Your Mouth – Portal to Your Body

Canadian Dental Hygienists Association Position Paper on the Links between Oral Health and General Health: Part I

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This paper discusses four aspects of systemic health and their association with periodontal disease. The conditions focused on are diabetes mellitus, heart disease, respiratory disease, and preterm low birth weight infants. The two-part article appeared originally in the CDHA journal,* Probe *(now the* Canadian Journal of Dental Hygiene*), in the 2004 May/June and 2004 July/August issues (Vol. 38, Nos. 1 and 2).

EXECUTIVE SUMMARY

A large body of research indicates a striking association between oral health and systemic health. Heart disease, preterm low birth weight babies, diabetes mellitus, and respiratory disease are being linked to periodontitis.

- Periodontal disease may exacerbate diabetes mellitus. Mechanical periodontal therapy combined with systemic antibiotics may provide better metabolic control of type 2 diabetes, with a 0.8% to 11% reduction in glycated hemoglobin.
- Persons with periodontal disease have a 1.04 to 2.8 fold greater risk of incurring cardiovascular disease than persons without periodontal disease. Of the different types of cardiovascular disease, stroke shows the most robust association.
- Women with periodontal disease may have 4 to 7.9 times the risk of having a preterm birth than do women with good oral health—this is considered a moderate to high risk. Early identification and treatment of periodontal disease during pregnancy may reduce the risk of premature birth and low birth weight.
- A moderate association may exist between oral health and respiratory disease, with an average odds ratio of 3.04 for those at risk of developing respiratory disease.

A number of possible biological pathways link oral disease to systemic disease:

- oral biofilm that harbours biological pathogens
- transient or chronic bacteremia
- immunologic injury caused by endotoxins
- direct injury by lipopolysaccharides

Since periodontal disease is a potentially modifiable risk factor, being both preventable and treatable in most cases, dental hygienists may have an opportunity to contribute to decreasing the

incidence and severity of these systemic diseases. This research opens the door for dental hygienists to work more collaboratively in interdisciplinary relationships with other health professionals. These findings can create opportunities for an integrated model of oral and general health and will strengthen the argument for an oral health system that is accessible to all citizens.

INTRODUCTION

> *A mid-16th century English proverb states that "the eyes are the window to the soul."*[1] *A 21st century proverb could well read, "the mouth is the portal to the body."*

A large body of research indicates a striking association between the multifactorial etiology of oral and systemic diseases. Heart disease, preterm low birth weight babies, diabetes mellitus, and respiratory disease are being linked to periodontitis.

The purposes of this position paper are to (1) gather comprehensive research information to offer a critical look at the relationships between oral health and systemic health outcomes; and (2) to present recommendations supporting clinical practice, policy making, and self-care decisions. This paper was posted on CDHA's website for comments. Members' feedback was incorporated into the document to help establish a consensus among the association's members on the recommendations. Experts in the oral health field were also consulted. This paper will be reviewed at regular intervals to ensure that it includes the current research.

Although increased attention has lately been paid to the mouth-body connection, this area of research has actually existed for 100 years. In 1909, Dr. William Hunter devised the "focal infection" or "focal sepsis" theory, stating that dental (septic) infection was the most important cause and complication of medical diseases.[2] More recently, the term "periodontal medicine" has been used to describe a new oral health field that examines how periodontal infections interact intimately with the morbidity and mortality of individuals with certain systemic conditions.

For example, diabetes mellitus is currently considered a risk factor for periodontal disease. This is supported by large epidemiologic studies using multifactorial statistical analysis to ensure the results are not skewed by confounding co-risk factors.[3]

This paper examines the other side of the coin—the ways in which oral disease affects systemic health, specifically, chronic heart disease, respiratory disease, diabetes mellitus, and preterm low birth weight babies. Each of these diseases is examined separately below. Due to space considerations, the suspected associations between oral health and *Helicobacter pylori* infection, nutrition, rheumatoid arthritis, stress, osteopenia, and Kindler syndrome will be considered in a later position paper.

The oral-systemic disease link is important because of the high occurrence of oral disease—approximately 10% to 15% of the world's population is affected by advanced periodontal disease[4] and more than 50% of adults 55 or older have periodontitis.[5] If periodontal disease is associated with systemic disease, then its prevention may have a significant positive impact on the general health of Canadians and thus limit the human and financial costs of systemic health issues. The following literature reviews will look at the research that explores oral and general

health associations as well as the intervention studies that show how dental hygiene treatment affects systemic health. Appendix A contains the definitions of terms as they are used in this paper.

METHODOLOGY

The methodological approach in this paper is a review of the literature. The primary focus centres on periodontal health status measures and their associations with systemic diseases. The researchers conducted a detailed search of relevant international English language epidemiological evidence from 1996 to 2003 using MEDLINE, EMBASE, and the Cochrane controlled trials register. The search also included "gray" literature—information not reported in the scientific periodical literature—and web sites known to contain publications on this topic. In addition, references cited in the articles were manually searched, as opposed to computer data base search. Lastly, we asked recognized experts in the topic area for other possibly relevant articles that may have otherwise not been identified.

In vivo and human studies identified in the literature search were included in this review; in vitro and animal studies were excluded. The research was classified according to the Canadian Task Force on the Periodic Health Examination Evidence Classification Scheme (see Appendix B).

DIABETES MELLITUS

Diabetes mellitus is a systemic disease characterized by hyperglycemia and it affects approximately 2 million people in Canada, about 6.4% of the population.[6] There are two types of diabetes: type 1, formerly called insulin-dependent diabetes, is caused by the complete or almost complete destruction of the pancreatic beta cells that produce insulin. Type 2, formerly called non-insulin-dependent diabetes, is the result of the body's inability to effectively use insulin so that glucose levels remain elevated. Risk factors for diabetes include a family history of diabetes, dyslipidemia, infertility, hirsutism, obesity, and smoking. Persistent poor glycemic control can lead to atherosclerosis, with complications such as retinopathy and nephropathy that may progress to blindness and end-stage renal disease.[7] It is important to determine what factors disrupt glycemic control in diabetics, given that the annual cost of diabetes is estimated at almost $9 billion,[8] costs attributed to health care, disability, work loss, and premature death.

Biological pathways

The following outlines the biologically based hypotheses to the link between periodontal disease and diabetes:[9-13]

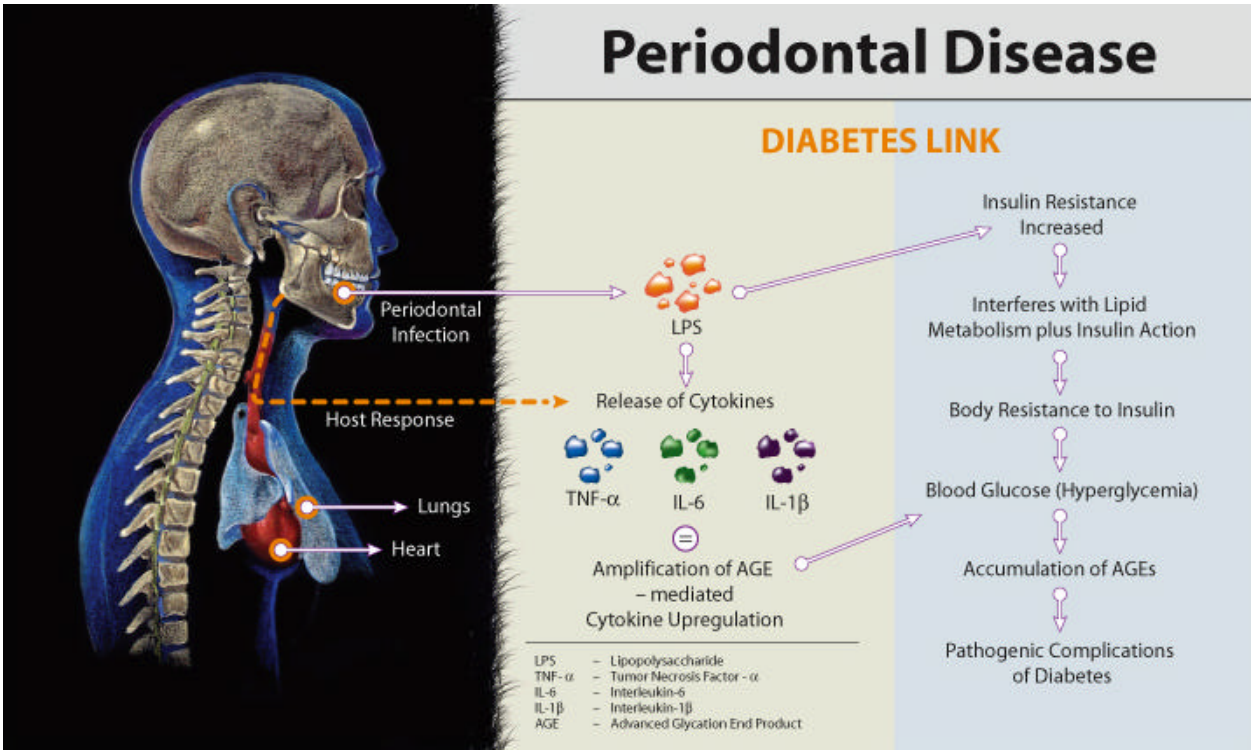
1. There is a subgingival microbial infection of the periodontium and pocket epithelium.
2. The periodontium is a gateway to the systemic circulation.
3. The cell wall of the micro-organism releases endotoxins such as lipopolysaccharide and other products that increase insulin resistance.

4. The host responds to such products by releasing proinflammatory cytokines such as tumor necrosis factor ? (TNF-?), interleukin-6 (IL-6), and interleukin-1 beta (IL-1ß) that interfere with lipid metabolism and insulin action.
5. The periodontal infection provides a source of micro-organism products such as lipopolysaccharides, which may amplify the magnitude of the advanced glycation end product-mediated cytokine upregulation.
6. When insulin is suppressed and the body becomes resistant to insulin, the increased level of glucose in the blood stream results in hyperglycemia.
7. Hyperglycemia results in the formation of advanced glycation end-products. The accumulation of advanced glycation end-products is linked to the development of the pathogenic complications of diabetes.

Research evidence

Substantial evidence supports diabetes as a risk factor for periodontal disease. Taylor in Teng et al. (2002)[14] conducted a MEDLINE literature review and found that 44 of the 48 primary reports on studies provided consistent evidence of greater prevalence, incidence, severity, extent, or progression of periodontal disease in diabetic patients, including those with either type 1 or type 2 diabetes mellitus.

A relatively new finding is that a history of chronic periodontal disease can disrupt glycemic control, suggesting a possible adverse two-way interrelationships between periodontal disease and diabetes mellitus.[14] The following three studies support this link. First, Taylor et al. (1996)[15] studied the Pima Indian Tribe, a population having a prevalence of type 2 diabetes mellitus of about 50%. This is the highest reported prevalence of type 2 diabetes mellitus in the world, making this community ideal for studying periodontal disease and diabetes mellitus.[16] Taylor et al. analyzed data collected in a longitudinal study of the Gila River Indian Community who are primarily Pima Tribe members. The data showed that those with severe periodontitis were up to six times more likely to have poor glycemic control, measured by glycated hemoglobin, at two- to four-year follow-ups.



Second, Collin et al. (1998)[17] conducted a longitudinal study of seniors with type 2 diabetes mellitus that showed glycemic control in patients with advanced periodontitis deteriorated during a follow-up of two to three years. However, the glycemic control improved in those having a better periodontal condition. Third, Taylor (July 2001)[9] analyzed cross-sectional data from NHANES III, using both the 1988–91 and 1992–94 data that support an association between periodontal infection and glycemic control problems in people with diabetes mellitus.

A considerable body of research shows that periodontal therapy has a positive effect on glycemic control. Three researchers conducted literature reviews. Grossi and Genco (1998)[12] and Grossi (2001)[18] reached the same conclusion in their reviews—that a beneficial effect on glycemic control is found when mechanical periodontal therapy includes the use of systemic antibiotics and that no significant improvement occurs when only mechanical therapy is used. Taylor (December 2001)[19] reviewed 10 studies and concludes that treating periodontal infection may have an important role in establishing and maintaining glycemic control. However, he calls for additional rigorous clinical investigations in diverse populations.

A number of other studies suggest that metabolic control of diabetes, measured by lower glycemic levels, is influenced by periodontal therapy, confirming the interrelationship between periodontal disease and diabetes mellitus. Table 1 contains a summary of the research.

Table 1. Treatment studies examining the impact of periodontal therapy on diabetes

Study	Study design	DM* type	Number subjects	F/U	Periodontal therapy	Metabolic control outcome	Evi-dence level
Rodrigues et al. 2003[20]	Randomized clinical study; no control	Type 2	30	3 mths	GI - full-mouth scaling and root planning (FMSRP) in combination with amoxicillin/clavulanic acid G2 – FMSRP only	G2 – Statistically significant 11% reduction in HbA_{1c} ($P < 0.05$)	11-3
Iwamoto et al. 2001[21]	Clinical study; no control	Type 2	13	1 mth	Anti-microbial treatment (local minocycline) and mechanical therapy	Average reduction of 0.49 pg/ml of circulating TNF-a ($P< 0.015$) and an average of 0.8% reduction in HbA_{1c} ($P< 0.007$)	11-3
Aldridge et al. 1995[22]	RCT	Type 1	31	2 mths	Oral hygiene instruction and mechanical therapy	No effect on glycated hemoglobin	1
Grossi et al. 1996[23]	RCT	Type 2	85	3, 6 and 12 mths	Ultrasonic therapy and one of the following four: Group 1: systemic doxycycline and subgingival irrigation with water Group 2: systemic doxycycline and subgingival irrigation with chlorhexidine Group 3: systemic doxycycline and subgivgival irrigation with povidone iodine Group 4: subgingival irrigation with water alone (placebo)	Ultrasonic therapy and doxycycline significantly reduced glycated hemoglobin (1% reduction $P< 0.04$)	1
Grossi et al. 1997[24]	RCT	Type 2	113	3 mths	Mechanical therapy combined with: 1. topical water and systemic doxycycline 2. topical chlorhexidine and systemic doxycycline 3. topical povidone-iodine and systemic doxycycline 4. topical CHX and placebo 5. control - topical water & placebo	Groups receiving doxycycline showed nearly 10% reduction in glycated hemoglobin	1
Christgau et al. 1998[25]	Prospective parallel treatment study	Type 1 and 2	a. 20 b. 20	4 mths	Phase one: oral hygiene instructions, mechanical therapy. Phase two: mechanical therapy and irrigation of pockets with chlorhexidine	No change in HbA_{1c}	11-1

* DM is diabetes mellitus

Rodrigues et al. (2003)[20] conducted a randomized study with 30 type 2 diabetes mellitus subjects. Subjects had chronic periodontal disease, assessed by at least one site having a probing depth =5 mm and two teeth with attachment loss =6 mm. Subjects were randomly assigned to

two treatment groups. Group 1 (G1) received full-mouth scaling and root planing in combination with amoxicillin/clavulanic acid (FMSRP & AC). Group 2 (G2) received FMSRP alone. Three months following therapy, both treatment groups showed statistically significant improvements in periodontal parameters (including number of sites with biofilm, and bleeding on probing). Although the G1 and G2 groups showed improvements in levels of glycated hemoglobin (HbA_{1c}), only the HbA_{1c} reduction in G2 was statistically significant at 11% ($P < 0.05$). There were minimal alterations to the changes in fasting glucose levels in both groups. In addition, this study showed that subjects with an elevated degree of diabetes mellitus severity and periodontal disease had the greatest reduction in HbA_{1c} levels. A drawback to this study was a lack of significant change in attachment levels after therapy. The researchers suggest that the lack of additional benefit for Group 1 from the amoxicillin may be due to non-sensitive micro-organisms in the periodontal pockets.

Although most of the intervention studies do not explore the details of the biological mechanism by which improved periodontal health leads to better glycemic control, Iwamoto et al. (2001)[21] attempt to define this mechanism. They examine the role of the proinflamatory cytokine, tumor necrosis factor ? (TNF-?), which is produced by periodontal infections. They conducted a study with 13 type 2 diabetes patients with periodontal disease who were given periodontal treatment consisting of antimicrobial therapy (local minocycline) and mechanical plaque debridement once a week for one month. Following periodontal treatment, they found an average reduction of 0.49 pg/ml of circulating TNF-? ($P< 0.015$) and an improvement in metabolic control of diabetes, measured by an average of 0.8% reduction in HbA_{1c} ($P< 0.007$). A drawback to this study is that the change in periodontal status showed only a 0.48 mm average reduction in probing depth one month after periodontal therapy—a result that was not statistically significant. This may be due to the fact that a one-month re-evaluation period is a relatively short time for changes in clinical attachment levels to occur.

The strongest research evidence comes from randomized controlled trials. However, our search uncovered only three randomized controlled trials that show the impact of periodontal treatment on glycemic control. Aldridge et al. (1995)[22] conducted the first single-blind randomized controlled trial with 31 subjects and showed that periodontal treatment consisting of oral hygiene instruction and scaling has no effect on glycated hemoglobin.

Grossi et al. (1996)[23] conducted a randomized controlled trial with 85 Pima Indians with type 2 diabetes mellitus. All subjects received subgingival ultrasonic debridement of the teeth and were then assigned randomly to one of the following four groups for treatment:

1. systemic doxycycline and subgingival irrigation with water
2. systemic doxycycline and subgingival irrigation with chlorhexidine
3. systemic doxycycline and subgingival irrigation with povidone iodine
4. subgingival irrigation with water alone (placebo)

The results indicated that subjects treated with doxycycline all experienced a significant reduction in glycated hemoglobin (1% reduction $P< 0.04$), suggesting that ultrasonic debridement plus systemic antimicrobial therapy has the potential to reduce the level of glycated hemoglobin in diabetic subjects.

Finally, Grossi et al. (1997)[24] conducted a randomized controlled trial with 113 subjects from the Gila River Indian Community, all of Pima or Pima/Papago heritage, with poorly controlled

type 2 diabetes mellitus and severe periodontal disease. The examiner was blinded to the assigned treatment group. Researchers report that periodontal treatment consisting of scaling and curettage combined with antimicrobial treatment (systemic doxycycline) for two weeks resulted in a statistically significant reduction of nearly 10% ($P \leq 0.04$) in glycated hemoglobin levels after three months and a 17% to 23% improvement in periodontitis. The glycated hemoglobin returned to basal level after six months when periodontal therapy was stopped.

Although all of the studies listed above, with the exception of Aldridge et al., indicate that periodontal therapy has a positive impact on glycemic control, two other studies refute this evidence. Christgau et al. (1998)[25] conducted a prospective parallel study comparing groups of well-controlled diabetics with healthy controls and found no connection between non-surgical periodontal therapy and diabetic control, measured by HbA_{1c}, at four-month follow-up. Periodontal therapy for moderate-to-advanced periodontitis consisted of two phases: the first included client motivation, oral hygiene instructions, supragingival scaling, emergency restorations, removal of overhanging margins, extractions of hopeless teeth, and splinting of mobile teeth. The second phase provided non-surgical periodontal therapy with subgingival scaling, root planing, and irrigation of all pockets with chlorhexidine. Hagiwara et al. (2002)[26] conducted a similar study and found no correlation between periodontal improvement and metabolic diabetes control. Rodrigues et al.[20] suggest that the lack of impact on glycemic control in these two studies may be because the subjects had only moderately controlled or well-controlled diabetes mellitus and that the study results may be different with subjects with a more severe degree of diabetes mellitus.

Discussion

The evidence overall shows that periodontal disease may contribute to poorer glycemic control in people with diabetes mellitus and supports the recent recognition of periodontal disease as the sixth complication of diabetes.[27] This review also highlights a considerable body of research showing that periodontal therapy may be associated with improved glycemic control and that the mode of therapy affects the outcome. The balance of evidence from the treatment studies suggests that mechanical periodontal therapy together with systemic antibiotics should be part of the standard of care of the diabetic client with peridontitis, since mechanical periodontal therapy by itself did not generally result in improvements in glycemic control. Also, the randomized controlled trial studies provide an argument for the inclusion of periodontal treatment in diabetes preventive measures.

Although some important information arises from this research, a few of the studies are somewhat limited by the small number of subjects and a heterogeneity in design, conduct, and results that restricts the ability to compare the studies. A further difficulty in comparing studies arises from the different ways in which periodontal disease is defined. A wide range of measurement parameters is used, including gingivitis, probing depths, clinical attachment level scores, and radiographically assessed alveolar bone loss. The most striking limitation is the low number of randomized controlled trials as this type of trial has the potential for providing the best evidence for the presence or absence of a causal relationship. In addition, the randomized controlled trials examining periodontal treatment interventions were carried out with only one population, Pima Indians. The ability to generalize to a larger population was therefore limited.

The lack of emphasis on Canadian Aboriginal peoples also limits the impact of these studies. The effect of diabetes on Canadian Aboriginal people is more pronounced than in the general population. For First Nations people living on reserves, the incidence of diabetes is three to five times higher than that of the Canadian population;[28] for the off-reserve Aboriginal population, it is twice as high as the non-Aboriginal population.[29] Of particular concern is the increasing incidence rate of type 2 diabetes mellitus that is now occurring in children on reserve 5 to 8 years of age, although it was previously limited to the adult population.[30,31]

Recommendations

Clinical

Some general suggestions for dental hygienists follow; however, all clinical decisions should be based on the needs of the specific client:

- Incorporate the bi-directional relationship of diabetes and chronic periodontitis into diagnostic and treatment decisions.
- Implement three levels of prevention, including primary, secondary, and tertiary. (See Appendix C.) The prevention and control of periodontal disease should be considered an integral part of diabetes control and prevention.
- Treat periodontitis in diabetic clients the same as in non-diabetic patients; however, diabetic clients with poor metabolic control should be seen more frequently and mechanical periodontal therapy combined with systemic antibiotics should be part of the standard of care.
- Assess glycemic control of diabetic clients by asking about their blood glucose self-monitoring practices and test results, including HbA_{1c} tests.
- Provide oral health promotion and disease prevention services for persons with diabetes in community health centres, health units, and public health programs.

Suggestions for other health professionals with clients with glycemic difficulties:

- Consider the periodontal status of clients with diabetes who have difficulty controlling glycemic levels.
- Refer clients to an oral health professional to reduce the prevalence of periodontal infection and inflammation.

Research

- Develop uniform study criteria for measuring periodontal disease.
- Further research is needed in the following areas:
  - studies to show that long-term periodontal care contributes to the long-term management of diabetes mellitus;
  - randomized controlled trials with more diverse populations and populations that are particularly susceptible to diabetes mellitus, such as Aboriginal peoples;
  - studies on health promotion initiatives to prevent the development of periodontal disease and diabetes mellitus.

HEART DISEASE

Cardiovascular diseases (CVD) (e.g. atherosclerosis, coronary thrombosis, ischemic heart disease, coronary heart disease, and peripheral vascular disease) affect a significant proportion of the Canadian population and comprise one of the major causes of death.[32] Atherosclerosis, which involves plaque-containing cholesterol, builds up in arteries and results in coronary thrombosis, ischemic heart disease (coronary artery disease), and stroke.

Infective endocarditis occurs when there is microbial infection of damaged heart valves or endocardium. Acute bacterial endocarditis has a rapid onset and death is usually the outcome unless prophylactic antibiotic therapy is prescribed to prevent the infection in the first place. Prophylactic antibiotics should be prescribed based on the most current American Heart Association guidelines. Subacute bacterial endocarditis has a more chronic course, where the problem may not be obvious until the onset of a low-grade fever, anemia, and debility. It is well accepted that dental procedures predispose susceptible patients to infectious endocarditis through transient oral bacteremias[33] and that antimicrobial prophylaxis should be administered prior to certain oral health procedures.[34] However, due to ethical considerations, it has not been possible to perform controlled clinical trials in humans to establish their effectiveness. The estimated frequency of infectious endocarditis varies from between 1 and 5 cases/100,000 population/year.[34]

Biological pathways

The current theory around this issue is that micro-organisms in infected gums may dislodge, enter the bloodstream, and spread throughout the body, inflaming coronary arteries and causing changes in blood pressure, heart rate, heart function and promoting blood clots, which can lead to heart attacks and strokes. Periodontal micro-organisms may also cause an infection in the lining or valves of the heart called infective endocarditis.

Authors propose three pathways linking oral infections to cardiovascular disease:

1. **Infection theories**[35,36]
   This involves the direct negative effect of bacteremia from a periodontal inflammation. Subgingival biofilms associated with periodontitis may act as reservoirs of gram-negative micro-organisms and create transient bacteremia that enter the bloodstream and have access to the lining of blood vessels. Bacteremia associated with *Porphyromonas gingivalis* may result in platelet aggregation that contributes to some atheroma formation and acute thromboembolic events.[37,38]

2. **Distant injury (focal sepsis) theory**[35,36]
   Injury results from the effects of circulating oral microbial toxins. Three mechanisms are involved.
   a. Endotoxins from the cell wall of oral micro-organisms are released and circulate throughout the body, causing the release of inflammatory mediators and clotting factors such as C-reactive protein and fibrinogen. These in turn increase platelet aggregation, damage endothelial cells, induce smooth muscle proliferation, and result in the formation of atheromas and subsequent atherosclerosis and thrombosis.[39,40] Some proof for this

comes from a growing body of evidence showing periodontal micro-organisms are found in atheromas.[40]

b. Products associated with bacteremia, such as micro-organism–derived lipopolysaccharides, trigger hyper-reactive leukocyte responses. Infections produce changes in lipid metabolism that may promote atherosclerosis.

c. Periodontal microbial infections may cause an immune response that results in a hyperinflammatory macrophage response. Macrophages release inflammatory mediators/proiflammatory cytokines, such as interleukin 1ß [IL-1ß], tumor necrosis factor- ? (TNF-?), TxA_2Il-1ß, MCP-1,[38] and PGE_2. The cytokines produced by the macrophages play a critical role in the formation of the atheroma in atherosclerosis.[39,41] This hypothesis is supported by recent findings that total cholesterol, low-density lipoprotein, and triglycerides are significantly higher in subjects with periodontitis than in controls.[41]

3. A link to glucose tolerance

Periodontal infection can reduce glucose tolerance, leading to an atherogenic serum lipid profile.[40]

Research evidence

There has been a proliferation of research on the link between cardiovascular disease and periodontal disease and tooth loss, focusing specifically on coronary heart disease, cerebrovascular ischemia, fatal cardiovascular disease, stroke, myocardial infarction, cerebrovascular accident, and the preclinical signs of cardiovascular disease. A brief description of the research showing a link is organized under categories of heart diseases. The research refuting this link is then presented. The research is also summarized in Table 2, and a discussion of the research follows.

Coronary heart disease, fatal coronary heart disease, and stroke

Beck et al. (1996)[36] conducted a prospective, longitudinal, cohort study with 1,147 men who received a dental examination and radiographs at approximately 3-year intervals for 18 years. They showed that periodontal diseases, as assessed by bone loss and worst probing pocket depth scores per tooth, increased the odds ratio (OR) of coronary heart disease by 1.5 (95% CI: 1.06 - 2.15), of fatal coronary heart disease by 1.9 (95% CI: 1.10 – 3.34), and of stroke by 2.8 (95% CI: 1.45 – 5.48). They used multiple logistic regression to control for the effects of age, smoking, diabetes mellitus, family history, body mass, blood pressure, and alcohol use.

Cerebrovascular accident and fatal cerebrovascular accident

Loesche et al. (1998)[42] conducted a cross-sectional study with 401 veterans who were at least 60 years of age. The researchers found that in the dentate group of 232 seniors, the presence of 15 to 28 teeth and an increased proportion of teeth with attachment loss >6 mm were significantly related to a cerebrovascular accident odds ratio of 1.04.

Wu et al. (2000)[43] examined data from a cross-sectional study, the First National Health and Nutrition Examination Survey (NHANES I) and its follow-up study (NHEFS), a representative sample of 9,962 U.S. adults. The exposure variable was periodontal disease and the outcome variables were incident and fatal events of cerebrovascular accident, instead of coronary heart disease, which is more often studied. First, they showed a significant association (relative risk 2.11, 95% CI, 1.3-3.42) between periodontitis and cerebrovascular accident—specifically nonhemorrhagic stroke but not hemorrhagic stroke—compared with no periodontal disease. Second, they demonstrated significant associations between periodontitis and fatal cerebrovascular accident. They used multivariate analyses and adjusted for a number of confounders and conclude that periodontal disease is a significant risk factor for cerebrovascular accident. One of the strengths of this study is that it included not only white men, but also white women and African Americans.

Elter et al. (2003)[44] conducted a study using the Dental Atherosclerosis Risk in Communities (ARIC) study data with 9,415 persons and found that attachment loss and edentulism were weakly associated with stroke/transient ischemic attack (OR 1.3, CI 1.02-1.7) and (OR1.4, CI 1.5-2.0). Logistic regression analysis controlled for confounders.

Joshipura et al. (2003)[40] in a 12-year Health Professionals Follow-Up Study (HPFS) cohort study with 41,380 men who were free of cardiovascular disease and diabetes at baseline showed that tooth loss and periodontal disease may be independent risk factors for stroke. They used a multivariate analysis and confounding variables—such as common risk factors shared by stroke, periodontal disease, and tooth loss—were accounted for. Men with 24 teeth or fewer at baseline were at higher risk of stroke compared with men with 25 teeth or more (hazard ratio 1.57; 95% CI, 1.24 to 1.98). Recent tooth loss showed little association. A modest association was found between baseline periodontal disease and ischemic stroke (Hazard ratio 1.33; 95% CI, 1.03 to 1.70). A self-assessment tool was used for the oral health assessment.

Coronary heart disease

DeStefano et al. (1993)[45] also analyzed National Health and Nutrition Epidemiologic Follow-Up Study (NHEFS) data, a 14-year follow-up of 9,760 participants who ranged from 25 to 74 years of age. This prospective cohort study showed a relative risk (RR) for myocardial infarction of 1.25 (95% confidence interval [CI]) for periodontal disease and 1.23 (95% CI) for complete edentulousness, compared with no dental disease. They found that men with periodontitis were 25% more likely to develop coronary heart disease than those with minimal periodontal disease. The risk was particularly high for men aged 29 to 49 who had a relative risk for coronary heart disease of 1.72 (95% CI).[45] They controlled for most major coronary heart disease risk factors. Smoking data, however, was not available for two-thirds of the participants.

Joshipura et al. (1996)[46] analyzed the Health Professionals Follow-Up Study (HPFS) composed of 44,119 men, 40 to 75 years of age, and found increased relative risk (RR) for coronary heart disease for people with both periodontal disease and tooth loss (RR 1.7) and periodontal disease and no tooth loss (RR 1.7). This was a 6-year follow-up study of subjects who reported no diagnosed coronary disease at baseline. A number of coronary risk factors, such as smoking and physical activity, were accounted for in the study.

Diagnosis of periodontitis in most studies is based on clinical or radiographic examination. However, it is also possible to diagnose serum antibodies to the primary pathogens responsible for periodontitis, *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis.* Some data indicate that the inflammatory and host responses, not the clinical signs of periodontitis, are associated with cardiac events and subclinical coronary artery disease. One study shows an association between levels of immunoglobulin G (IgG) antibodies to periodontal pathogens and coronary artery disease.

Pussinen et al. (2003)[47] conducted the first study using serum antibodies as a form of diagnosis and found a link between serum IgG-antibodies to these two periodontal pathogens and coronary heart disease. Using a multivariate linear regression model, they found that of the 1,163 subjects studied, those with a high combined antibody response had an odds ratio of 1.5 (95% CI, 0.95 to 2.50, P=0.077) for coronary heart disease.

Cardiovascular disease

Grau et al. (1997)[48] conducted a case-control study where cases consisted of 166 subjects with cerebrovascular ischemia and controls consisted of 166 non-stroke neurological subjects. Dental status, which was blindly assessed, was determined by a total dental index (TDI) that reflects caries, periapical lesions, periodontitis, and other dental lesions. Using a multiple logistic regression analysis, the researchers concluded that chronic dental infection might be associated with an increased risk for cerebrovascular ischemia (OR = 2.6; 95% CI, 1.18 - 5.7), independent of current smoking, diabetes mellitus, and pre-existing vascular diseases.

Preclinical signs of cardiovascular disease

The two following studies are set apart from the above studies since they measure the relationship between periodontal disease and the preclinical signs, instead of the clinical signs, of cardiovascular disease. The intima-media wall thickness of the carotid artery is a measure of preclinical atherosclerosis and is associated with coronary heart disease and with incident stroke.[49] First, Beck et al. (2001)[49] conducted a prospective study with 6,017 black subjects and showed that periodontitis is associated with these preclinical signs of atherosclerosis. Using a multivariable logistic regression model, they found that individuals with severe periodontal disease, measured by attachment loss, had 1.3 times the odds of having thick carotid arterial walls (greater than and equal to 1 mm) compared with individuals with less severe disease (OR 1.31, CI 1.03 to 1.66). Second, Desvarieux et al. (2003)[50] reports preliminary findings from 711 participants in a prospective study that shows a possible relationship between tooth loss (which is a marker of past periodontal disease) and subclinical cardiovascular disease/subclinical atherosclerosis, measured with a carotid scan using ultrasound. The cohort was free of baseline cardiovascular disease. Regression models were used to account for conventional risk factors. The prevalence of carotid plaque increased with the number of missing teeth, with an average of 44% of those missing zero to nine teeth having artery plaque, and 61% ($P<0.05$) of those with 10 to 19 missing teeth having artery plaque. The researchers found a significant relationship between tooth loss and periodontal disease and suggest that this is related to subclinical atherosclerosis.

Fatal cardiovascular disease

Morrison et al. (1999)[51] conducted a cardiovascular mortality follow-up on 10,368 individuals without coronary artery disease and on 11,251 individuals with cerebrovascular and coronary heart disease from the Nutrition Canada Survey. Participants were followed retrospectively for assessment of cardiovascular mortality status from the National Mortality Database. They found an RR of 2.15 (95% CI: 1.25-3.72) for severe gingivitis; 1.37 (95% CI: 0.80-2.35) for periodontitis; and 1.90 (95% CI: 1.17-3.10) for edentulousness for fatal coronary heart disease.

Similar findings are reported in an epidemiological study by Jansson et al. (2001)[52] with 1,393 men and women. Plaque and oral health scores, measured with missing teeth, apical lesions, caries lesions, and marginal bone loss, were adjusted for age, gender, smoking, and cardiovascular disease at baseline and showed a significant correlation to fatal cardiovascular disease.

Peripheral vascular disease and peripheral arterial disease

Studies of the link between oral health and cardiovascular disease and coronary heart disease are common. However, less common are studies showing the link between oral health and peripheral vascular disease, which can be divided into two areas, peripheral arterial disease and peripheral venous disorders, both of which can potentially lead to heart disease or stroke. Mendez et al. (1998)[53] found an association between periodontal disease and peripheral vascular disease (OR = 2.27; 95% CI: 1.32-3.9) after controlling for several other risk factors. Hung et al. (2003)[54] conducted a prospective study with 45,136 male subjects, 342 of whom were identified with peripheral arterial disease during a 12-year follow-up period. Periodontal disease and tooth loss were self-reported. The strongest association between cumulative incident tooth loss and peripheral arterial disease was found among men with periodontal disease (RR 1.88, 95% CI, 1.27 - 2.77, P=0.09).

Studies refuting association between periodontal disease, and cardiovascular disease and coronary heart disease deaths

There are many studies showing that various types of oral infections are possible risk factors for coronary heart disease and cardiovascular disease. Two studies that refute this connection follow. Tuominen et al. (2003)[55] analyzed information from 6,527 men and women, aged 30 to 69, from the Mini-Finland Health Survey. They found that when the data, collected during a mean 12-year follow-up, were adjusted for established coronary heart disease risk factors, there was no statistically significant association between oral health indicators and coronary heart disease deaths. Oral health indicators included gingival inflammation, periodontal pocket depths, dental plaque status, and edentulousness. Hujoel et al. (2000)[56] uses the same data set, NHANES I follow-up study, as did Wu et al. (2000) and DeStephano et al. (1993), but reached very different conclusions. Hujoel et al. did not find a significant association between cardiovascular disease and periodontitis and gingivitis after adjustment for known cardiovascular risk factors.

Table 2. The association of heart disease, the systemic outcome, with periodontal disease and tooth loss (Evidence Level 11-2)

Reference	Study type	Logistic regression analysis	# Subjects case/ controls	PVD	CVD	CHD	CVI	Fatal CHD/ CVA/ CVD	CVA/ Stroke	MI	Pre-clinical signs of CVD	Oral Exposure
Beck et al. 1996[36]	Prospec-tive, longitu-dinal	Yes	1,147 men			1.5 OR		1.9 OR	2.8 OR			PD
De Stefano et al. 1993[45]	Prospec-tive cohort NHEFS	Yes, but did not control for smoking	9,760							1.25 RR		PD
"	"	"	"							1.23 RR		E
"			Men aged 29-49			1.72 RR						PD
Pussinen et al. 2003[47]	FPAIS	Yes	1,163			1.5 OR						IgG-antibodies to periodontal pathogens
Joshipura et al. 1996[46]	HPFS		44,119 men			1.7 RR						PD and tooth loss
"	"					1.7 RR						PD and no tooth loss
Joshipura et al. 2003[40]	HPFS	Yes	41,380 men						1.57 HR			Fewer than or equal to 24 teeth
"	"	"							Little associ-ation			Recent tooth loss
"	"	"							1.33 HR			PD
Grau et al. 1997[48]	Case/ control	Yes	166/166				2.6 OR					PD
Morrison et al. 1999[51]	NCS		10,368 with-out CAD; 11,251 with CVD					2.15				Severe gingivitis
"								1.37				Periodontitis
"								1.9				Edentulousness
Jansson et al. 2001[52]	Epidemio-logical	Yes	393 men and women					Signif-icant corre-lation				PD
Mendez et al. 1998[53]		Yes		2.27 OR								PD
Hung et al. 2003[54]	Prospec-tive HPFS		45,136 men	1.88 RR								Cumulative tooth loss & PD
Beck et al. 2001[49]	Prospec-tive	Yes	6,017 African Americans								1.31 OR	PD – severe
Loesche et al. 1998[42]	Cross-sectional		401 senior veterans						1.04 OR			15 to 28 teeth and an increased proportion of teeth with attachment loss >6 mm
Wu et al. 2000[43]	Cross-sectional NHANES & NHEFS	Yes	9,962 black, & Caucasian men and women					Signif-icant asso-ciation s fatal CVA	2.11 RR, non-hemorr hagic stroke			PD
Desvarieux et al. 2003[50]	Prospec-tive	Yes	711								44%	0 to 9 missing teeth
"	"	"									61%	10 to 19 missing teeth

Reference	Study type	Logistic regression analysis	# Subjects case/ controls	PVD	CVD	CHD	CVI	Fatal CHD/ CVA/ CVD	CVA/ Stroke	MI	Pre-clinical signs of CVD	Oral Exposure
Tuominen et al. 2003[55]	12-year follow-up MFHS	Yes	6,527 men and women					No association				PD
Hujoel et al. 2000[56]	NHANES follow-up study	Yes	8,032		No association							PD and gingivitis
Elter et al. 2003[44]	Dental ARIC study	Yes	9,415						OR 1.3			Attachment loss
"	"	"							OR 1.4			Edentulism

PD Periodontal disease
E Edentulism
CVI Cerebrovascular ischemia
CVA Cerebrovascular accident
PVD Peripheral vascular disease
MI Myocardial infarction

OR Odds ratio
RR Relative risk
HR Hazard ratio

ARIC Dental Atherosclerosis Risk in Communities Study
HPFS Health Professionals Follow Up Study
NHANES National Health and Nutrition Examination Survey
NHEFS National Health and Nutrition Epidemiologic Follow-Up Study
NCS Nutrition Canada Survey
MFHS Mini-Finland Health Survey
FPAIS Finland Platelet Aggregation and Inflammation Study

Discussion

The balance of the evidence suggests that periodontal disease and tooth loss may be independent risk factors for cardiovascular disease. The associations between oral conditions and cardiovascular disease are consistent across different population samples—including international studies from Canada, the United States, and Finland—and different measures of periodontitis, for example, bone loss and probing depth. However, there is insufficient evidence to show a definitive causal relationship between periodontal disease and tooth loss and cardiovascular disease. There is only minor opposition to the suggested association, since all but 2 of the 17 studies indicated that periodontal disease and tooth loss might be independent risk factors for cardiovascular disease. A summary of the strength of the associations follows, showing that persons with periodontal disease have a 1.04 to 2.8 fold greater risk of incurring cardiovascular disease than persons without periodontal disease. Of the different types of cardiovascular disease, stroke shows the most robust association.

- Cardiovascular accident, stroke
  - OR 2.8 for periodontal disease
  - HR 1.33 to 1.57 for periodontal disease and fewer than or equal to 24 teeth
  - RR 2.11 for periodontal disease
  - OR 1.04 for attachment and tooth loss
- Cardiovascular ischemia
  - OR 2.6 for periodontal disease
- Peripheral vascular disease
  - OR 2.27 for periodontal disease
  - RR 1.88 for periodontal disease and tooth loss

- Coronary heart disease
  - OR 1.5 for periodontal disease
  - RR 1.7 to 1.72 for periodontal disease and tooth loss
- Fatal cardiovascular disease
  - OR 1.37 to 2.15 for periodontal disease, severe periodontal disease and tooth loss
- Myocardial infarction
  - RR 1.23 to 1.25 for periodontal disease and edentalousness
- Preclinical signs of cardiovascular disease
  - OR 1.31 periodontal disease

Although the OR (odds ratio) and RR (relative risk) showed a low-to-moderate association of 1.04 to 2.8, modest associations may have a significant impact within the population since the prevalence of both periodontitis and cardiovascular disease is very high. There is a dose-response relationship to this association whereby the severity of periodontal disease influences the strength of the association, as shown in Beck et al. (1996)[36] and Beck et al. (2001).[49] The association is also characterized by the quality of the host response as the antibody response was related to a high incidence of coronary heart disease. In one of the studies, Beck et al. (1996)[36] found that periodontal disease—compared with more established risk factors such as smoking, diabetes, hypertension, and elevated serum triglycerides— may be associated with excess risk of coronary heart disease/stroke.

Although almost all of the studies measured the clinical signs of cardiovascular disease, two studies by Beck et al. (2001)[49] and Desvarieux et al. (2003)[50] were different in that they found an association between periodontal disease and tooth loss and preclinical signs of cardiovascular disease. These two studies established that oral health studies could successfully use ultrasound measurement of the intima-media wall thickness, a quick and non-invasive way to measure atherosclerosis.

Since periodontitis and atherosclerosis have many risk factors in common, including diet, smoking, and diabetes mellitus, it is important for research evidence to include a multifactorial regression model to control for these common risk factors. Fortunately, all of the research studies used a multiple logistic regression model to analyze the data and control for confounding health issues. Only one researcher, DeStefano et al. (1993),[45] noted that smoking data were not available for two-thirds of subjects and therefore they could not control for this potential confounder.

In general, the reviewed studies used a large number of subjects with the majority (nine) using between 1,000 and 11,000 subjects and three studies using over 40,000 subjects. This makes it possible to generalize to a larger population. Although most of the studies had a large number of subjects, some studied only segments of the population, such as men, African-Americans, and veterans. This made it difficult to generalize to the larger population.

There are several other limitations to the research. Most of the associations had a small-to-medium magnitude or a weak association. It therefore may be possible that the associations are due to various types of bias in the studies: additional confounders not accounted for, such as genetic and environmental factors that increase susceptibility to both chronic oral infection and cardiovascular disease; or the fact that good oral health is an indicator of good general health care practices.

The study type also presented limitations. Unfortunately, none of the studies were classified as having level 1 or level 11-1 evidence (see Appendix B for Evidence Classification Scheme). Therefore a causal role for periodontal disease and tooth loss in cardiovascular disease cannot be established. The majority of the studies were classified as level 11-2, with the majority being prospective longitudinal or cross-sectional cohort studies and only one being a case-control study, therefore suggesting an association only. Another limitation is the total absence of intervention studies.

Inconsistencies in the various study designs preclude a rigorous systematic review. Study comparison was also difficult due to inconsistent quantitative assessments of oral health or periodontal disease. A wide variety of the following combinations of measures were used: bone loss, pocket depth scores, and attachment loss. Furthermore, while most studies used clinical assessments, some did not measure level or severity of infection and others used self-reporting, a method that has been questioned as imprecise.[57]

Furthermore, a number of the studies were secondary analyses from data that were not gathered specifically to investigate an association between oral health and heart disease. Therefore, to confirm the risk factor more clearly, it would be helpful to have studies designed specially for this purpose.

Periodontal disease may some day be considered next to smoking and diabetes as having a strong association with cardiovascular disease. Before this occurs, however, more extensive interventional, longitudinal research is needed to determine to what extent treatment of periodontal disease will decrease the incidence of heart disease.

Recommendations

Clinical

Oral procedure guidelines for individuals at risk for developing infective endocarditis include three steps.[58,59] However, dental hygienists should use their own clinical judgment in individual cases or special circumstances.

1. Clients at high and moderate risk for infectious endocarditis who are undergoing dental procedures that will induce bleeding should be given antibiotic prophylaxis according to the most current American Heart Association recommendations. (See Appendix D for definitions of "at-risk" and a list of oral procedures that create a risk of bacteremia.) It should be noted that antibiotic prophylaxis does not preclude infective endocarditis; it only minimizes the risks, since a considerable portion of oral micro-organisms do not respond to the ß-lactam class of antibiotics (which includes amoxicillin, the current popular antibiotic). It is therefore important to implement step 2 to minimize gingival inflammation and prevent the initiation of periodontal disease.
2. Establish and maintain good oral health:
    - Apply antiseptic mouth rinses, such as chlorhexidine gluconate and povidone-iodine, via gentle oral rinsing for about 30 seconds immediately before dental procedures.
    - Frequent home use of antiseptic rinses is not recommended due to the potential for developing resistant micro-organisms.

- Frequent dental hygiene treatments are recommended to maintain periodontal health.
- Encourage clients to make use of Pre-medication Alert Wallet Cards. These cards are completed by cardiologists to alert the dental hygienists to a client's risk factors and required protection from bacterial endocarditis, so that antibiotic treatment may be administered immediately prior to any invasive treatment. (For a copy of the card, visit <www.americanheart.org/presenter.jhtml?identifier=11086>.)

3. Educate clients concerning periodontal health:
   - Emphasize the importance of maintaining good periodontal health through frequent dental hygiene treatment and appropriate home care methods.
   - Ensure that clients who have other risk factors for cardiovascular disease or who may already have cardiovascular disease are informed about the potential correlation between periodontal disease and cardiovascular disease.

Research

There is a need for additional research in intervention longitudinal studies and health promotion and its impact on periodontal disease and cardiovascular disease.

PRETERM LOW BIRTH WEIGHT BABIES

Preterm birth and low birth weight (PLBW) in infants create a significant public health problem, causing perinatal morbidity, including neurological abnormalities, mild learning disabilities, breathing problems (such as asthma), and developmental problems.[61] Two estimates of costs are associated with PLBW infants: first, the costs associated with the care of preterm infants and neonatal intensive care add over US$5 billion to US$10 billion annually to the costs of childbirth.[62,63] Second, costs for care per child over the lifetime are estimated at US$500,000.[63]

Established risk factors for PLBW include an older maternal age (>34 years) as well as younger (<17 years); African-American ancestry; low socio-economic status; inadequate prenatal care; drug, alcohol, and tobacco abuse; hypertension; diabetes mellitus; and multiple pregnancies.[62] Many of these are also risk factors for periodontal disease.[62] There is also evidence that several different types of microbial infections are also risk factors. Acute infections involving distant organ systems, such as the genitourinary tract, are implicated in adverse pregnancy outcomes, including preterm birth, rubella, shigellosis, encephalitis, and pneumonia.[64] Emerging evidence points to the role of periodontal infection in PLBW. Given that 25% to 100%[65] of pregnant women experience gingivitis—a preventable and treatable condition—research to determine if oral diseases are independent risk factors for PLBW is warranted.

Biological pathways

The biological mechanism to support a link between maternal periodontal disease and PLBW infants involves micro-organisms in the oral cavity that may enter the bloodstream passively through the inflamed periodontal pocket wall or through invasive oral procedures. The maternal periodontal infection then influences the fetoplacental unit in the following three ways:[62,66,67]

1. **Action of the proinflammatory mediators**
   Periodontal diseases are associated with chronic gram negative anaerobic infections or those resulting in local and systemic elevations of proinflammatory prostaglandins, including prostaglandin E_2 (PGE_2) and cytokines (IL-1, IL-6, and TNF-?). It is the artificially high levels of the prostaglandins that foster premature labour.

2. **The action of the periodontal reservoir of LPS**
   The oral micro-organisms themselves are not directly implicated in the PLBW; rather, the periodontal infection provides a source of microbial products such as lipopolysaccharides (LPS), which trigger the release of immune modulators such as prostaglandin E_2 (PGE_2) and cytokines—TNF?, IL-6, interleukin–1ß (IL-1 ß). These immune modulators in turn target the placenta to influence the course of pregnancy.

3. **Direct micro-organism assault on the fetoplacental unit**
   This mechanism involves translocation of periodontal pathogens to the fetoplacental unit, through the blood.

Research evidence

Four separate lines of evidence currently relate oral infection to pregnancy outcome: microbiological studies, case-control studies, prospective longitudinal studies, and intervention studies. Some of these are randomized controlled trials, testing the hypothesis that periodontal treatment of at-risk mothers will decrease the incidence of preterm low birth weight infants.

The first line of evidence is found in several microbiological studies of amniotic fluid, maternal and fetal cord serum, and gingival crevicular fluid (GCF). The first two studies look at GCF and amniotic fluid and the role of PGE_2 and IL-1ß. Damare et al. (1997)[68] conducted a small study showing a high correlation in the levels of PGE_2 and IL-1ß in maternal GCF and amniotic fluid. Offenbacher et al. (1998)[61] conducted a similar study and found that the GCF of 48 mothers of PLBW infants had higher levels of PGE_2 than mothers of infants with normal birth weight.

Two other studies examined maternal and fetal serum (see Table 3) and similarities in the antibody responses. Offenbacher et al. (1999)[69] analyzed blood samples from fetal cords for the presence of immunoglobulin M (IgM) antibody against various periodontal pathogens. Of the PLBW serum samples, 33.3% tested positive for IgM against the test micro-organism. However, only 17.9% of the normal birth weight samples tested positive. Recently, Madianos et al. (2001)[70] analyzed maternal plaque and serum, as well as fetal cord serum from 400 births. In the fetal serum, IgM seropositivity to maternal periodontal pathogens was 2.9 fold higher in preterm versus normal births (19% vs. 6.9%, respectively; $P = 0.0015$ chi square). These studies suggest that the oral pathogens may be translocating to the fetoplacental unit.

Each study suggests that periodontal infection is a source of microbial products that affect the pregnancy outcome. The studies also suggest that maternal periodontal infections, resulting in blood-borne micro-organisms that can translocate to the fetus, provide a systemic challenge to the fetus and induce an immunologic response. They show it is the inflammatory and host responses, not the clinical signs of periodontitis, that are associated with preterm births.

Table 3. Microbiological studies of fetal serum

Study	Serum analysis	PLBW/PT	Normal birth
Offenbacher et al. (1999)[69]	IgM	33.3% of PLBW tested positive	17.9% tested positive
Madianos et al. (2001)[70]	IgM	19% of PT tested positive	6.9% tested positive

The second line of evidence comes from examining two case-control studies, where the case is defined as a low birth weight infant and a control is defined as a normal birth weight infant. Offenbacher et al. (1996)[71] studied 124 pregnant or postpartum mothers and found that periodontal disease is a statistically significant risk factor for low birth weight in infants. Using a multivariate logistic regression model, there was an odds ratio (OR) of 7.9 (95% CI, 6.27–9.58) for preterm low birth weight cases (PLBW) (n = 93). In other words, mothers with periodontal infection had more than seven times the risk of delivering a PLBW infant. One shortcoming of this study is that periodontal status was determined for all but 10% of the subjects, three days following the birth of their child. However, case-control studies usually assume that the exposure occurred prior to the outcome. In this study, it was not possible to determine whether these mothers had active periodontal disease prior to the birth or during pregnancy. Therefore, it is not possible to show causality.

A case-control study by Dasanayake (1998)[72] involving 55 pairs of women in Thailand does not clearly support the link between periodontal disease and PLBW. Oral health status was measured using the Community Periodontal Index of Treatment Needs (CPITN) and Decayed, Missing, and Filled Teeth scores (DMTF). On the one hand, it shows that having good oral health reduces the probability of a low birth weight infant (OR 0.3). Good periodontal health (measured by healthy sextants) presented an odds ratio of 0.3 (95% CI, 0.12–0.72), that is, mothers with more healthy areas of gingiva had a lower risk of giving birth to a low birth weight infant. However, it did not show that having *poor* periodontal health increases the chances of having a low birth weight infant. Poor periodontal health presented an odds ratio of 1.1 (95% CI, 0.12–0.72) for low birth weight. Data was analyzed using a conditional logistic regression analysis to control for other known risk factors. The study also did not find a significant association between some of the known risk factors, such as smoking, alcohol, and coffee consumption, and low birth weight. However, there may have been confounding factors at play in this study or the results could indicate that the link between periodontal disease and low birth weight does not exist in some populations.

The third line of evidence comes from two prospective studies. Preliminary results from a relatively large prospective study by Jeffcoat et al. (2001)[73] with approximately 1,300 mothers concluded that maternal periodontitis is an independent risk factor for preterm birth. Periodontitis in the mother was assessed at 21 to 24 weeks gestation. The researchers used multivariable logistic regression to calculate the adjusted odds ratio. For severe periodontitis, it was reported at 4.45 (95% CI, 2.16–9.18) for infants born before 37 weeks gestational age. The odds ratio increased to 7.07 (95% CI, 1.70–27.40) for delivery before 32 weeks gestational age. This prospective study and the case-control studies reported above are recorded in Table 4.

Table 4. Case-control studies and prospective studies showing the link between periodontal disease and PLBW

Study	Outcome/odds ratio	Oral exposure
Offenbacher et al. 1996[71]	PTB 7.9	Periodontal disease
Dasanayake 1998[72]	LBW 1.1	Poor periodontal health
Dasanayake 1998[72]	LBW .3	Good periodontal health
Jeffcoat et al. 2001[73]	PTB 4 to 7	Severe or generalized periodontal disease

Preliminary findings are now available from the largest longitudinal prospective study reported to date on periodontal status in pregnant women. Offenbacher et al. (2001)[64] report on 814 deliveries with periodontal examinations performed at enrolment and again within 48 hours postpartum, with blinded examiners. The results provide strong support for the hypothesis that maternal periodontal disease is a risk factor for preterm birth, low birth weight, and fetal growth restriction, independent of other major risk factors. Also, incidence/progression of periodontal disease, defined as 4+ sites with an increase of 2+ mm periodontal disease, also contributes significant risk for fetal growth restriction. Although the number of neonatal deaths in the study was too small to be reliable, they indicated that neonatal mortality was linked with more severe maternal periodontal disease.

The fourth line of evidence comes from three intervention studies using periodontal treatment for pregnant mothers with existing oral health problems. (The two randomized controlled trials are listed in Table 5.) The first study conducted by Mitchell-Lewis et al. in 2001[74] showed a prevalence of 18.9% preterm low birth weight infants without periodontal treatment for the pregnant mothers versus 13.5% with treatment. Periodontal treatment included oral hygiene instruction and full-mouth debridement, including scaling, polishing with fluoridated paste, and dental sealants. Subjects included 164 women, 60% African-American and 39% Hispanic, between the ages of 12 to 19. There were several drawbacks to this study. One is that the effect of the intervention did not reach statistical significance. The second concern is that oral clinical exams were only conducted following delivery; therefore it was impossible to determine if periodontal disease or gingivitis existed prior to delivery. In addition, only four of the study subjects had periodontal disease. They did, however, display poor oral health habits, abundant plaque and calculus, and gingivitis. Although statistical significance was not reached, this was an early study that suggested the need for further exploration of this association.

Lopez et al. (2002)[75] conducted the first randomized controlled trial of its type with 351 women with periodontal disease. Results suggest that periodontal disease is an independent risk factor for preterm low birth weight. Periodontal therapy consisted of plaque control instructions, scaling, root planing, and chlorhexidine rinse once a day. In addition, 18% of the treatment group had severe periodontitis and were given metronidazole 250 mg plus amoxicillin 500 mg three times a day for seven days. The study took place in Chile with a population of low socio-economic status women of Spanish and local Aboriginal descent, predominantly Caucasian. For the first group, periodontal therapy was completed before 28 weeks of gestation and maintenance therapy was provided every 2 to 3 weeks until delivery. The second group received periodontal therapy postpartum. The incidence of PLBW in the first group, which was treated, was 1.84% (N 3/163)—significantly lower than in the control group, which was10.11% (N19/188). Women with periodontal disease have more than four times greater risk of having a PLBW infant than

periodontally healthy women. This figure was calculated from a multiple logistic regression model where mothers with periodontal disease had an odds ratio of 4.70; 95% confidence interval, 1.29 to 17.13.

Jeffcoat et al. (2003)[76] also conducted a randomized controlled trial with 366 women (85% African-American) with periodontitis between 21 and 25 weeks gestation to determine whether treatment of periodontitis reduces the risk of spontaneous preterm birth (SPTB). Subjects were randomly assigned to one of three treatment groups: (1) dental prophylaxis (tooth cleaning and polish) plus placebo capsule three times a day; (2) scaling and root planing plus placebo capsule three times a day; and (3) scaling and root planing plus metronidazole 250 mg three times a day for one week. Results show that the rate of preterm birth at <35 weeks was 4.9% for the first group (prophylaxis plus placebo), 3.3% for the third group (scaling and root planing plus metronidazole), and the lowest rate of 0.8% for the second group (scaling and root planing plus placebo). The rate of preterm birth was 6.3% in the reference or untreated group. Results also show as much as an 84% reduction in spontaneous preterm birth at <35 weeks gestation in subjects receiving scaling and root planing compared with the prophylaxis plus placebo group.

Table 5. Intervention randomized controlled trials, Level 1 studies

Study	**Risk ratios (RR) Odds ratios (OR) and percentage 95% confidence interval (CI) for preterm birth**	
Jeffcoat et al. 2003[76]	**SRP + placebo**	**SRP + metronidazole**
PTB <37 weeks	0.5 RR (CI, 0.2–1.3)	1.4 RR (CI, 0.7–2.9)
PTB <35 weeks	0.2 RR (CI, 0.02–1.4)	0.7 RR (CI, 0.2–2.4)
Lopez et al. 2002[75]	Treatment group 1.84% (3/163)	
	Control group 10.11% (19/188), OR 4.70; 95% CI, 1.29–17.13	

PTB Preterm birth SRP Scaling and root planing

Discussion

Collectively, the results from the case-control, prospective, and intervention studies show a possible link or correlation between periodontal disease and PLBW and preterm birth, and suggest that periodontal treatment may reduce the risk of PLBW. The studies suggest that exacerbation of existing periodontal disease, as well as pregnancy-induced gingivitis, may be harmful to the fetus. Women with periodontal disease may have 4 to 7.9 times the risk of having a preterm birth than women with good oral health. Using a risk factor of 7, Offenbacher and Beck calculate that as much as 18% of the total incidence of PLBW could be eliminated if

periodontal disease is eliminated. This would result in the prevention of 45,000 preterm births in the United States each year, with a savings of $1 billion in intensive care costs alone.[77]

Although case-control and prospective studies provide important information, randomized controlled trials are the only studies that can show a cause-and-effect association between periodontal infection and PLBW and provide convincing evidence that treatment of periodontal disease will reduce the risk of PLBW. This report includes two such studies that suggest early identification and treatment of periodontal disease during pregnancy can reduce the risk of premature birth and low birth weight. Unfortunately, both these studies contain weaknesses. The results from these two trials are limited in their generalizability to the population at large or to women without periodontal disease, for two reasons. First, the reference groups for the studies consisted only of individuals with oral health problems. Second, in one of the randomized controlled trials, there was a predominantly African-American population. Therefore, additional research is needed to determine if there is a definitive causal link between periodontal disease and PLBW babies.

Research studies are more easily compared when criteria for definitions are consistent. Fortunately, the studies all appear to agree that low birth weight is defined as a birth weight less than 2,500 g and that preterm delivery is defined as prior to 37 weeks of gestational age. However, the studies show a large variation in oral health measurements. For example, Offenbacher et al. (1996)[71] and Jeffcoat et al. (2003)[76] use a similar periodontal status measurement, defined as mean clinical attachment levels (CAL mm/site) and Offenbacher also included probing depths and bleeding on probing. Dasanayake (1998)[72] measured periodontal status by using the Decayed, Missing and Filled Teeth index (DMFT) and the Community Periodontal Index of Treatment Needs (CPITN). Finally, Offenbacher et al. (2001a)[64] used a three-level definition of periodontal disease—periodontally healthy mothers, a mild disease group, and a moderate-severe group. The moderate-severe group was defined as =4 sites with at least 5 mm periodontal disease and 2 mm attachment loss at =4 sites. The use of different types of measurement makes the translation of research findings into clinical guidelines more complex.

Many of the risk factors that are generally accepted as related to preterm delivery are interrelated, such as smoking, alcohol consumption, socio-economic status, and age of mother. Therefore, unless the research studies control for these factors using a multivariate logistical model, the associations are questionable. Unfortunately, only four studies in this report used a multivariate logistical model in the statistical analysis.

There are some commonly held beliefs about recommendations for oral health care of pregnant women. The American Dental Association, for example, suggests that elective oral health care should be avoided, if possible, during the first trimester and the last one-half of the third trimester.[78] This recommendation takes into account the periods of greater vulnerability and risk of harm to the developing embryo or fetus. In light of the results of recent research, there may be a need to re-evaluate this recommendation, taking into account the potential risk of harm to the developing embryo if periodontal treatment is not provided.

Recommendations

Clinical

In light of the possible link between periodontal infection and adverse pregnancy outcomes, and the intervention studies showing that treatment of periodontal disease may reduce the risk of PLBW infants, the following are some suggestions for dental hygienists. All clinical decisions, however, should be based on the needs of the specific client:

- Consider educating pregnant clients and those contemplating pregnancy about the correlation between periodontal disease and PLBW babies and the implications.
- Consider periodontal therapy as a necessary part of prenatal care for all clients.
- Preventive oral health education should be a part of prenatal public health education.
- Oral health outreach should be provided to those individuals who do not seek preventive care during pregnancy.

Research

Suggestions for further research:

- Studies on the link between periodontal disease and PLBW infants should be conducted, particularly randomized controlled trials, with larger numbers of participants, and a wider spectrum of participants, including more ethnically and economically diverse general populations.
- Studies to prove oral health education and community support prevent PTLBW.
- Universal criteria should be used in studies for defining periodontal disease.

RESPIRATORY DISEASE

Respiratory diseases (RD) include chronic obstructive pulmonary diseases (COPD) such as bronchitis and emphysema, and acute respiratory diseases including influenza, pneumonia, and acute bronchitis. Over 3 million Canadians have serious respiratory diseases that account for $12.8 billion of expenditures per year, including the direct visible costs of hospitalization, drugs, and physician visits as well as the indirect costs associated with disability and mortality.[78] Hospital inpatients develop pneumonia more than 5% of the time, and pneumonia accounts for the majority of admissions to hospitals from nursing homes. This increases hospital inpatient time and costs and causes significant morbidity and mortality.[80] Ventilator-associated pneumonia, from hospital-acquired (nosocomial) bacterial pneumonia, is a leading cause of death from hospital-acquired infections with a crude mortality rate of approximately 30%.[81]

Biological pathways

Several biological mechanisms are hypothesized to explain the link between microbial infections and pneumonia.[66,80,82]

1. Oral micro-organisms are aspirated into the respiratory tract and host defence mechanisms fail to eliminate the micro-organisms causing aspiration pneumonia.
2. Dental plaque acts like a reservoir for respiratory pathogen colonization. Periodontal disease-associated enzymes in saliva may modify mucosal surfaces to promote adhesion and

colonization by respiratory pathogens. Periodontal disease-associated enzymes may destroy salivary pellicles on pathogenic micro-organisms, causing them to adhere to mucosal surfaces. These pathogens are then shed into the salivary secretions and aspirated into the lung to cause infection.

3. Respiratory pathogens adhering to plaque in clients with periodontitis may be abundant following treatment with antibiotics. These micro-organisms are aspirated into the lung, causing pneumonia.
4. Cytokines originating from periodontal tissues may contribute to respiratory inflammation by altering respiratory epithelium.

Research evidence

This section first examines some cross-sectional, longitudinal, and retrospective studies. Random controlled trials are then discussed. The final portion looks at research from the nursing field reporting on physician and nurse involvement with oral health and the link between poor oral health and ventilator-associated pneumonia.

The following summarizes evidence from eight epidemiological studies indicating an association between oral infections and respiratory infections. (See Table 6 for an evidence table of the research showing odds ratios.) Three studies show a high degree of respiratory pathogen colonization of plaque in institutionalized populations and the researchers suggest that the mechanism for this colonization is poor oral hygiene. Other reviewers agree that the mechanism is poor oral hygiene.[80,83] Russell et al. (1999)[84] conducted a cross-sectional study comparing 28 institutionalized seniors with 30 community-dwelling senior outpatient controls. They found that 14% versus 0% respectively showed positive for respiratory pathogen colonization of plaque. Oral colonization of plaque was also associated with COPD and with higher plaque scores. They suggest that deficient plaque control is related to respiratory pathogen colonization of plaque.

El-Solh et al. (2003)[85] confirms Russell et al.'s results in a study that included 95 institutionalized seniors and analysis with a logistic regression model. The El-Solh study suggests that aerobic micro-organisms that colonize dental plaque may play a significant role in aspiration pneumonia. This study also suggests a potential link between functional status—measured by activities of daily living—and anaerobic pulmonary aspiration in the elderly. The researchers postulate that poor oral hygiene related to a decrease in activities of daily living combined with difficulty accessing professional dental care lead to colonization of dental plaque by the respiratory disease micro-organisms.

Fourrier et al. (1998)[86] conducted a prospective study of 57 patients in an intensive care setting. Over time, there were increases in both dental plaque and respiratory pathogens in the dental plaque, which were associated with pneumonia. The researchers suggest that poor oral health may predispose institutionalized patients to oral colonization by respiratory pathogens.

Several studies show a connection between poor oral hygiene and respiratory disease in an institutionalized population and a community dwelling population. The first study examines both of these populations. Terpenning et al. (2001)[87] conducted a study with prospective enrolment of subjects with retrospective analysis of the data. Of the 358 enrolled veteran subjects, 50

developed aspiration pneumonia and 28 of those were dentate. A logistic regression model, which controlled for established medical risk factors in aspiration pneumonia, indicated that the dentate subjects with oral health problems had a higher risk of developing aspiration pneumonia, decayed teeth (OR 1.2), presence of organisms for decay in saliva (OR 6.2), and periodontal disease (OR 4.2). Oral health problems were measured by oral hygiene, dental caries, periodontal disease, number of teeth, chewing potential, and presence of removable prostheses.

The next study examines an institutionalized population. Mojon et al. (1997)[88] demonstrated that poor oral hygiene might be a major risk factor for respiratory tract infection in an elderly institutionalized population. They studied 302 seniors in a medical care facility and found that individuals with poor oral hygiene and the presence of a potential dental emergency had a greater risk for respiratory tract infections (RR 1.9; 95% CI, 1.1–3.9). The oral exam included an evaluation of hygiene, periodontal disease, caries, and mucosal disorders.

The next three studies examine community dwelling populations. Scannapieco et al. (1998)[89] analyzed the National Health and Nutrition Examination Survey I (NHANES I) and suggest an association between poor oral hygiene and chronic respiratory disease. In this cross-sectional epidemiological study, oral hygiene was measured with the oral hygiene index (OHI), including oral debris and/or calculus. Of the 234 subjects, 41 developed chronic respiratory disease. Multivariate analyses controlled for relevant covariates. Logistic regression analysis of data was used to determine that subjects with the maximum OHI value (poor oral health) were 4.5 times more likely (OR 4.5; 95% CI, 1.06–18.99) to have a chronic respiratory disease than those with an OHI of zero. No link was found between periodontal disease and respiratory disease and between poor oral health and acute respiratory diseases.

In contrast to Scannapieco et al. (1998), Hayes et al. (1998)[90] conducted a prospective, cross-sectional, longitudinal, epidemiological study using data from the Veterans Affairs Dental Longitudinal Study (DLS) and Normative Aging Study (NAS). They found that periodontal disease measured with alveolar bone loss at baseline was associated with risk for subsequent development of COPD. The bone loss was measured with periapical radiographs. Of the 1,118 subjects who initially enrolled in the study, only about one-quarter developed COPD over the subsequent 25 years. Subjects in the worst population quintile had alveolar bone loss of >20% per site. The risk of COPD was 1.8 times greater for those subjects with the worst alveolar bone loss versus those with <20% alveolar bone loss per site. A logistic regression model accounted for known risk factors associated with COPD. One drawback to this study is that baseline pulmonary function was not adjusted for in the logistic regression analysis and may be confounding the association.

Scannapieco and Ho (2001)[91] report on a retrospective study of cross-sectional data from the National Health and Nutrition Examination Survey III (NHANES III) database. They show an association between periodontal disease and COPD. Variables such as smoking, diabetes mellitus, alcohol use, education, income, sex, age, and socio-economic status were controlled for using a logistic regression analysis. Oral health status was assessed using the decayed, missing, or filled, surfaces/teeth (DMFS/T) index, and periodontal health was measured using attachment level, gingival bleeding, and the dental health index. Subjects with mean attachment loss (MAL) = 3.0 mm had a higher risk of COPD (OR 1.45; 95% CI, 1.02–2.05). There was also a possible dose-response relationship, whereby lung function diminished with increasing periodontal attachment loss.

Table 6. Associations between oral health and respiratory disease, Level II studies

Reference	Study design	Subjects	Exposure	Outcome	Odds ratio/risk ratio	95% CI
Terpenning et al. 2001[87]	Prospective enrolment, retrospective analysis of data	358 community dwelling and institutionalized veterans	Decayed teeth Organisms for decay Periodontal disease	Aspiration pneumonia	OR 1.2 OR 6.2 OR 4.2	1.1-1.4 1.4-27.5 1.6-11.3
Mojon et al. 1997[88]	Longitudinal	302 institutionalized seniors	periodontal disease, caries, and mucosal disorders and the presence of oral disorder that could develop into a dental emergency	Respiratory tract infection	RR 1.9	1.1-3.9
Scannapieco et al. 1998[89]	Cross-sectional	234 community dwelling subjects	Oral hygiene index (OHI)	Respiratory disease (n=41)	OR 4.5	1.06-18.99
Hayes et al. 1998[90]	Cross-sectional, longitudinal	1,118 community dwelling veterans	Alveolar bone loss	COPD (n= 297)	RR 1.8	
Scannapieco and Ho 2001[91]	Cross-sectional	13,792 community dwelling subjects	Attachment loss	COPD	OR 1.45	1.02-2.05

OR Odds ratio
RR Risk ratio
COPD Chronic obstructive pulmonary disease
CI Confidence interval

The following summarizes four randomized controlled trials showing that oral hygiene treatment reduces the risk of pneumonia for high-risk subjects and one study showing that oral hygiene treatment lowers colonization of respiratory pathogens. Table 7 is an evidence table of the randomized controlled studies dealing with this topic.

DeRiso et al. (1996)[92] conducted a randomized controlled trial with 353 subjects in an intensive care unit. Subjects receiving an oral rinse of 0.12% chlorhexidine gluconate twice per day had a 65% reduction in the incidence of nosocomial infection (OR 0.32; 95% CI, 0.14–0.72) and 69% reduction in respiratory tract infection, compared with the control group who received no oral rinse.

Pugin et al. (1991)[93] conducted a double-blind randomized controlled trial with 52 patients requiring mechanical ventilation. Subjects received either an oral antibiotic rinse, which was also

swallowed, or a placebo. The rinse consisted of polymyxin B sulfate, neomycin sulfate, and vancomycin hydrochloride (PNV). Colonization by gram negative micro-organisms and staphylococcus aureus, as well as pneumonia, occurred five times less frequently in the PNV group than in the placebo group (16% and 78% respectively, $p > .0001$).

Yoneyama et al. (1999)[94] conducted a randomized controlled trial and reported that the risk of pneumonia was 1.67 times higher (95% CI, 1.01–2.75) in the control group than in the group that received oral hygiene treatment, including application of 1% povidone iodine to the pharynx and oral hygiene care. The test group consisted of 184 subjects and the control group 182. Treatment group results are as follows: odds ratio 0.60, 95% confidence interval 0.36-0.99.

Fourrier et al. (2000)[95] conducted a randomized controlled trial with 30 treatment and 30 control intensive care unit subjects on mechanical ventilation. The treatment group received dental plaque antiseptic decontamination with 0.2% chlorhexidine gel, applied three times per day. The group receiving oral decontamination had a significantly reduced rate of nosocomial infection (OR 0.27; 95% CI, 0.09–0.80).

Abe et al. (2001)[96] conducted a study composed of 54 seniors with daily nursing care, 21 healthy seniors, and 22 healthy young subjects as controls. They found that the seniors with daily nursing care who gargled with a saline solution had a lower colonization of respiratory pathogens than the elderly control subjects without oral care. However, this study has been challenged for its lack of baseline data and poor statistical analysis.[97]

Table 7. Effect of oral care interventions on risk of respiratory disease (RCT studies), Level 1 Studies

Reference	Subjects	Intervention	Outcome	Odds ratio	95% CI
DeRiso et al. 1996[92]	353 ICU subjects	0.12% chlorhexidine gluconate 2X/day	Nosocomial infection	OR 0.32	0.14–0.72
Pugin et al. 1991[93]	52 subjects on mechanical ventilation	PNV (polymyxin B sulfate, neomycin sulfate, and vancomycin hydrochloride)	Pneumonia	5 times less frequently	
Yoneyama et al. 1999[94]	366 nursing home residents	1% povidone iodine and oral hygiene care	Pneumonia	0.60	0.36-0.99
Fourrier et al. 2000[95]	30 treatment, 30 control ICU subjects	0.2% chlorhexidine gel 3X/day	Nosocomial infection	OR 0.27	0.09-0.80

Additional contributing factors to the development of respiratory disease are noted in the nursing and critical care medicine literature. "Neither nursing home staff nor physicians appear to give high priority to the oral care of residents."[85] In addition, nurses primarily use sponge toothettes for intubated ICU patients' oral care, despite the toothettes' ineffectiveness.[98] Even though tooth brushing is an independent nursing action, it is not routinely performed for critically ill patients. Micro-organisms from the mouth may then become aspirated into the lower respiratory tract. Infection sets in when the micro-organisms multiply and the host defence mechanisms fail to

eliminate them. Prevention of respiratory disease would thus involve better oral health care for ICU patients. Several authors in the nursing field agree with this call for better oral care when they suggest that the teeth of ICU patients should be brushed regularly—some say every 2 to 4 hours—to prevent ventilator-associated pneumonia.[99-101]

Discussion

The balance of epidemiological research shows a moderate association between oral health/periodontal disease and respiratory disease. The associations are consistently positive, with only one study challenging this by showing no association between periodontal disease and respiratory disease, possibly due to weaknesses in this study that will be discussed later in this section. It is difficult to quantitatively combine the results of the studies, since they have a high degree of variation in the outcome—which included COPD, pneumonia and respiratory disease—and in the exposure—which included attachment loss, alveolar bone loss, and caries. However, with all of the differences in the studies aside, the OR ranged from a low value of 1.2 to a moderate value of 6.2 with a moderate average of 3.04. Although the risk is moderate, due to the prevalence of respiratory disease, even a moderate risk can have major implications for population health. Another highlight of this research is that one of the studies showed a possible dose-response relationship, whereby lung function diminished with increasing periodontal attachment loss.

There are several limitations in this research. Some of the risk factors for respiratory disease and for poor oral health include poor nutritional status, mediocre functional status, and smoking.[97] Although some of the studies controlled for smoking, many did not control for all of these factors, resulting in the possibility that confounding variables skewed the results. Secondly, two of the studies had small numbers of subjects. In Scannapieco et al. (1998),[89] the combination of a small subject size and the fact that respiratory disease is uncommon in community dwelling populations may preclude detection of statistical significance of a link between periodontal disease and respiratory disease. There are two other concerns with Scannapieco et al. (1998).[89] Chronic respiratory disease may be an inaccurate diagnosis, since it was not assessed using laboratory and/or radiographic tests, and the oral indices in the NHANES have been challenged as being insensitive.[80,89]

Although the number of randomized controlled trials are low, they indicate that dental hygiene treatment may decrease the prevalence of oral respiratory pathogen colonization and reduce the risk of respiratory infection in high-risk subjects. The intervention research does support providing preventive oral health care to the elderly, especially those in institutional settings, who are at high risk of developing respiratory disease. Reduction in plaque may be particularly important due to its potential role as a reservoir for respiratory pathogens and the development of nosocomial pneumonia. Periodontal disease along with other factors, such as smoking, environmental pollutants, viral infections, allergies and/or genetic factors may play a role in the development of respiratory disease.

There are several limitations in the randomized controlled trials. First, the number is small, limiting the strength of the evidence. Second, there are a small number of subjects in two of the studies, Pugin et al. (1991)[93] and Fourrier et al. (2000).[95] Third, two of the studies—DeRiso et al. (1996)[92] and Fourrier et al. (2000)[95]—did not provide any oral health status data. Due to these

limitations, it may not be possible to conclude definitively that poor oral health causes respiratory disease. Thus there is a need for further randomized controlled trials to verify the importance of oral hygiene treatment in respiratory disorders.

The factors involved in the pathogenesis of respiratory disease and periodontal disease are multidimensional with considerable overlap. Although the microbial mechanisms are uncertain, the randomized controlled trials and associational research indicate that respiratory pathogens adhere to plaque. Plaque buildup results from poor oral hygiene, which may originate with inattention to oral care by institutionalized seniors, ICU patients, physicians, and nurses. These factors, combined with difficulty in accessing professional oral health care, may contribute to colonization of plaque by respiratory disease pathogens. Increased attention to oral health in this high-risk population may result in a lower incidence of respiratory disease.

Recommendations

Clinical

Some general suggestions for dental hygienists follow; however, all clinical decisions should be based on the needs of the specific client:

- There is a need for dental hygienists to provide health promotion and disease prevention services for individuals at high risk for respiratory infection in intensive care units and long-term care facilities.
- There is a need for education in oral health care and the possible links with respiratory disease for intensive care unit and long-term care facility staff.

Research

- Randomized controlled trials with larger subject numbers.
- Research to delineate the best procedure for oral health care in intensive care units.

CONCLUSIONS

Is the mouth really the portal to the body? The biological theories suggest that plaque harbours biological pathogens, which lead to chronic or acute bacteremia and to systemic damage by endotoxins and lipopolysaccharides. These processes may lead to chronic and acute systemic infections. The epidemiological evidence, although preliminary, suggests that oral health and oral infections may have an association with the occurrence and severity of a wide variety of systemic conditions and diseases such as heart disease, preterm low birth weight babies, respiratory disease, and diabetes mellitus. The association is not indicated simply by clinical signs of periodontal disease, but by molecular criteria, such as immune and inflammatory mediators. Since periodontal disease is a potentially modifiable risk factor, being both preventable and treatable, an opportunity may exist for dental hygienists to play a key role in decreasing the incidence and severity of these systemic diseases.

The studies show a small-to-large association between periodontal disease and some systemic disorders, including diabetes mellitus, heart disease, preterm low birth weight babies and respiratory disease. Conclusions from the research are as follows:

- Periodontal disease may exacerbate diabetes mellitus and mechanical periodontal therapy combined with systemic antibiotics may provide better metabolic control of type 2 diabetes, with a .8% to 11% reduction in glycated hemoglobin.
- Persons with periodontal disease may have a 1.04 to 2.8 fold greater risk of incurring cardiovascular disease than persons without periodontal disease; of the different types of cardiovascular disease, stroke shows the most robust association.
- Women with periodontal disease may have 4 to 7.9 times the risk of having a preterm birth than women with good oral health. This may be considered a moderate to high risk. Also, early identification and treatment of periodontal disease during pregnancy may reduce the risk of premature birth and low birth weight.
- A moderate association may exist between oral health and respiratory disease, with an average odds ratio of 3.04, for those at risk of developing respiratory disease.

Periodontal infections are quite common, with advanced disease affecting about 10% to 15% of the population worldwide.[4] As the population ages, the prevalence of periodontal disease is bound to increase as more people are retaining their teeth. Although the association between oral health and general health varies from small to large depending on the specific health issue, due to the high prevalence of some health issues, even a small to moderate risk can have major implications for population health. Taking these demographic issues into consideration, preventing periodontal disease may have a greater role to play in general health in the near future.

Dental hygienists can play an active role in translating this research knowledge into information that the public can use to make decisions about their own health. This information may be the motivating factor for good oral health, since there is now evidence of its link to other conditions that are traditionally considered more serious. There is also an important on-going role for dental hygienists in assessing health risks and referring clients for periodontal assessments. The growing realization of the association between oral health and systemic health brings increased responsibilities for dental hygienists to be more aware of the potential impact of their treatment. The research in this paper also points to roles for dental hygienists in health promotion and disease prevention, roles that need to be further developed. There should be dental hygienists in every hospital, intensive care unit, health unit, and community health centre. These roles will make it increasingly important for dental hygienists to have knowledge of and experience in interdisciplinary practice.

To help clarify the role of oral health promotion in the incidence and management of systemic diseases, further research is required through randomized controlled trials and longitudinal interventional studies that attempt to reduce the risk for a particular systemic disease, following treatment or prevention of periodontal infections. Only through randomized controlled trials can we reach the conclusion that periodontal disease causes or exacerbates systemic disease. There is also a need for further studies showing consistency or differences in associations in different populations, such as low-income groups, multicultural groups, Aboriginal peoples, and women.

The associations identified in this paper can significantly affect the importance of the role of the dental hygiene profession, change how oral health is perceived, and change the discipline of periodontal medicine. This research also opens the door for dental hygienists to work more collaboratively in interdisciplinary relationships with other health professionals. This evidence

will create opportunities for an integrated model of oral health and general health and strengthen the argument for an oral health system that is accessible to all citizens.

APPENDIX A

Definitions

This section defines terms as they are used in this report.

Bacteremia: the presence of micro-organisms in the bloodstream. Transient bacteremia can be caused by oral micro-organisms entering the bloodstream through chewing, toothbrushing, flossing, periodontal infections, and some dental procedures.

Case-control study: a retrospective study in which people with a condition are compared with people without it, but who are similar in other characteristics

Causality: a cause for systemic diseases can be determined only by means of a randomized controlled trial (RCT). This study design allows the potential causal factors to be controlled by the investigator, who assigns persons randomly to the experimental and control groups.

Confidence interval (CI): the range within which the true size of effect lies with a given degree of assurance. A 95% confidence interval is the interval that includes the true value in 95% of cases.

Cross-sectional study: a study in which the health conditions of a group of people who are, or are assumed to be, a sample of a particular population are assessed at one time.

Gingivitis: an infectious inflammatory process limited to the gingiva.

Infection: invasion and proliferation of micro-organisms or other pathogenic micro-organisms in body tissues and the reaction of the tissues to their presence.

Logistic regression: statistical analysis that allows the separation and measurement of the relative contributions of a number of factors from among many risk factors that are present at the same time. For example, logistic regression can be used to describe how periodontal infection independently contributes to preterm low birth weight in infants, when other risk factors such as smoking are also present. Multiple/multivariate/multifactorial/multivariable logistic regression is the relationship between the dependent variable and more than one independent variable. Conditional logistic regression is used to investigate the relationship between an outcome and a set of prognostic factors in cohort and matched case-control studies.

Longitudinal study: a study in which the same group of people is studied on two or more occasions.

Nosocomial pneumonia: hospital acquired pneumonia

Odds ratio (OR): measurement of risk used in case-control studies where risks are examined retrospectively for those with and without disease. It is calculated by taking the number of people with a disease who were exposed to the risk factor over the number of people with the disease who were not exposed. It is a way of comparing whether the probability of a certain event is the

same for two groups. An odds ratio of 1 implies that the event is equally likely in both groups; an odds ratio greater than one implies that the event is more likely in the first group. An odds ratio less than one implies that the event is less likely in the first group. Case-control studies use OR.

Prospective study: a study where information on an exposure of interest is used to compare eventual outcomes.

Relative risk factor (RR): measurement of how much a particular risk factor influences the risk of a particular outcome. A relative risk of 2 means that a person has a two-fold increased risk of having a particular outcome. Cohort studies use RR.

P value: when statistical analysis of the study data differs between the control and experimental group or the before-and-after treatment group finds a P value greater than .05 (5%), the difference is considered non-significant. In order to have significant results, the p value must be less than 5% (.05). meaning the results were not just due to chance.

Periodontal disease: periodontal diseases are caused by chronic gram-negative micro-organisms that accumulate in plaque biofilms and result in the inflammatory destruction of the structures of the periodontium, including the periodontal ligament, cementum, alveolar and supporting bone. These diseases result from exposure of the periodontium to dental plaques, biofilms that accumulate on the teeth. The inflammation around the tooth may allow micro-organisms or their products, including lipopolysaacharides, peptidoglycan fragments, and hydrolytic enzymes, into the systemic circulation. The host response to periodontal infections results in the local production of cytokines and biological mediators including interleukins and prostaglandins as well as the introduction of serum antibodies.[33]

Randomized controlled trial (RCT): the strongest experimental design in which subjects are randomly assigned to treatment groups, with one group being a control group. The RCT provides the most powerful research evidence and can show causality.

Retrospective study: a study that begins with an outcome and investigates back for exposure information.

Systemic disease: a disease that affects the whole body

Therapeutic seeding: within the context of a diabetic client, it refers to a clinician's discussion with a pre-symptomatic client regarding his or her susceptibility to diabetes and suggestions for life style changes that include exercise, weight loss or control, and knowledge of risk factors.

APPENDIX B

Canadian Task Force on the Periodic Health Examination Evidence Classification Scheme

Levels of evidence*

I: Evidence obtained from at least one properly randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

* Criteria developed by the Canadian Task Force on the Periodic Health Examination. Goldbloom R, Battista RN. The Periodic Health Examination: 1. Introduction. *CMAJ* 1986; 134(7):721-3.

APPENDIX C

Three levels of oral disease prevention for the diabetic client

Hein* suggests the following three levels of prevention for clients with diabetes or at risk of developing diabetes:

- Primary prevention, which is aimed at pre-symptomatic yet susceptible individuals and includes health promotion and therapeutic seeding.
- Secondary prevention includes early diagnosis and screening for type 2 diabetes using glucometers at the chairside, for clients considered by history and clinical findings to be at risk for diabetes. This suggestion is of particular importance, given the suggestion by Lamster and Lalla** that some patients are seen in their dentist's office on a more regular basis than they are seen in a physician's office.
- Third level prevention (or tertiary prevention) is rehabilitation of the chronic diabetic client, including minimizing the loss of periodontal support.

* Hein C. Getting it right in long-term management of chronic periodontitis associated with diabetes, Part 1. Contemporary Oral Hygiene. 2003;3(9): 24-31.

** Lamster IB, Lalla E. Periodontal disease and diabetes mellitus: discussion, conclusions, and recommendations. Ann Peridontol. 2001;6: 146-49.

APPENDIX D

Oral procedures creating risk of bacteremia[58,59]

The following is a list of oral procedures that create a risk for bacteremias: periodontal treatment and prophylactic cleaning of teeth or implants where bleeding is anticipated, periodontal surgery, scaling, root planing, probing, recall maintenance, initial placement of orthodontic bands but not brackets, intraligamentary local anesthetic injections, oral irrigators or air abrasive polishing devices, dental extractions, implant placement and tooth reimplantation, endodontic surgery or instrumentation beyond the root apex, and subgingival placement of antibiotic fibers or strips.

Cardiac conditions requiring prophylaxis for dental treatment[59,60]

High risk

- Prosthetic cardiac valves, including bioprosthetic and homograft valves.
- Previous infective endocarditis, even in the absence of heart disease.
- Complex congenital cardiac malformations (e.g., single ventricle states, transposition of the great arteries, tetralogy of Fallot).
- Surgically constructed systemic/pulmonary shunts.

Moderate risk

- Rheumatic and other acquired valvular dysfunction even after valvular surgery.
- Hypertropic cardiomyopathy.
- Mitral valve prolapse with valvular regurgitation and/or thickened leaflets
- Non-complex congenital cardiac malformations.

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