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***Grado en Odontología***

**SYSTEMIC IMPACT OF PERIODONTAL  
DISEASE**

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## **Abstract:**

**Introduction:** Periodontal disease is an infectious inflammatory disease of multifactorial origin, affecting the supporting tissues of the teeth and can lead to tooth loss. Bacteria can reach the bloodstream and thus reach other parts of the body through the ulcerated periodontal pockets. Periodontal disease may therefore be linked to certain systemic diseases such as diabetes, cardiovascular diseases, pregnancy complications, respiratory diseases and Alzheimer's disease, and could be a risk factor for them.

**Objective:** Performing a literature review, with the aim of understanding how periodontal disease affects certain systemic conditions and what the effects are.

**Material and methods:** A literature search was carried out in different databases such as Pubmed, Google Scholar, with the use of keywords limited by inclusion and exclusion criteria.

**Results:** It has been observed that periodontal disease can have an effect on systemic diseases such as: diabetes (in this specific case the relationship is bidirectional), cardiovascular diseases (in particular atherosclerosis), pregnancy complications (such as premature births, low birth weight infants and pre-eclampsia), respiratory diseases (including COPD), and Alzheimer's disease.

**Conclusion:** Numerous studies have correlated periodontitis with systemic pathologies. Because this relationship exists, the implication of each must be understood in order to make a proper diagnosis and ensure appropriate management

of the patient. However, the benefits of periodontal treatments on general health are not yet proven. It is therefore new research on periodontal therapeutics that must be initiated in the future.

**Key words:** Periodontitis, periodontal disease and treatment, systemic disease, diabetes, cardiovascular disease, pregnancy outcomes, respiratory disease, Alzheimer's disease.

## **Resumen:**

**Introducción:** La enfermedad periodontal es una enfermedad inflamatoria infecciosa de origen multifactorial, que afecta a los tejidos de soporte de los dientes y puede provocar la pérdida de estos. Las bacterias pueden llegar al sistema sanguíneo y así alcanzar otras partes del cuerpo a través de las bolsas periodontales ulceradas. Por tanto, la enfermedad periodontal puede estar relacionada con ciertas enfermedades sistémicas como la diabetes, las enfermedades cardiovasculares, las complicaciones del embarazo, las enfermedades respiratorias y la enfermedad de Alzheimer, y podría ser un factor de riesgo para ellas.

**Objetivo:** Realización de una revisión bibliográfica, con el objetivo de comprender cómo afecta la enfermedad periodontal a determinadas condiciones sistémicas y cuáles son sus efectos.

**Metodología:** Se realizó una búsqueda bibliográfica en diferentes bases de datos como, Pubmed, Google Scholar, con el uso de palabras clave limitadas por criterios de inclusión y exclusión.

**Resultados:** Se ha observado que la enfermedad periodontal puede repercutir en enfermedades sistémicas como: la diabetes (en este caso la relación es bidireccional), las enfermedades cardiovasculares (en particular la aterosclerosis), las complicaciones del embarazo (como los partos prematuros, bajo peso al nacer y la preeclampsia), las enfermedades respiratorias (EPOC) y la enfermedad de Alzheimer.

**Conclusión:** Numerosos estudios han correlacionado la periodontitis con patologías sistémicas. Dado que existe esta relación, es necesario comprender la implicación de cada una de ellas para realizar un diagnóstico adecuado y asegurar un tratamiento apropiado del paciente. Sin embargo, los beneficios de los tratamientos periodontales sobre la salud general aún no están demostrados. Por lo tanto, es necesario iniciar nuevas investigaciones sobre la terapéutica periodontal en el futuro.

**Palabras clave:** Periodontitis, enfermedad periodontal y tratamiento, enfermedad sistémica, diabetes, enfermedad cardiovascular, resultados del embarazo, enfermedad respiratoria, enfermedad de Alzheimer.

## 1. Introduction

Periodontology is defined as the study of the periodontium which are the supporting tissues of the tooth, be it anatomical, histological, physiological, pathological or therapeutic. It is the most medicalized discipline in dentistry. Periodontitis is an inflammatory and infectious disease, caused by bacteria in dental plaque, which results in the progressive destruction of the supporting tissues of the teeth. (1)

### ***1.1 Anatomy of the periodontium:***

The periodontium is the set of structures supporting the tooth which includes gingiva, alveolar bone, periodontal ligament, cementum. (2)

The gingiva belongs to the masticatory mucosa covering the alveolar process, it is made of an epithelial layer and the lamina propria which is a connective tissue. The alveolar bone is the part of the bone which forms and supports the socket of the teeth. The periodontal ligament surrounds the teeth and is made of cellular connective tissue. The cementum is a specialized, mineralized tissue that covers the root of the teeth. The primary function of the periodontium is to hold the tooth to the bone, and to protect it. Over more, it allows the distribution and reabsorption of the masticatory forces and those generated by occlusal contacts. (3)

Clinical examination of a healthy periodontium shows a pale pink gingiva of firm consistency with an orange peel granular surface appearance. It has a scalloped contour that follows the cemento-enamel junction and forms a papilla in the interdental spaces.

The other way round, when the gum becomes unhealthy, we can talk of periodontal disease. However, periodontal diseases are still little known to the general public.

## **1.2 Periodontal disease**

### *1.2.1 Evolution of periodontal disease*

Periodontal disease is an infectious disease whose main etiological agent is the presence of gram-negative anaerobic bacteria that cause an inflammatory reaction in the periodontal tissues. They are therefore multifactorial infectious diseases that usually begin with an inflammation of the gum (gingivitis) that gradually spreads to the deep tissues (periodontitis). The first step to periodontal diseases is the appearance of dental plaque. It is a biofilm that is deposited on the surface of the teeth and forms a whitish deposit; it is composed of cells, saliva and food. Saliva is a major actor of calculus formation, which is deposited at the base of the teeth and pushes back the gums. Subsequently, it causes an early lesion. (4)

The growth of the dental plaque will initially cause inflammatory manifestations, then secondarily, depending on the nature of the flora and the individual risk factors, a destruction of the gingival collagen, which then leads to the onset of gingivitis. If there is destruction of the alveolar bone, it will be periodontitis.

### *1.2.2 Gingivitis and periodontitis*

Gingivitis is a gingival inflammation without loss of attachment, the lesions are located at the gum margin tissue and the superficial periodontium. It results in redness, bleeding, swelling, increased gingival sensitivity and a smooth texture. It is the consequence of an accumulation of plaque in the gingival margin. (5)

Periodontitis is associated with the loss of connective attachment to the alveolar bone and the appearance of periodontal pockets. Clinically it appears as a more or less marked gum inflammation, an increase in dental mobility and secondary migrations that may destabilize the occlusion. The different degrees of periodontal disease are

defined according to several criteria: the presence and extent of bacterial plaque (calcified plaque more commonly known as calculus), the degree of inflammation or bleeding, the extent of attachment loss assessed with a periodontal probe. (6)

### *1.2.3 Diagnosis*

Clinical signs (bleeding, oedema, redness, halitosis, periodontal pocket) are the first elements of the diagnosis. This will require a more rigorous evaluation of the loss of attachment by the X-ray examination and by measuring, with a graduated periodontal probe the depth of periodontal pockets. (6)

### *1.2.4 Risk Factors*

Risk factors associated with the development of periodontal disease may be local, systemic and/or genetic. Bacterial colonization is not sufficient to cause disease. These risk factors include poor oral hygiene, smoking, age, gender, education, frequency of dental visits, certain systemic diseases or stress, as well as different host responses and differences in pathogenic flora. (5)

### *1.2.5 Prevention and treatment*

Periodontal diseases can affect the overall health of the patient. People are often unaware that they are affected and how to prevent them. Indeed, a good oral hygiene is essential for periodontal health (daily brushing of the teeth and regular visits to the dentist).

The treatment is based on several techniques, from the gentlest (scaling, antibiotics) to the most aggressive (surgery). (5)

### *1.2.6 Bacteriology of periodontal disease*

Periodontal diseases are associated with an increase in number of bacteria. The presence of gingivitis leads to an increased microbial load compared to that of the healthy periodontium since its appearance is most often linked to an absence or poor oral hygiene.

The composition of the plaque also changes as it progresses in the apical direction: the proportion of Gram-negative bacteria increases (between 15 and 50%) and anaerobic bacteria increase compared to facultative anaerobes in established lesions.

(7) The correlation has become evident between bacterial accumulation and the inflammatory response of gingival tissue. However, the nature or progression of the inflammatory process can be altered by various systemic influences like the hormonal changes or the medication intake.

When a periodontitis appears, the proportion of anaerobes rises to 90% in a periodontal pocket, the majority of which are Gram-negative bacteria. It is the appearance of certain groups of bacteria or specific bacteria in the plaque which is at the origin of periodontitis thanks to their greater capacity to induce bone lysis. The dominant bacterial flora varies greatly depending on the form of periodontitis, the stage of the disease, and according to the patients.

The periodontopathogenic bacteria most active in tissue destruction are *Actinobacillus actinomycetemcomitans*, *Tannerella forsythensis*, *Porphyromonas gingivalis*, *Prevotella intermedia* and *Fusobacterium nucleatum*. (8)

### *1.2.7 Immunology*

There are several lines of defense against periodontal disease. The first line of defense is the non-specific innate immunity mainly represented by neutrophils, monocytes, macrophages, natural killer cells which are the innate immune cells, and complement. The reaction is local and rapid. The specific acquired immunity intervenes in the second line of defense represented by the T and B lymphocytes. It is mainly provided at the periodontal level by immunoglobulins: IgA, IgG and IgM. (9)

Periodontopathogenic bacteria lyse the periodontium both directly and indirectly:

- Directly, by releasing enzymes and cytotoxic substances that will have a bacterial proteolytic action.
- Indirectly, by causing the synthesis of lytic enzymes in the host they infect. This amplification is responsible for the destruction of connective tissue and also bone. The release of inflammatory mediators activates certain degradation mechanisms.

Bacterial invasion thus provokes an immune response accompanied by a disruption of tissue homeostasis, the periodontal tissues are modified.

The pathogenic micro-organisms that infect the cells have bacterial endotoxins on their outer membrane. They stimulate macrophages which trigger an inflammatory and immune defense reaction. It causes an elevation of markers of the acute phase response, including C-reactive protein which is the inflammation protein in peripheral blood, cytokines and proteins such as tumor necrosis factor (TNF- $\alpha$ ), various interleukins IL-1, IL-6, IL-8 and free radicals, metabolites of oxygen like nitric oxide, active oxygen, hydrogen peroxide, released during phagocytosis and which create significant tissue damage when found in excessive quantities. Cytokines are

responsible for periodontal inflammation, tissue collagenase synthesis which reduces collagen levels and causes local tissue resorption.

Physiologically, to achieve a balance between bone resorption and growth, the proteins receptor activator of nuclear factor kappa-B ligand and osteoprotegerin modulate the level of osteoblasts and osteoclasts. If the ratio is altered by pro-inflammatory cytokines in the direction of a decrease in osteoprotegerin or an increase in protein receptor activator, this results in pathological bone resorption. Bacterial proteinases increase the pathogenic flora, sustain the inflammatory process and inhibit tissue repair.

### ***1.3 Relationship between periodontal disease and systemic disease***

W.D. Miller, a 19th century American dentist and microbiologist, stated in 1891, that bacteria from oral infections could be found in other parts of the body, leading to disease. (10) Even though this theory has not been demonstrated, many dentists at this time decided to perform teeth extractions in order to avoid systemic diseases.

Several recent studies show that periodontal disease can be associated with certain systemic diseases. It is now proven that certain systemic pathologies can modify the expression of periodontal diseases. In particular, periodontitis has been associated with diabetes, cardiovascular disease and complications of pregnancy.

Nowadays we know that there is a link between periodontal diseases and systemic diseases. This statement is based on the fact that there is a mechanism that allows bacteria from the oral cavity to enter the bloodstream and thus infiltrate the organs. Subsequently these bacteria can have some influence on systemic diseases. (10)

To date, two possible mechanisms are known to explain the presence of bacteria in the bloodstream.

### *1.3.1 Metastatic infection hypothesis*

The metastatic infection also called the focal infection, is an infectious disease mediated by microorganisms from a distant location in the body. When periodontal tissue is damaged due to overly aggressive tooth brushing, or ulcerations due to eating, bacteria as well as their toxins have an easy access to the bloodstream and can survive and circulate to reach other organs. Especially in immunocompromised patients who already have systemic pathologies, bacteremia induces more easily an infection of other organs, which can lead to an immunological reaction. (11)

Rosenow explains that bacteria from oral cavity and their toxins are migrating to a greater extent in sites where the predominant composition is mesenchymal tissues, notably joints, muscles and neuronal sheaths. Some studies have shown that bacteria have been localized in arteries and that they can resist a certain time alive. (12)

### *1.3.2 Inflammatory hypothesis*

The other possible mechanism is the systemic involvement comes from the inflammatory cascade initiated in the mouth. When leukocytes and endothelial cells meet bacterial antigens in the bloodstream, they produce pro-inflammatory mediators, such as C-Reactive protein and prostaglandin. With prolonged exposure, bacterial antigens develop and settle into immune complexes with the help of circulating antibodies to exacerbate the systemic inflammatory process. (10)

## **1.4 Systemic diseases**

### *1.4.1 Diabetes*

Among the systemic effects of periodontal disease, diabetes is now known to be strongly associated to periodontitis. Diabetes is defined as chronic hyperglycemia.

It is diagnosed when fasting blood glucose is greater than or equal to 1.26 g/L (7 mmol/L) in the blood or when blood glucose levels are above 2g/L (11.1 mmol/L) at any time of the day. There are two types of diabetes. Type 1 diabetes is of autoimmune origin. In most cases, there is a genetic susceptibility associated with environmental factors. Type 2 diabetes is a non-autoimmune disease and therefore different from type 1 diabetes, with obesity being the primary cause. (13)

A two-way relationship between diabetes and periodontal disease has been suggested in the literature. Specifically, it has been found that diabetic individuals have a higher risk of developing periodontal disease. Conversely, the presence of severe chronic periodontitis may increase the risk of poor glycemic control.

### *1.4.2 Cardiovascular diseases*

Periodontal disease is frequently associated with cardiovascular disease. Cardiovascular diseases are all diseases that affect the heart and vessels. Each of the anatomical components of the heart can be affected (myocardium, endocardium, pericardium, valves, automatic tissue, vessels), either during embryonic development or later in an acquired form.

Cardiovascular diseases are the leading cause of death in the world.

According to the WHO, cardiovascular diseases include a number of disorders affecting the heart and blood vessels such as:

- Hypertension (high blood pressure),

- Coronary heart disease (heart attack or infarction),
- Cerebrovascular disease (stroke),
- Peripheral arterial diseases,
- Heart failure,
- Rheumatic heart disease,
- Congenital heart disease,
- Cardiomyopathies. (14)

Atherosclerosis (atheromatous plaques) is at the origins of most cardiovascular disorders. This is a chronic, slowly progressing inflammatory disease, corresponding to vascular remodeling due to an accumulation of lipids, complex carbohydrates, blood limescale deposits and blood products. Cardiovascular diseases associated with atherosclerosis are defined as a group of diseases that include the following cardiac pathologies: angina, myocardial infarction, ischemic cerebrovascular diseases and peripheral arterial diseases. (15)

Over the last few decades, several research have been carried out to study the association between cardiovascular diseases related to atherosclerosis and periodontitis.

#### *1.4.3 Pregnancy outcomes*

The adverse consequences of pregnancy are a major public health concern because of the human and economic consequences. Pregnancy outcomes include spontaneous abortion, congenital malformations, lower or higher birth rate, preterm birth or stillbirth.

Pregnancy in woman increases the risk of gingival inflammation and periodontal disease can be a risk for pregnancy outcomes including lower birth rate, preterm birth

and pre-eclampsia (gestational hypertension that can appear after 20 weeks of pregnancy). According to the WHO, low weight birth corresponds to baby born under 2.500kg, and a preterm birth appears when pregnancy is achieved before 37 weeks knowing that the normal duration of a pregnancy is 40 weeks. Those complications can lead to either neuronal, respiratory problems, anomalies or death. The study of pregnancy outcomes impacted by periodontal disease has been discussed and analyzed for about thirty years now. (16)

#### 1.4.4 Respiratory diseases

Respiratory diseases concern the nasal tracts, bronchial tubes and lungs. There are acute diseases such as pneumonia and bronchitis, and chronic diseases such as asthma and COPD (Chronic Obstructive Pulmonary Disease) which limits the amount of airflow. Respiratory infections can be caused by viruses, bacteria, fungi or parasites. The most common respiratory infection is bacterial pneumonia. The treatments mainly concern an improvement in lifestyle and may involve the use of corticosteroids and bronchodilators. (17)

The search for a correlation between periodontitis and COPD has become a focus of interest because the pathogens of the oral cavity can cause directly a pneumonia. That is why several studies investigate this concept.

#### 1.4.5 Alzheimer's disease

Alzheimer's disease dementia is defined by the association of a dementia syndrome and, on histological examination of the brain, by the existence of amyloid plaques, neurofibrillary degeneration and neuronal loss. The dementia syndrome corresponds to the following medical definition: disorders of cognitive functions (memory, language,

executive functions, etc.) that are sufficiently important to affect daily life and that have lasted for at least 6 months. (18)

For those patients, oral health is then a challenge as in advanced stages they may forget how to brush their teeth, floss, or rinse. The consequences of Alzheimer are multiple in terms of oral conditions as the lack of hygiene can lead to caries or periodontal problems. But also, since recently it has been observed that some oral pathogens may play a role in the development of Alzheimer's disease.

Several articles on rheumatoid arthritis, chronic kidney disease, certain cancers, have established a link with periodontitis. For the most part, the limited number of studies on each of these conditions does not allow clear associations with periodontitis to be established. (15)

## 2. Objectives:

### Principal objective:

- Determine which systemic diseases are impacted by periodontal disease and in which way.

### Secondary objectives:

- Determine the symptoms and signs associated with periodontal disease in patients with systemic disease.
- Identify the patient's needs and the type of treatment required in the case of periodontal disease associated with systemic disease.

### **3. Materials and methods:**

The study is a literature review, conducted in depth in international databases, such as Pubmed, Google scholar. The documents selected were articles published in journals thesis. The search was also carried out through the service of the of the university library which permits to access free documents.

The search was done using the following keywords: « periodontal disease », « diagnosis of periodontal disease », « relationship between periodontal disease and systemic disease », « impact of periodontal disease and its treatment », « diabetes and periodontal disease », « cardiovascular disease and periodontal disease », « pregnancy and periodontal disease », « COPD and cardiovascular diseases », « Alzheimer's disease and periodontal disease ».

Articles were selected when they were in French, English or Spanish.

Once the selection of documents in the database had been carried out, the inclusion and exclusion criteria were used to select the articles. Several articles were not selected because they were in a different language for example, others because they were repeated in different databases, others because when reading the full text, it did not explain exactly what we were looking for.

While collecting the articles for the study, we included articles that were published from the year 2009 to 2021. Exceptions have been made for two studies about diabetes and periodontal disease published in 2006, one study about pre-eclampsia published in 2005 and one study issued in 2006 dealing with respiratory disease. Those four articles were still chosen due to their relevance with our topic. Only the studies made in humans were chosen and studies on animals were excluded.

## 4. Results and Discussion

### a) Diabetes

Diabetes mellitus is a metabolic disorder characterized by the presence of hyperglycemia due to a defect in insulin secretion or insulin action, or both. There are two main types of diabetes that are quite distinct with equivalent consequences. Type 1 diabetes, which represents about 6% of diabetic patients, it has an autoimmune origin. It leads to an absolute lack of insulin. Type 2 diabetes, representing 92% of diabetic patients, linked to a dysfunction of the glucose-receiving cell, resulting in a relative deficiency of insulin. Diabetes is characterized by three symptoms which are polyuria, polydipsia and polyphagia and which allow the clinical diagnosis of the presence of diabetes in a patient. (13)

For this literature review a number of articles, that trace studies done to show the link between systemic diseases and periodontal disease, were selected. Indeed, since 2003, periodontitis has been identified as the sixth most common complication in diabetic patients.

With the following studies several relationships have been demonstrated between diabetes and periodontal diseases. The first thing is that diabetes and periodontal disease have a two-way relationship. Indeed, diabetes has an influence on periodontal conditions and vice versa.

B. L. Mealey, T. W. Oates published in 2006 a review of epidemiological studies published during the last two decades. They talked about the fact that diabetes increases the risk of developing periodontal disease and that periodontal disease may have an impact on the glycemic control of the patient even though it lacks evidence at this point. (19)

In a study carried out in 2009, I. Sanz-Sánchez and A. Bascones-Martínez made a literature review 36 scientific articles that were about types of diabetes and their complications including oral complications. We come to the conclusion that this bidirectional relationship does exist, and that today periodontitis is the sixth most frequent complication of patient with diabetes. (20)

In 2014, two scientists, L. I. Holla and P. Stankoa, conducted a literature review with articles on the relationship between periodontal diseases and diabetes. They concluded that the relationship is strong, that diabetes increases the severity of periodontitis. On the other hand, what is still less clear is the association between periodontitis and glycemic control. In fact, it has been shown that periodontitis can accelerate insulin resistance, which affects poor blood sugar control. However, studies have also shown that periodontitis can help glycemic control in type 2 diabetic patients. (21)

Through the literature we can see that it was first shown that patients with diabetes were more likely to develop periodontal disease and that the evolution of this condition was more severe and had a poorer prognosis. But in the last two decades it has been established that periodontal diseases also have an impact on diabetes. We are now talking about a two-way relationship. Several authors have initiated the study of the possible influence of periodontitis as a risk factor in the development of diabetes.

We currently know from studies that diabetes is a risk factor for the development of periodontitis.

In 2006, three scientists from Singapore made a review of studies to demonstrate the impact of diabetes on periodontal diseases. They reach the conclusion that the destruction of the periodontium is related with the glycemic control of the patient. They also talked about therapy in patient with diabetes and their reactions toward it. (22)

With a study carried out in 2012, M. M. Galvis, Y. P. M. Zuluaga, A. Saldarriaga Saldarriaga come to the conclusion that periodontal diseases are more frequent in patient with diabetes and that diabetes have an influence on the immunological and inflammatory host response. (23)

The same year as the previous article P. M. Preshaw et al. reviewed several studies and articles reaching various conclusions. One of them being that the risk of suffering from periodontitis is three times higher in the diabetic population than in the non-diabetic population. (24)

As it is a two-way relationship, periodontitis is also a risk factor for diabetes. Several articles and studies have been conducted to prove this.

A study made in 2010 by R. Santos Tunes et al, explains that according to the Third National Health and Nutrition Examination Survey (NHANES III) in the United States, there is more periodontal patient with diabetes as a systemic condition than periodontal patient without any systemic disease. They also conclude that there is a need of more evidence about the influence of periodontal disease on diabetes. (25)

Once this bi-directional relationship is known to exist, we can try to demonstrate the mechanism by which periodontal disease affects diabetes and the reverse.

Different mechanisms have been proposed to explain the bidirectional relationship between diabetes and periodontal disease. Among these, the authors attribute the hyperactive inflammatory response in diabetics to the presence of periodontal pathogens that would trigger exaggerated inflammation leading to periodontal tissue destruction. Secondly, the presence of high glucose levels may activate the production of pro-inflammatory cytokines. Thirdly, delays in healing and impaired immune

responses such as impaired neutrophil phagocytosis and chemotaxis may also predispose diabetic patients to develop periodontitis. (26)

With the link between periodontal disease and diabetes established, it is important to consider whether treating periodontitis can have a positive effect on diabetes management.

In 2010, a meta-analysis was conducted with the use of 639 studies and come to the result that diabetic patient with therapy of periodontal disease shows a decrease of 0.40% of the glycated hemoglobin A1C. (27)

There are also specificities and influences of each periodontal treatment. The evidence is still quite limited and sometimes contradictory. However, hyperglycemia in subjects with periodontal disease is higher than in healthy subjects. Periodontal management could lower glycated hemoglobin A1C by 0.40%, and surgical periodontal treatment would lower glycated hemoglobin A1C by a further 0.25% compared to non-surgical periodontal treatment. The effect of periodontal disease on glucose homeostasis is harmful. (28)

This implies that there is a factor which must be taken into account in diabetes treatment protocols, it is oral health care. These studies demonstrate how correct treatment of periodontitis and maintenance of periodontal health may improve blood glucose control. Studies also concluded that the presence of periodontitis negatively affects blood sugar control and increases the risk of developing diabetes. In brief, the presence of periodontitis in an individual seems to have a significant impact on the metabolic control of diabetes.

The role of the dental surgeon is therefore to diagnose and screen for diabetes but also to treat periodontal disease to improve the patient's general health. In a well-balanced diabetic patient, all periodontal therapies can be used, including surgery. The

initiation of treatment requires a complete dental examination including a periodontal assessment. Scaling must be more frequent and rigorous than in non-diabetic patients.

(28)

It would be necessary to involve the dental surgeon in the reinforcement of prevention, to detect early the periodontal affections related to diabetes, to develop an awareness of the health professionals, to include the care of periodontology in the prevention of the systemic pathologies.

### b) Cardiovascular diseases

Cardiovascular pathologies and periodontal disease are both chronic, multifactorial pathologies and share a number of modifiable and non-modifiable risk factors such as age, gender, education and socio-economic status, tobacco, obesity, diabetes and stress.

Over the last few decades, several research have been carried out to study the association between cardiovascular diseases related to atherosclerosis and periodontitis. A review of recent literature on the epidemiological evidence of an association between periodontitis and cardiovascular events related to atherosclerosis concluded that there is an increased risk of cardiovascular events in patients diagnosed with periodontitis.

In 2012, a paper was published in the journal of vascular surgery which had for aim to find a connection between periodontal diseases and cardiovascular diseases in particular stroke. In total thirteen English studies were analyzed. The analysis showed that the global risk of stroke in individuals with periodontitis was 1.47 times higher than

in individuals without periodontitis for the prospective studies and 2.63 times higher in retrospective studies. (29)

In a study paper made in 2013 by M. S. Tonetti, and T. E. Van Dyke which has reviewed epidemiological studies as well as the results of intervention trials, it has been shown that the presence of periodontitis can lead to the appearance of cardiovascular diseases in the future. However, the intervention trials studied did not show clear evidence of relationship between atherosclerosis and periodontitis. (30)

Recently, in 2020 the meta-analysis of H. Larvin et al, tried to find evidence that periodontist can be a risk factor for cardiovascular diseases. They looked at thirty longitudinal cohort studies and found that there is a higher risk for having periodontal diseases in patients with periodontitis, especially in men with severe periodontal condition. They claim in their paper that the risk of cardiovascular disease increases from 9% in mild periodontal disease, 23% in moderate and 25% in severe ones. (31)

A study made in Canada by two scientists in 2020, reported according to Bradford Hill criteria analysis, that there was not enough demonstration to make any conclusion on the association of periodontitis and cardiovascular disease. They reviewed systemic reviews and meta-analysis and tried to know if patients with periodontal diseases treated surgically could reduce the risk for developing cardiovascular disease. (32)

Many studies have focused on the relationship between cardiovascular disease and periodontal disease, and it is now recognized that periodontitis has an increased risk of developing cardiovascular conditions. However, a direct causal link between periodontitis and cardiovascular diseases related to atherosclerosis has not yet been established.

There are a number of possible mechanisms that could be responsible for the increased inflammatory responses in cardiovascular disease due to periodontal diseases.

An article from 2015, by H. A. Schenkein and B. G. Loos, permits to understand the mechanisms that links the two types of diseases and explains the increase in the inflammatory response due to periodontitis. (33)

Another article, published in 2017, has evaluated the level of antibodies to *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis* in 576 participants. Scientists have also assessed the periodontal condition of the patients as well as the presence of cardiovascular disease and tried to find a correlation between these facts. They come to the conclusion that those bacteria are associated with cardiovascular conditions, but it was not significant when they take into account other risk factors such as smoking, age, gender or alcohol consumption. (34)

In 2018, Aarabi et al, made a research to describe the different mechanism and to find evidence that can confirm them. They described the process of bacteremia, in which a bacteria originated from the periodontium can reach the vascular system. They reported that 23 species of oral bacteria were observed in atherosclerotic plaque samples. (35)

The link between periodontal disease and cardiovascular disease, particularly atherosclerosis, is based on inflammatory mechanisms initiated by bacteria associated with periodontal lesions, which then influence the initiation or propagation of atherosclerotic lesion. Several studies support certain plausible biological mechanisms to explain the causal link between these two conditions. It could be an indirect immunoinflammatory reaction which would be induced by an increase in the secretion of pro-inflammatory marker/mediators: certain cytokines IL-1, IL-6, TNF- $\alpha$ , C-Reactive protein

and oxidative stress involved in atherogenesis. These cytokines have been observed in higher concentrations in patients suffering from periodontal disease and in lower concentrations in those treated. (33)

Another hypothesis is that there would be a direct bacterial reaction. Indeed, according to several studies, there is an association between the level of antibodies and the presence of cardiovascular conditions. Periodontal bacteria graft themselves to a localized vascular lesion and favor the recruitment of macrophages which participate in atherogenesis. Thus, they participate in the development of the atheromatous lesion. According to Damgaard et al, levels of circulating IgG antibodies against *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis* are correlated with loss of periodontal attachment and could be used as a biomarker for periodontitis and cardiovascular disease. Bacteria from the oral cavity have been found in atheromatous plaques. (34)

As it has been shown that periodontal disease can be a risk factor for cardiovascular disease, it is interesting to look at the effect of periodontitis treatment on a patient's possible cardiovascular condition. Thus, to see if periodontal treatment as well as good oral hygiene can have a positive effect on the risk of cardiovascular diseases.

A report of E. Rocca-Millan et al, published in 2018 analyzed the effect of periodontal treatment on patients with atherosclerotic cardiovascular disease. Ten articles were chosen and had for result that the C-reactive protein, which plays an important role in atherosclerotic cardiovascular disease, decreased in a significant way in patient receiving non-surgical periodontal treatment. (36)

In 2020, M. Sanz et al, have made a report reviewing the literature relating periodontal diseases and cardiovascular diseases. The goal was to make an update about the epidemiological findings at this day, to explain the mechanisms and to describe the

impact of periodontal treatment on the cardiovascular condition. It permits to give recommendations to dentist when confronted with cardiac patients. (37)

According to some studies, the treatment of moderate to severe periodontitis would reduce the level of systemic inflammation mediators and improve endothelial function. In the study of, we can observe, after periodontal treatment and giving the patient oral hygiene instructions, the decrease in the C-reactive protein, TFN- $\alpha$  and IL-6. We can conclude that periodontal therapy provides a reduction in the inflammation. This study is limited by the fact that the treatments are different, they can be surgical or mechanical and the severity of the periodontal disease of the patient is unknown. (36)

To this day, it is known that there is a link between periodontal disease and cardiovascular disease. The mechanisms of action of periodontal bacteria in the cardiac system are known and are still being studied. Conclusions about the future of cardiac patients according to their periodontal condition is increasingly being demonstrated.

Furthermore, it is recommended that periodontists and cardiologists work closely together when patients with cardiovascular disease are newly diagnosed with periodontitis in order to optimize the care provided and reduce the risk of cardiovascular events. Although it is not evident that periodontal treatment reduces the risk of cardiovascular disease or prevents its complications, it is interesting for the dentist to inform the patient about the possible cardiovascular complications when he presents a periodontal disease. When a patient has a cardiovascular disease, he should be informed about the possible benefits of preventing periodontal disease through good oral hygiene and treatment if necessary. (37)

### c) Pregnancy outcome

The prevalence of periodontal diseases in pregnant women is high. Due to hormonal changes that occur during pregnancy and promote an inflammatory response, pregnant women are more likely to develop periodontitis or gingivitis.

In an article published in the United States in 2008, pregnant women were found to suffer from gingivitis in 60-75% of cases and from periodontitis in 30% of pregnant women. In addition, pyogenic granuloma appears in 5% of pregnant women. Other oral conditions are mentioned without any relevant aspect for our study. (38)

The relationship between periodontitis and various complications of pregnancy, such as premature or very premature births, reduced fetal weight and pre-eclampsia, has been studied since 1996 with the first research, made by Offenbacher et al. which suggests that there is a relationship between maternal periodontal health and preterm birth. According to this study, a pregnant woman with periodontitis was seven times more likely to have a preterm birth. (39)

Nowadays, the scientific world is highlighting the fact that premature births can be linked to systemic diseases. By definition, a birth is considered premature when a baby is born before completing 37 weeks of gestation.

In a study made six years ago by scientists of India, the link between periodontal disease and premature births has been tested. With the help of 40 pregnant women between the ages of 18 and 35, the periodontal condition of these women was investigated by dividing them into two groups: those who had given birth before 37 weeks, meaning prematurely, and those who had given birth after a full 37 weeks. Results showed that periodontal status among women who delivered before the right time was poorer and showed signs of bleeding and pockets, which means that there would be a link between periodontal disease and preterm birth. (40)

Several studies are also trying to prove that periodontal disease may play a role in infant birth weight.

In 2016, A. Teshome, and A. Yitayeh conducted a review of case control studies made between 2005 and 2015 to find a relationship between periodontitis or poor periodontal status and preterm birth, and preterm low birth weight. In the end they used 10 studies and 9 of them have for result that periodontal disease could be a risk factor for bad pregnancy outcomes. The estimated risk of premature delivery for a pregnant woman with periodontitis was 2.83 compared to women without periodontitis. Although this study was done with the observation of 2423 pregnant women, it is not known if these women had other potential risk factors and if they were taken into account. (41)

A review of literature has been made in 2012 by three scientists of Saudi Arabia, they used a lot of type of studies to prove the relationship between periodontal disease and pregnancy outcome as well to find the causes of these results. It has been found that the increase of progesterone would permit the gingival infection to go through all the body. Intra-amniotic levels of prostaglandins, and tumor necrosis factor, increase gradually throughout pregnancy until a critical level is attained to trigger early delivery. Another suggestion is that premature delivery can be triggered when the fetus is exposed to periodontal bacteria leading to an inflammatory reaction. (42)

This relationship is bidirectional, periodontal disease can have an unfavorable risk for pregnancy: premature delivery, newborn with low birth weight, and conversely pregnancy can present a risk for the periodontal tissues.

However, in a study made in 2017 by M. Fogacci et al. with the same method as the previous study, no association were found between periodontal diseases and pregnancy outcomes. Indeed, there were no significant differences between both groups in terms of clinical attachment level, probing pocket depth, plaque index and

gingival bleeding index. The conclusion was that periodontal condition is not a risk factor for preterm low birth weight. (43)

We can also wonder if there is a possibility that periodontal disease could have an impact on the risk of developing preeclampsia. Several studies have also reported an association between periodontitis and this systemic disease. It is a common disease of pregnancy, associated with high blood pressure and the appearance of protein in the urine that appears after 20 weeks of gestation.

The study by BARAK et al, reported that 50% of placentas from patients diagnosed with pre-eclampsia showed the presence of periodontopathogenic bacteria whereas only 14% of placentas were contaminated in the control group. The presence of periodontopathogenic bacteria in the placenta was associated with pre-eclampsia. (44)

In 2013, A meta-analysis of observational studies was conducted by B.J. Wei, Y.J. Chen, L. Yu, and B. Wu. Through all the studies used, 1089 patient with pre-eclampsia were observed and analyzed. This study brings the conclusion that pregnant women with periodontal conditions have higher risk of suffering from pre-eclampsia and suggests that periodontal disease is a risk factor for it, although the degree of severity of periodontal disease of the selected patients was not mentioned. (45)

Periodontal diseases have many common risk factors in common with preterm birth, low birth weight, and pre-eclampsia such as age, smoking, low socio-economic status and systemic health status. This is one of the limitations of the studies discussed above, as the patients investigated may present these risk factors and thus have a related pregnancy complication related to them.

To explain the possible relationship between periodontal disease and low birth weight preterm infants, possible biological hypotheses have been advanced that propose a link between preterm birth and periodontal disease.

The periodontal tissues in periodontitis will release pro-inflammatory mediators (PGE<sub>2</sub>, TNF $\alpha$ , IL-1 $\beta$ , IL-6, IL-8) and increase the CRP level in the systemic circulation. This inflammatory cascade can cause placental damage and pre-eclampsia. There are therefore two hypotheses according to the studies. (42)

- Periodontopathogenic bacteria and their degradation products penetrate the placenta.
- The production and release of molecules involved in inflammation; their increase can act as a trigger for the onset of childbirth.

In general, the more severe the periodontal disease, the more likely preterm delivery and low birth weight, and there is an inverse relationship between average birth weight and the severity of periodontal infections. (46)

Understanding the multidirectional and dynamic links between pregnancy and periodontal disease can improve the preventive measures and the comfort of the patient's life.

At this point in time, several randomized control trials on the effect of periodontal treatment and the reduction of the risk of premature births show contradictory results and conclusions. Periodontal treatment in pregnant women may reduce the risk for having a low birth weight but the quality of evidence is quite low. (47)

In a nutshell, it is known that the relationship between the two multifactorial pathologies of periodontal disease and preterm delivery exists, but without a proven causal link to date. For the odontologist, without being alarmist, the precautionary principle must be considered in the management of periodontal diseases for all women who present a known medical risk for preterm births. This implies stabilizing tissue loss as early as possible and scheduling several check-ups until delivery. Although the effect of periodontal treatments on pregnancy outcome is not yet clear, it is widely recognized

that it is safe to perform periodontal treatments, such as scaling during the second or third trimester of pregnancy. (48)

#### d) Respiratory diseases

Recent studies have associated periodontal disease with respiratory disease. It would therefore be possible that periodontal disease, may influence the course of some respiratory infections such as bacterial pneumonia and chronic obstructive pulmonary disease (COPD).

In an observational study published in 2015 by T.C. Shen et al. searchers have made a cohort study based on a population of 22 323 patients with chronic obstructive pulmonary disease diagnosed between 2000 and 2010. They concluded that COPD patients are more at risk of developing periodontal disease than the general population. Their results also argue that the risk of periodontal disease is proportional to the control of COPD. In addition, patients receiving corticosteroid treatment would be at higher risk of developing periodontal disease. Periodontal disease would be an independent risk factor for COPD and oral and periodontal microorganisms would be involved in bacterial pneumonia. (49)

The meta-analysis based on 14 observational studies by Zeng et al, from 2012 identified a significant association between periodontal disease and COPD. These results include the observation of 3 988 patients who had COPD. However, the existence of a causal relationship remains uncertain due to publication bias such as the difference of prevalence of COPD depending on the place in the world. Indeed, developing countries have higher rate of COPD than developed countries. (50)

A 2006 study of 19 articles provided the following results, potential risk factors for pneumonia were identified as being the presence of periodontal bacteria and that

maintaining oral hygiene particularly with the daily use of 0.12% chlorhexidine rinses reduced the progression or onset of pneumonia. (51)

However, there are several studies that do not find a link between periodontal and respiratory diseases.

We can see this in the paper from X. Zhou et al, released in 2020. Indeed, the scientists conducted a case control study over 60 patients who shared periodontal diseases as well as COPD and a control group of 60 other patients. Although the participants in the case study presented higher plaque index, fewer remaining teeth and the higher presence of periodontal bacteria the differences between the two groups are not large enough to be able to state that periodontitis is a risk factor for COPD. (52)

A number of studies have found a relationship between periodontal disease and respiratory disease. Nevertheless, at present the level of evidence is still insufficient.

A weakness that can be found in these studies is that the co-morbidities associated with COPD must also be taken into account: high blood pressure, diabetes, hyperlipidemia, asthma, arterial and coronary diseases, kidney disease, strokes.

In the study of Bansal et al, it is explained that oral bacteria could become involved in respiratory diseases through several mechanisms. It could be either a direct reaction of pathogens by inhalation, or an aspiration of oral pathogens present in dental plaque. Dental plaque is a direct source of *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* which can be released from oral secretions and contaminate the respiratory system. Or it could be the reaction of enzymes associated with periodontitis and present in saliva: they can modify mucosal surfaces to promote the adhesion and colonization of respiratory pathogens. Indeed, mucins can be altered which reduces their ability to eliminate respiratory pathogens. (53)

Although the connection between periodontal disease and respiratory disease is still lacking evidence to date, there is still a need for further research. It may be important to consider periodontal treatment in patients with respiratory disease in order to possibly improve their living conditions and general health. As a matter of fact, Bansal et al, suggest that improved oral hygiene, use of oral disinfectants and treatment of periodontal diseases, either by antibiotherapy or clinical interventions, could be a way to reduce the incidence of respiratory infections. (53) Shen et al. claim that periodontal treatment in these patients could reduce the risk of adverse respiratory events, disease exacerbations, and thus mortality. Moreover, patients with COPD had a fewer demand of medication when they have been periodontally treated. (49)

To date there is a lack of studies and mainly intervention studies to really establish a link between periodontitis and respiratory diseases and to show that periodontal treatment can significantly improve the health of patients suffering from respiratory conditions.

#### e) Alzheimer's disease

Over the last decade, there has been increasing evidence of a microbial and inflammatory origin of Alzheimer's disease with the discovery of bacteria, viruses and fungal species in the brains of Alzheimer's patients.

In 2014, S.S. Martande et al, assessed in their study the periodontal condition of 58 patients with Alzheimer's disease and 60 patients without any neurological disease. It was found that patients with Alzheimer had more periodontal problems than in the other group of patients. They concluded that patients who lose their cognitive function find it more difficult to respect good oral hygiene and therefore lose their periodontal status.

(54)

The deterioration of oral health due to progressive cognitive impairment that affects oral hygiene habits is the first level of evidence for an association between Alzheimer's disease and periodontal disease.

C.K. Chen et al, conducted a research in 2017, they analyzed patient with chronic periodontics and patients without, then they evaluated the risk of Alzheimer's disease in both groups of patients. Patients with chronic periodontitis for 10 years presented higher risk for developing Alzheimer in the future. They described the fact that there are other risk factors for Alzheimer that must be taken into account such as depression, stroke, traumatic brain injury and that patients with this neurological disease present impairment in their chewing function leading to higher risk for developing Alzheimer's disease. (55)

The study of K. Abbayya et al, permits to understand better the possible mechanisms in which the periodontal disease plays a role in Alzheimer. It appears that the inflammation that is present in periodontal disease contributes to the development of Alzheimer's disease. (56)

It is proposed that periodontitis may lead to the progression of Alzheimer's disease through two likely mechanisms:

- Periodontitis precedes inflammation
- The bacterial and viral influence of periodontal disease.

In the first mechanism, periodontal pathogens and the host response increase the levels of pro-inflammatory cytokines. A range of cytokines and pro-inflammatory agents are released into the systemic circulation. These pro-inflammatory molecules can compromise the blood-brain barrier and access brain regions. This can lead to adverse effects resulting in neuronal damage.

The second mechanism may involve invasion of the brain by bacteria and viruses residing in the dental plaque biofilm. Indeed, periodontopathogenic bacteria contribute to inflammation. Among the pathogens linked to periodontitis, *Porphyromonas gingivalis* has been associated with C-reactive protein levels in elderly patients. (56)

Yet the 2016 study by Ide et al, found no significant relationship between baseline serum *Porphyromonas gingivalis* antibody levels and rates of cognitive decline among the 60 patients involved in the research. (57)

However, in a study conducted in 2015 by A. Kamer et al, a link has been found between periodontal problems and the level of amyloid  $\beta$  plaques. Indeed, it has been found in relatively healthy and elderly patients that present moderate to severe periodontitis. Amyloid plaques are accumulations that form around neurons, particularly in certain neurodegenerative diseases such as Alzheimer's disease. Among other things, this formation of plaques prevents neurons and neurotransmitters from functioning properly. (58)

At present, we cannot say that periodontitis may be a potential risk factor for the development of Alzheimer's disease. There is still insufficient data to really support a causal relationship. One of the reasons for the lack of data is the difficulty of studies and recruitment of elderly people, and of obtaining regular periodontal follow-up. However, some studies suggest that periodontal disease may occur before the specific pathology of Alzheimer's disease and that a causal effect could be determined. (59)

Studies should therefore be continued. Indeed, there is still no effective treatment for this disease, so it would be interesting to assert certain risk factors for Alzheimer's disease.

At this stage, the main objective of care is to maintain a good state of oral health to allow feeding in the best conditions and to avoid the development of inflammatory,

infectious and painful pathologies. But there are still no clear recommendations for the treatment or prevention of periodontitis in individuals with Alzheimer's disease.

## Conclusion

Preterm birth, pre-eclampsia, diabetes, cardiovascular disease, respiratory disease and Alzheimer's disease are systemic conditions with a high prevalence rate in the population. The consequences related to these diseases are important for patients and for health systems.

Nowadays, periodontal infection appears more and more as a factor of disruption of homeostatic balances, likely to lead to pathological manifestations at a distance from the original site. Indeed, the pathophysiology of these diseases follows the same thread: an inflammatory state. It is therefore very important to set up the necessary periodontal treatments, all the more so if the patient's general condition is not totally controlled. It is fundamental to be able to prevent these conditions in patients at risk and to optimize the range of care offered to those who already have these conditions. The dental surgeon plays a key role in the diagnosis, screening, treatment and follow-up of his patients. We know that periodontal treatment helps to reduce systemic inflammatory markers. The modification of behavioral risk factors (stress, lifestyle habits, hygiene, smoking, sedentary lifestyle) contributes to periodontal treatment, which is why there must be a real multidisciplinary collaboration between the various health professionals: general practitioner, nutritionist, psychologist, tobaccologist. It is the practitioner's responsibility to take all the necessary precautions, he must identify and evaluate the risks to which the patient is exposed during treatment.

## Responsibilities

This work provides knowledge about patients sharing two specific conditions: systemic disease and periodontal disease. It provides a better understanding of patient need and management. The control and consequences of periodontal diseases on systemic

diseases and vice versa permits to make an easier early diagnosis, and the patient can then be treated consequently. From a social point of view, it is relevant because this theme can help to improve the quality of life of patients.

These patients are usually followed by caregivers of several disciplines which sometimes lack coordination. This results in additional unnecessary treatments which are usually expensive. This can be avoided with the help of preventive measures when practitioners work hand in hand and ensure a good follow-up of patients.

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## Infection and inflammatory mechanisms

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### Abstract

This introductory article examines the potential mechanisms that may play a role in the associations between periodontitis and the systemic conditions being considered in the EFP/AAP Workshop in Segovia, Spain. Three basic mechanisms have been postulated to play a role in these interactions; metastatic infections, inflammation and inflammatory injury, and adaptive immunity. The potential role of each alone and together is considered in *in vitro* and animal studies and in human studies when available. This is not a systematic or critical review, but rather an overview of the field to set the stage for the critical reviews in each of the working groups.

Key words: cardiovascular disease; infection; inflammation; pathogenesis; periodontitis; systemic diseases

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Two disorders/diseases can simultaneously occur or may develop sequentially where progression or exacerbation of one disease may affect the second disease. In parallel with Koch's postulates, which are used to identify the aetiological agents of an infectious disease, the criteria for a causal association between two diseases have been defined and are known as the Bradford Hill criteria. These include epidemiological association, biological plausibility and the impact of intervention of one on the second disease.

A large body of evidence exists relevant to the association of periodontitis with diabetes mellitus, cardiovascular disease and dental focal infections. Three mechanisms

have been postulated to play a role in non-oral manifestations of oral diseases (Thoden van Velzen et al. 1984): metastatic infections, dissemination of bacterial toxins and immunological injury. The word *metastasis* comes from the Greek "displacement"; *μετά*, *meta*, "next", and *στάσις*, *stasis*, "placement". *Metastasis*, or *metastatic disease*, has been defined as the spread of a disease from one organ or part of the body to another non-adjacent organ or body part. The definition is not limited by the common usage involving malignant tumour cells; infection and inflammation have the capacity to *metastasize* (Chiang & Massague 2008).

In the context of the relationship between periodontal disease and systemic diseases, the underlying assumption is that periodontitis is an infection that causes an inflammatory disease that metastasizes. This can be metastasis of the infection (bacteremia and infection at non-oral sites caused by oral bacteria or other direct bacterial actions), inflammation and inflammatory mediators having an impact on systemic inflammation

mediated by innate immune cells and mediators, activation of adaptive immunity and the systemic consequences, or an undefined combination of any or all of these potential mechanisms. However, it is plausible, if unlikely based on available data, that the associations are the result of common risk factors and not causally related. From our understanding of the biology of the relationship between periodontitis and systemic disease, it remains clear that the relationship is not linear, but complex.

The purpose of this introductory Supplement article is to discuss the potential mechanisms underpinning the associations between periodontal disease and systemic conditions. This not intended to be a systematic or critical review, but than an overview of the possibilities based upon our understanding of the systemic consequences of periodontal infection and inflammation. The classification of Gonzalez-Periz et al. (2009), Kinane et al. (2005) has been modified for the purposes of this Supplement article, where metastatic infections and bacterial toxins will be considered

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## The impact of periodontal infection on systemic diseases

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### Summary

Systemic health is often closely linked to the state of the oral cavity: many systemic diseases and conditions have oral manifestations. Likewise, oral microbiological infections may also affect one's general health status. Indeed, animal and population-based studies now suggest that periodontal diseases may be linked with systemic diseases and conditions including cardiovascular diseases, diabetes, respiratory diseases, adverse pregnancy outcomes, and osteoporosis. Better understanding of this correlation will help both dental and medical professionals to determine the best approach to patient care.

This review will focus on the current knowledge linking periodontal infections to a set of systemic diseases. While a number of interactions have been identified, additional research will be required to determine whether these associations are causal or coincidental, and to evaluate disease pathogenesis and potential therapeutic interventions. These findings place oral health in the perspective of systemic health, and they suggest that the dental and medical professions should develop even closer ties in the future.

**key words:** periodontal diseases • systemic diseases • cardiovascular diseases • diabetes • respiratory diseases • adverse pregnancy outcomes • osteoporosis

**Full-text PDF:** [http://www.MedSciMonit.com/pub/vol\\_9/no\\_12/3776.pdf](http://www.MedSciMonit.com/pub/vol_9/no_12/3776.pdf)

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*Case Report*

## Anatomy of the periodontium: A biological basis for radiographic evaluation of periradicular pathology

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The periodontium surrounds and supports the teeth and consists of four major components; gingiva, periodontal ligaments, cementum/dentin, and alveolar bone/lamina dura, with collective function of keeping the tooth in position despite varying changes and responses during mastication. A near-normal radiograph of periradicular tissues was used as the basis for evaluation of some common periradicular radiographic pathologies. Apical periodontitis was 70 (58.33%), alveolar abscess 32 (26.66%), and apical granulomas 15 (12.50%). A background anatomy of the periodontium is advocated as a precondition for accurate evaluation of periradicular pathologies.

**Key words:** Periodontium, periradicular, pathology.

### INTRODUCTION

The periodontium surrounds and supports the teeth. It consists dominantly of four major components; gingiva, periodontal ligaments, cementum and the alveolar bone. They collectively function as a unit to keep the tooth in position, despite varying responses during mastication. In occlusal wear, the cementum is deposited apically to compensate the loss. Periodontal ligament has high turnover of cells that allows the teeth to be suspended in the socket. In response to applied force, bones resorb on the pressure side and are deposited on the tension side (Piezoelectric effect) (Skoog et al., 2007; Manbachi and Cobbold, 2011). Gingiva as an integral part of the periodontium, is not reflected radiographically, because it is a soft tissue, but has its peculiar pathology. However, the morphological characteristics of the gingiva depends on several factors like the dimension of the alveolar process,

the form of teeth, events that occur during tooth eruption, the eventual inclination and position of the fully erupted teeth (Skoog et al., 2007; Seba et al., 2014). Gingiva and the periodontal ligaments though not appearing radiographically have collagen, ground substance, cells, nerves and blood vessels in common (Berkovitz, 2004). The alveolar process, lamina dura, periodontal ligament space and the bulk of the root dentine are visible in dental periapical radiographs. Alveolar process is the bone of the jaw containing the sockets, and it is made up of buccal and lingual cortical plates, with a central spongy bone. The radiographically visible tooth supporting structures are alveolar processes, cementum/dentine, and alveolar bone/lamina dura. The radiographic health of this tissue determines the periodontal status of the teeth. Changes in the lamina dura are associated with dental disease and

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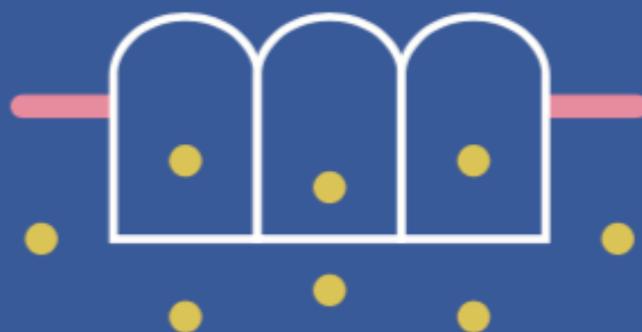
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# 03. Maladies systémiques et problèmes parodontaux

## Guide à l'attention des cliniciens

- De nombreux troubles systémiques peuvent influencer sur l'apparition et la progression des parodontites, ou peuvent affaiblir les structures parodontales.
- La nouvelle classification des récessions gingivales est basée sur la perte d'attache interproximale et y associe différents paramètres cliniques, comme le phénotype gingival, ou les caractéristiques de la surface radiculaire exposée.
- Les forces occlusales peuvent endommager les dents et le système d'attache parodontale.
- Les affections développementales ou acquises associées aux dents ou aux prothèses peuvent prédisposer aux maladies du parodonte.
- Les abcès parodontaux et les lésions endo-parodontales peuvent également affecter le parodonte.



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InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-.

## Gingivitis and periodontitis: Overview

Last Update: February 27, 2020; Next update: 2023.

### Introduction

Many people have inflamed gums every now and then. A gum inflammation (gingivitis) usually doesn't cause any major problems at first. But it may spread to other parts of the periodontium (the soft tissue and bone responsible for keeping our teeth firmly anchored) and cause damage there. The medical term for inflammation of the periodontium is periodontitis. Over time, periodontitis can cause teeth to loosen.

Good oral hygiene can help to prevent gingivitis. Only if you clean your teeth properly can treatment by a dentist stop – or at least slow down – the progression of periodontitis. It's also very important to carry on taking good care of your teeth after having treatment, in order to prevent periodontitis from getting worse.

### Symptoms

The main signs of gingivitis are red, swollen and bleeding gums. The gums bleed when you clean your teeth, and sometimes for no obvious reason too. Gingivitis generally doesn't cause any pain or other symptoms, so it remains undetected for quite some time.

Periodontitis often doesn't cause any symptoms either until it has become advanced. As well as red and bleeding gums, it can also lead to sensitive teeth and receding gums ("long teeth"), sore gums and bad breath. If the gums are inflamed, they may start pulling away from the neck of the tooth. This causes gaps to form between the teeth and the gums, known as gum pockets (or periodontal pockets). At a more advanced stage, periodontitis can cause teeth to shift position, start wobbling or hurt when you chew.



### Causes

The most common cause of inflamed gums is plaque. Plaque is a thin film that is mainly made up of bacteria and is hardly visible at first. It is mainly found where the tooth and gum meet, and may feel a bit "furry" when you run your tongue over it. The bacteria in the plaque "eat" sugars in food in your mouth, and their waste products can cause the gums to become inflamed and swollen. You can get rid of plaque by cleaning your teeth properly. In other words, good oral hygiene can reduce the risk of gingivitis and periodontitis.

The likelihood of developing gingivitis and periodontitis is also increased by various factors, including

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## NEW CLASSIFICATION OF PERIODONTAL AND PERI-IMPLANT DISEASES

Guest editors:  
Mariano Sanz y Panos N. Papapanou

new classifi-  
cation of pe-  
riodontal and  
peri-implant  
diseases



Contents lists available at ScienceDirect

## Microbial Pathogenesis

journal homepage: [www.elsevier.com/locate/micpath](http://www.elsevier.com/locate/micpath)

## Periodontal-disease-associated biofilm: A reservoir for pathogens of medical importance



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### ABSTRACT

The ecological diversity of the periodontal microenvironment may provide suitable conditions for the colonization of species not usually considered members of the oral microbiota. In this investigation, we aimed to determine the prevalence and levels of pathogenic species of medical relevance in the microbiota of individuals with distinct periodontal clinical status. Subgingival biofilm was obtained from patients with periodontal health (H, n = 81), gingivitis (G, n = 55), generalized aggressive (AgP, n = 36) or chronic periodontitis (CP, n = 98), and analyzed for 39 microbial taxa using a checkerboard DNA–DNA hybridization technique. Microbial differences among groups, as well as associations between clinical and microbiological parameters were sought by non-parametric and univariate correlation tests. *Neisseria* spp., *Peptostreptococcus anaerobius*, *Candida albicans*, enterobacteria, *Pseudomonas aeruginosa*, *Escherichia coli*, *Clostridium difficile* and *Olsenella uli* were detected in high mean prevalence and counts in the subgingival microbiota of the study population. Species that were more related to periodontal inflammation and tissue destruction at the patient and site levels included enterobacteria, *C. albicans*, *Neisseria* spp., *P. aeruginosa*, *O. uli*, *Hafnia alvei*, *Serratia marcescens* and *Filifactor alocis* ( $p < 0.05$ ). In contrast, *Fusobacterium necrophorum*, *Lactobacillus acidophilus*, *Staphylococcus aureus* and *Streptococcus pneumoniae* were associated with periodontal health ( $p < 0.05$ ). Pathogenic species of medical importance may be detected in high prevalence and levels in the periodontal microbiota. Regardless of their role in periodontal health or disease, the periodontal biofilm may be a source for dissemination and development of systemic infections by these pathogenic microorganisms.

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### 1. Introduction

Periodontal diseases are among the most common oral infectious diseases associated with the establishment of a highly pathogenic biofilm that triggers an immune/inflammatory host

response, leading to the destruction of supporting periodontal tissues and eventual tooth loss [1,2]. In addition to the substantial economic burden and negative impact of these diseases on quality of life [3,4], oral bacteria and periodontal infections have been indicated as potential risk factors for several systemic diseases [5–8]. Due to the anatomical proximity of the periodontal biofilm to the gingival blood stream, periodontal pockets may act as reservoirs of microbial pathogens and their products, as well as inflammatory mediators and immuno-complexes that may disseminate to other sites of the human body [7,9]. The highly complex periodontal microbiota plays a major role in the establishment of periodontal health as well as the development of periodontal diseases. This microbiota comprises mostly commensal

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## The Oral Microbial Consortium's Interaction with the Periodontal Innate Defense System

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### Abstract

The oral microbial consortium is the most characterized polymicrobial microbial community associated with the human host. Extensive sampling of both microbial and tissue samples has demonstrated that there is a strong association between the type of microbial community found in the gingival crevice and the status of innate host mediator expression. The strong clinical association between the microbial community and the innate host response in both clinically healthy and diseased tissue suggests that the oral consortium has a direct effect on periodontal tissue expression of innate defense mediators. A preliminary study in germ-free mice has demonstrated that the oral commensal consortium has direct effect on IL-1 $\beta$  expression, indicating that this microbial community may contribute to the strong protective status of healthy gingival tissue. Likewise, the lipopolysaccharide composition and invasion characteristics of *Porphyromonas gingivalis*, an oral bacterium strongly associated with periodontitis, suggest that it may be a keystone member of the oral microbial community and facilitate a destructive change in the protective gingival innate host status.

### The Microbial Oral Community Is the Most Completely Characterized Group of Bacteria That Persistently Colonize the Host

EXAMINING THE POTENTIAL SYMBIOTIC RELATIONSHIPS in the oral cavity is greatly aided by the extensive studies that have characterized the composition of dental plaque. Dental plaque is an oral microbiological consortium that forms a biofilm on the tooth and tooth root surface. The first characterization of dental plaque was performed by van Leeuwenhoek in 1683 where he described gingival bacteria as "animacules" that contributed to the beginning of the science of bacteriology (Dobell, 1958). Subsequently, descriptive studies performed throughout the twentieth century demonstrated that dental plaque was a distinct structure containing layers of different morphological types that formed on the tooth and tooth root surface in an orderly ecological succession (Socransky and Haffajee, 1994). Microbiological analyses revealed that the composition of commensal oral bacteria and the bacterial load isolated from healthy sites is significantly different from that found in diseased sites. In healthy sites the microbial load is low ( $10^2$ – $10^3$  isolates may be cultured from an individual healthy sulcus) (Darveau *et al.*, 1997) consisting of mostly gram-positive streptococci (e.g., *Streptococcus gordonii*) and Actinomyces with about 15% gram-negative rod species, including *Fusobacterium nucleatum*. In contrast, characterization of the periopathogenic microbial flora has revealed that the microbial load is higher ( $10^5$ – $10^8$  microorganisms may be cultured from an individual pocket), and there is an increase in the number of gram-negative organisms (15–50%) (Tanner *et al.*,



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## Oral Inflammatory Diseases and Systemic Inflammation: Role of the Macrophage

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### Abstract

Inflammation is a complex reaction to injurious agents and includes vascular responses, migration, and activation of leukocytes. Inflammation starts with an acute reaction, which evolves into a chronic phase if allowed to persist unresolved. Acute inflammation is a rapid process characterized by fluid exudation and emigration of leukocytes, primarily neutrophils, whereas chronic inflammation extends over a longer time and is associated with lymphocyte and macrophage infiltration, blood vessel proliferation, and fibrosis. Inflammation is terminated when the invader is eliminated, and the secreted mediators are removed; however, many factors modify the course and morphologic appearance as well as the termination pattern and duration of inflammation. Chronic inflammatory illnesses such as diabetes, arthritis, and heart disease are now seen as problems that might have an impact on the periodontium. Reciprocal effects of periodontal diseases are potential factors modifying severity in the progression of systemic inflammatory diseases. Macrophages are key cells for the inflammatory processes as regulators directing inflammation to chronic pathological changes or resolution with no damage or scar tissue formation. As such, macrophages are involved in a remarkably diverse array of homeostatic processes of vital importance to the host. In addition to their critical role in immunity, macrophages are also widely recognized as ubiquitous mediators of cellular turnover and maintenance of extracellular matrix homeostasis. In this review, our objective is to identify macrophage-mediated events central to the inflammatory basis of chronic diseases, with an emphasis on how control of macrophage function can be used to prevent or treat harmful outcomes linked to uncontrolled inflammation.

**Keywords:** innate immune system, macrophage, oral disease, inflammation, resolution

### Introduction

Inflammation is the physiological response of the body to injury. The inflammatory response can be either acute and of short duration or chronic, which does not resolve and leads to pathology. The major function of innate immune cells most studied during the inflammatory process is the identification and



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## Current understanding of the relationship between periodontal and systemic diseases

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### Abstract

Periodontal disease (PD) is among the most common infectious diseases affecting humans. While the burden of periodontal disease on oral health has been extensively investigated, a possible specific relationship between the disease and systemic health is a relatively new area of interest. More recently it has been suggested that PD has an etiological role in the development of atherosclerotic cardiovascular disease, diabetes mellitus, and preterm low-birth weight, among others. In this review, we critically evaluate the current knowledge on the relation between PD and systemic diseases overall, and specifically with cardiovascular diseases. The best available evidence today suggests that the infection and inflammatory reaction associated with PD may contribute toward systemic disease. It is critical that dentists and physicians are well informed of the potential general health impact of periodontal disease so that they are in a position to knowledgeably counsel patients.

Periodontal disease (PD) is among the most common infectious diseases afflicts humans. Its presence has been documented for thousands of years, and it has been the subject of intense study. Progressive periodontal disease is characterized by the destruction of the alveolar bones of the jaws and the other supporting structures of the teeth. As a consequence, PD has been identified as one of the 2 major causes of tooth loss, in addition to dental caries.<sup>1</sup> In addition to its effect on oral tissues, PD has been linked to a multiplicity of systemic diseases including cardiovascular disease (CVD), diabetes mellitus (DM), and preterm low-birth weight, and many more including cancer. Although this putative relationship has been reported in many publications, the nature of such a linkage remains to be fully vetted and understood. The concept that oral disease could impact systemic health is not novel. Hippocrates suggested that tooth extraction might cure arthritis. More recently, in 1891, Miller<sup>2</sup> reported that bacteria from mouth infections could seed distant sites in the body leading to pathology. As recently as the 1970's, full mouth extraction for children with leukemia was advocated as a way to prevent sepsis.<sup>3</sup>

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## Oral inflammation and bacteremia: implications for chronic and acute systemic diseases involving major organs

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## Affiliations

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**Abstract**

Gingivitis and periodontitis are both highly prevalent gum diseases characterized by an accumulation of a polymicrobial biofilm (dental plaque) around teeth and inflammation in adjacent soft tissues. During dental procedures, even tooth brushing, these bacteria and their components, such as endotoxin, can easily disseminate into the systemic circulation through minor or major gingival injuries. Particularly in immuno-compromised subjects or patients with preexisting pathologic conditions, bacteremia may lead to bacterial infection of distant organs, which may cause immunological reactions. Oral bacteria and endotoxins have been found in sepsis, infective endocarditis, lung infection, liver disease and many other potentially lethal disorders. This article presents a review of the possible pathologic consequences of bacteremia originating in the oral cavity and points out the most commonly affected organs as well as preventive and treatment measures. At the present time, plaque control by subjects and/or dental professionals is one of the most effective means to prevent the onset and progression of oral bacteremia-induced systemic diseases.

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### JADA, ADA NEWS SHARE TOP READERSHIP SCORES; JADA EARNS AWARDS

The ADA News and JADA are locked in a virtual tie for best-read publication in dentistry, and both are well ahead of their nearest competition, an independent survey on dental publications shows.

Using a formula to determine average readership percentages for major dental publications, PERQ/HCI Corp. calculated 2005 readership scores of 71 percent for both The Journal of the American Dental Association and the ADA News.

That score places ADA publications a full 8 percentage points ahead of their closest competitor among 15 dental publications ranked in this year's PERQ/HCI FOCUS study. The New Jersey-based corporation is an independent research firm that studies the health care publishing industry.

The 2005 FOCUS survey was mailed to a sample of 1,000 U.S. dentists randomly selected from the ADA's lists of members and nonmembers, general dentists and specialists in active private practice. Dentists were asked about their reading habits (cover to cover, read articles of interest, skim, review table of contents and choose articles of interest).

Other selected findings from the FOCUS survey:

- dentists in practice for 15 years or less rated JADA at 66 percent, giving it a slight edge over the ADA News at 65 percent, though both publications surpassed their competition;
- dentists in practice for 15 years or more rated ADA News as best read at 75 percent, with JADA a close second at 73 percent;

- more dentists save JADA for future reference than any other dental publication.

On another front, the Journal of the American Dental Association garnered three awards for excellence in publishing in the Society of National Association Publication's annual awards competition.

JADA won silver EXCEL awards in the design excellence and cover illustration (March 2004) categories, as well as a bronze award for general excellence among scholarly journals, the organization, better known as SNAP, announced last month.

"We are delighted that SNAP has continued to recognize our publications," said Laura A. Kosden, publisher and associate executive director, ADA Publishing Division. "This visibility enhances their value and our ongoing efforts to meet the needs of our readers."

JADA was among some 1,130 entries in SNAP's 2004 awards competition. SNAP is a nonprofit professional society serving association publishers and communications professionals nationwide.

"Congratulations on your fine work and exemplary product," wrote Marilee Peterson, SNAP executive director. "Your efforts have truly identified [the] American Dental Association Publishing Division as a leader in the field."

### ORAL BACTERIA FOUND IN ARTERIAL PLAQUE

Two oral bacteria have been found in arterial plaque, according to a study published in the March issue of the American Heart Association's journal *Atherosclerosis, Thrombosis and*

*Vascular Biology*.

Scientists have found remnants of oral bacteria's DNA in arteries, which signaled that bacteria had entered the bloodstream. However, scientists have not been able to grow periodontal bacteria isolated from arterial plaque in Petri dishes, even though the same species of bacteria swabbed from oral plaque can be cultured in Petri dishes. As a result, they could not be sure that the DNA was from oral bacteria destroyed by the immune system in the bloodstream, or if live oral bacteria were involved directly in arterial plaque formation.

To find bacteria that are infectious to both the oral and vascular tissues, Ann Progulsk-Fox, Ph.D., a professor of oral biology at the University of Florida College of Dentistry, and colleagues attempted to grow bacteria from arterial plaque directly on human artery cells. They obtained a section of a diseased carotid artery from a 74-year-old, partially edentulous man who was undergoing surgery to remove an arterial blockage. After the arterial section was removed, researchers rinsed it, placed it on ice and took it to Dr. Progulsk-Fox's nearby laboratory in a sealed, sterile container.

Within six hours of the sample's leaving the operating room, researchers pureed plaque from the artery and incubated it with a mixture of healthy arterial cells and liquid growth medium. After 24 hours, researchers separated the cells from the slurry in the flask, washed them several times, and subjected them to a series of fluorescent baths containing antibodies sensitive to *Porphyromonas gingivalis* and



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Lignes directrices de pratique clinique

## Définition, classification et diagnostic du diabète, du prédiabète et du syndrome métabolique

Comité d'experts des Lignes directrices de pratique clinique de l'Association canadienne du diabète

La version préliminaire de ce chapitre a été préparée par Ronald Goldenberg MD, FRCPC, FACE, Zubin Punthakee MD, MSc, FRCPC

### MESSAGES CLÉS

- L'hyperglycémie chronique liée au diabète est associée à d'importantes complications microvasculaires et macrovasculaires à long terme.
- Une glycémie à jeun d'au moins 7,0 mmol/L, une glycémie 2 heures après l'ingestion de 75 g de glucose d'au moins 11,1 mmol/L ou un taux d'hémoglobine glycosylée (HbA<sub>1c</sub>) d'au moins 6,5 % sont des facteurs prédictifs de rétinopathie. Par conséquent, un diagnostic de diabète peut être posé en fonction de chacun de ces trois critères.
- Le terme « prédiabète » renvoie à une anomalie de la glycémie à jeun, à une intolérance au glucose ou à un taux d'HbA<sub>1c</sub> variant entre 6,0 et 6,4 %, lesquels exposent les personnes à un risque élevé de diabète et de complications liées à la maladie.

### Définitions de diabète et de prédiabète

Le diabète sucré est un trouble métabolique caractérisé par la présence d'une hyperglycémie attribuable à un défaut de la sécrétion d'insuline ou de l'action de l'insuline, ou des deux. L'hyperglycémie chronique liée au diabète est associée à des complications microvasculaires à long terme assez spécifiques touchant les yeux, les reins et les nerfs, ainsi qu'à un risque accru de maladie cardiovasculaire. Les critères diagnostiques du diabète sont fondés sur les seuils de glycémie associés aux maladies microvasculaires, la rétinopathie en particulier.

Le terme « prédiabète » renvoie à une anomalie de la glycémie à jeun, à une intolérance au glucose (1) ou à un taux d'hémoglobine glycosylée (HbA<sub>1c</sub>) variant entre 6,0 et 6,4 %, lesquels exposent les personnes à un risque élevé de diabète et de complications liées à la maladie.

### Classification du diabète

Le tableau 1 est un résumé de la classification du diabète de type 1, du diabète de type 2 et du diabète gestationnel. L'annexe 1 porte sur la classification étiologique du diabète. Il peut être difficile dans certains cas de faire la distinction entre le diabète de type 1 et de diabète de type 2 au moment du diagnostic; toutefois, cette distinction est importante, car leurs stratégies de prise en charge sont différentes. Les signes physiques d'une insulino-résistance et les marqueurs auto-immuns (tels que les auto-anticorps anti-îlots de Langerhans et antiglutamate décarboxylase) peuvent s'avérer utiles, mais leur utilisation à titre de

test diagnostique dans ce contexte n'a pas fait l'objet d'études adéquates. Bien que de très faibles taux de peptide C obtenus après plusieurs mois de stabilité clinique pourraient favoriser un diagnostic de diabète de type 1 (2), ils ne sont pas utiles en présence d'hyperglycémie aiguë (3). L'approche prudente consiste à faire appel au jugement clinique, à utiliser un traitement sûr et à assurer un suivi continu.

### Critères diagnostiques

#### Diabète

Les critères diagnostiques du diabète sont résumés dans le tableau 2 (1). Ces critères sont fondés sur des épreuves faites à partir de sang veineux et sur les méthodes utilisées en laboratoire.

Une glycémie à jeun de 7,0 mmol/L correspond environ à une glycémie 2 heures après l'ingestion de 75 g de glucose de 11,1 mmol/L ou plus, et les deux mesures sont les meilleurs prédicteurs d'une rétinopathie (5–11).

Une relation semblable à celle de la glycémie à jeun ou de la glycémie après 2 heures existe entre le taux d'HbA<sub>1c</sub> et la rétinopathie, à une valeur seuil d'environ 6,5 % (5–7,11,12). Bien que le diagnostic de diabète soit fondé sur le seuil d'HbA<sub>1c</sub> pour la survenue d'une maladie microvasculaire, le taux d'HbA<sub>1c</sub> est également un facteur de risque cardiovasculaire continu et il est un meilleur prédicteur des complications macrovasculaires que la glycémie à jeun ou la glycémie après 2 heures (13,14). Quoique de nombreuses personnes chez qui un diabète a été diagnostiqué à partir du taux d'HbA<sub>1c</sub> n'auront pas de diabète selon les critères diagnostiques traditionnels fondés sur la glycémie, et vice versa, il n'en demeure pas moins que l'utilisation du taux d'HbA<sub>1c</sub> dans le diagnostic du diabète présente plusieurs avantages (15). Le taux d'HbA<sub>1c</sub> peut être mesuré à tout moment de la journée, ce qui le rend plus commode que la glycémie à jeun ou la glycémie mesurée 2 heures après l'ingestion de 75 g de glucose. Comme le taux d'HbA<sub>1c</sub> indique la glycémie moyenne au cours des deux ou trois derniers mois, il permet également d'éviter le problème de la variabilité quotidienne de la glycémie (1).

Le taux d'HbA<sub>1c</sub> lorsqu'il est utilisé comme critère diagnostique, doit être mesuré au moyen d'un test validé et normalisé selon la référence du NGSP-DCCT (National Glycohemoglobin Standardization Program – Diabetes Control and Complications Trial). Il est important de noter que le taux d'HbA<sub>1c</sub> peut être trompeur chez les

# CARDIOVASCULAR DISEASES

## The Problem



Globally, cardiovascular diseases are the number one cause of death and they are projected to remain so. An estimated 17 million people died from cardiovascular disease in 2005, representing 30% of all global deaths. Of these deaths, 7.2 million were due to heart attacks and 5.7 million due to stroke. About 80% of these deaths occurred in low- and middle-income countries. If current trends are allowed to continue, by 2030 an estimated 23.6 million people will die from cardiovascular disease (mainly from heart attacks and strokes).<sup>1</sup>

Cardiovascular diseases include:

- coronary heart disease (heart attacks),
- cerebrovascular disease,
- raised blood pressure (hypertension),
- peripheral artery disease,
- rheumatic heart disease,
- congenital heart disease, and
- heart failure.

The major causes of cardiovascular disease are tobacco use, physical inactivity, and an unhealthy diet.

Over 80% of cardiovascular disease deaths take place in low- and middle-income countries and occur almost equally in men and women.

### Risk Factors

- Tobacco use, an unhealthy diet, and physical inactivity increase the risk of heart attacks and strokes.
- High blood pressure has no symptoms, but can cause a sudden stroke or heart attack.
- Diabetes increases the risk of heart attacks and stroke.
- Being overweight increases the risk of heart attacks and strokes.<sup>2</sup>
- Low socioeconomic status increases the chances of exposure to risk factors and increases the vulnerability to develop CVD.

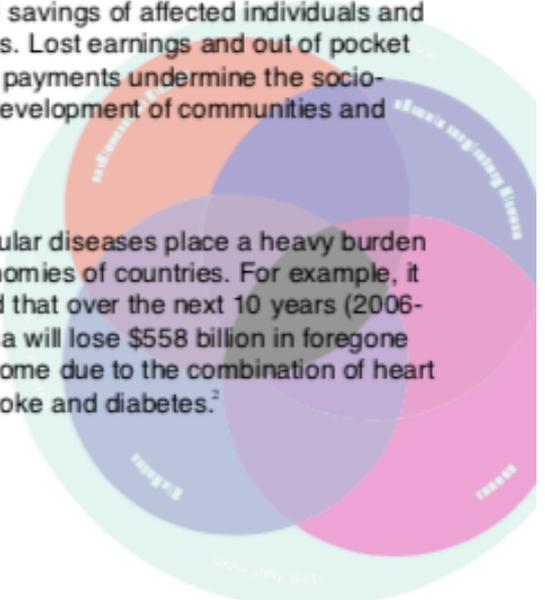
### The Economic Costs of Cardiovascular Diseases

#### Individuals and families

Cardiovascular diseases affect many people in middle age, very often severely limiting the income and savings of affected individuals and their families. Lost earnings and out of pocket health care payments undermine the socio-economic development of communities and nations.<sup>2</sup>

#### Countries

Cardiovascular diseases place a heavy burden on the economies of countries. For example, it is estimated that over the next 10 years (2006-2015), China will lose \$558 billion in foregone national income due to the combination of heart disease, stroke and diabetes.<sup>2</sup>





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## Prevalence of periodontal disease, its association with systemic diseases and prevention

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### Abstract

Periodontal diseases are prevalent both in developed and developing countries and affect about 20-50% of global population. High prevalence of periodontal disease in adolescents, adults, and older individuals makes it a public health concern. Several risk factors such as smoking, poor oral hygiene, diabetes, medication, age, hereditary, and stress are related to periodontal diseases. Robust evidence shows the association of periodontal diseases with systemic diseases such as cardiovascular disease, diabetes, and adverse pregnancy outcomes. Periodontal disease is likely to cause 19% increase in the risk of cardiovascular disease, and this increase in relative risk reaches to 44% among individuals aged 65 years and over. Type 2 diabetic individuals with severe form of periodontal disease have 3.2 times greater mortality risk compared with individuals with no or mild periodontitis. Periodontal therapy has been shown to improve glycemic control in type 2 diabetic subjects. Periodontitis is related to maternal infection, preterm birth, low birth weight, and preeclampsia. Oral disease prevention strategies should be incorporated in chronic systemic disease preventive initiatives to curtail the burden of disease in populations. The reduction in the incidence and prevalence of periodontal disease can reduce its associated systemic diseases and can also minimize their financial impact on the health-care systems. It is hoped that medical, dental practitioners, and other health-care professionals will get familiar with perio-systemic link and risk factors, and need to refer to the specialized dental or periodontal care.

**Keywords:** Periodontal disease, epidemiology, risk factors, systemic disease, preventive strategy

### Introduction

Periodontal disease is a chronic inflammatory disease of periodontium and its advanced form is characterized by periodontal ligament loss and destruction of surrounding alveolar bone.<sup>1</sup> It is the main cause of tooth loss and is considered one of the two biggest threats to the oral health.<sup>1,2</sup> There are approximately 800 species of bacteria identified in the oral cavity<sup>3</sup> and it is hypothesized that complex interaction of bacterial infection and host response, modified by behavioral factors such as smoking, can result in periodontal disease.<sup>4</sup>

The aim of the review is two-fold: (1) To evaluate the prevalence of periodontal disease in different populations, risk factors, and its association with systemic diseases and (2) to discuss the strategies and measures to prevent and control periodontal disease.

## Association between periodontitis in pregnancy and preterm or low birth weight: Review of the literature

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<http://www.medicinaoral.com/medoral/medoral/1309medoral1309p609.pdf>

### Abstract

The aim of this paper is to describe the pathogenic mechanisms that could explain the relationship between periodontitis and adverse pregnancy outcomes, and to review the evidence from systematic reviews and interventional studies, regarding the association between the clinical indicators of periodontitis and the incidence of low birth weight or preterm births.

Preterm birth and low birth weight are world wide leading perinatal problems and have evident public health implications, due to the fact that their incidence doesn't decrease in spite of the many attempts at their prevention. Both intrauterus infections and bacterial vaginosis of the mother are well known risk factors, but distant infections, even subclinical, may also produce preterm births. Periodontitis is a chronic infection by anaerobic gram-negative organisms and may produce local and systemic infection, so a possible association between periodontitis and adverse pregnancy outcomes has been suggested.

Since 1996, a number of studies have investigated the potential relationship between periodontitis and preterm and low birth weight. However, results have been controversial and more research is needed in order to confirm or discard this association.

**Key words:** Periodontitis, preterm birth, low birth weight, pregnancy.

### Introduction

Periodontitis can be considered a continuous pathogenic and inflammatory challenge at a systemic level, due to the large epithelium surface that could be ulcerated in the periodontal pockets. This fact allows bacteria and their products to reach other parts of the organism, creating lesions at different levels. Even some bacterial species, like *Porphyromona gingivalis* and *Aggregatibacter actinomycetemcomitans* (previously named *Actinobacillus actinomycetemcomitans*) can directly invade cells and tissues (1). This exposition to Gram-negative bacteria and their products can generate an immuno-inflammatory response with potential damages to different organs and systems (1,2). Thus, in the last decade, periodontal infections have

been associated with different systemic diseases (1), e.g.: osteoporosis, diabetes mellitus, respiratory diseases, pre-eclampsia, cardiovascular diseases, infections and preterm low birth weight.

At the World Workshop in Periodontics of 1996, the term "periodontal medicine" was introduced to define a discipline focused on the evaluation of the relationship between these pathologies and periodontitis both in humans and animal models (3). This is a two-way relationship, as periodontitis can have a great influence on individual systemic health, and systemic diseases may influence periodontal health as well (3). Several mechanisms have been described to explain these interactions:

• Periodontal bacteria may get introduced into the blood stream and cause infections after colonizing other sites of



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## From focal sepsis to periodontal medicine: a century of exploring the role of the oral microbiome in systemic disease

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### Abstract

The oral microbiome is established within a few minutes after birth and consists of stable multi-species communities that engage in a dynamic equilibrium with the host immune system. Dental caries, endodontic infections and periodontal diseases are bacterially driven diseases that are caused by dysbiotic microbiomes. Over a century ago, the focal infection theory implicated these infections in the aetiology of several systemic diseases, ranging from arthritis to neurodegenerative diseases. However, a lack of concrete evidence, combined with the urgency with which clinicians embraced this approach without regard for appropriate case selection, led to its demise within 30 years. In the last decade of the 20th century, the concept of periodontal medicine was introduced to explain the correlations that were being observed between periodontitis and cardiovascular disease, rheumatoid arthritis, Alzheimer's disease, pulmonary disease, pre-term delivery of low birth weight infants and metabolic disease. It was proposed that periodontal pathobionts played a causal role in the initiating or exacerbating certain diseases either by direct invasion or by stimulating a florid immune-inflammatory response that extended into the systemic circulation. This review will examine the strength of current evidence in establishing a causal link between oral pathobionts and systemic disease.



**Keywords:** focal infection, periodontal medicine, oral microbiome, oral pathobiont, periodontitis, systemic disease

### The oral microbial ecosystem – real estate and habitats

## PRÉVALENCE, INCIDENCE ET FACTEURS DE RISQUE DE LA MALADIE D'ALZHEIMER

[Joël Ankri](#)

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Review J Periodontol. 2006 Aug;77(8):1289-303. doi: 10.1902/jop.2006.050459.

## Diabetes mellitus and periodontal diseases

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### Abstract

**Background:** The purpose of this review is to provide the reader with practical knowledge concerning the relationship between diabetes mellitus and periodontal diseases. Over 200 articles have been published in the English literature over the past 50 years examining the relationship between these two chronic diseases. Data interpretation is often confounded by varying definitions of diabetes and periodontitis and different clinical criteria applied to prevalence, extent, and severity of periodontal diseases, levels of glycemic control, and complications associated with diabetes.

**Methods:** This article provides a broad overview of the predominant findings from research published in English over the past 20 years, with reference to certain "classic" articles published prior to that time.

**Results:** This article describes current diagnostic and classification criteria for diabetes and answers the following questions: 1) Does diabetes affect the risk of periodontitis, and does the level of metabolic control of diabetes have an impact on this relationship? 2) Do periodontal diseases affect the pathophysiology of diabetes mellitus or the metabolic control of diabetes? 3) What are the mechanisms by which these two diseases interrelate? and 4) How do people with diabetes and periodontal disease respond to periodontal treatment?

**Conclusions:** Diabetes increases the risk of periodontal diseases, and biologically plausible mechanisms have been demonstrated in abundance. Less clear is the impact of periodontal diseases on glycemic control of diabetes and the mechanisms through which this occurs. Inflammatory periodontal diseases may increase insulin resistance in a way similar to obesity, thereby aggravating glycemic control. Further research is needed to clarify this aspect of the relationship between periodontal diseases and diabetes.

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# Diabetes mellitus: Su implicación en la patología oral y periodontal

## *Diabetes: oral and periodontal implications*

Sanz-Sánchez I\*, Bascones-Martínez A\*\*

### RESUMEN

*Introducción:* La diabetes es una enfermedad metabólica de alta prevalencia y con gran morbilidad, por lo que las medidas preventivas de las complicaciones derivadas y el control de la enfermedad son esenciales. Los objetivos son: a) diferenciar las rutas patogénicas que intervienen en la diabetes mellitus tipo 1 y 2; b) conocer cuáles son las complicaciones de la diabetes a nivel general y a nivel oral; c) hacer un repaso de la asociación entre la diabetes y la enfermedad periodontal.

*Material, métodos y resultados:* Para la realización de este trabajo se han analizado 36 artículos científicos y un libro de texto. Para la búsqueda se han empleado la base de datos MEDLINE y Cochrane.

*Discusión:* Existen dos rutas patogénicas que diferencian claramente la diabetes tipo 1 de la 2. Además, nos vamos a encontrar con un gran número de posibles complicaciones a largo plazo. Especial mención requiere la asociación existente entre la periodontitis y la diabetes.

**Palabras clave:** Diabetes, metabolic syndrom, insulin, autoimmunity, periodontitis, caries, oral disease.

### SUMMARY

*Introduction:* Diabetes is a high prevalent metabolic disease with a high morbidity. That is why preventive measurements of the linked complications and the control of the disease are essential. The objectives are: a) differentiate the pathogenic ways that take place in diabetes mellitus type 1 and 2; b) to know which are the general and oral complications of diabetes; c) make a summary of the association between diabetes and periodontal disease.

*Materials, methods and results:* For the preparation of this work, we employed 36 scientific articles and one text book. The MEDLINE and Cochrane databases have been used to make the search.

*Discussion:* We can find two clearly different pathways that differentiate diabetes type 1 from type 2 have been analysed. We can also find lots of long term complications. The association between diabetes and periodontal disease requires a special mention.

**Key words:** Diabetes, metabolic syndrom, insulin, autoimmunity, periodontitis, caries, oral disease.

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Sanz-Sánchez I, Bascones Martínez A. Diabetes mellitus: Su implicación en la patología oral y periodontal. *Au. Odontoestomatol* 2009; 25 (5): 249-263.

# Bidirectional association between diabetes mellitus and inflammatory periodontal disease.

## A review

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**Background.** Diabetes mellitus is a metabolic disorder characterized by hyperglycemia. The abnormal glucose metabolism results from defects in insulin production or insulin action, or both. For decades, it was suspected that diabetes contributed to poorer oral health and the increased frequency of periodontitis. More recently it was found that periodontitis could adversely affect glycemic control in diabetics. This review focuses on the bidirectional relationship between diabetes mellitus and periodontitis.

**Methods and Results.** A review of the literature on periodontal disease in diabetes using the following key words: periodontitis/periodontal disease and diabetes mellitus, hyperglycemia/glycemic control.

**Conclusions.** There is strong evidence for an association between diabetes mellitus and inflammatory periodontal disease. Diabetes mellitus increases the risk for and severity of periodontitis, and periodontal diseases can aggravate insulin resistance and affect glycemic control. Periodontal treatment improves glycemic control in type 2 diabetics; control of periodontal infection is not only important for oral health, it may also improve overall health.

**Key words:** diabetes mellitus, periodontitis, hyperglycemia, glycemic control, periodontal treatment

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### INTRODUCTION

Diabetes mellitus (DM) is a chronic disease, characterized by hyperglycemia due to a defect in insulin secretion by pancreatic  $\beta$  cells, a decrease in insulin sensitivity, or a combination of both<sup>1</sup>. The current classification of diabetes is based upon the pathophysiological mechanisms of each form of the disease<sup>1,2</sup>. Type 1 diabetes results from autoimmune destruction of pancreatic  $\beta$  cells, typically leading to a complete loss of insulin secretion. This form is usually present in children and adolescents. The lack of insulin production in patients with type 1 diabetes makes the use of exogenous insulin necessary to sustain life, hence the former name "insulin-dependent diabetes" (ref.<sup>2</sup>). Type 2 diabetes, previously called non-insulin dependent diabetes, results from insulin resistance, which alters the availability of endogenously produced insulin in the target cells<sup>1,2</sup>. Type 2 diabetic patients can be undiagnosed for many years as the hyperglycemia appears gradually and often without symptoms<sup>3</sup>.

Gestational diabetes usually has its onset in the third trimester of pregnancy, and adequate treatment reduces perinatal morbidity. Most women with gestational diabetes return to a normoglycemic state after parturition; however, a history of gestational diabetes significantly increases the risk of subsequently developing type 2 diabetes<sup>4</sup>.

Periodontal disease (PD) is a chronic inflammatory disease of the tissues that support and attach the teeth

to the jaws<sup>5</sup>. Although it is initiated and maintained by a mixed endogenous gram-negative bacterial infection, the onset and progression of the disease is a result of the inflammatory host response. PD is characterized by gingival inflammation, periodontal pocket formation, loss of connective tissue attachment, and alveolar bone resorption, ultimately resulting in tooth loss<sup>6-8</sup>.

The relationship between diabetes mellitus and periodontitis has appeared in the literature for over 70 years; however, with conflicting data. Numerous studies in various populations have demonstrated that individuals with diabetes tend to have a higher prevalence of and more severe periodontitis than nondiabetics<sup>9</sup>. Periodontal disease is the most prevalent oral complication in patients with type 2 DM (ref.<sup>10,11</sup>). In a classic cross-sectional study, type 1 diabetes has been associated with a fivefold increased prevalence of periodontitis in teenagers<sup>12</sup> and with greater bleeding index, probing pocket depth and clinical attachment level<sup>13,14</sup>. Today, chronic periodontitis has been identified as the sixth complication of diabetes alongside retinopathy, nephropathy, neuropathy, macrovascular disease and poor wound healing<sup>15</sup>.

### Link between diabetes mellitus and inflammatory periodontal diseases: data from epidemiological studies

Diabetes mellitus and periodontal diseases are both chronic, common, multifactorial diseases in the population, especially in those over 60 years of age, and are related.

## Diabetes as a Risk Factor for Periodontal Disease: Current Status and Future Considerations

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### Abstract

**Introduction:** Over the past decade, there has been an emerging interest in the inter-relationship between systemic conditions and oral health. Diabetes is perhaps one of the best documented conditions that have been closely linked with periodontal disease. This paper reviews the role of diabetes as a risk factor in periodontal disease. The treatment implications in the management of periodontal disease as an integral component of diabetes care is also discussed in light of the current understanding of the pathogenesis of these 2 chronic conditions. **Materials and Methods:** Epidemiological, clinical and laboratory studies examining the relationship between diabetes and periodontal diseases were selected from both medical and dental journals. **Results:** The severity of periodontal destruction has been shown to be related to the direct and indirect effects of glycaemic control, with other factors also being implicated. Although some studies have pointed towards a bi-directional relationship between glycaemic control and periodontal health, it is still not clear if improvement in periodontal health could lead to improved metabolic control. **Conclusion:** Diabetes and periodontal disease are closely related in many ways, though the effect of periodontal disease on diabetes control remain to be determined, with larger intervention studies. In light of the increasing evidence of the relationship between diabetes and periodontal disease, management of oral health should form an integral part of diabetes management.

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**Key words:** Diabetes mellitus, Infection, Periodontitis

### Introduction

Diabetes mellitus (DM) is a common and growing global health problem. It is highly prevalent in Asian communities. Hong Kong, Pakistan, and Singapore are among the countries with the highest prevalence of diabetes in the adult population. In Singapore, the prevalence of DM among adult Singaporeans increased from 1.9% in 1975, 4.7% in 1984 and 8.6% in 1992<sup>1</sup> to about 9% in 1998.<sup>2</sup> However, in the recent National Health Survey 2004, there had been a decline to 8.2%.<sup>3</sup>

Diabetes is a chronic and complex disease that requires continuous lifelong management to reduce the high morbidity and premature mortality caused by its associated complications. These complications can be reduced, if not completely prevented, with optimal glycaemic control.

However, it was found that about 50% of 1697 Singapore patients surveyed at hospitals and government outpatient clinics had glycated haemoglobin levels in the suboptimal or unacceptable levels.<sup>4</sup> With poor glycaemic control, the social and financial burden of DM is substantial, as a considerable amount of medical resources are utilised for the management of its many complications, namely, retinopathy, diabetic nephropathy, diabetic foot complications, increased risk of hypertension and dyslipidaemia, and ischaemic heart disease.<sup>5</sup> DM is the sixth commonest cause of death in Singapore, accounting for 9.3% of all deaths if all diabetes-related deaths are considered.<sup>6</sup> Thus, early diagnosis and aggressive treatment of the disease can delay or prevent the progression of the major chronic complications as mentioned, due to macrovascular (coronary artery disease)<sup>7</sup> and microvascular

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## DIABETES Y ENFERMEDAD PERIODONTAL: HACIA UN MODELO CLÍNICO BIDIRECCIONAL\*

DIABETES AND PERIODONTAL DISEASES: TOWARDS A BIDIRECTIONAL CLINICAL MODEL

Marisol Miranda Gavís,<sup>1</sup> Yenny Paola Montoya Zukraga,<sup>2</sup> Andrés Saldarriaga Saldarriaga<sup>3</sup>

### RESUMEN

La diabetes mellitus es una de las enfermedades sistémicas con mayor prevalencia en la población mundial y, a su vez, es considerada un problema de salud pública. Esta alteración es catalogada como uno de los factores de riesgo más importantes asociados a la enfermedad periodontal. Se realizó entonces una revisión de literatura sobre la relación diabetes-enfermedad periodontal. Entre los principales resultados se encontró que la prevalencia de la periodontitis es más alta en pacientes diabéticos que en los no diabéticos, y que la prevalencia de diabetes es mayor en personas con periodontitis respecto a un grupo control. En conclusión, se establece una relación desde tres hipótesis diferentes: la diabetes como factor de riesgo para la aparición y progresión de la periodontitis, la infección periodontal como agravante de un difícil control glucémico, y la existencia de una relación bidireccional entre ambas. Se propone un nuevo modelo clínico que explica esta relación.

**Palabras clave:** clasificación, diabetes mellitus, enfermedad, periodontitis, productos finales de glicosilación avanzada, progresión de la enfermedad.

### ABSTRACT

Diabetes mellitus is one of the most prevalent systemic diseases in world population and is considered a public health problem. This disorder is classified as one of the most important risk factors associated with periodontal disease. We thus undertook a literature review on the relation between diabetes and periodontal disease. Among the main results, we found that the prevalence of periodontitis is higher in diabetics than in non-diabetics, and also that the prevalence of diabetes is higher in people with periodontitis when compared to a control group. In conclusion, we established a relationship from three different hypothesis: diabetes as a risk factor for the onset and progression of periodontitis, periodontal infection as related to an aggravation of low glycemic control, and the existence of a bidirectional relationship between these two diseases. We propose a new clinical model that explains this bidirectional relationship.

**Keywords:** classification, diabetes Mellitus, disease, periodontitis, advanced glycosylation end products (AGE), disease progression.

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\* Artículo de revisión sobre la relación diabetes-enfermedad periodontal.

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## Periodontitis and diabetes: a two-way relationship

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### Abstract

Periodontitis is a common chronic inflammatory disease characterised by destruction of the supporting structures of the teeth (the periodontal ligament and alveolar bone). It is highly prevalent (severe periodontitis affects 10–15% of adults) and has multiple negative impacts on quality of life. Epidemiological data confirm that diabetes is a major risk factor for periodontitis; susceptibility to periodontitis is increased by approximately threefold in people with diabetes. There is a clear relationship between degree of hyperglycaemia and severity of periodontitis. The mechanisms that underpin the links between these two conditions are not completely understood, but involve aspects of immune functioning, neutrophil activity, and cytokine biology. There is emerging evidence to support the existence of a two-way relationship between diabetes and periodontitis, with diabetes increasing the risk for periodontitis, and periodontal inflammation negatively affecting glycaemic control. Incidences of macroalbuminuria and end-stage renal disease are increased twofold and threefold, respectively, in diabetic individuals who also have severe periodontitis compared to diabetic individuals without severe periodontitis. Furthermore, the risk of cardiorenal mortality (ischaemic heart disease and diabetic nephropathy combined) is three times higher in diabetic people with severe periodontitis than in diabetic people without severe periodontitis. Treatment of periodontitis is associated with HbA<sub>1c</sub> reductions of approximately 0.4%. Oral and periodontal health should be promoted as integral components of diabetes management.

**Keywords:** Diabetes, Diabetes complications, Periodontal diseases, Periodontitis, Type 1 diabetes mellitus, Type 2 diabetes mellitus

### The two-way relationship between diabetes and periodontitis

## Impact of Periodontitis on the Diabetes-Related Inflammatory Status

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August 26, 2010

### TOPICS:

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# Diabetes and periodontal disease: a two-way relationship

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## IN BRIEF

- Explains the current knowledge regarding the links between diabetes and periodontal disease.
- Provides information on the main types of diabetes and explains how to interpret blood glucose and glycated haemoglobin values that patients may report to you.
- Gives practical guidance for the dental team in assessing and managing periodontal status in people with diabetes.

PRACTICE

Periodontitis and diabetes are common, complex, chronic diseases with an established bidirectional relationship. That is, diabetes (particularly if glycaemic control is poor) is associated with an increased prevalence and severity of periodontitis, and, severe periodontitis is associated with compromised glycaemic control. Periodontal treatment (conventional non-surgical periodontal therapy) has been associated with improvements in glycaemic control in diabetic patients, with reductions in HbA1c of approximately 0.4% following periodontal therapy. For these reasons, management of periodontitis in people with diabetes is particularly important. The dental team therefore has an important role to play in the management of people with diabetes. An emerging role for dental professionals is envisaged, in which diabetes screening tools could be used to identify patients at high risk of diabetes, to enable them to seek further investigation and assessment from medical healthcare providers.

## INTRODUCTION

Periodontitis and diabetes are both highly prevalent conditions, and the association between these two common diseases has been recognised by dental professionals for many years. Epidemiological studies have clearly identified that diabetes is a major risk factor for periodontitis, increasing the risk approximately three-fold compared to non-diabetic individuals, particularly if glycaemic control is poor.<sup>1</sup> In recent years, the precise relationship between periodontitis and diabetes has been the subject of much interest, given that both conditions are highly prevalent, and also because it has become increasingly clear that there are interactions between the two diseases that have important clinical implications for dental professionals, physicians and, most importantly, patients. This narrative review aims to summarise our current understanding of the relationship between diabetes and periodontitis and to discuss the clinical implications of these findings for the dental professional. Relevant literature was identified from Medline and PubMed database

searches together with scrutiny of reference lists from published articles.

## PERIODONTAL DISEASE

Inflammatory periodontal diseases are the most common chronic inflammatory conditions of man, affecting – if including gingivitis as well as periodontitis – up to 90% of the world's population.<sup>2</sup> When considering severe periodontitis (which typically refers to the presence of pocketing  $\geq 6$  mm), the prevalence is generally estimated to be around 5–15% of adults globally.<sup>3</sup> Consistent with this are the findings of the 2009 Adult Dental Health Survey for England, Wales and Northern Ireland, which identified that 8% of adults have at least one pocket of 6 mm or deeper.<sup>4</sup> The inflammation in the periodontal tissues that characterises periodontitis is initiated by the accumulation of the subgingival biofilm; however, susceptibility to disease is determined by a number of factors independent of the absolute levels of plaque. Pre-eminent among these are the major environmental risk factors for periodontitis, tobacco smoking<sup>5</sup> and diabetes.<sup>6</sup>

The tissue damage that results from the chronic inflammation in the periodontal tissues (loss of attachment, breakdown of periodontal ligament fibres and alveolar bone resorption) is largely irreversible. It is also typically painless, so may remain unnoticed for many years unless the patient is seen by a dental healthcare professional. The consequences of periodontitis, such as gingival bleeding, compromised aesthetics, recurrent

periodontal infections, tooth mobility and tooth loss, may all have negative impacts on daily living and quality of life, with implications for function, comfort, self-confidence, social interactions and food choices.<sup>7,8</sup>

## DIABETES

Diabetes is a group of metabolic disorders characterised by hyperglycaemia (elevated blood sugar). The main types of diabetes are type 1 diabetes, type 2 diabetes and gestational diabetes.

Type 1 diabetes (in the past, referred to as insulin-dependent diabetes, or juvenile diabetes) describes a condition in which there is a failure to produce insulin as a result of autoimmune destruction of the insulin-producing  $\beta$ -cells in the pancreas. Genetic susceptibility is a major risk factor in type 1 diabetes, and in susceptible individuals, the onset of diabetes appears to be triggered by environmental factors such as viral infections and diet, rather than being related to lifestyle factors. The onset of type 1 diabetes is usually in childhood or young adulthood. Type 1 diabetes constitutes about 5–10% of all cases of diabetes, but accounts for more than 90% of diabetes cases in young people less than 25 years old. Complications arise as a result of hyperglycaemia and include acute conditions such as diabetic ketoacidosis, as well as chronic disorders such as nephropathy, neuropathy, cardiovascular disease, and acute coronary syndrome. Many patients with type 1 diabetes do not develop serious long-term complications, however,

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## Effect of Periodontal Treatment on Glycemic Control of Diabetic Patients

A systematic review and meta-analysis

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### Abstract

#### OBJECTIVE

There is growing evidence that periodontitis may affect general health. This study was assigned to explore the robustness of observations that periodontal therapy leads to the improvement of glycemic control in diabetic patients.

#### RESEARCH DESIGN AND METHODS

A literature search (until March 2009) was carried out using two databases (MEDLINE and the Cochrane Library) with language restriction to English. Selection of publications was based on 1) original investigations, 2) controlled periodontal intervention studies where the diabetic control group received no periodontal treatment, and 3) study duration of  $\geq 3$  months.

#### RESULTS

Screening of the initial 639 identified studies and reference checking resulted in five suitable articles. A total of 371 patients were included in this analysis with periodontitis as predictor and the actual absolute change in A1C ( $\Delta$ A1C) as the outcome. The duration of follow-up was 3–9 months. All studies described a research population of type 2 diabetic patients in whom glycemic control improved after periodontal therapy compared with the control group (range  $\Delta$ A1C:  $\Delta$ -1.17 up to  $\Delta$ -0.05%). The studies in a meta-analysis demonstrated a weighted mean difference of  $\Delta$ A1C before and after therapy of -0.40% (95% CI -0.77 to -0.04%,  $P = 0.03$ ) favoring periodontal intervention in type 2 diabetic patients. Nevertheless, this improvement in %A1C must be interpreted with care due to limited robustness as evidenced by heterogeneity among studies (59.5%,  $P = 0.04$ ).

#### CONCLUSIONS

The present meta-analysis suggests that periodontal treatment leads to an improvement of glycemic control in type 2 diabetic patients for at least 3 months.

# Treating periodontal disease may improve metabolic control in diabetics

## Abstracted from

Simpson TC, Needleman I, Wild SH, Moles DR, Mills EJ.

Treatment of periodontal disease for glycaemic control in people with diabetes. Cochrane Database of Systematic Reviews 2010, Issue 5.

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## Questions: Is there a relationship between periodontal therapy and glycaemic control in people with diabetes?

**Data sources** The Cochrane Oral Health Group's Trials Register, The Cochrane Central Register of Controlled Trials (CENTRAL), Medline, EMBASE, CINAHL, ZETOC, ISIWeb of Knowledge and LILACS databases were searched together with hand searches of the journals *Annals of Periodontology* (1996 to 2003) and *Periodontology 2000* (1993 to 2003). There were no language restrictions.

**Study selection** This review included randomised controlled trials of people with type 1 or 2 diabetes mellitus (DM) with a diagnosis of periodontitis. Suitable interventions included mechanical periodontal therapy with or without adjunctives and oral hygiene education.

**Data extraction and synthesis** The titles and abstracts of all identified papers were examined by two review authors independently. All included trials were assessed for risk of bias. Data were collated in evidence tables, grouped according to research design and assessed for possible meta-analysis on the basis of homogeneity of main characteristics.

**Results** Seven studies were included and three studies had results pooled into a meta-analysis. The effect for the mean percentage difference in HbA1c for scaling/root planing and oral hygiene (+/- antibiotic therapy) versus no treatment/usual treatment after 3/4 months was -0.40% (95% confidence interval (CI) fixed effect -0.78% to -0.01%), representing a statistically significant reduction in HbA1c ( $P = 0.04$ ) for scaling/root planing. One study was assessed as being at low risk of bias with the other two at moderate to high risk of bias. A subgroup analysis examined studies without adjunctive antibiotics -0.80% (one study: 95% CI -1.73% to 0.13%;  $P = 0.09$ ), with adjunctive antibiotics in the test group -0.36% (one study: 95% CI -0.83% to 0.11%;  $P = 0.14$ ), and with antibiotics in both test and control groups after 3/4 months -0.15% (one study: 95% CI -1.04% to 0.74%;  $P = 0.74$ ).

**Conclusions** There is some evidence of improvement in metabolic control in people with diabetes, after treating periodontal disease. There are few studies available and individually these lacked the power to detect a significant effect. Most of the participants in the study had poorly controlled type 2 DM and there was little data from randomised trials on the effects on people with type 1 DM. Improving periodontal health is an important objective in itself. However, in order to understand the potential of this treatment to improve glycaemic control among people with diabetes, larger, carefully conducted and reported studies are needed.

## Commentary

This is the first Cochrane review dealing with the effect of periodontal therapy on the activity/severity of a systemic disease. This work is without doubt the best available summary of the scientific literature addressing the effect of periodontal treatment in metabolic control in people with diabetes. Results are in favour of a significant effect of periodontal therapy in reducing HbA1c levels. Although still quite imprecise and apparently modest, this effect might translate into an important public health benefit, given the high prevalence of periodontitis on the one hand, and the mortality, morbidity and cost of diabetes on the other.

Other randomized controlled trials are still needed, and relevant implications for researchers are provided in this systematic review. Today, there is a broad consensus about the high quality of Cochrane systematic reviews, and the work by Simpson *et al.* fulfils all the quality requirements. This commentary will focus on some considerations that can help the general dental practitioner (GDP) to apply the results of this systematic review to his/her practice.

## Screening

First, it is important for the GDP to ask new patients systematically about their diabetes status, and to cooperate actively with general practitioners and diabetologists. As stated by Simpson *et al.*, "health providers may wish to explore ways of increasing co-operation between medical and dental/periodontal professionals involved in the care of people with diabetes". Then a full periodontal examination should be recommended for all known diabetic patients, as part of their routine oral health management. Indeed, people with diabetes experience periodontal disease more frequently and with greater severity than the general population.<sup>1,2</sup>

This paper is based on a Cochrane Review published in the Cochrane Library 2010, issue 5 (see [www.thecochranelibrary.com](http://www.thecochranelibrary.com) for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and the Cochrane Library should be consulted for the most recent version of the review.

# Association between periodontal disease and stroke

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**Objective:** Periodontitis is a very common human infection. There is evidence that periodontitis is associated with cerebrovascular disease (CVD) and stroke. The aim of this study is to examine the relationship between periodontal disease and CVD in observational studies.

**Methods:** An electronic search of the English literature using PubMed was conducted. A meta-analysis of the studies reporting on the risk of stroke in patients with periodontitis was performed.

**Results:** Six prospective and seven retrospective studies met the inclusion criteria. Patients with both hemorrhagic and ischemic cerebrovascular events, fatal and nonfatal, were included. Definition of periodontitis was taken directly from included studies. Most studies have been adjusted for common cardiovascular risk factors. Separate statistical analysis was performed for prospective and retrospective studies. Overall adjusted risk of stroke in subjects with periodontitis was 1.47 times higher than in subjects without (95% confidence interval, 1.13-1.92;  $P = .0035$ ) in prospective and 2.63 times (95% confidence interval, 1.59-4.33;  $P = .0002$ ) in retrospective studies. The application of the trim and fill algorithm does not change the initial significant inference.

**Conclusions:** There is evidence that periodontitis is associated with increased risk of stroke. However, the results of this meta-analysis should be interpreted with caution because of the heterogeneity of the studies as well as the differences in periodontitis definition. (*J Vasc Surg* 2012;55:1178-84.)

Gingivitis and periodontitis are among the most common human infections. It has been estimated that in the United States, at least 35% of adults aged 30 years and older have periodontitis: 22% have a mild form, and 13% have a moderate or severe form.<sup>1</sup> Cerebrovascular disease (CVD) is among the most prevalent causes of death and disability in industrialized countries. Stroke is the third leading cause of death in the United States, with 60.9 deaths per 100,000 people in 2000.<sup>2</sup>

Periodontitis has been shown to increase the systemic inflammatory response, which has been implicated in atherosclerosis and CVD. Periodontitis results from a complex interplay between chronic bacterial infection and the inflammatory host response, leading to irreversible destruction of tooth-supporting tissues, with tooth loss as a common end point.<sup>3</sup> Approximately 40% of elders are edentulous.<sup>4</sup> Periodontitis is associated with elevated markers of inflammation<sup>5</sup> that are indicators of CVD and stroke risk. Tooth loss, a marker of past periodontal dis-

ease, has been related to subclinical atherosclerosis and carotid artery plaque prevalence.<sup>6</sup> Bacteria from periodontal pockets can enter the bloodstream during activities such as chewing or tooth brushing,<sup>7</sup> and periodontal pathogens were identified in carotid plaques,<sup>8</sup> but their role in atherogenesis is not clear.

This meta-analysis was conducted to examine the relationship between periodontal disease and CVD in observational studies. The aim was to obtain pooled estimates on the association between periodontal disease and incidence of CVD.

## METHODS

A literature search was undertaken using the MEDLINE database to identify all publications on CVD and periodontitis until December 2010. The keywords used were "stroke," "cerebral ischemia," "cerebrovascular disease," and "periodontitis." Only full-length original articles were included in the analysis. The search was restricted to original studies published in English-language journals, conducted on humans. The inclusion criteria in the meta-analysis included: (1) observational studies that provided a risk estimate of CVD for patients with periodontitis; (2) cases defined as subjects with fatal or nonfatal ischemic or hemorrhagic cerebrovascular event; (3) exposure defined as periodontal diseases; (4) exposure was treated as a categorical variable.

Initial database search using the keywords "periodontitis" and "stroke" or "cerebral ischemia" or "cerebrovascular disease" revealed 146 abstracts. Twelve studies were excluded because they were published in other than English-language journals. Nine more studies were excluded because they were conducted in nonhu-

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*J Periodontol*. 2013 Apr;84(4 Suppl):S24-9. doi: 10.1902/jop.2013.1340019.

## Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases

Maurizio S Tonetti<sup>1</sup>, Thomas E Van Dyke, working group 1 of the joint EFP/AAP workshop

Collaborators, Affiliations

PMID: 23631582 DOI: 10.1902/jop.2013.1340019

### Abstract

**Background:** This consensus report is concerned with the association between periodontitis and atherosclerotic cardiovascular disease (ACVD). Periodontitis is a chronic multifactorial inflammatory disease caused by microorganisms and characterized by progressive destruction of the tooth supporting apparatus leading to tooth loss; as such, it is a major public health issue.

**Aims:** This report examined biological plausibility, epidemiology and early results from intervention trials. **PLAUSIBILITY:** Periodontitis leads to entry of bacteria in the blood stream. The bacteria activate the host inflammatory response by multiple mechanisms. The host immune response favors atheroma formation, maturation and exacerbation.

**Epidemiology:** In longitudinal studies assessing incident cardiovascular events, statistically significant excess risk for ACVD was reported in individuals with periodontitis. This was independent of established cardiovascular risk factors. The amount of the adjusted excess risk varies by type of cardiovascular outcome and across populations by age and gender. Given the high prevalence of periodontitis, even low to moderate excess risk is important from a public health perspective.

**Intervention:** There is moderate evidence that periodontal treatment: (i) reduces systemic inflammation as evidenced by reduction in C-reactive protein (CRP) and improvement of both clinical and surrogate measures of endothelial function; but (ii) there is no effect on lipid profiles--supporting specificity. Limited evidence shows improvements in coagulation, biomarkers of endothelial cell activation, arterial blood pressure and subclinical atherosclerosis after periodontal therapy. The available evidence is consistent and speaks for a contributory role of periodontitis to ACVD. There are no periodontal intervention studies on primary ACVD prevention and there is only one feasibility study on secondary ACVD prevention.

**Conclusions:** It was concluded that: (i) there is consistent and strong epidemiologic evidence that periodontitis imparts increased risk for future cardiovascular disease; and (ii) while in vitro, animal and clinical studies do support the interaction and biological mechanism, intervention trials to date are not adequate to draw further conclusions. Well-designed intervention trials on the impact of periodontal treatment on prevention of ACVD hard clinical outcomes are needed.

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## Risk of incident cardiovascular disease in people with periodontal disease: A systematic review and meta-analysis

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## Abstract

### Objectives

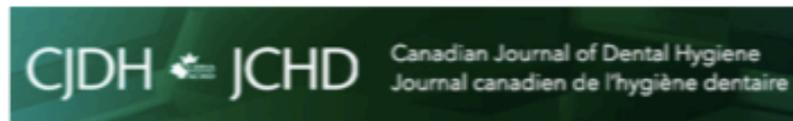
Cardiovascular disease (CVD) is a major cause of mortality; periodontal disease (PD) affects up to 50% of the world's population. Observational evidence has demonstrated association between CVD and PD. Absent from the literature is a systematic review and meta-analysis of longitudinal cohort studies quantifying CVD risk in PD populations compared to non-PD populations. To examine the risk of incident CVD in people with PD in randomised controlled trials and longitudinal cohort studies.

### Material and Methods

We searched Medline, EMBASE and Cochrane databases up to 9th Oct 2019 using keywords and MeSH headings using the following concepts: PD, CVD, longitudinal and RCT study design. CVD outcomes included but were not restricted to any CVD, myocardial infarction, coronary heart disease (CHD) and stroke. Diagnosis method and severity of PD were measured either clinically or by self-report. Studies comparing incident CVD in PD and non-PD populations were included. Meta-analysis and meta-regression was performed to determine risk of CVD in PD populations and examine the effects of PD diagnosis method, PD severity, gender and study region.

### Results

Thirty-two longitudinal cohort studies were included after full text screening; 30 were eligible for meta-analysis. The risk of CVD was significantly higher in PD compared to non-PD (relative risk [RR]: 1.20, 95% CI: 1.14–1.26). CVD risk did not differ between clinical or self-reported PD diagnosis (RR = 0.97, 95% CI: 0.87–1.07). CVD risk was higher in men (RR: 1.16, 95% CI: 1.08–1.25) and severe PD (RR: 1.25, 95% CI: 1.15–1.35). Among all types of CVD, the risk of stroke was highest (RR = 1.24; 95% CI: 1.12–1.38), the risk of CHD was also increased (RR = 1.14; 95% CI: 1.08–1.21).



[Can J Dent Hyg](#). 2020 Feb; 54(1): 32–41.  
Published online 2020 Feb 1.

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PMID: [33240362](#)

Language: English | [French](#)

## An umbrella review of systematic reviews of the evidence of a causal relationship between periodontal disease and cardiovascular diseases: Position paper from the Canadian Dental Hygienists Association

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### Abstract

Previous position papers have confirmed associations between periodontal disease and cardiovascular disease. Causal associations have not been confirmed and have been the source of much confusion for oral health professionals and the public.

#### Aim:

To investigate whether sufficient evidence exists for a causal relationship between periodontal disease and cardiovascular disease.

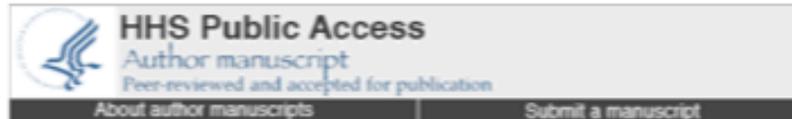
#### Methods:

The PICO question was “For adults in good general health who are diagnosed with periodontal disease, will receiving non-surgical periodontal therapy (NSPT), as compared to not receiving NSPT, lower their risk for cardiovascular diseases?” Only systematic reviews (SRs) with or without meta-analyses (MAs) of randomized controlled trials published in the English language between 2007 and 2019 were included. Databases searched included PubMed, MEDLINE, EbscoHost, CINAHL, Scopus, Cochrane Registry of Systematic Reviews, and Clinical Trials Registry. Quality assessments were conducted by both authors using the PRISMA checklist. The Bradford Hill criteria were used to determine evidence for causality.

#### Results:

Of 53 cardiovascular disease studies retrieved, 7 met the inclusion criteria, of which 6 contained MAs. Results were mixed for various periodontal interventions lowering the risk for cardiovascular outcomes. Only one SR used cardiovascular events as a direct outcome; the other 6 used various surrogate measures.

#### Conclusions:



[J Clin Periodontol](#). Author manuscript; available in PMC 2015 Aug 31.

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J Clin Periodontol. 2013 Apr; 40(0 14): S51–S69.

PMID: [23627334](#)

doi: [10.1111/jcpe.12060](#)

## Inflammatory Mechanisms Linking Periodontal Diseases to Cardiovascular Diseases

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### Abstract

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#### Aims

In this paper, inflammatory mechanisms that link periodontal diseases to cardiovascular diseases (CVD) are reviewed.

#### Materials and Methods and Results

This paper is a literature review. Studies in the literature implicate a number of possible mechanisms that could be responsible for increased inflammatory responses in atheromatous lesions due to periodontal infections. These include increased systemic levels of inflammatory mediators stimulated by bacteria and their products at sites distant from the oral cavity, elevated thrombotic and hemostatic markers that promote a prothrombotic state and inflammation, cross-reactive systemic antibodies that promote inflammation and interact with the atheroma, promotion of dyslipidemia with consequent increases in proinflammatory lipid classes and subclasses, and common genetic susceptibility factors present in both disease leading to increased inflammatory responses.

#### Conclusions

Such mechanisms may be thought to act in concert to increase systemic inflammation in periodontal disease and to promote or exacerbate atherogenesis. However, proof that the increase in systemic inflammation attributable to periodontitis impacts inflammatory responses during atheroma development, thrombotic events, or myocardial infarction or stroke is lacking.

**Keywords:** Periodontitis, Cardiovascular Diseases, Atherosclerosis, Inflammation

### 1. Introduction: Atherosclerosis and periodontitis as inflammatory diseases

**Fundamentals of inflammation in atherogenesis and atherosclerosis ([Figure 1](#))**

J Oral Microbiol. 2017; 9(1): 1374154.

PMCID: PMC5646634

Published online 2017 Sep 10. doi: [10.1080/20002297.2017.1374154](https://doi.org/10.1080/20002297.2017.1374154)

PMID: [29081914](https://pubmed.ncbi.nlm.nih.gov/29081914/)

## Immunoglobulin G antibodies against *Porphyromonas gingivalis* or *Aggregatibacter actinomycetemcomitans* in cardiovascular disease and periodontitis

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### ABSTRACT

**Objectives:** The aim was to elucidate whether levels of circulating antibodies to *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis* correlate to loss of attachment, as a marker for periodontitis and cardiovascular disease (CVD).

**Design:** Sera were collected from 576 participants of the Danish Health Examination Survey (DANHES). Immunoglobulin G antibodies against lipopolysaccharide (LPS) and protein antigens from the a, b and c serotypes of *A. actinomycetemcomitans* and *P. gingivalis* were quantified by titration in ELISA plates coated with a mixture of antigens prepared by disintegration of bacteria.

**Results:** Levels of antibodies against *P. gingivalis* (OR = 1.48) and *A. actinomycetemcomitans* (1.31) associated with periodontitis, as determined by univariable logistic regression analysis. These antibody levels also associated with CVD (1.17 and 1.37), respectively. However, after adjusting for other risk factors, including age, smoking, gender, alcohol consumption, overweight, and level of education using multivariable logistic regression analysis, only increasing body mass index (BMI; 1.09), previous smoking (1.99), and increasing age (decades) (2.27) remained associated with CVD. Increased levels of antibodies against *P. gingivalis* (1.34) remained associated with periodontitis after adjusting for other risk factors.

**Conclusions:** CVD and periodontitis were associated with levels of IgG antibodies to *P. gingivalis* or *A. actinomycetemcomitans* in univariable analyses, but only the association of *P. gingivalis* antibody levels with periodontitis reached statistical significance after adjustment for common confounders. Age, in particular, influenced this relationship.



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Published online 2018 Jul 6. doi: [10.3390/ijms19071978](https://doi.org/10.3390/ijms19071978)

PMID: [29986441](https://pubmed.ncbi.nlm.nih.gov/29986441/)

## Roles of Oral Infections in the Pathomechanism of Atherosclerosis

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### Abstract

Oral infections occur frequently in humans and often lead to chronic inflammations affecting the teeth (i.e., caries), the gingival tissues surrounding the teeth (i.e., gingivitis and endodontic lesions), and the tooth-supporting structures (i.e., periodontitis). At least four basic pathogenic mechanisms have been proposed that involve oral inflammations in the pathogenesis of atherosclerosis: (1) low level bacteremia by which oral bacteria enter the blood stream and invade the arterial wall; (2) systemic inflammation induced by inflammatory mediators released from the sites of the oral inflammation into the blood stream; (3) autoimmunity to host proteins caused by the host immune response to specific components of oral pathogens; (4) pro-atherogenic effects resulting from specific bacterial toxins that are produced by oral pathogenic bacteria. In this narrative review, we summarize published experimental evidence related to these four mechanisms and discuss their impact on the pathogenesis of atherosclerosis.

**Keywords:** coronary artery disease risk, stroke risk, myocardial infarction, periodontitis, endodontic lesions, chronic inflammation

### 1. Introduction

Atherosclerosis is a chronic inflammatory condition affecting arterial blood vessels [1,2]. Due to its causal role in the pathogenesis of cardiovascular diseases (CVD), atherosclerosis is closely related to one of the most frequent causes of morbidity and mortality worldwide [3]. In Europe, CVD is responsible for about 40% of all deaths, killing over 3.9 million people each year, the majority of deaths resulting from heart disease and stroke [4]. Coronary death, myocardial infarction (MI), and stroke represent “hard” or major CVD events, whereas examples for “soft” outcomes are angina pectoris, revascularization and peripheral artery disease, which are not so life threatening [1].

About 50% of MIs occur without significant previous symptoms and despite significant progress in the acute care of MI patients, the 4-week lethality after the first MI could not be lowered significantly below 50% [5]. Therefore, early detection of high-risk patients plays an important role in prevention. The classic risk factors identified i.e., on the basis of the Framingham Heart Study [6], account for only about half of the cardiovascular events occurring in the population, and almost half of all hard CVD events occur in patients lacking a classic risk factor [7,8]. For instance, the fraction of CHD deaths occurring in people with cholesterol levels that are lower than the population mean amounts to about 40% [6,7]. The precise causes underlying the “missing risk factor paradox” are currently unclear. One hypothesis is that the contribution of inflammation to CVD risk is not sufficiently covered by the

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Med Oral Patol Oral Cir Bucal. 2018 Nov; 23(6): e681–e690.

PMCID: PMC6261003

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PMID: [30341272](https://pubmed.ncbi.nlm.nih.gov/30341272/)

### Periodontal treatment on patients with cardiovascular disease: Systematic review and meta-analysis

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**Conflict of interest statement:** None.

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#### Abstract

##### Background

Atherosclerotic cardiovascular disease is the main cause of mortality in developed countries. It is a chronic and systemic inflammatory disease with a multifactorial etiology. Periodontal disease is one of the many factors that contribute to its development.

##### Objective

To analyze the effects of periodontal treatment on cardiovascular risk parameters in patients with atherosclerotic cardiovascular disease.

##### Material and Methods

A systematic research was conducted in the Pubmed/Medline databases for clinical trials published up to and including the year 2017.



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PMCID: PMC7027895  
PMID: [32011025](https://pubmed.ncbi.nlm.nih.gov/32011025/)

## Periodontitis and cardiovascular diseases: Consensus report

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## Abstract

### Background

In Europe cardiovascular disease (CVD) is responsible for 3.9 million deaths (45% of deaths), being ischaemic heart disease, stroke, hypertension (leading to heart failure) the major cause of these CVD related deaths. Periodontitis is also a chronic non-communicable disease (NCD) with a high prevalence, being severe periodontitis, affecting 11.2% of the world's population, the sixth most common human disease.

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## Oral health during pregnancy.

Morgan MA<sup>1</sup>✉, Crall J, Goldenberg RL, Schullin J

### Author information ▶

The Journal of Maternal-fetal & Neonatal Medicine : the Official Journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians  
Sep 2009, 22(9):733-739  
DOI: 10.3109/14767050902926954 PMID: 19488943

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## Abstract

### Objectives

To assess how obstetrician-gynecologists address oral health during pregnancy.

### Methods

Questionnaires were mailed to obstetrician-gynecologists in March 2008.

### Results

The response rate was 41%, with 351 respondents included in the final analysis. Most obstetrician-gynecologist agree that routine dental care during pregnancy is important (84%), periodontal disease can have adverse effect pregnancy outcome (84%), and treating periodontal disease positively affects pregnancy outcome (66%). They seldom ask pregnant patients whether they have recently seen a dentist (73%), ask about current oral health (5) or provide information about oral care (69%). Over a third (38%) do not advise patients to see a dentist for routine prophylaxis, 80% of these saying they had not previously thought about it. Most respondents (77%) reported that patients be declined dental services because of pregnancy. Over half (52%) indicated lack of insurance as a substantial barrier to oral care.

### Conclusion

Obstetrician-gynecologists recognize the importance of good oral health during pregnancy but largely do not act on it. Improved training in the importance of oral health, recognizing oral health problems, and knowledge of procedure safety during pregnancy may make doctors more comfortable with assessing oral health and more likely to act with patients.

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Periodontal infection as a risk factor for preterm low birth weight

April 2010 · Journal of Indian Society of Periodontology 14(2):114-20 · [Follow journal](#)DOI: [10.4103/0972-124X.70832](https://doi.org/10.4103/0972-124X.70832)Source · [PubMed](#)License · [CC BY 2.0](#)

D Gandhimadhi · R Mythili

Research Interest ⓘ

Citations

Recommendations

Reads ⓘ

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### Abstract

There is an overwhelming body of evidence strongly suggesting that periodontal infection may have a significant negative impact on pregnancy outcome in some women. The aim of this study was to determine the association, if any, between periodontal disease and preterm low birth weight. A total of 211 mothers between the ages of 17 and 35 were grouped into two categories based on the gestational age and weight of the baby as cases (< 37 weeks, < 2500 g) and controls (>37 weeks, >2500 g). Relevant obstetric history and information on other primary risk factors for preterm low birth weight were obtained. Investigation reports on blood group, Rh factor and hemoglobin (Hb) were also gathered. Oral assessments included: simplified oral hygiene index (OHI-S), gingival bleeding index, probing pocket depth and clinical attachment level (CAL). Cases had significantly more attachment loss and probing pocket depth, poor oral hygiene, more percentage of sites with attachment loss (Extent) and more mean attachment loss per site (Severity) and less Hb than controls. The number of visits for prenatal care and the percentage of sites with CAL $\geq$ 2mm (Extent 2) remained significant when compared to other variables. The study indicated that periodontal disease is a contributing factor for preterm low birth weight.

Public Full-text ⓘ



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doi: [10.4103/0972-124X.164751](https://doi.org/10.4103/0972-124X.164751)

PMCID: PMC4645536  
PMID: [26644716](https://pubmed.ncbi.nlm.nih.gov/26644716/)

## Maternal periodontal disease and preterm birth: A case-control study

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### Abstract

#### Background and Objective:

Preterm birth (PTB) is an important issue in public health and is a major cause for infant mortality and morbidity. There is a growing consensus that systemic diseases elsewhere in the body may influence PTB. Recent studies have hypothesized that maternal periodontitis could be a high-risk factor for PTB. The aim of the present study was to investigate the relationship between maternal periodontitis on PTB.

#### Materials and Methods:

Forty systemically healthy primiparous mothers aged 18–35 years were recruited for the study. Based on inclusion and exclusion criteria, they were categorized into PTB group as cases and full term birth group (FTB) as controls. PTB cases ( $n = 20$ ) defined as spontaneous delivery before <37 completed weeks of gestation. Controls (FTB) were normal births at or after 37 weeks of gestation. Data on periodontal status, pregnancy outcome variables, and information on other factors that may influence adverse pregnancy outcomes were collected within 2 days of labor. Data were subjected to Student's *t*-test and Pearson's correlation coefficient statistical analysis.

#### Results:

Statistically significant difference with respect to the gestational period at the time of delivery and birth weight of the infants in (PTB) group ( $<0.001$ ) compared to (FTB) group was observed. Overall, there was statistically significant poor periodontal status in the (PTB) group compared to (FTB) group. The statistical results also showed a positive correlation between gestational age and clinical parameters.

#### Conclusion:

An observable relationship was noticed between periodontitis and gestational age, and a positive correlation was found with respect to PTB and periodontitis. Further studies should be designed to establish periodontal disease as an independent risk factor for PTB/preterm low birth weight.



[Pan Afr Med J](#). 2016; 24: 215.

PMCID: PMC5075444

Published online 2016 Jul 12. doi: [10.11604/pamj.2016.24.215.8727](https://doi.org/10.11604/pamj.2016.24.215.8727)

PMID: [27800070](https://pubmed.ncbi.nlm.nih.gov/27800070/)

## Relationship between periodontal disease and preterm low birth weight: systematic review

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The Pan African Medical Journal - ISSN 1937-8688. This is an Open Access article distributed under the terms of the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

### Abstract

#### Introduction

Periodontal disease is a neglected bacterial infection that causes destruction of the periodontium in pregnant women. Yet its impact on the occurrence of adverse pregnancy outcomes has not systematically evaluated and there is no clear statement on the relationship between periodontal disease and preterm low birth weight. The objective of this study was to summarize the evidence on the impact of periodontal disease on preterm low birth weight.

#### Methods

We searched the following data bases from January 2005 to December 2015: CINAHL (cumulative index to nursing and allied health literature), MEDLINE, AMED, EMBASE (excerpta medica database), Cochrane library and Google scholar. Only case-control studies with full text in English were eligible. Critical appraisal of the identified articles was done by two authors independently to provide the possible relevance of the papers for inclusion in the review process. The selected Case control studies were critically appraised with 12 items structured checklist adapted from national institute of health (NIH). Odds ratio (OR) or risk ratios (RR) were extracted from the selected studies. The two reviewers who selected the appropriate studies also extracted the data and evaluated the risk of bias.

#### Results

Of 229 articles, ten studies with a total of 2423 participants with a mean age ranged from 13 to 49 years were met the inclusion criteria. The studies focused on preterm birth, low birth weight and /or preterm low birth weight and periodontitis. Of the selected studies, 9 implied an association between periodontal disease and increased risk of preterm birth, low birth weight and /or preterm low birth weight outcome (ORs ranging from 2.04 to 4.19) and only one study found no evidence of association.



*Open Dent J.* 2012; 6: 79–84.

PMCID: PMC3355349

Published online 2012 May 9. doi: [10.2174/1874210601206010079](https://doi.org/10.2174/1874210601206010079)

PMID: [22615718](https://pubmed.ncbi.nlm.nih.gov/22615718/)

## Causes of Adverse Pregnancy Outcomes and the Role of Maternal Periodontal Status – A Review of the Literature

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### Abstract

Preterm (PT) and Low birth weight (LBW) are considered to be the most relevant biological determinants of newborn infants survival, both in developed and in developing countries. Numerous risk factors for PT and LBW have been defined in the literature. Infections of the genitourinary tract infections along with various biological and genetic factors are considered to be the most common etiological factors for PT/LBW deliveries. However, evidence suggests that sub-clinical infection sites that are also distant from the genitor-urinary tract may be an important cause for PT/LBW deliveries. Maternal periodontal status has also been reported by many authors as a possible risk factor for PT and LBW, though not all of the actual data support such hypothesis. The aim of this paper is to review the evidence from various published literature on the association between the maternal periodontal status and adverse pregnancy outcomes. Although this review found a consistent association between periodontitis and PT/LBW, this finding should be treated with great caution until the sources of heterogeneity can be explained.

**Keywords:** Etiology, low birth weight, literature review, maternal periodontal status, preterm delivery, pregnancy.

### INTRODUCTION

Preterm (PT) delivery is defined as delivery before the end of 37 weeks of gestation (less than 259 days). The international definition of low birth weight (LBW) adopted by the 29th World Health assembly in 1976 is a birth weight of less than 2500 grams [1]. PT infants who are born with a LBW are termed preterm low birth weight (PLBW). The rate of PT birth appears to be increasing world-wide and efforts to prevent or reduce its prevalence have been largely unsuccessful. The importance of PT and LBW deliveries comes from their capacity to predict the increased risk of mortality among infants born with this condition. PT births account for 75% of perinatal mortality and more than half the long-term morbidity [2]. Moreover, World Health Organization (WHO) aims to reduce the number of LBW deliveries, since this is a known predictor of childhood morbidity and mortality [3]. WHO had given

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## No association between periodontitis and preterm low birth weight: a case-control study

[Mariana Fampa Fogacci](#) , [Elaine de O. C. Cardoso](#), [Davi da S. Barbirato](#), [Denise Pires de Carvalho](#) & [Carmelo Sansone](#)

*Archives of Gynecology and Obstetrics* **297**, 71–76(2018)

1259 Accesses | 4 Citations | 1 Altmetric | [Metrics](#)

### Abstract

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#### Purpose

This study aimed to investigate the association between periodontitis in pregnant women and adverse pregnancy outcomes by heeding confounding risk factors for preterm low birth weight infants.

#### Methods

This study was reported according to The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. A case-control study was conducted. Medical records of all pregnant women attending a prenatal care clinic were screened. Those between 21 and 34 years and gestational age of 28–32 weeks were

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### FULL TEXT LINKS



*J Periodontol.* 2005 Jan;76(1):134-7. doi: 10.1902/jop.2005.76.1.134.

## Severe pregnancy complication (preeclampsia) is associated with greater periodontal destruction

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Affiliations

PMID: 15830648 DOI: 10.1902/jop.2005.76.1.134

### Abstract

**Background:** Preeclampsia is a pregnancy-specific disease which is one of the leading causes of maternal and fetal morbidity and mortality. The etiology of preeclampsia remains elusive. The underlying pathology may be related to a generalized intravascular hyperinflammatory state. Since the placental histopathologic lesions of acute atherosclerosis, seen in preeclampsia, bear resemblance to those seen in atherosclerosis, and recent evidence links atherosclerosis with chronic infection, we decided to investigate a possible link between preeclampsia and chronic periodontal infection.

**Methods:** Thirty primigravidas, 15 suffering from preeclampsia, had full mouth periodontal examinations. Gingival crevicular fluid samples were taken for laboratory immunological assessment. Similar examination and sampling were performed in 15 age- and maternal status-matched controls.

**Results:** Significantly higher periodontal probing depth and clinical attachment level scores were found in the preeclamptic group compared with controls (2.98 versus 2.11 and 3.33 versus 2.30, respectively). Plaque index, gingival index, and mean gingival overgrowth scores were very similar in both groups. Furthermore, prostaglandin E2 (PGE2), tumor necrosis factor (TNF)-alpha, and interleukin (IL)-1beta levels were all significantly higher in the preeclamptic group (247.4 ngr/sample versus 89.1 ngr/sample, 8.03 pgr/sample versus 4.03 pgr/sample, and 175.7 pgr/sample versus 62.2 pgr/sample, respectively).

**Conclusion:** The above results suggest a possible association between periodontal inflammation and preeclampsia.

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## Periodontal Disease and Risk of Preeclampsia: A Meta-Analysis of Observational Studies

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### Abstract

#### Background

Many epidemiological studies have found a positive association between periodontal disease (PD) and the risk of preeclampsia, but the magnitude of this association varies and independent studies have reported conflicting findings. We performed a meta-analysis to ascertain the relationship between PD and preeclampsia.

#### Methods

The PubMed database was searched up to January 12, 2013, for relevant observational studies on an association between PD and the risk of preeclampsia. Data were extracted and analyzed independently by two authors. The meta-analysis was performed using comprehensive meta-analysis software.

#### Results

Thirteen observational case-control studies and two cohort studies, involving 1089 preeclampsia patients, were identified. Based on a random-effects meta-analysis, a significant association between PD and preeclampsia was identified (odds ratio=2.79, 95% confidence interval CI, 2.01–3.01,  $P<0.0001$ ).

#### Conclusions

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## The Relationship Between Maternal Periodontal Status of and Preterm and Low Birth Weight Infants in Iran: A Case Control Study

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### Abstract

#### Aim and Background:

It has been suggested that periodontitis is associated with systemic alterations such as adverse pregnancy outcomes. However, some conflicting results have been reported. This study was conducted to determine the association between periodontitis and preterm birth (PTB), low birth weight (LBW) to obtain information which is necessary for the planning of preventive programs of periodontal disease for pregnant women in this area.

#### Materials & Methods:

This case-control study was performed on 264 mothers. The index used to determine oral hygiene and periodontal diseases is Community Periodontal Index Treatment Needs (CPITN).

#### Results:

The mothers in the sample group with single delivery delivered 8 times low birth weight infants more than the mothers in the control group with single delivery. And also the mothers in the sample group with multiple deliveries; delivered 10 times low birth weight infants and 8 times premature infant more than the mothers in the control group.

#### Conclusion:

More studies should be carried out in through preventing and treating periodontal diseases, expenses incurred due to preterm labor and low birth weight decrease and the society will witness fewer mental problems suffered by such children as they grow up. So we can emphasize the importance of periodontal care in prenatal health programs. And we may suggest that a special program of periodontal disease prevention for pregnant women is very necessary.



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## Treating periodontal disease for preventing adverse birth outcomes in pregnant women

Monitoring Editor: [Zipporah Iheozor-Ejirofor](#),<sup>✉</sup> [Philippa Middleton](#), [Marco Esposito](#), [Anne-Marie Glenny](#), and Cochrane Oral Health Group

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### Abstract

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#### Background

Periodontal disease has been linked with a number of conditions, such as cardiovascular disease, stroke, diabetes and adverse pregnancy outcomes, all likely through systemic inflammatory pathways. It is common in women of reproductive age and gum conditions tend to worsen during pregnancy. Some evidence from observational studies suggests that periodontal intervention may reduce adverse pregnancy outcomes. There is need for a comprehensive Cochrane review of randomised trials to assess the effect of periodontal treatment on perinatal and maternal health.

#### Objectives

To assess the effects of treating periodontal disease in pregnant women in order to prevent or reduce perinatal and maternal morbidity and mortality.

#### Search methods



REVIEW ARTICLE

# Oral health challenges in pregnant women: Recommendations for dental care professionals



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## KEYWORDS

Fetus;  
Dental problems;  
Teratology;  
Women's health

**Abstract** Pregnancy is a dynamic state leading to several physiological transient changes in the body systems including the oral cavity. In order to maintain good oral health, the dental treatment should not be withheld. The dental management of pregnant patients involves special considerations. This review article discusses common dental problems a pregnant woman faces along with the relevant treatment implications, the risks of various medications to both mother and fetus and common dental problems a pregnant women faces. In addition, the management of related dental problems in the pregnant patients and appropriate scheduling of dental surgical procedures during pregnancy has been discussed.

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# Risk of Periodontal Diseases in Patients With Chronic Obstructive Pulmonary Disease

## A Nationwide Population-based Cohort Study

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**Abstract:** Several studies have reported an association between chronic obstructive pulmonary disease (COPD) and periodontal diseases. However, a large-scale population-based cohort study was previously absent from the literature. Therefore, we evaluated the risk of periodontal diseases in patients with COPD in a nationwide population.

From the National Health Insurance claims data of Taiwan, we identified 22,332 patients with COPD who were newly diagnosed during 2000 to 2010. For each case, two individuals without COPD were randomly selected and frequency matched by age, sex, and diagnosis year. Both groups were followed up till the end of 2011.

The overall incidence of periodontal diseases was 1.19-fold greater in the COPD group than in the comparison group (32.2 vs 26.4 per 1000 person-years; 95% confidence interval [CI] 1.15–1.24). Compared with non-COPD patients, the adjusted hazard ratios of patients with COPD increased with the number of emergency room visits (from 1.14 [95% CI 1.10–1.19] to 5.09 [95% CI 4.53–5.72]) and admissions (from 1.15 [95% CI 1.10–1.20] to 3.17 [95% CI 2.81–3.57]). In addition, the adjusted hazard ratios of patients with COPD treated with inhaled corticosteroids (1.22, 95% CI 1.11–1.34) and systemic corticosteroids

(1.15, 95% CI 1.07–1.23) were significantly higher than those of patients not treated with corticosteroids.

Patients with COPD are at a higher risk of developing periodontal diseases than the general population. Our results also support that the risk of periodontal diseases is proportional to COPD control. In addition, patients who receive corticosteroid treatment are at a higher risk of developing periodontal diseases.

(*Medicine* 94(46):e2047)

**Abbreviations:** CAD = coronary artery disease, CDS = cluster of differentiation 8, CI = confidence interval, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, ER = emergency room, HR = hazard ratio, ICD-9-CM = International Classification of Disease 9th Revision Clinical Modification, LHD2000 = Longitudinal Health Insurance Database 2000, NHI = National Health Insurance, NHRI = National Health Research Institutes.

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F-CS and C-HK contributed equally.

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There are no conflicts of interests.

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by persistent and usually progressive airflow limitation and is associated with an enhanced chronic inflammatory response in the airways and the lungs. Comorbidities that occur frequently in patients with COPD include certain infections, cardiovascular diseases, diabetes, metabolic syndrome, skeletal muscle dysfunction, osteoporosis, anxiety, depression, impaired cognitive function, and lung cancer.<sup>1</sup> These comorbid conditions can have a significant impact on the prognosis of the disease.

Periodontal diseases are defined as any disorder of the tissues surrounding and supporting the teeth; the term usually refers to the inflammatory disorders of gingivitis and periodontitis.<sup>2</sup> These diseases are highly prevalent and may affect up to 90% of the worldwide population.<sup>3</sup> They are mainly caused by the bacterial biofilm that accumulates on the teeth, but other genetic and environmental factors also contribute to the conditions.<sup>4,5</sup> Compared with COPD, similar comorbid diseases such as cardiovascular diseases, diabetes, and osteoporosis have been reported in association with periodontal diseases.<sup>6–8</sup>

Patients who have an underlying respiratory disorder may face some special challenges in establishing and maintaining oral health. These factors include the illness itself and the associated medical therapies.<sup>9</sup> Several studies have reported the association between COPD and periodontal diseases.<sup>10–14</sup> For example, Zeng et al<sup>12</sup> recently performed a meta-analysis using 14 observational studies and identified a significant association between periodontal diseases and COPD (odds ratio [OR] 2.08, 95% confidence interval [CI] 1.48–2.91,  $P < 0.001$ ).

## Periodontal Disease and Risk of Chronic Obstructive Pulmonary Disease: A Meta-Analysis of Observational Studies

Xian-Tao Zeng,<sup>1</sup> Ming-Li Tu,<sup>2</sup> Dong-Yan Liu,<sup>1</sup> Dong Zheng,<sup>3</sup> Jing Zhang,<sup>2</sup> and WeiDong Lang<sup>1,3,\*</sup>

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Conceived and designed the experiments: XTZ WDL. Performed the experiments: XTZ MLT DYL. Analyzed the data: XTZ DZ. Contributed reagents/materials/analysis tools: XTZ. Wrote the paper: XTZ DZ JZ. Critically reviewed paper: MLT WDL.

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### Abstract

#### Background

Many epidemiological studies have found a positive association between periodontal disease (PD) and risk of chronic obstructive pulmonary disease (COPD), but this association is varied and even contradictory among studies. We performed a meta-analysis to ascertain the relationship between PD and COPD.

#### Methods

PubMed and Embase database were searched up to January 10, 2012, for relevant observational studies on the association between PD and risk of COPD. Data from the studies selected were extracted and analyzed independently by two authors. The meta-analysis was performed using the Comprehensive Meta-Analysis software.

#### Results

Fourteen observational studies (one nested case-control, eight case-control, and five cross-sectional) involving 3,988 COPD patients were yielded. Based on random-effects meta-analysis, a significant association between PD and COPD was identified (odds ratio=2.08, 95% confidence interval=1.48–

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### FULL TEXT LINKS



Review [J Periodontol.](#) 2006 Sep;77(9):1465-82. doi: 10.1902/jop.2006.060010.

# Systematic review of the association between respiratory diseases and oral health

Amir Azarpazhooh<sup>1</sup>, James L Leake

Affiliations

PMID: 16945022 DOI: [10.1902/jop.2006.060010](#)

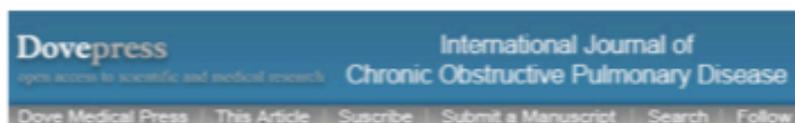
## Abstract

**Background:** The purpose of this review was to investigate evidence for a possible etiological association between oral health and pneumonia or other respiratory diseases.

**Methods:** The following data sources were used: Ovid MEDLINE (In-Process & Other Non-Indexed Citations, Daily Update, and OLDMEDLINE); Cumulative Index to Nursing & Allied Health Literature; Evidence Based Medicine of Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews; Database of Abstracts of Reviews of Effects; EMBASE; Health and Psychosocial Instruments; HealthSTAR; International Pharmaceutical Abstracts; PubMed; and Google Scholar from the earliest record until July 2005. Studies were selected from randomized controlled clinical trials and longitudinal, cohort, case-control, and epidemiological studies. Searches were limited to English language and human studies.

**Results:** A total of 728 articles were searched for relevancy, determined by article title, abstract, and full copy, resulting in a yield of 19 studies that met our inclusion criteria. These articles were read and scored independently by the reviewers to obtain the evidence for this review: 1) the potential risk factors for pneumonia were identified as the presence of cariogenic and periodontal pathogens, dental decay, and poor oral hygiene in five studies; 2) a weak association between periodontal disease and chronic obstructive pulmonary disease (COPD) was identified in four poor to fair studies; and 3) 10 studies were retained providing evidence that interventions aiming to improve oral health reduced the progression or occurrence of pneumonia.

**Conclusions:** 1) There is fair evidence (II-2, grade B recommendation) of an association of pneumonia with oral health (odds ratio [OR]=1.2 to 9.6 depending on oral health indicators). 2) There is poor evidence of a weak association (OR<2.0) between COPD and oral health (II-2/3, grade C recommendation). 3) There is good evidence (I, grade A recommendation) that improved oral hygiene and frequent professional oral health care reduces the progression or occurrence of respiratory diseases among high-risk elderly adults living in nursing homes and especially those in



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## Periodontal Status and Microbiologic Pathogens in Patients with Chronic Obstructive Pulmonary Disease and Periodontitis: A Case–Control Study

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### Abstract

#### Purpose

To evaluate clinical periodontal status and microbiologic pathogens in patients with chronic obstructive pulmonary disease (COPD) and periodontitis.

#### Patients and Methods

We conducted a case–control study of 60 periodontitis patients with COPD (case group) and 60 periodontitis patients with normal pulmonary function (control group). Their periodontal status and respiratory function were clinically examined. Real-time polymerase chain reaction assays were used to measure five dental pathogens and four respiratory pathogens in subgingival dental plaque. Spearman's rank correlation coefficients ( $r^2$ ) were calculated to assess correlations of pathogens. Principal component analysis (PCA) was employed to assess the similarity of bacterial diversity between the two groups. Logistic regression was performed to examine the associations of periodontal variables and pathogens with COPD risk.

## Influence of periodontal disease on systemic disease: inversion of a paradigm: a review

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### Abstract

Medicine and dentistry interface at many levels. For example, the focal infection theory, popular at the outset of the 1900s, suggested that systemic ailments could be traced to dental infections, which, in those days, were common, chronic, and often untreated. With the advent of modern dental and medical treatment, particularly antibiotics, this relationship was largely forgotten. Until recently, the discovery of relationships between periodontal disease and heart ailments, maternal oral health and prematurity of offspring, bidirectional interrelationships between diabetes and periodontal diseases, relationship of oral infections and chronic respiratory diseases and relationship between skeletal and oral bone mineral density, has brought a shift in the perspective. Research is now focused on the potential impact of periodontal diseases on systemic health. Thus, the impact of oral infection in systemic health defined a novel branch in Periodontology termed Periodontal medicine.

**Keywords:** Periodontal diseases, oral infection, systemic health

### Introduction

The organization of health profession into specialties and sub specialties according to body organs and systems is often more pragmatic than scientific. The human organism is a single unit composed of a seemingly infinite number of biologic processes so intertwined that abnormalities of almost any of its parts or processes have profound effects in multiple body areas. The link between the oral cavity and general health is similar and it can be stated very correctly, "The mouth is the window to your body's health". It can show signs of illnesses, general infections and nutritional deficiencies [1].

### The turning of tide in dentistry

# Periodontal Health Condition in Patients With Alzheimer's Disease

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## Abstract

**Objective:** To compare periodontal health status in individuals with and without Alzheimer's disease (AD). **Methods:** A total of 58 individuals with AD and 60 cognitively normal (ND) adult individuals, ranging in age from 50 to 80 years, were assessed for periodontal health status. Individuals with AD were further divided as mild, moderate, and severe, based on degree of cognitive impairment as evaluated using Mini-Mental State Examination. Gingival index (GI), plaque index (PI), probing depth (PD), clinical attachment level (CAL), and percentage of bleeding sites (%BOP) were evaluated. **Results:** All the evaluated periodontal parameters were higher in individuals with AD than that in ND individuals, and the periodontal status deteriorated with the progression of AD. There were significant differences in mean GI, PI, PD, CAL, and %BOP between all the groups. **Conclusion:** The periodontal health status of individuals with AD deteriorates with disease progression and was closely related to their cognitive function.

## Keywords

Alzheimer's disease, dementia, chronic periodontitis, oral health

## Introduction

Alzheimer's disease (AD) is the most common type of dementia affecting the elderly people. Alzheimer's disease is characterized by progressive degeneration in the central and peripheral neurological system<sup>1</sup> and presents with progressive memory loss and cognitive impairments.<sup>2</sup> Memory loss involves not only difficulty in remembering recent events but also impairments in holding information in mind over short periods of time.<sup>3,4</sup> Alzheimer's disease is thought to progress uniformly from the earliest signs of impaired memory to severe cognitive loss, terminating inevitably in complete incapacity and death.<sup>5</sup>

According to World Alzheimer's report 2010, there are an estimated 35.6 million people with dementia worldwide. This number will nearly double every 20 years and much of the increase will be in developing countries. About 58% of people with dementia live in developing countries. The fastest growth in the elderly population is taking place in China, India, and their South Asian and Western Pacific neighbors. Alzheimer's disease mainly affects people older than 65 years, with a greater predilection for women, although there is a growing awareness of cases that start before the age of 65.<sup>6</sup>

Patients with AD experience limitations in medical and social conditions which may also complicate overall personal and medical care.<sup>7</sup> Deficiencies in the care of these elderly patients may result in several systemic and intraoral health

problems including malnutrition, hygiene defects, pressure ulcers, and respiratory disturbances.<sup>8,9</sup> Impaired cognition may severely affect daily activities, and poor oral hygiene execution may lead to caries and eventual loss of teeth.<sup>10-12</sup> Chronic periodontitis (CP) is a peripheral, infectious disease and is one of the leading cause for tooth loss.<sup>13</sup> According to the Third National Health and Nutrition Examination Survey (NHANES

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## Association between chronic periodontitis and the risk of Alzheimer's disease: a retrospective, population-based, matched-cohort study

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### Abstract

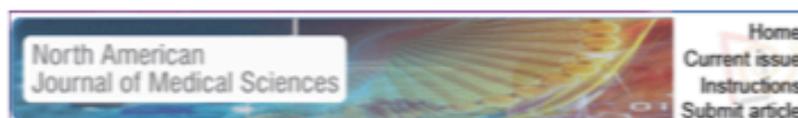
#### Background

Although recent short-term cross-sectional studies have revealed that chronic periodontitis (CP) may be a risk factor for increased cognitive impairment in patients with Alzheimer's disease (AD), systematic reviews and long-term longitudinal studies have provided less clear evidence regarding the relationship between CP and AD. Therefore, we conducted a retrospective cohort study using the National Health Insurance Research Database (NHIRD) of Taiwan to determine whether patients with CP are at increased risk of developing AD.

#### Methods

We conducted a retrospective matched-cohort study using the NHIRD of Taiwan. We identified 9291 patients newly diagnosed with CP between 1997 and 2004. A total of 18,672 patients without CP were matched to the patient cohort according to sex, age, index year, co-morbidity and urbanisation level. Cox proportional hazards regression analyses were performed to evaluate the subsequent risk of AD.

#### Results



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## Association between Periodontitis and Alzheimer's Disease

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### Abstract

Alzheimer's disease (AD) is a neurodegenerative disease which significantly increases with age. Its onset can be either early or late. AD is characterized by the salient inflammatory features, microglial activation, and increased levels of proinflammatory cytokines which contribute to the inflammatory status of the central nervous system (CNS). Whereas, periodontitis is a common oral infection associated with the gram negative anaerobic bacteria. Periodontitis can be marked as a "low-grade systemic disease" by release of proinflammatory cytokines into systemic circulation and elevation of C-reactive protein (CRP). Inflammation is known to play a pivotal role in both the disease process serving as a connecting link between periodontitis and AD. The present review throws a light on possible enigmatic link between AD and periodontitis. This review is designed by collecting data from PubMed database using key words like "Alzheimer's disease", "inflammation", "periodontitis", and "proinflammatory cytokines".

**Keywords:** Alzheimer's disease, Inflammation, Periodontitis, Proinflammatory cytokines

### Introduction

Alzheimer's disease (AD) is a fatal neurodegenerative disease associated with elderly age group and a major health problem in the geriatric subject's worldwide. The incidence of AD significantly increases with age, reaching almost 50% in subjects aged 85 years.[1] As the population ages and life span increases, the prevalence of AD will increase even further and is expected to affect around 14 million people in the next 50 years. A decrease in the prevalence of AD can be achieved by switching to newer treatment approaches which can be effective against probable risk factors for AD and can also delay the onset.[2]

AD could be either early or late onset. Early onset AD is thought to be genetically determined; whereas late onset or sporadic AD, which includes the majority of patients, is believed to be a result of interaction between genetic and environmental factors. Age is a major risk factor for AD. Other risk

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## Periodontitis and Cognitive Decline in Alzheimer's Disease

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Conceived and designed the experiments: MI MH VHP CH. Performed the experiments: MH AS RS VH JF PI RR RT UP JT. Analyzed the data: CH DC. Contributed reagents/materials/analysis tools: MH JF RR JT VHP CH. Wrote the paper: CH MI DC.

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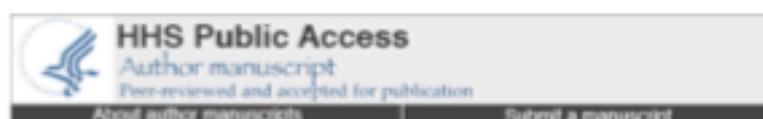
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### Abstract

Periodontitis is common in the elderly and may become more common in Alzheimer's disease because of a reduced ability to take care of oral hygiene as the disease progresses. Elevated antibodies to periodontal bacteria are associated with an increased systemic pro-inflammatory state. Elsewhere raised serum pro-inflammatory cytokines have been associated with an increased rate of cognitive decline in Alzheimer's disease. We hypothesized that periodontitis would be associated with increased dementia severity and a more rapid cognitive decline in Alzheimer's disease. We aimed to determine if periodontitis in Alzheimer's disease is associated with both increased dementia severity and cognitive decline, and an increased systemic pro inflammatory state. In a six month observational cohort study 60 community dwelling participants with mild to moderate Alzheimer's Disease were cognitively assessed



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## Periodontal disease associates with higher brain amyloid load in normal elderly

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### Abstract

#### Background

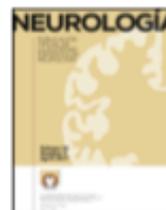
The accumulation of amyloid  $\beta$  plaques ( $A\beta$ ) is a central feature of Alzheimer's disease (AD). First reported in animal models, it remains uncertain if peripheral inflammatory/infectious conditions in humans can promote  $A\beta$  brain accumulation. Periodontal disease, a common chronic infection, has been previously reported to be associated with AD.

#### Methods

Thirty-eight cognitively normal, healthy, community residing elderly (mean age 61; 68% female) were examined in an Alzheimer's Disease research center and a University-based Dental School. Linear regression models (adjusted for age, ApoE and smoking) were used to test the hypothesis that periodontal disease assessed by clinical attachment loss was associated with brain  $A\beta$  load using <sup>11</sup>C-PIB PET imaging.

#### Results

After adjusting for confounders, clinical attachment loss ( $\geq 3$ mm), representing a history of periodontal inflammatory/infectious burden, was associated with increased <sup>11</sup>C-PIB uptake in  $A\beta$  vulnerable brain regions ( $p=0.002$ ).



## REVIEW ARTICLE

### Association between periodontal disease and dementia: A literature review<sup>☆</sup>



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#### KEYWORDS

Periodontitis;  
Alzheimer disease;  
Dementia;  
Inflammation;  
Risk factors;  
Review

#### Abstract

**Introduction:** Periodontal disease and dementia are very prevalent, especially in elderly populations. Multiple studies have shown a link between these diseases; however, the conditions are highly heterogeneous and so is the diagnostic methodology, which may hinder interpretation and comparison of the results. The aim of this article is to provide a critical review of the literature linking these 2 processes.

**Development:** We retrieved 22 studies, most of which were retrospective, and analysed various methodological variables including study population, diagnosis of periodontitis, definition of dementia, adjusted variables, and results. The different aetiopathogenic mechanisms that may affect the progression and interaction of these 2 conditions were also analysed.

**Conclusions:** Although available evidence indicates a positive association between periodontitis and dementia, both the strength of that association and the presence of a causal relationship have yet to be determined.

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#### PALABRAS CLAVE

Periodontitis;  
Enfermedad de  
Alzheimer;

Asociación entre enfermedad periodontal y demencia. Revisión de la bibliografía

#### Resumen

**Introducción:** La enfermedad periodontal y la demencia son enfermedades muy prevalentes, especialmente en poblaciones envejecidas. Numerosos estudios han demostrado una relación entre ambas afecciones, pero la alta heterogeneidad en el diagnóstico, así como la metodología

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