

REVIEW ARTICLE

Systemic manifestations of oral diseases

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ABSTRACT

The oral cavity is the site of much infectious and inflammatory disease which has been associated with systemic diseases such as diabetes, cardiovascular disease and pre-term low births. This article emphasizes on the oral-systemic disease connection which is now a rapidly advancing area of research. The possible systemic diseases which arise from oral microorganisms are hereby focused.

Key words: Cardiovascular disease, diabetes, oral microorganisms, oral-systemic connection, pre-term low births

INTRODUCTION

The oral cavity might well be thought of as the window to the body as oral manifestations accompany many systemic diseases. But with recent research it may be said that the oral cavity has opened a door for many systemic diseases. The concept of ‘focal infection’ was propounded by Dr. William Hunter in 1910, whereby disease at a distant site, such as the mouth, could contribute to diseases such as anaemia, gastritis, colitis and so on. This theory is currently being carefully reconsidered. At the landmark conference at the University of North Carolina in Chapel Hill in March 1997 was devoted to this theme, that periodontal disease itself can instigate conditions such as cardiovascular disease, low birth weight babies, and that periodontal therapy may contribute to the control of diabetes.^[1]

In addition, conditions such as diabetes have been shown to increase the risk of periodontal disease. Conversely periodontal therapy may improve the diabetic condition by stabilizing the systemic blood sugar levels.

New studies reveals increased incidence of coronary heart disease and stroke linked to high incidence of periodontal bone loss.^[1,2]

It is becoming increasingly clear that infections and chronic inflammatory conditions such as periodontitis may influence

the atherosclerotic process. They may increase haemostatic variables which promote haemostatic plugs and thrombi and rheological variables (which affect blood flow), both of which play important roles in the pathogenesis of vascular diseases (viz ischemic heart disease, stroke, and peripheral arterial disease).^[1]

PATHOBIOLOGICAL MECHANISMS

Evidence obtained over the past decade clearly identifies inflammation as a critical mediating factor in the development of cardiovascular diseases,^[3] in which prostaglandins and other inflammatory mediators are greatly elevated.^[3,4] C-reactive protein is increased in individuals with periodontal infections and is also an important risk factor for myocardial infarction.^[3,5] These types of associations have led to the simplistic model that inflammatory mediators from periodontal infections may impact on other, remote organs and tissues; or that systemic spread of periodontal pathogens may settle out on blood vessel walls and there promote atheroma formation.^[3]

PATHWAY FOR ORAL INFECTION

Three mechanisms or pathways linking oral infections to secondary systemic effects have been proposed. These are metastatic spread of infection from the oral cavity as a result of transient bacteremia, metastatic injury from the effects of circulating oral microbial toxins, and metastatic inflammation caused by immunological injury induced by oral microorganisms.^[6,7]

1. Metastatic infection from oral cavity via transient bacteremia:.....Subacute infective endocarditis, acute bacterial myocarditis, brain abscess, cavernous sinus thrombosis, sinusitis, lung abscess/infection, Ludwig’s angina,orbital cellulitis, skin ulcer, osteomyelitis, prosthetic joint infection
2. Metastatic injury from circulation of oral microbial

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toxins :.....Cerebral infarction, acute myocardial infarction, abnormal pregnancy outcome, persistent pyrexia, idiopathic trigeminal neuralgia, toxic shock syndrome, systemic granulocytic cell defects, chronic meningitis

3. Metastatic inflammation caused by immunological injury from oral organisms :.....Behcet's syndrome, chronic urticaria, uveitis, inflammatory bowel disease, Crohn's disease.^[6,8,9]

PERIODONTAL DISEASES AND ITS LINK TO SYSTEMIC DISEASES

The extent of the inflammatory burden caused by periodontal disease can influence systemic diseases with a similar inflammatory pathology and *vice versa*, raising an important issue regarding periodontal and systemic health affecting each other. It is relevant that uncontrolled diabetes mellitus is associated with more severe destructive periodontal disease. This damage appears to be worse in smokers and an association with existing cardiovascular disease has been identified.^[10]

Three biological mechanisms have been proposed to explain the association between periodontal disease and cardiovascular disease [Figure 1]:

- Bacteria from the periodontal infection enter the blood and invade heart and blood vessel tissue causing harmful effects.
- The body responds to the periodontal infection with the production of inflammatory mediators that travel through the blood and cause harmful effects on the heart and blood vessels.
- Bacterial products such as lipopolysaccharides enter the blood and cause harmful effects on the heart and blood vessels.^[11]

Periodontal disease and cardiovascular disease

Several laboratory and animal studies have demonstrated that the oral bacterium *Porphyromonas gingivalis* can colonize cells in the coronary artery and produce structural and immunologic changes associated with early heart disease.^[12] Bacteria that naturally attach to our teeth are displaced and pass into the bloodstream during a dental procedure, flossing, or even chewing food. These microbes while relatively harmless in the mouth, have an affinity for damaged endothelial cells or blood clots in the heart, where they attach, multiply, and form larger bacterial colonies that trigger the endocarditis. Scientists have shown that immune cells called monocytes are prominently found in early inflammatory lesions linked to endocarditis.^[13] What's been puzzling is the monocytes tend to disappear from the lesions over time without becoming macrophages, a scavenging immune cell formed from monocytes that removes debris from tissues, such as the damaged, bacteria-laden cells linked to endocarditis. C-reactive protein has been reported to be elevated in

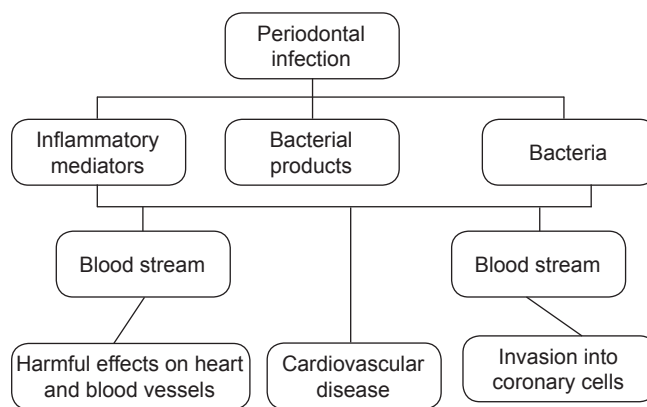


Figure 1: Pathway showing periodontal infection leading to cardiovascular disease

people with periodontal disease, and recent studies found that testing for this protein may be predictive of developing heart disease.^[14] Periodontitis and atherosclerosis have complex aetiologies, genetic and gender predispositions and may share pathogenic mechanisms as well as common risk factors. C-reactive protein (CRP) is gaining recognition as a risk factor for atherosclerosis. Recent work by Slade *et al.*^[1,15] has demonstrated increased levels of CRP in patients with periodontitis even after controlling for established risk factors for elevated CRP. The severity and chronicity of periodontal disease provides a rich source of subgingival microbial and host response products and effects over a long time period. Thus there are clear mechanisms whereby diseases such as periodontitis, which is a chronic inflammatory condition initiated by microbial plaque, could contribute to cardiovascular disease. Two main processes: the bacteraemia or lipopolysaccharide related responses; and the hyper-responsive monocyte phenomenon show promise in providing the aetiopathogenic link between these two diseases.^[1]

PERIODONTAL DISEASE AND DIABETES

The data from well-designed clinical studies indicate that periodontal diseases may have a significant impact on the maintenance and ongoing treatment of diabetic patients as shown in Figure 2. Several studies have shown that diabetic patients with periodontal disease are able to maintain lower blood glucose levels more easily and with lower doses of insulin once their periodontal disease has been treated effectively. These types of findings have significant long-term health benefits for these patients: prevention of the onset of diabetic complications including blindness and kidney failure not only affects a patient's quality of life, they also have a significant benefit for our already overtaxed healthcare system.^[3,16]

Periodontal disease and preterm birth

Oral infections seem to increase the risk for or contribute to low birth weight in newborns. Low birth weight, defined as a birth

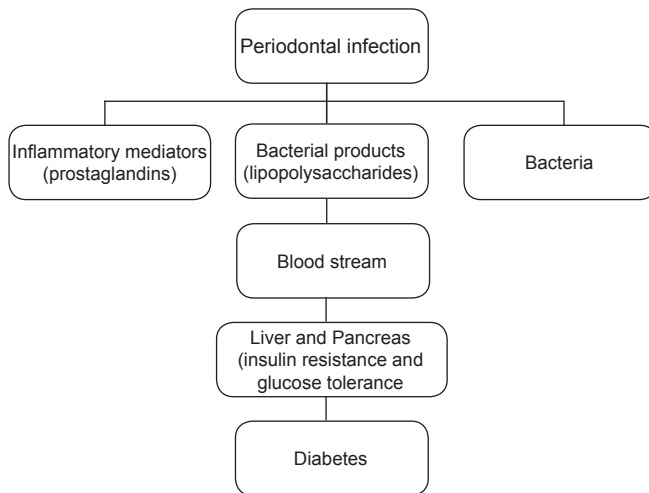


Figure 2: Pathway showing link between periodontal infection and diabetes

weight of <2,500 g, is a major public health problem in both developed and developing countries. Evidence of increased rates of amniotic fluid infection, chorioamnion infection, and chorioamnionitis supports an association between preterm birth or low birth weight and infection during pregnancy.^[6,17] This suggests that distant sites of infection or sepsis may be targeting the placental membranes.^[6,18] Human case-control studies have demonstrated that women who have low-birth-weight infants as a consequence of either preterm labor or premature rupture of membranes tend to have more severe periodontal disease than mothers with normal- birth-weight infants.^[6,17]

In some reports, treatment of periodontal infections was associated with reduced pre-term births and with improved diabetic control.^[3,19] It has been proposed that preterm labour is induced by infection or inflammation at a distant site from the uterus which leads to the release of prostaglandins (pro-inflammatory molecules) that cause inappropriately timed uterine contractions.^[3,4]

Bacteria from a mother's mouth can be transmitted through the blood and amniotic fluid in the womb to her unborn child. This could contribute to the risk of a premature delivery, a low birth weight baby, premature onset of contractions, or infection of the newborn child.

Cecilia Gonzales- Martin and colleagues from Queen Mary University of London tested the gastric aspirates (stomach contents containing swallowed amniotic fluid) of 57 newborn babies and found 46 different species of bacteria in the samples out of which 2 were recognized as coming from the mouth. Research by using DNA techniques to confirm the bacteria from the newborn matches the bacteria in the respective mother's mouth is in progress.^[20]

In light of the possible association between periodontal disease and preterm low birth weight babies, women who are considering pregnancy or who are pregnant should have

access to oral health services (including oral health promotion, disease prevention and treatment).^[21]

OTHER SYSTEMIC DISEASES CAUSED BY ORAL INFECTIONS

Aspiration of oral bacterial pathogens has been linked to pneumonia in the institutionalized elderly.^[3,22] In light of the clear association between periodontal disease and pneumonia in health-compromised seniors in intensive and long-term care, high-risk seniors should have access to oral health services (including oral health promotion, disease prevention- and treatment).^[21]

Further, patients with blood dyscrasias and white blood cell defects benefit by more frequent periodontal maintenance through the reduction of oral bacterial loads and the subsequent infections which often follow in these immunocompromised individuals.^[3,23]

CONTROVERSIES AND FUTURE STUDIES

There have been a very large number of studies conducted to test the validity of the relationships, for example, between periodontal destruction and prevalence of myocardial infarction and stroke. While some research centres in the USA, South America and Germany have shown increased risks for stroke of up to four-fold, other research groups can find no relationship.

Here we need to emphasize that the investigation into oral-systemic disease connections is a rapidly advancing area of research, and that new information is constantly appearing in the literature. Further studies on periodontal infections and systemic inflammation as a cause or as an exacerbating factor for the progression of cardiovascular diseases, metastasis from primary tumors in the oral cavity and if there is a link of immunological diseases is needed.

Increase in inter-professional collaboration and communication between dental hygienists and other health professionals is the need of the hour. We need to emphasize that the investigation into oral-systemic disease connections is a rapidly advancing area of research, and that the early identification of oral disease may contribute to the early diagnosis and treatment for a number of systemic diseases. A need for additional knowledge is required to link the inter-relationships between dentistry and medicine to further improve the management of overall health of patients which will further strengthen the partnership between dental and medical communities.

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