

Comparative cross-sectional studies

- Alpagot T, Silverman S, Lundergan W, Bell C, Chambers DW. Crevicular fluid elastase levels in relation to periodontitis and metabolic control of diabetes. *J Periodont Res.* 2001;36(3):169-74.
- Bridges RB, Anderson JW, Saxe SR, George K, Bridges SR. Periodontal status of diabetic and non-diabetic men: effects of smoking, glycemic control, and socioeconomic factors. *J Periodontol.* 67:1185-92.
- Campbell MJ. Epidemiology of periodontal disease in diabetic and the non-diabetic. *Aust Dent J.* 1972;17(4):274-78.
- Collin HL, Uusitupa M, Niskanen L, Kontturi-Harhi V, Markkanen H, Koivisto AM, Meurman JH. Periodontal findings

in elderly patients with non-insulin dependent diabetes mellitus. *J Periodontol.* 1998;69:962-66.

- De Pomereau V, Dargent-Pare C, Robert JJ, & Brion M. Periodontal status in insulin dependent diabetic adolescents. *J Clin Periodontol.* 1992;19:628-32.
- Emrich LJ, Shlossman M, Genco RJ. Periodontal disease in non-insulin dependent diabetes mellitus. *J Periodontol.* 1991;62(2):123-31.
- Falconbridge AR, Bradshaw WC, Jenkins PA, Baum JD. The dental status of a group of diabetic children. *Br Dent J.* 1981;151(8):253-55.
- Firatli E, Yilmaz O, Onan U. The relationship between clinical attachment loss and the duration of the insulin-dependent diabetes mellitus (IDDM) in children and adolescents. *J Clin Periodontol.* 1996;23(4):362-66.
- Goteiner D, Vogel R, Deasy M, Goteiner C. Periodontal and caries experience in children with insulin-dependent diabetes mellitus. *J Am Dent Assoc.* 1986;113(2):277-79

- Hugoson A, Thorstensson H, Falk H, Kuylenstierna J. Periodontal conditions in insulin-dependent diabetics. *J Clin Periodontol.* 1989;16(4):215-23.
- Karjalainen KM, Knuuttila ML. The onset of diabetes and poor metabolic control increases gingival bleeding in children and adolescent with insulin dependent diabetes mellitus. *J Clin Periodontol.*, 1996;23:1060-67.
- Morton AA, Williams RW, Watts TL. Initial study of periodontal status in non-insulin dependent diabetics in Mauritius. *J Dent.* 1995;23(6):343-45.
- Oliver RC, Tervonen T. Periodontitis and tooth loss: comparing diabetics with the general population. *J Am Dent Assoc.* 1993;124 (12):71-76.
- Pinson M, Hoffman WH, Garnick JJ, Litaker MS. Periodontal disease and type 1 diabetes mellitus in children and adolescents. *J Clin Periodontol.* 1995;22(2):118-23.
- Sznajder N, Carraro JJ, Rugna S, Sereday M. Periodontal finding in diabetic and non-diabetic patients. *J Periodontol.* 1978;49(9):445-48.
- Thorstensson H, Hugoson A. Periodontal disease experience in adult long-duration insulin-dependent diabetics. *J Clin Periodontol.* 1993;20(5):352-58.
- Trevonen T, Knuuttila M. Relation of diabetes control to periodontal pocketing and alveolar bone level. *Oral Surg Oral Med Oral Pathol.* 1986;61:346-49.
- Unal T, Firatli E, Sivas A, Meric H, Oz H. Fructosamine as a possible monitoring parameter in non-insulin dependent diabetes mellitus patients with periodontal disease. *J Periodontol.* 1993;64:191-94.

Prospective cohort studies

- Firatli E. The relationship between clinical periodontal status and insulin-dependent diabetes mellitus. Results after 5 years. *J Periodontol.* 1997;68(2):136-40.
- Pohjamo L, Tervonen T, Knuuttila M, Nurkkala H. Adult diabetic and nondiabetic subjects as users of dental services. A longitudinal study. *Acta Odontologica Scandinavica.* 1995;53(2):112-14.
- Trevonen T, Karjalainen K. Periodontal disease related to diabetic status. A pilot study of the response to periodontal diabetic status. A pilot study of the response to periodontal therapy in type 1 diabetes. *J Clin Periodontol.* 1997;24(7):505-10.

Clinical trials

- Tervonen T, Knuuttila M, Pohjamo L, Nurkkala H. Immediate response to non-surgical periodontal treatment in subjects with diabetes mellitus. *J Clin Periodontol.* 1991;18:65-68.
- Wesfelt E, Rylander H, Blohme G, Jonasson P, Linhe J. The effect of periodontal therapy in diabetics. Results after 5 years. *J Clin Periodontol.* 1996;23:92-100.

REFERENCE LIST D

List of studies cited in: Taylor GW, Manz C, Borgnakke W. Diabetes, periodontal diseases, dental caries, and tooth loss: a review of the literature. *Comp Cont Educ Dent.* 2004;25(3):179-190.

Adverse effect of diabetes on periodontal health

- Albrecht M, Banoczy J, Tamas G Jr. Dental and oral symptoms of diabetes mellitus. *Comm Dent Oral Epidemiol.* 1988;16(6):378-80.
- Alpagot T, Silverman S, Lundergan W, et al. Crevicular fluid elastase levels in relation to periodontitis and metabolic control of diabetes. *J Periodontol Res.* 2001;36(3):169-74.
- Bacic M, Plancak D, Granic M. CPITN assessment of periodontal disease in diabetic patients. *J Periodontol.* 1988;59(12):816-22.
- Belting CM, Hiniker JJ, Drummet CO. Influence of diabetes mellitus on the severity of periodontal disease. *J Periodontol.* 1964;35:476-80.
- Benveniste R Bixler D, Conneally PM. Periodontal disease in diabetics. *J Periodontol.* 1967;38(4):271-79.
- Bridges RB, Anderson JW, Saxe SR, et al. Periodontal status of diabetic and non-diabetic men: effects of smoking, glycemic control, and socioeconomic factors. *J Periodontol.* 1996;67(11):1185-92.
- Campbell MJ. Epidemiology of periodontal disease in the diabetic and the non-diabetic. *Aust Dent J.* 1972;17(4):274-78.
- Cianciola LA, Park BH, Bruck E, et al. Prevalence of periodontal disease in insulin-dependent diabetes mellitus (juvenile diabetes). *J Am Dent Assoc.* 1982;104(5):653-60.
- Cohen DW, Friedman LA, Shapiro J, et al. Diabetes mellitus and periodontal disease: two-year longitudinal observations. *J Periodontol.* 1970;41(12):709-12.
- de Pommereau V, Dargent-Pare C, Robert JJ, Brion M. Periodontal status in insulin-dependent diabetic adolescents. *J Clin Periodontol.* 1992;19(9 Pt 1):628-23.
- Dolan TA, Gilbert GD, Ringelberg ML, et al. Behavioral risk indicators or attachment loss in adult Floridians. *Clin Periodontol.* 1997;24(4):223-32.
- Emrich LJ, Sclossman M, Genro RJ. Periodontal disease in non-insulin-dependent diabetes mellitus [see comments]. *J Periodontol.* 1991;62(2):123-31.
- Faulconbridge AR, Bradshaw WC, Jenkins PA, et al. The dental status of a group of diabetic children. *Br Dent J.* 1981;151(8):253-55.
- Finestone AJ, Boorujy SR. Diabetes mellitus and periodontal disease. *Diabetes.* 1967;16(5):336-40.
- Firatli E, Yilamz O, Onan U. The relations between clinical attachment loss and the duration of insulin-dependent diabetes mellitus (IDDM) in children and adolescents. *J Clin Periodontol.* 1996;23(4):362-66.
- Firatli E. The relationship between clinical periodontal status and insulin-dependent diabetes mellitus. Results after 5 years. *J Periodontol.* 1997;68(2):136-40.
- Galea H, Aganovic I, Aganovic M. The dental caries and periodontal disease experience of patients with early onset insulin dependent diabetes. *Int Dent J.* 1896;36(4):219-24.
- Glavind L, Lund B, Loe H. The relationship between periodontal state and diabetes duration *J Periodontol.* 1968;39(6):341-47.
- Goteiner D, Vogel R, Deasy M, et al. Periodontal and caries experience in children with insulin-dependent diabetes mellitus. *J Am Dent Assoc.* 1986;113(2):277-79.
- Grossi SG, Zambon JJ, HO AW, et al. Assessment of risk for periodontal disease. I. Risk indicators for attachment loss. *J Periodontol.* 1994;65(3):260-67.
- Guven Y, Satman I, Dincag N, et al. Salivary peroxidase activity in whole saliva of patients with insulin-dependent (type-1) diabetes mellitus. *J Clin Periodontol.* 1996;23(9):879-81.
- Harrison R, Bowen WH. Periodontal health, dental caries, and metabolic control in insulin-dependent diabetic children and adolescents. *Pediatr Dent.* 1987;9(4):283-86.
- Hove KA, Stallard RE. Diabetes and the periodontal patient. *J Periodontol.* 1970;41(12):713-18.
- Hugoson A, Thorstensson H, Falk H, et al. Periodontal conditions in insulin-dependent diabetics. *J Clin Periodontol.* 1989;16(4):215-23.
- Kjellman O, Henrickson CO, Berghagen N, et al. Oral conditions in 105 subjects with insulin-treated diabetes mellitus. *Sven Tandlak Tidskr.* 1970;63(2):99-110.
- Mackenzie RS, Millard HD. Interrelated effects of diabetes, arteriosclerosis, and calculus on alveolar bone loss. *J Am Dent Assoc.* 1963;66:191-98.
- Morton AA, Williams RW, Watts TLP. Initial study of periodontal status in non-insulin-dependent diabetics in Mauritius. *J Dent.* 1995;23(6):343-354.
- Nelson RG, Shlossman M, Budding LM, et al. Periodontal disease and NIDDM in Pima Indians. *Diabetes Care.* 1990;13(8) 836-40.
- Novaes Junior AB, Gutierrez FG, Novaes AB. Periodontal disease progression in type II non-insulin-dependent diabetes mellitus patients (NIDDM). Part 1 - Probing pocket depths and clinical attachments. *Braz Dent J.* 1996;7(2):65-73.

- Novaes Junior AB, Pereira AL, de Moraes N, et al. Manifestations of insulin-dependent diabetes mellitus in the periodontium of young Brazilian patients. *J Periodontol.* 1991;62(2):116-22.
- Oliver RC, Tervonen T. Periodontitis and tooth loss: comparing diabetes with the general population. *J Am Dent Assoc.* 1993;124(12):71-76.
- Pinson M, Hoffman WH, Garnick JJ, et al. Periodontal disease and type 1 diabetes mellitus in children and adolescents. *J Clin Periodontol.* 1995;22(2):118-23.
- Ringelberg ML, Dixon DO, Francis AO, et al. Comparison of gingival health and gingival crevicular fluid flow in children with and without diabetes. *J Dent Res.* 1977;56(2):108-11.
- Rylander H, Ramberg P, Blohme G, et al. Prevalence of periodontal disease in young diabetics. *J Clin Periodontol.* 1987;14(1):38-43.
- Sandler HC, Stahl SS. Prevalence of periodontal disease in a hospitalized population. *J Dent Res.* 1960;39(3):439-49.
- Shlossman M, Knowler WC, Pettitt DJ, et al. Type 2 diabetes mellitus and periodontal disease. *J Am Dent Assoc.* 1990;121(4):532-36.
- Sznajder N, Carraro JJ, Rudna S, et al. Periodontal findings in diabetic and nondiabetic patients. *J Periodontol.* 1978;49(9):445-48.
- Szpunar SM, Ismail AI, Eklund SA. Diabetes and periodontal disease: analyses of NHANES I and NHANES [Abstr #1605]. *J Dent Res.* 1989;68(Spec issue):383.
- Taylor GW. Exploring interrelationships between diabetes and periodontal disease in African Americans. *Compend Contin Educ Dent.* 2001;22(3):42-48.
- Taylor GW, Burt BA, Becker MP, et al. Glycemic control and alveolar bone loss progression in type 2 diabetes. *Ann Periodontol.* 1998;3(1):30-39.
- Taylor GW, Burt BA, Becker MP, et al. Non-insulin dependent diabetes mellitus and alveolar bone loss progression over 2 years. *J Periodontol.* 1998;69(1):76-83.
- Tervonen T, Karjalainen K, Knuutila M, et al. Alveolar bone loss in type 1 diabetes subjects. *J Clin Periodontol.* 2000;27:567-71.
- Tervonen T, Karjalainen K. Periodontal disease related to diabetic status. A pilot study of the response to periodontal therapy in type 1 diabetes. *J Clin Periodontol.* 1997;24(7):505-10.
- Tervonen T, Knuutila M. Relation of diabetes control to periodontal pocketing and alveolar bone level. *Oral Surg Oral Med Oral Pathol.* 1986;61(4):346-49.
- Thorstensson H, Hugoson A. Periodontal disease experience in adult long-duration insulin-dependent diabetics. *J Clin Periodontol.* 1993;20(5):352-58.
- Wolf J. Dental and periodontal conditions in diabetes mellitus. A clinical and radiographic study. *Proc Finn Dent Soc.* 1977;73(4-6 suppl):1-56.
- Yavuzilmaz E, Yumak O, Akdoganli T, et al. The alterations of whole saliva constituents in patients with diabetes mellitus. *Aust Dent J.* 1996;41(3):193-97.
- Bi-directional relationship*
- Ainamo J, Lahtinen A, Uitto VJ. Rapid periodontal destruction in adult humans with poorly controlled diabetes. A report of 2 cases. *J Clin Periodontol.* 1990;17(1):22-28.
- Albrecht M, Banoczy J, Tamas Jr G. Dental and oral symptoms of diabetes mellitus. *Comm Dent Oral Epidemiol.* 1988;16(6):378-80.
- Alpagot T, Silverman S, Lundergan W, et al. Crevicular fluid elastase levels in relation to periodontitis and metabolic control of diabetes. *J Periodontol Res.* 2001;36(3):169-74.
- Bacic M, Plancak D, Granic M. CPITN assessment of periodontal disease in diabetic patients. *J Periodontol.* 1988;59(12):816-22.
- Barnett ML, Baker RL, Yancey JM, et al. Absence of periodontitis in a population of insulin-dependent diabetes mellitus (IDDM) patients. *J Periodontol.* 1984(7):402-05.
- Bridges RB, Anderson JW, Saxe SR, et al. Periodontal status of diabetic and non-diabetic men: effects of smoking, glycemic control, and socioeconomic factors. *J Periodontol.* 1996;67(11):1185-92.
- de Pommereau V, Dargent-Pare C, Robert JJ, et al. Periodontal status in insulin-dependent diabetic adolescents. *J Clin Periodontol.* 1992;19(9 Pt 1):628-23.
- Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. *N Eng J Med.* 1993;329(14):977-86.
- Finestone AJ, Boorujy SR. Diabetes mellitus and periodontal disease. *Diabetes.* 1967;16(5):336-40.
- Firatli E. The relationship between clinical periodontal status and insulin-dependent diabetes mellitus. Results after 5 years. *J Periodontol.* 1997;68(2):136-40.
- Galea H, Aganovic I, Aganovic M. The dental caries and periodontal disease experience of patients with early onset insulin dependent diabetes. *Int Dent J.* 1896;36(4):219-24.
- Gislen G, Nilsson KO, Mattsson L. Gingival inflammation in diabetic children related to degree of metabolic control. *Acta Odontol Scand.* 1980;38(4):241-46.
- Goteiner D, Vogel R, Deasy M, et al. Periodontal and caries experience in children with insulin-dependent diabetes mellitus. *J Am Dent Assoc.* 1986;113(2):277-79.
- Gusberti FA, Syed SA, Bacon G, et al. Puberty gingivitis in insulin-dependent diabetic children. I. Cross-sectional observations. *J Periodontol.* 1983;54(12):714-20.
- Harrison R, Bowen WH. Periodontal health, dental caries, and metabolic control in insulin-dependent diabetic children and adolescents. *Pediatr Dent.* 1987;9(4):283-86.
- Hayden P, Buckely LA. Diabetes mellitus and periodontal disease in an Irish population. *J Periodontol Res.* 1989;24(5):298-02.
- Hove KA, Stallard RE. Diabetes and the periodontal patient. *J Periodontol.* 1970;41(12):713-18.
- Karikoski A, Murtomaa H, Ilanne-Parikka P. Assessment of periodontal treatment needs among adults with diabetes in Finland. *Int Dent J.* 2002;52(2):75-80.
- Karjalainene KM, Knuutila ML. The onset of diabetes and poor metabolic control increases gingival bleeding in children and adolescents with insulin-dependent diabetes mellitus. *J Clin Periodontol.* 1996;23(12):1060-67.
- Kjellman O, Henrickson CO, Berghagen N, et al. Oral conditions in 105 subjects with insulin-treated diabetes mellitus. *Sven Tandlak Tidsskr.* 1970;63(2):99-110.
- Moore PA, Weyant RJ, Mongelluzzo MB, et al. Type 1 diabetes mellitus and oral health assessment of periodontal disease. *J Periodontol.* 1999;70(4):409-17.
- Nichols C, Laster LL, Bodak-Gyovai LZ. Diabetes mellitus and periodontal disease. *J Periodontal disease. J Periodontol.* 1978;49(2):85-88.
- Novaes AB Jr, Gutierrez FG, Novaes AB. Periodontal disease progression in type II non-insulin-dependent diabetes mellitus patients (NIDDM). Part 1 – Probing pocket depths and clinical attachments. *Braz Dent J.* 1996;7(2):65-73.
- Oliver RC, Tervonen T. Periodontitis and tooth loss: comparing diabetes with the general population. *J Am Dent Assoc.* 1993;124(12):71-76.
- Pinson M, Hoffman WH, Garnick JJ, et al. Periodontal disease and type 1 diabetes mellitus in children and adolescents. *J Clin Periodontol.* 1995;22(2):118-23.
- Rylander H, Ramberg P, Blohme G, et al. Prevalence of periodontal disease in young diabetics. *J Clin Periodontol.* 1987;14(1):38-43.
- Safkan-Seppala B, Ainamo J. Periodontal conditions in insulin-dependent diabetes mellitus. *J Clin Periodontol.* 1992;19(1):24-29.
- Sandberg GE, Sundberg HE, Fjellstrom CA, et al. Type 2 diabetes and oral health A comparison between diabetic and non-diabetic subjects. *Diabetes Res Clin Pract.* 2000;50:27-34.
- Sandholm L, Swanljung O, Rytomaa I, et al. Periodontal status of Finnish adolescents with insulin-dependent diabetes mellitus. *J Clin Periodontol.* 1989;16(10):617-20.

- Sastrowijoto SH, Hillemans P, van Steenberg TJ, et al. Periodontal condition and microbiology of healthy and diseased periodontal pockets in type 1 diabetes mellitus patients. *J Clin Periodontol.* 1989;16(5):316-22.
- Seppala B, Ainamo J. A site-by-site follow-up study on the effect of controlled versus poorly controlled insulin-dependent diabetes mellitus. *J Clin Periodontol.* 1994;21(3):161-65.
- Seppala B, Seppala M, Ainamo J. A longitudinal study on insulin-dependent diabetes mellitus and periodontal disease. *J Clin Periodontol.* 1993;20(3):161-65.
- Taylor GW. Exploring interrelationships between diabetes and periodontal disease in African Americans. *Compend Contin Educ Dent.* 2001;22(3):42-48.
- Taylor GW, Burt BA, Becker MP, et al. Glycemic control and alveolar bone loss progression in type 2 diabetes. *Ann Periodontol.* 1998;3(1):30-39.
- Tervonen T, Karjalainen K, Knuuttila M, et al. Alveolar bone loss in type 1 diabetes subjects. *J Clin Periodontol.* 2000;27:567-71.
- Tervonen T, Karjalainen K. Periodontal disease related to diabetic status. A pilot study of the response to periodontal therapy in type 1 diabetes. *J Clin Periodontol.* 1997;24(7):505-10.
- Tervonen T, Knuuttila M. Relation of diabetes control to periodontal pecketing and alveolar bone level. *Oral Surg Oral Med Oral Pathol.* 1986;61(4):346-49.
- Tervonen T, Oliver RC. Long-term control of diabetes mellitus and periodontitis. *J Clin Periodontol.* 1993;20(6):431-35.
- Tsai C, Hayes C, Taylor GW. Glycemic control of type 2 diabetes and severe periodontal disease in the US adult population. *Community Dent Oral Epidemiol.* 2002;30(3):182-92.
- UKPDS Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *UK Prospective Diabetes Study (UKPDS) Group. Lancet.* 1998;54(12):714-20.
- Unal T, Firatly E, Sivas A, et al. Fructosamine as a possible monitoring parameter in non-insulin dependent diabetes mellitus patients with periodontal disease. *J Periodontol.* 1993;64(3):191-94.
- Wolf J. Dental and periodontal conditions in diabetes mellitus. A clinical and radiographic study. *Proc Finn Dent Soc.* 1977;73(4-6 suppl):1-56.
- Dental caries*
- Akyuz S, Oktay C. The relationship between periodontitis and tooth decay in juvenile diabetes mellitus cases and in healthy children. *J Marmara Univer Dent Fac.* 1990;1(1):58-65.
- Albrecht M, Banoczy J, Tamas G Jr. Dental and oral symptoms of diabetes mellitus. *Community Dent Oral Epidemiol.* 1988;16(6):378-80.
- Bacic M, Ciglar I, Granic M, et al. Dental status in a group of adult diabetic patients. *Community Dent Oral Epidemiol.* 1989;17(6):313-16.
- Bernick SM, Cohen DW, Baker L, et al. Dental disease in children with diabetes mellitus. *J Periodontol.* 1975;46(4):241-45.
- Cherry-Peppers G, Ship JA. Oral health in patients with type II diabetes and impaired glucose tolerance. *Diabetes Care.* 1993;16(4):638-41.
- Ciglar I, Sutalo J, Vuksan V, et al. Nutrition dental caries, and diabetes mellitus. *Diab Croat.* 1985;14:239-46.
- Collin HL, Uusitupa M, Niskanen L, et al. Caries in patients with non-insulin-dependent diabetes mellitus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1998;85(6):680-85.
- Edblud E, Lundin SA, Sjodin B, et al. Caries and salivary status in young adults with type 1 diabetes. *Swed Dent J.* 2001;25(2):53-60.
- Falk H, Hugoson A, Thorstensson H. Number of teeth, prevalence of caries and periapical lesions in insulin-dependent diabetics. *Scand J Dent Res.* 1989;97(3):198-206.
- Faulconbridge AR, Bradshaw WC, Jenkins PA, et al. The dental status of a group of diabetic children. *Br Dent J.* 1981;151(8):253-55.
- Galea H, Aganovic I, Aganovic M. The dental caries and periodontal disease experience of patients with early onset insulin dependent diabetes. *Int Dent J.* 1896;36(4):219-24.
- Goteiner D, Vogel R, Deasy M, et al. Periodontal and caries experience in children with insulin-dependent diabetes mellitus. *J Am Dent Assoc.* 1986;113(2):277-79.
- Harrison R, Bowen WH. Periodontal health, dental caries, and metabolic control in insulin-dependent diabetic children and adolescents. *Pediatr Dent.* 1987;9(4):283-86.
- Jones RB, McCallum RM, Kay EJ, et al. Oral health and oral health behaviour in a population of diabetic outpatient clinic attenders. *Community Dent Oral Epidemiol.* 1992;20:204-07.
- Kirk JM, Kinirons MJ. Dental health of young insulin dependent diabetic subjects in Northern Ireland. *Community Dent Health.* 1998;8(4):335-41.
- Kjellman O, Henrickson CO, Berghagen N, et al. Oral conditions in 105 subjects with insulin-treated diabetes mellitus. *Sven Tandlak Tidsskr.* 1970;63(2):99-110.
- Leeper SH, Kalkwarf KL, Strom EA. Oral status of "controlled" adolescent type 1 diabetics. *J Oral Med.* 1985;40(3):127-33.
- Lin BP, Taylor GW, Allen DJ, et al. Dental caries in older adults with diabetes mellitus. *Spec Care Dentist.* 1999;19(1):8-14.
- Matsson L, Koch G. Caries frequency in children with controlled diabetes. *Scand J Dent Res.* 1975;7(4):20-23.
- Moore PA, Weyant RJ, Etzel KR, et al. Type 1 diabetes mellitus and oral health: assessment of coronal and root caries. *Community Dent Oral Epidemiol.* 2001;29(3):183-94.
- Narhi TO, Meurman JH, Odont D, et al. Oral health in the elderly with non-insulin-dependent diabetes mellitus. *Spec Care Dentist.* 1996;16(3):116-22.
- Pohjamo L, Knuuttila M, Burkkala H, et al. Increment of caries in diabetic adults. A two-year longitudinal study. *Community Dent Health.* 1991;8(4):343-48.
- Pohjamo L, Knuuttila M, Tervonen T, et al. Caries prevalence related to the control of diabetes. *Proc Finn Dent Soc.* 1988;84(4):247-52.
- Sandberg GE, Sundberg HE, Fjellstrom CA, et al. Type 2 diabetes and oral health A comparison between diabetic and non-diabetic subjects. *Diabetes Res Clin Pract.* 2000;50:27-34.
- Sarnat H, Eliaz R, Geiman G, et al. Carbohydrate consumption and oral status of diabetic and nondiabetic young adolescents. *Clin Prev Dent.* 1985;7(4):20-23.
- Sterky G, Kjellman O, Hogberg O, et al. Dietary composition and dental disease in adolescent. A pilot study. *Acta Paediatr Scand.* 1971;60(4):461-64.
- Swanlung O, Meurman JH, Torkko H, et al. Caries and saliva in 12-18 year-old diabetics and controls. *Scan J Dent Res.* 1992;100(6):310-13.
- Tavares M, Dapaola P, Soparkar P, et al. The prevalence of root caries in diabetic population. *J Dent Res.* 1991;70(6):979-83.
- Tenovuo J, Alanene P, Larjava H, et al. Oral health of patients with insulin-dependent diabetes mellitus. *Scand J Dent Res.* 1986;94(4):338-46.
- Twetman S, Aronsson S, Bjorkman S. Mutans streptococci and lactobacilli in saliva from children with insulin-dependent diabetes mellitus. *Oral Microbiol Immunol.* 1989;4(3):165-68.
- Twetman S, Johansson I, Birkhed D, et al. Caries incidence in young type 1 diabetes mellitus patients in relation to metabolic control and caries-associated risk factors. *Caries Res.* 2002;36(1):31-35.
- Twetman S, Norderford T, Stahl, et al. Two-year longitudinal observations of salivary status and dental caries in children with insulin-dependent diabetes mellitus. *Pediatr Dent.* 1992;14(3):184-88.
- Wegner H. Dental caries in young diabetics. *Caries Res.* 1971;5(2):188-92.
- Wegner H. Increment of caries in young diabetics. *Caries Res.* 1975;9(1):90-91.
- Wolf J. Dental and periodontal conditions in diabetes mellitus. A clinical and radiographic study. *Proc Finn Dent Soc.* 1977;73(4-6 suppl):1-56.