Oral - Systemic Health Connection?

A Brief Overview

Introduction

Medical and dental specialists often partner together in the care of patients. Common examples of this partnership include the use of prophylactic antibiotic therapy to reduce the risk of endocarditis prior to dental procedures and the care of trauma patients with maxillo-facial injuries. The partnership has typically had a narrow focus as illustrated by the preceding examples but the need to broaden this partnership is rapidly approaching based on a growing body of scientific evidence that supports a connection between oral health and a number of systemic diseases. While no direct causal relationship has been established, scientific evidence continually mounts that indicates that an increase in oral bacteria appears to affect a number of physical reactions in the body — specifically in people with susceptibility to a number of specific diseases or those that might be adversely affected due to their physical condition — cardiovascular disease, diabetes mellitus, respiratory disease, adverse pregnancy outcomes, and transplants. At the same time, a number of studies have shown that a reduction in oral bacteria and its subsequent inflammatory response improves the status of some patients susceptible to adverse changes in these same systemic conditions.
Periodontal Disease and Inflammation

An intact mucosal lining of the body being penetrated by calcified structures colonized by bacteria create an environment that produces a unique inflammatory response that, left untreated, results in the production of pro-inflammatory cytokines, destruction of tissue, and opportunistic bacterial penetration into the systemic circulation. The inflammatory response results in periodontitis or periodontal disease and is estimated to affect nearly 50 percent of Americans over the age of 30 years. Periodontal disease if untreated will ultimately result in the loss of bone that supports the teeth and is the leading cause of adult tooth loss.

Over 400 different species of bacteria reside in plaque biofilms at the interface of the gingival sulcus and the tooth, many of which are gram negative and anaerobic.1 Inflammation is initiated as the host immune system is overcome by invasive bacteria releasing endotoxins from gram negative bacteria, chemotactic peptides, organic acids, and protein toxins.2 Host enzymes are subsequently released in response — most notably from monocytes that include proinflammatory cytokines such as interleukin-1(IL-1), IL-6, tumor necrosis factor-α (TNF-α), and prostaglandin E2 (PGE2).3

Ulcerated sulcular epithelium may serve as one entry portal into the systemic circulation. The cumulative surface area of ulcerated pocket epithelium in severe periodontal disease patients has been estimated to be from 8 to 20 cm (about the size of the palm of a hand).4,5 Normal chewing has been shown to cause systemic endotoxemia in 40 percent of these patients compared with 12 percent of periodontally healthy patients — the endotoxin concentration in the bloodstream was five times higher in those with periodontitis.5,7

Significantly higher serum inflammatory markers such as C-reactive protein (CRP), IL-6, and fibrinogen are found in the peripheral blood of patients with periodontitis — particularly in those patients harboring highly virulent Gram-negative Porphyromonas gingivalis, Prevotella intermedia, and Tannerella forsythens.5,8,10 Periodontal treatment in intervention trials has been shown to reduce not only localized inflammation, but also resulted in decreased serum levels of IL-6, TNF-α and CRP.11-14

With the stage set by the inflammatory response, let’s take a look at several clinical conditions and the scientific evidence that support the connection between oral and systemic health.

Periodontal Pathogens and Vascular Disease

Recent studies by Fiehn identified DNA from pathogenic periodontal microbes in atherosclerotic plaques removed from carotid and femoral arteries.23 One interesting finding from this study is that none of the tissue specimens were able to reproduce oral bacteria growth under anaerobic conditions. Dögan compared bacterial levels in subgingival plaque samples of periodontal patients with and without a history of recent myocardial infarction.24 Elevated levels were detected only in those patients with a recent history of myocardial infarction, suggesting increased bacteria loads may present a systemic health risk.

Desvarieux reported a direct relationship, independent of CRP levels, between the thickness of the tunica intima and tunica media of the carotid artery (indicating atherosclerotic plaque formation) and the presence of five periodontal microbial pathogens, P. gingivalis, A. actinomycetemcomitans, T. forsythens, Treponema denticola, and Micromonas micros.25 Other researchers have confirmed invasive oral bacteria in carotid artery plaque26 as well as tissue samples taken from aortic aneurysms.27,28 P. gingivalis has been the focus of a number of studies indicating a seropositive connection with coronary heart disease and stroke patients29,30 as well as being shown to induce monocyte chemoattractant protein-1 to recruit monocytes in human umbilical vein endothelial cells31,32 and increasing the cellular production of elastase/gelatinase (MMP-9), implicated in atheroma plaque rupture.32 The recruitment and attachment of monocytes to the endothelial lining of blood vessels is hypothesized to initiate vascular atheroma formation.

The relationship of inflammation to cardiovascular disease has begun to focus on immunogenic heat shock protein 60 (HSP60) as a signaling molecule capable of mediating and influencing a range of inflammatory responses correlated in both the bacteria and the host.33 A number of researchers have independently reported a connection between chronic periodontitis, atherosclerosis, and HSP60.34,35 Clinical studies have indicated a relationship between oral health and cardiovascular disease.36-47 However, due to the obvious risk factors shared in common, such as diabetes, smoking, diet, elevated serum CRP, etc., it is unlikely that a direct singular causal relationship will be established.48-50 Nevertheless, it is critical to weigh the existing evidence and continue to test the hypothesis that a positive clinical impact on atherosclerotic diseases may be attained by effectively treating periodontal disease and maintaining oral health over time.
Periodontal Pathogens and Diabetes

The relationship between diabetes mellitus (DM) and periodontal disease has been the subject of more than 200 articles published in English during the past 50 years. The overall available data strongly suggests that diabetes is a risk factor for gingivitis and periodontitis, so much as to call periodontitis the “sixth complication of diabetes,” along with retinopathy, neuropathy, nephropathy, macrovascular diseases and altered wound healing. Conversely, evidence has been increasing that periodontitis may affect the metabolic state of diabetic patients by worsening glycemic control and increasing the risk of diabetic complications. While the exact mechanism is unknown, a bidirectional relationship between the two conditions is suggested.

Acute bacterial and viral infections have been shown to increase insulin resistance in people without diabetes, often persisting for months after clinical recovery. The chronic inflammatory state potentially induced by periodontitis may increase insulin resistance in a similar manner in diabetics. In conjunction with chronic gram-negative bacteria present in periodontitis, glycemic control is negatively impacted.

A two-year longitudinal study of Type 2 DM patients reported those with severe periodontitis to have a six times greater risk for worsening glycemic control than patients without periodontitis. Studies also support a connection by evaluating other diabetic complications. An 11-year case control study reported that 82 percent of diabetic patients with severe periodontitis had one or more macrovascular complications such as angina, MI, heart failure, transient ischemic attack and stroke as opposed to 21 percent of DM patients without periodontitis. After adjusting for common risk factors, a prospective longitudinal trial of 628 patients found a 2.3 higher mortality rate from ischemic heart disease and an 8.5 times higher diabetic nephropathy rate in patients with severe periodontitis than those with milder periodontitis or no periodontal disease.

A recent meta-analysis of 10 intervention trials reported that periodontal therapy without antibiotics reduced HbA1c levels 0.4 percent from baseline on average and the addition of systemic antibiotics resulted in a 0.7 percent average reduction, neither of which reached statistical significance. Given the conflicting nature of the research to date, the evidence indicates that the connection appears strongest in patients with the poorest diabetic control and most severe periodontitis. In turn, these appear to be the patients in which co-coordinated treatment and management have the greatest effect.

Periodontal Pathogens and Pregnancy Outcomes

In obstetrics, as in medicine in general, there are very few “good” infections, and virtually all infections are considered a potential threat to the outcome of the pregnancy. Microbiological studies have reported relatively consistent findings that indicate that the risk of pre-term birth is greatest (4.7 risk ratio) among those patients exhibiting an inflammatory response, as indicated by the increase in cord serum levels of CRP, IL-1, IL-6, TNF, PGE2, and 8-isoprostane. These studies support the hypothesis that maternal periodontal infection without a protective maternal antibody response is associated with systemic bacteria transmission to the fetus.

In the medical literature, there are 13 epidemiologic case-control studies available, six find an association between periodontitis and pregnancy complications, three conclude an association may exist, and four noted no association. In the 10 available cohort studies, six indicated an association, one suggested an association may be present, and three reported no association. All of these studies varied in sample size, diversity of populations (race, sex, socioeconomic, etc.), and definition criteria for periodontal disease and pregnancy outcomes.

Only three randomized intervention studies have been published. All three studies reported a reduction in the rate of preterm delivery and an increase in birth weight. It should be noted that the results were not always statistically significant due to the sample size and may not have broad implication across all populations as the majority of the women participating were black and/or of low socioeconomic status.

A recent multi-center randomized, controlled intervention study concluded that while periodontal treatment is safe during pregnancy and effectively reduces periodontal disease, it did not significantly alter rates of preterm birth in samples of women judged to have early to moderate periodontitis. Patients with severe periodontitis were not the primary focus of the study. In weighing the available evidence, there does not appear to be a down-side to minimizing maternal chronic periodontal infection; the benefit for the fetus, while implied, still remains to be proven.
Periodontal Pathogens and Pneumonia

While little evidence exists that periodontal disease increases the risk of community-acquired pneumonia, there is evidence to support a connection in nosocomial occurrences. The risk of developing pneumonia for mechanically ventilated patients is estimated to be six to 21 times greater due to the bacteria that colonize the tube surface. Scannapieco compared bacteria in dental plaque in patients treated in medical ICUs to controls and found not only a greater level of colonization but a number of pathogens known to cause pneumonia only in the plaque of patients treated in the ICU – up to 100 percent of the aerobic flora was S. aureus, P. aeruginosa, or one of several enteric species. A separate finding was also made in the same study that indicated patients exposed to antibiotics in the same hospital setting had a greater chance of dental plaque being colonized by respiratory pathogens. The hypothesis is that competitive beneficial flora is inhibited. A number of similar studies corroborate the relationship of poor oral hygiene and respiratory pathogens in institutionalized patients.

A number of oral intervention studies have been conducted and a majority reported a reduced risk of pneumonia in nosocomial populations, as has a meta-analysis of studies published from 1966 to 2002. While studies also suggest oral intervention may help prevent ventilator-associated pneumonia, a recent double-blind multicenter trial showed no significant effect of oral intervention in the prevention of ventilator-associated pneumonia. Further study is needed to confirm efficacy as well as contributing factors such as medication induced xerostomia.

Conclusion

Caution is warranted while scientific evidence is weighed to determine the precise connection between oral and systemic health and what recommendations are to be made to patients. The American Dental Association (ADA) and American Medical Association (AMA) are co-sponsoring media events to highlight the trends in the current research emphasizing the need for cooperation among organized medicine. While further research is necessary to reach definitive conclusions on the connection between oral and systemic health, it has never been more important to:

- Practice good dental hygiene,
- Receive regular dental care,
- Include questions on dental health during a visit with a medical practitioner,
- Include questions on medical health during a visit with a dental practitioner, and
- Promote communication between medical and dental specialists.

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References:
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References:


