

Gum Bugs Hit Heart: State-of-the-Science

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ABSTRACT

Gingival bleeding is a hallmark of chronic periodontal disease; it is likely that the bacteria associated with this disease may produce a low level bacteraemia over extended time periods and the periodontal bacteria enter the bloodstream and travel to major organs like the heart. Microbial infections associated with periodontal disease contribute to cardiovascular disease via transient bacteraemia. Inflammatory and immunological mechanisms which may link periodontal infection and athermanous diseases may be numerous and diverse, potentially involving various cellular and molecular components, direct effects of bacteremia and indirect effects of periodontal tissue inflammation.

Keywords: Perio-cardio pathogenesis, Atheroma, periodontitis, Anthrogenes

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INTRODUCTION

Oral Health continues to be a major public health problem worldwide and despite the major advances in understanding, prevention and treatment, which have occurred over a past century, common oral conditions, such as gingivitis and chronic periodontitis, are still among the most prevalent microbial diseases of mankind. Over the past 50 years, there has nevertheless, been a significant increase in the number of people retaining more of their natural teeth, such that this increasingly dentate population is at further risk of periodontal disease. The mouth is thus, a significant contributor to both the total burden of infection and the total burden of inflammation and, to overall health being.

Periodontal disease is a chronic mixed infection of gram-positive microorganisms such as *Peptostreptococcus micros* and *Streptococcus intermedius* and gram-negative bacteria such as *Porphyromonas gingivalis*, *Prevotella intermedia*, *Bacteroides forsythus*, *Actinobacillus actinomycetemcomitan* (1). It is of insidious outset in that the affected individuals may not be aware of any symptoms in the earlier stages of disease development. The chronic infection of periodontitis may develop symptom-free for many years prior to the clinical manifestation and thus the periodontal disease goes untreated for years (2).

Gingival bleeding is a hallmark of chronic periodontal disease; it is likely that the bacteria associated with this disease may produce a low level bacteraemia over extended time periods and the periodontal bacteria enter the bloodstream and travel to major organs like the heart. In addition to the direct effects of microorganisms on vascular tissue, it is also feasible that indirect effects involving inflammatory and immune factors may also be responsible for contribution of periodontitis to the etiology of cardiovascular disease.

Cardiovascular Diseases including acute myocardial infection and angina pectoris are major health problems in developing countries and are considered amongst most common medical problems in the general population. (3)

Annual mortality from CVD is about 12 million cases per year and are responsible for 30% of all deaths. (4,5)

CVD are estimated to have led to 1.59 million deaths in India in year 2000 and this figure is projected to increase to 2.03 million for the year 2012.(6)

Beck J *et al* (7) Offenbacher *et al* (8) and Ernesto D *et al* (9) proposed that the pro-atherogenic markers from chronic bacterial infection of periodontitis may promote and modify atherosclerosis (7,8) by a

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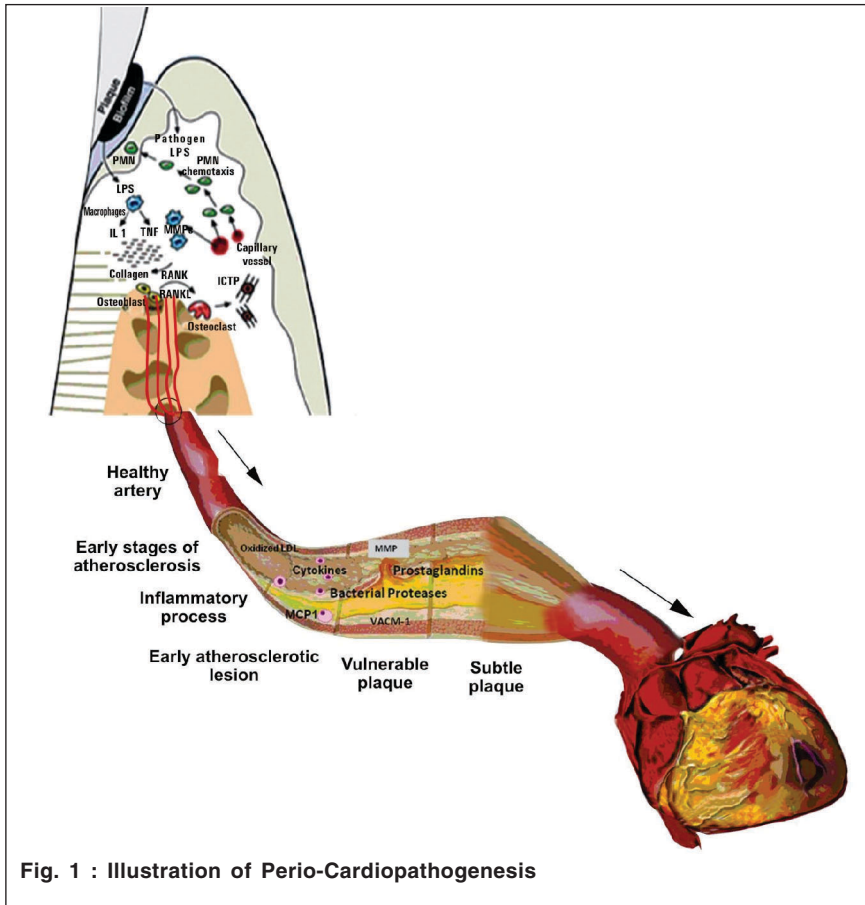


Fig. 1 : Illustration of Perio-Cardiopathogenesis

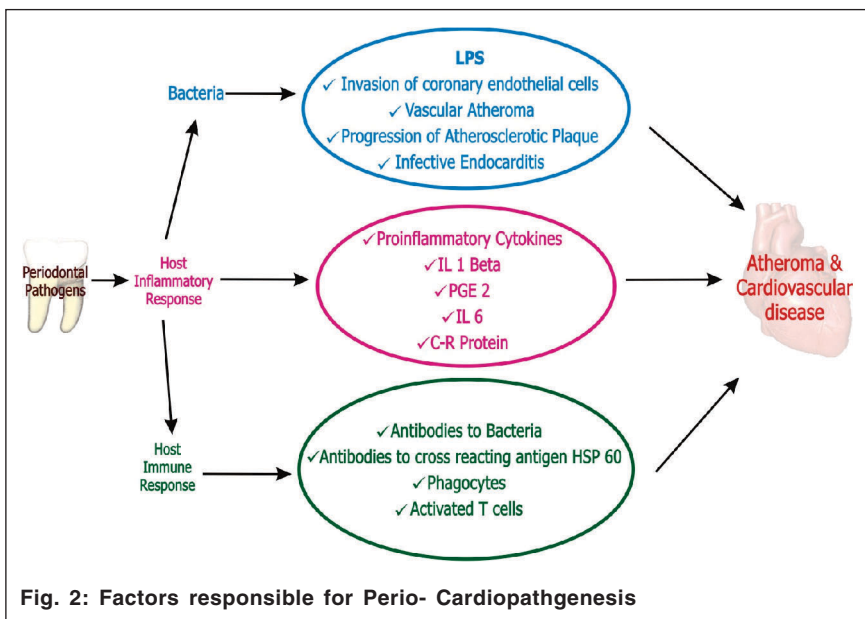


Fig. 2: Factors responsible for Perio- Cardiopathogenesis

mechanism that involves bacterial pathogens, bacterial antigens, endotoxins and inflammatory cytokines. The interaction between microorganisms, microbial products, lipopolysaccharides (LPS) and the host immune /

inflammatory response is fundamental in interpreting the sequence of events leading to perio-cardio pathogenesis (10) (Fig. 1).

All of these factors either contribute or modify the process of atherogenesis (7).

These atherosclerotic plaques result in decreased vascular patency and /or decreased compliance of vessel wall and ultimately these plaques may embolize and/or rupture leading to vessel obstruction and a cardiovascular pathology (Fig. 2).

PERIO- PATHOGENS AS ATHEROGENS

Microbial infections associated with periodontal disease contribute to cardiovascular disease via transient bacteraemia. Transient bacteremias from inflamed gingival tissues introduces the pathogenic microorganisms from sub-gingival plaque bio-films into the bloodstream causing pathologic damage to blood vessels and promote clot formation. Periodontal pathogens themselves have been shown to increase platelet aggregation and thromboembolic events (11,12). The pathogens associated with periodontal infection were identified on atheromas, which supports the etiological role of these pathogens in cardiovascular disease (13). Studies on human atheromas obtained during endarterectomy have found multiple periodontal pathogens in the atheromas, including *P.gingivalis*, *P.Intermedia*, *B.forsythus* and *A. Actinomycescomitansq* (14,15).

P. gingivalis, the major bacterial pathogen in adult periodontitis possess platelet-aggregation capability unique among sub gingival plaque microorganisms (16,17,18) and is a common inhabitant of atheromatous plaques removed from carotid and coronary arteries. *P. gingivalis* can induce platelet activation and aggregation through the expression of collagen-like platelet aggregation-associated proteins which play a role in increased serum lipid levels, (19) thrombus formation (20,21), enhanced atheroma formations as well as increased calcification of the atherosclerotic plaques and increased levels of proinflammatory mediators such as IL-6, vascular cell adhesion molecule-1, and matrix metalloproteinase-2 in an animal model (12,22).

P. gingivalis and other pathogenic bacteria are able to induce foam cell formation (an important characteristic of cardiovascular disease) in macrophage cell line, which is mediated by LPS fraction of the cell. LPS promotes atherosclerosis and thrombus formation (23,24) and the rupture of the atherosclerotic plaque appear to be an important factor in acute coronary syndrome (25).

Finally, *P. gingivalis* has been shown to produce a mammalian endothelin-converting enzyme, which activates endothelin, a powerful vasoconstrictor involved in hypertension (26).

PERIO-CARDIOPATHOGENESIS: STATE-OF-THE-SCIENCE

Periodontal disease represents an excellent and a unique model of chronic infection. The relationship between cardiovascular disease and periodontal infection can be dependent on the risk factors both diseases have in common (27,28,29), but there may be a more direct relationship resulting from the systemic effects of periodontal disease. Inflammatory and immunological mechanisms which may link periodontal infection and atheromatous diseases may be numerous and diverse, potentially involving various cellular and molecular components, direct effects of bacteremia and indirect effects of periodontal tissue inflammation.(30,31).

Inflammatory mechanisms

Various studies have also shown an association between dental health and acute myocardial infarction and atherosclerosis (32,33,34).

Inflammatory periodontitis increase the risk of cardiovascular disease (31,34). Subjects with the severe probing depths and bone loss at baseline had higher risk for developing cardiovascular disease than those with minimal periodontal diseases or gingivitis (35,36,37). The inflammation-induced injury damages the intact gingival tissue barrier allowing the bacteria access into the systemic circulation.

Gram-negative pathogens may cause

vascular events via LPS and inflammatory cytokines, contributing to the pathogenesis of cardiovascular disease (31) macrophages can be stimulated by many factors produced during periodontal infections, leading to the production of IL-1 α and β , TNF- α , IL-6, (all of which stimulate bone resorption) and matrix metalloproteinase (which digests collagen).

An additional factor is an exaggerated host response to LPS mediated by the existence of hyper responsive monocytic cells. Such monocytes play a role in atheroma formation and provide a biological basis that link the periodontal infection to cardiovascular disease. The interaction between monocytes and LPS may be related also to thrombogenesis, atheroma and congestive heart disease (38,39,40).

Various cytokines and intercellular adhesion molecule -1(ICAM-1) can initiate platelet adhesion and aggregation, promotes the formation of lipid-laden foam cells and the deposition of cholesterol in the intima. Also cytokines released from monocyte, together with periodontal pathogens will increase smooth muscle proliferation leading to thickening of the vessel wall that predisposes to atheroma formation (41,42).

Periodontal infection contribute to elevated systemic C- reactive protein (CRP) level, which depend upon the severity of the disease after adjusting for age, smoking, body mass index, triglycerides and cholesterol (43,44). Elevation of C- reactive protein has been found to be a predictor of increased risk for cardiovascular diseases (39). The link between cardiovascular disease and periodontitis is explained by the fact that levels of von willebrand's factor antigen are higher in patient's with giant cell arteritis and gram-negative infection of relevance to thrombogenesis. Endotoxins from gram-negative bacteria will induce the release of von willebrand's factor antigen from human endothelial cells (45).

Immune response

Periodontal pathogens stimulate a strong

immune response, leading to a marked response of high levels of serum IgG antibodies (46). Periodontal pathogens like *P. gingivalis* (40); *A. actinomycetemcomitans*, and *B. forsythus* express HSP (Heat shock proteins) homology to GroEL, the bacterial homologue of human HSP 60. Induction of HSP-60 as a response to environmental and metabolic stress in the infected host tissue which share antigenic determinants with bacterial heat shock protein can lead to production of antibodies to cross reacting antigens, and immune complex formation, ultimately resulting in immune complex-mediated pathology (40,41).

The periodontal infection causes a T-cell response leading to an increased number of CD8 T-suppressor cells and a decreased count of CD4 T-helper cells (41,42).

Genetics

It suggests that persons jointly affected by periodontitis and cardiovascular disease exhibit a genetically determined hyper inflammatory immune response to bacterial attack. Abnormally elevated secretion of tissue damaging and pro-inflammatory mediators like PG-2 and IL1-b from peripheral blood monocytes in hyper inflammatory positive phenotype individuals lead to the increased risk for both periodontitis and congestive heart disease.

CONCLUSION

Periodontal disease is highly prevalent; especially in the late middle age when coronary artery disease is also most common. Hence, even a modest effect of periodontal disease on the incidence of cardiovascular disease makes this exposure an important public concern. Dental and medical practitioners should be aware of this silent risk factor of gingival and periodontal disease to intelligently interact with inquiring patients to maintain medical surveillance of their cardiovascular status. Thus, it may then be fair to conclude that the gums are a foundation for health and well being of the whole body and not just the only mouth. Given the clear indicators present and the additional benefit of a

lifetime of happy smiles and healthy teeth, the advantage of regular check-ups and other preventive care for teeth and gums are apparent to prevent the initiation or progression of perio-cardiopathogenesis.

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