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### **Review Articles**

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### Periodontal Medicine-Oral Systemic Interrelation

#### Abstract

Periodontal disease refers to the inflammatory processes that occur in the tissues surrounding the teeth in response to bacterial accumulations, or dental plaque, on the teeth. The bacterial accumulations cause an inflammatory response from the body. The chronic and progressive bacterial infection of the gums leads to alveolar bone destruction and loss of tissue attachment to the teeth. A growing body of scientific evidence has shown that severe periodontitis may enhance susceptibility to certain important systemic diseases and conditions, for example, cardiovascular disease, diabetes mellitus, adverse pregnancy outcomes, and pulmonary infections. Therefore, patients diagnosed with periodontal disease may be at higher risk due to a compromised immune system. Dental and medical practitioners should be aware of the clinical implications of these inter-relationships and treat affected patients in collaboration for better oral and general health.

#### **Key Words**

Periodontal disease, cardiovascular disease, diabetes mellitus, adverse pregnancy outcome, pulmonary infection.

#### Introduction

For decades, physicians and dentists have paid close attention to their own respective fields, specializing in medicine pertaining to the body and the oral cavity, respectively. However, recent findings have strongly suggested that oral health may be indicative of systemic health. Currently, this gap between allopathic medicine and dental medicine is quickly closing, due to significant findings supporting the association between periodontal disease and systemic conditions such as cardiovascular disease, type 2 diabetes mellitus, adverse pregnancy outcomes, and osteoporosis (1).

Periodontitis, one of the most common diseases of humans, is an infectious condition that can result in the inflammatory destruction of periodontal ligament and alveolar bone. In light of the extensive microbial plaques associated with periodontal infections, the chronic nature of these diseases, and the exuberant local and systemic host response to microbial assault, it is reasonable to hypothesize that these infections may influence overall health and the course of some systemic diseases (2).

The term Periodontal Medicine, as first suggested by Offenbacher (1996), can be viewed as a broad term that defines a rapidly emerging branch of Periodontology

focusing on the wealth of new data establishing a strong relationship between periodontal health or disease and systemic health or disease. This means a two-way relationship in which periodontal disease in an individual may be a powerful influence on an individual's systemic health or disease as well as the more customarily understood role that systemic disease may have in influencing an individual's periodontal health or disease (3). The possibility that morbidity and mortality from systemic diseases may be reduced by improving periodontal health makes it imperative that this relationship be examined more closely (4).

### Nature of periodontal disease as infectious burden to systemic health

It is estimated that 104 normal or commensal microbes reside on the surfaces of teeth, prosthetic implants, dentures, dental restorations, and the mucosal epithelia lining the oral cavity, respiratory tract, gastrointestinal tract, and urinary tract. The oral cavity contains almost half the commensal bacteria in the human bodyapproximately six billion microbes representing 300 to 500 species (5). In certain conditions, some of these microorganisms may become opportunistic species that contribute to local and/or systemic infections. It is known that the oral microbial ecosystem is highly dynamic and <sup>1</sup> Bansi M Bhusari <sup>2</sup> Rizwan M Sanadi <sup>3</sup> Kavita G Pol

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the oral cavity faces a constant challenge of opportunistic infections and various oral complications of systemic diseases and disorders (6).

Periodontal lesions are recognized as continually renewing reservoirs for the systemic spread of bacterial antigens, Gramnegative bacteria, cytokines, and other proinflammatory mediators (1, 7). In a patient with moderate-to advanced periodontitis and a relatively complete dentition, it has been estimated that the total area of pocket epithelium in direct contact with subgingival biofilms is surprisingly large, being approximately 72 cm2- the size of the palm of the human hand (8).

Oral, especially periodontal, infections have been regarded as a source of focal infections for a long time. Miller originally published his 'focal infection theory' in 1891, indicating that "micro-organisms or their waste products obtain entrance of parts of the body adjacent to or remote from the mouth (5)."

Three different mechanisms by which oral bacteria may contribute to non-oral diseases have been described (9):

(1) Metastatic infection caused by translocation of bacteria;

(2) Metastatic injury related to microbial toxins; and

(3) Metastatic inflammation due to immune injury.

The focal infection concept has recently been given more attention by the dental and medical communities. This is largely due to improvements in methods of sampling, cultivation, and identification of bacteria that revealed the presence of microorganisms well known to be oral colonisers in a variety of infected non-oral sites (10). It is also possible that periodontal bacteria or their products can directly invade the periodontal tissues. This represents a distinct mechanism by which periodontal disease-associated bacteria may gain access to the systemic circulation (2).

Moreover, periodontal diseases may also exacerbate existing heart conditions. It is known that poor dental hygiene and periodontal or periapical infections may produce bacteraemias even in the absence of dental procedures (5). Bacteremias can be provoked by mastication and oral hygiene procedures such as toothpicking, flossing and toothbrushing. The extent to which bacteremia of oral origin occurs appears to be directly related to the severity of gingival inflammation. Thus, the best means to prevent bacteremia from the oral cavity is the maintenance of periodontal health (2).

### Organ Systems and Conditions Possibly Influenced by Periodontal Infection (11)

### Cardiovascular System:

Atherosclerosis Coronary heart disease Angina Myocardial infarction

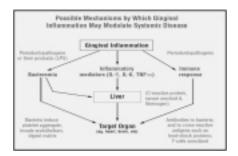
*Endocrine System:* Diabetes mellitus

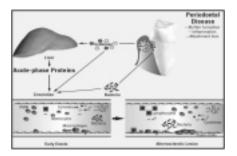
*Reproductive System:* Preterm low birth-weight babies Acute bacterial pneumonia

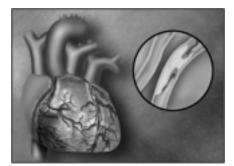
*Respiratory System:* Chronic obstructive pulmonary disease

### Cardiovascular diseases and Periodontal disease:

Cardiovascular disease (CVD) is a common cause of death, accounting for 29% of deaths worldwide (12). Estimates from the year 2002 show that more than 70 million Americans were diagnosed with one of the forms of CVD, which include high blood pressure, coronary heart disease (myocardial infarction and angina pectoris), peripheral arterial disease, and stroke, with atherosclerosis as the principal cause of all CVDs. Atherosclerosis is thus responsible for 50% of all mortality in the United States, Europe, and Japan (13). After adjustment of other risk factors, studies indicate that severe periodontal disease is associated with a 25% to 90% increase in risk for CVD (14). One study showed that 91% of patients with CVD demonstrated moderate to severe periodontitis, while 66% of cardiologically healthy patients had periodontitis. The same study showed a statistically significant correlation between coronary artery disease and periodontitis (15).







Periodontal disease & cardiovascular disease

Periodontal diseases might affect heart disease through the mechanism of oral bacteria, bacterial toxins, and induced inflammatory mediators entering the blood stream and contributing to chronic, systemic vascular challenge, directly resulting in platelet aggregation, adhesion, and vasculitis, with the subsequent cholesterol deposition, thromboembolic events, and atheroma formation (4, 8). Another possibility is that the inflammation caused by periodontal disease induces inflammatory cell infiltration into major vessels, vascular smooth muscle proliferation, vascular fatty degeneration, and increasing plaque build-up, which contribute to swelling and thickening of the arteries (5). These events may lead to atherosclerosis and atheroma formation. and result in obstruction of normal blood flow, restricting the amount of nutrients and oxygen required for the heart to function properly, and eventually increase the risk of heart attacks.

In addition, CVD and periodontal diseases have a number of common characteristics and may share a similar causative pathway through a hyper-inflammatory phenotype, for example, increased release of inflammatory cytokines and relevant mediators (4).

Whatever mechanisms are involved, it is evident that periodontitis may affect the host's susceptibility to systemic disease through subgingival biofilms acting as reservoirs of gram-negative bacteria and creating transient bacteremia, through release of microbial toxins and through a reservoir of inflammatory mediators. In parallel, all these factors are capable of predisposing the host to vascular changes or disorders. Further studies are required to find ways of intercepting these pathological changes, which may involve developing new generations of antimicrobial, antiinflammatory, anti-infective or antithrombotic therapeutic agents (16).

## Diabetes mellitus and Periodontal disease:

Diabetes mellitus is a metabolic disorder characterized by hyperglycaemia due to the defective secretion or activity of insulin. The condition affects more than 16 million people in the United States (17). Diabetes mellitus can be divided into three classifications according to signs and symptoms: type 1, type 2, and gestational. Type 1 diabetes mellitus results from the destruction of beta-cells within the islets of Langerhans of the pancreas, which leads to complete insulin deficiency. Type 2 diabetes mellitus ranges from insulin resistance progressively leading to pancreatic beta-cell failure. Lastly, gestational diabetes mellitus is a glucose intolerance that begins during pregnancy. The number of adults diagnosed

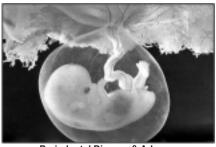
with type 2 diabetes worldwide is expected to grow from 135 million in 1995 to approximately 300 million in 2025 (18). People with type 2 diabetes constitute 90% of the diabetic population (19).

It has been known for years that patients with uncontrolled diabetes have a high risk for periodontal diseases (5). While in recent years, at least one study has shown a twoway relationship between periodontal disease and diabetes mellitus. Increasing scientific evidence shows that acute infections may alter the endocrinologicmetabolic status of the host, thus leading to difficulty with glycaemic control. Periodontal infection may adversely influence glycaemic control in diabetes and decrease insulin-mediated glucose uptake by skeletal muscle, resulting in poor glycaemic control. Moreover, induced production of pro-inflammatory mediators in periodontal disease also mediates insulin resistance and reduces insulin action (8). It is conceivable that unresolved periodontal disease could also increase blood sugar, contribute to increased periods of time when the body functions with high blood sugar, and make it harder for patients to control their blood sugar, putting poorly controlled patients with diabetes at a higher risk of the complications of the condition (5).

It has been shown that periodontal treatment directed at elimination of pathogenic species and controlling inflammation may have a positive impact on glycaemic control by restoring insulin sensitivity in poorly controlled patients with diabetes, possibly by suppressing glycosylation of proteins, formation of advanced glycation endproducts, and activities of matrix metalloproteinases and other inflammatory mediators (8). Recent studies have shown that effective control of periodontal infection in patients with diabetes may reduce the level of advanced glycation endproducts in the serum (20). In this regard, prevention of periodontal diseases and control of established periodontal diseases should be considered an integral part of diabetes control (19).

### Adverse pregnancy outcomes (PLBW) and Periodontal disease:

Preterm low-birth weight (PLBW), as defined by the 29th World Health assembly in 1976, is a birth weight of less than 2500 grams with a gestational age of less than 37 weeks. Low birth weight can be a result of this short gestational period and/or retarded intrauterine growth (1). Preterm and / or low birth weight (PT/LBW) continues to be a significant cause of infant morbidity and mortality. PT/LBW is associated with risk for mortality in the first year of life, with developmental problems in childhood, and with risk of several diseases in adulthood (21). The prevalence of preterm birth varies from 6% to 15% of all deliveries, depending on the population studied, and the prevalence has risen in recent years (22). It is known that various risk factors, such as older (greater than 34 years) and younger (less than 17 years) maternal age, inadequate prenatal care, smoking, drug and alcohol abuse, hypertension, genitourinary tract infection, diabetes mellitus, and multiple pregnancies contribute to adverse pregnancy outcomes (4, 5, 23).



Periodontal Disease & Adverse Pregnancy Outcome

However, the recognised risk factors alone do not wholly account for the high prevalence of preterm low-birth-weight infants. An important factor contributing to this problem is the effect of maternal burden of infection such as bacterial infection of the genitourinary tract and bacterial vaginosis (5, 24, 25). Other than local infection of the genitourinary tract, potential infections distant from the placental complex or the genitourinary tract, due to an indirect action of translocated bacterial products such as lipopolysaccharide (LPS) and/or the action of maternally induced inflammatory mediators may adversely affect pregnancy outcomes (5, 25, 26). Therefore, periodontal disease might be a newly considered risk factor of adverse pregnancy

Periodontal pathogens, being gramnegative anaerobic bacterial species, may cause inflammation of the placental membrane. Bacterial lipopolysaccharide triggers release of a variety of biologically active mediators [(eg: interleukin I-beta (IL-1?), tumor necrosis factor-alpha (TNF-?) & prostaglandin E2 (PGE2)] which may contribute to premature labour. Periodontal infections may also impair foetal growth and trigger increased levels of biological fluids that induce preterm labour. Case control studies showed that preterm deliveries were 7.5-fold more common in women with severe periodontal disease than in those with good periodontal health. Women whose periodontal condition worsens during pregnancy have an even higher risk of having a premature baby (5). Hence, periodontal disease has the potential to influence preterm low birth weight through an indirect mechanism involving inflammatory mediators or a direct bacterial assault on the amnion (27).

### Respiratory diseases and Periodontal disease:

The pneumonias are a group of diseases caused by a wide variety of infectious agents, including bacteria, mycoplasma, fungi, parasites, and viruses, resulting in infection of the pulmonary parenchyma. Pneumonia can be a life-threatening infection, especially in the elderly and immunocompromised patient and it is a significant cause of morbidity and mortality in patients of all ages. It is also possible that other pulmonary diseases may be adversely influenced by oral conditions. Chronic bronchitis is an inflammatory condition associated with excessive tracheobronchial mucous production sufficient to cause cough with expectoration for at least 3 months of the year for 2 or 3 successive years. Emphysema is the destruction of the air spaces distal to the terminal bronchiole with destruction of the alveolar septa. Chronic obstructive pulmonary disease (COPD) is characterized by chronic obstruction to airflow due to chronic bronchitis and / or emphysema. It is possible that aspiration of (oral) bacteria may exacerbate the course of COPD(2)

It is known that one of the most common routes of infection for bacterial pneumonia is aspiration of oropharyngeal contents (28). Oral bacteria have been implicated in the pathogenesis of this disease and, in this regard, dental plaque might be an important reservoir for these potential pathogens (29). It has been shown that bacteria that grow in the mouth and throat can be aspirated into the lower respiratory tract and lungs to contribute to respiratory diseases such as pneumonia or worsening lung conditions. A recent epidemiological study showed that people with poor oral hygiene were 4.5-fold more likely to have chronic respiratory

disease than those with satisfactory oral hygiene (5). A 25-year longitudinal study showed that alveolar bone loss due to periodontal diseases at baseline was an independent predictor of chronic obstructive pulmonary disease incidence (30). However, there is no strong evidence that periodontal diseases directly cause chronic obstructive pulmonary disease. Rather, periodontal disease may be an indicator of risk for lung disease, and these two disease conditions may share a common host susceptibility factor related to an underlying inflammatory response trait (4). Perhaps aspiration of saliva into which oral bacterial antigens, lipopolysaccharide and enzymes have been released promotes inflammation and infection of the lower airway. It is also possible that host-derived mediators such as cytokines and prostaglandins, which are elevated in the saliva of subjects with periodontal disease, promote lung inflammation and infection if aspirated into the lower airway. The possibility that bacteria in oral biofilms influence respiratory infection suggests that good oral hygiene may prevent the aspiration of large numbers of oral bacteria into the lower airway and thus prevent initiation or progression of respiratory infection in susceptible individuals. Further studies are required to verify the importance of oral conditions in the pathogenesis of lung diseases such as COPD(16).

#### Suggestions for the treatment of patients with systemic diseases or conditions (5)

### Cardiovascular diseases:

Patients with CVD and those known to be at risk for CVD, from family history or from examination, for example, hypercholesterolaemia, should be advised to have a comprehensive periodontal examination and to undergo appropriate periodontal treatment as indicated on the basis of dental history and the findings of a periodontal examination. The importance of long-term control of periodontal diseases should be part of comprehensive health education for such patients.

### **Diabetes mellitus**

Patients with diabetes, especially those for whom control of the disease proves to be difficult and those at risk of developing the disease, should be advised to have a comprehensive periodontal examination and to undergo appropriate periodontal treatment as indicated. Physicians should recognise periodontitis as a complication of diabetes mellitus and as a condition that, if **Conclusion** left unresolved, can complicate the management of diabetes mellitus. From a dental point of view, patients with diabetes mellitus should have a functioning dentition maintained or receive adequate oral rehabilitation for good function.

### Pregnancv

Expectant mothers should be advised to have a comprehensive periodontal examination prior to pregnancy or as soon thereafter as possible and preventive periodontal care should be instituted to prevent pregnancy gingivitis. Appropriate periodontal treatment at a suitable stage of pregnancy should be delivered to pregnant women with active periodontitis to help reduce the risks of adverse pregnancy outcomes.

### **Pulmonary diseases**

Patients with chronic obstructive pulmonary diseases and those at risk of developing such diseases should be advised to have a comprehensive periodontal examination and to undergo appropriate periodontal treatment as indicated.

### Dentist and doctor collaboration for better health

The advent of so-called periodontal medicine will promote a strong collaboration of dental professionals and medical professionals for better diagnosis and treatment across specialities. With medical doctors and dentists working closely together, more patients with systemic diseases are likely to be successfully treated, and patients will benefit from predictable treatment regimens to save and rehabilitate their dentition. The promotion of health and management of disease should require interdisciplinary education, updated knowledge and treatment strategies, and state-of-the-art health care delivery. While recognising and upholding the separateness of the dental and medical professions and sustaining and expanding the body of knowledge and practice that has developed since the foundation of dentistry as a separate profession from medicine, further integration of dental and general medicine requires a better communication between dentists and medical doctors, and more responsibilities and effective team approaches in the clinical management of their shared patients for better oral health and general health (5).

Extraordinary progress is being made in understanding the relationship between periodontal disease and systemic health. Periodontitis, one of the oldest and most common diseases of humans, was once generally believed to be an inevitable consequence of aging. However, we have learned over time that not all people, nor all populations, are at equal risk of developing periodontitis. An increasing body of epidemiological and experimental work has helped to identify specific risk factors and risk indicators, permitting better understanding of what makes an individual more susceptible to periodontal disease. This new knowledge gives increasing emphasis to the important role that systemic factors, diseases, and conditions may play in the causation and progression of periodontal disease. Dentistry has also become more cognizant of the extent to which behavioral factors play a role in risk. One goal of such investigations is that they may enable us to better identify individuals susceptible to periodontal disease in order to more effectively prevent and treat the disease (4).

The advent of periodontal medicine may also change the traditional objectives of periodontal treatment. The evaluation of success may shift from one focused on preventing attachment loss to one focused more on measurable reductions in the bacterial infection burden or reducing the levels of inflammatory mediators at involved sites. Oral health is an important component of general health, and individuals with periodontitis may be at risk for other diseases as well. The future of dental practice will be dramatically altered if subsequent research confirms that periodontal disease is a true risk factor for systemic disease and that the initiation or progression of these medical conditions can be reduced by periodontal treatment (4).

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