

**Relevance of periodontal disease as a precursor to systemic disorders in companion animals****Relevância da doença periodontal como precursora de afecções sistêmicas em animais de companhia**

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**ABSTRACT**

Periodontal disease (periodontitis) is an oral condition characterized by the involvement of the periodontium, that is, structures that protect and support the teeth. It is commonly diagnosed in small animals, especially in the elderly, and is a frequent cause of tooth loss in both dogs and cats. The etiological factor of periodontal disease is the organized sub- and supragingival plaque and numerous factors are responsible for the predisposition of the disease such as age, race, size and immunity of the patient. The symptomatology of the affected animals varies according to the degree of involvement of the disease, but they usually include halitosis, hyperemia, bleeding and gingival retraction, odontoliths, contact gingival ulcers, furcation exposure and tooth loss. The diagnosis is based on history, complete anamnesis, thorough examination of the oral cavity associated with extra and intraoral x-rays. The periodontal treatment has the purpose of eliminating the causal agent, removing dental stones, tooth extractions and polishing the remaining dental elements. In addition to local changes, periodontal disease can cause systemic damage, due to the rich vascularization of the periodontium and tooth movement in the tooth socket, allowing bacteria and their metabolites to enter the lymphatic and blood vessels during patient chewing, causing organ failure. In view of the high incidence of periodontal disease in pets and the consequent local and systemic changes, the objective of the current work was to carry out a bibliographic survey on this oral condition in dogs and cats, highlighting the damage to other organs due to bacteremia. In this context, the scientific literature emphasizes that the systemic immune response secondary to bacteremia predisposes the formation of immune complexes in the bloodstream that adhere to the walls of the endothelium causing local inflammation and endothelial lysis of the heart, kidneys, liver, lungs, bones, among others, reflecting on diverse symptomatology. Thus, it is assumed that early diagnosis and treatment of periodontal disease can prevent the establishment and local progression of oral disease and, consequently, systemic impairments that directly affect the quality of life and survival of the affected.

**Keywords:** Bacteremia. Oral cavity. Periodontitis. Veterinary dentistry.

## RESUMO

A doença periodontal (periodontite) é a afecção oral caracterizada pelo comprometimento do periodonto, ou seja, estruturas que protegem e sustentam os dentes. É comumente diagnosticada em pequenos animais, especialmente nos senis, sendo causa frequente de perdas dentárias tanto em cães como em gatos. O fator etiológico da doença periodontal é a placa bacteriana sub e supragengival organizada e inúmeros fatores são responsáveis pela predisposição da doença como idade, raça, porte e imunidade do paciente. A sintomatologia dos animais acometidos varia de acordo com o grau de acometimento da doença, mas normalmente incluem halitose, hiperemia, sangramento e retração gengival, odontólitos, úlceras gengivais de contato, exposição de furca e perda dentária. O diagnóstico baseia-se no histórico, anamnese completa, exame minucioso da cavidade oral associado a raios-x extra e intra-orais. O tratamento periodontal tem como finalidade a eliminação do agente causal, remoção de cálculos dentários, extrações dentárias e polimento dos elementos dentários remanescentes. Além das alterações locais, a doença periodontal pode acarretar danos sistêmicos, devido à rica vascularização do periodonto e da movimentação do dente no alvéolo dentário, possibilitando que bactérias e seus metabólitos adentrem os vasos linfáticos e sanguíneos durante a mastigação do paciente, causando insuficiência de órgãos. Perante a elevada incidência da doença periodontal em animais de companhia e das consequentes alterações locais e sistêmicas, o objetivo do atual trabalho foi realizar levantamento bibliográfico sobre esta afecção oral em cães e gatos, ressaltando os danos em outros órgãos em decorrência da bacteremia. Neste contexto, a literatura científica enfatiza que a resposta imunológica sistêmica secundária à bacteremia predispõe a formação de imunocomplexos na corrente sanguínea que se aderem às paredes dos endotélios causando inflamação local e lise endotelial do coração, rins, fígado, pulmões, ossos, entre outros, refletindo em sintomatologia diversa. Assim, admite-se que o diagnóstico e tratamento precoces da doença periodontal possam evitar o estabelecimento e progressão local da afecção oral e, conseqüentemente de comprometimentos sistêmicos que afetam diretamente a qualidade de vida e sobrevida dos acometidos.

**Palavras-chave:** Bacteremia. Cavidade oral. Periodontite. Odontologia veterinária.

## 1 INTRODUCTION

The veterinary dentistry of small animals is a specialty that has been gaining recognition among veterinarians and guardians of dogs and cats, progressing considerably in recent decades due to advances in specific products, diagnostic and treatment techniques, which provide an increase in the quality of care (ROZA, 2004; COLMERY, 2005).

In this sense, among the several conditions that commonly affect the oral cavity of domestic animals, periodontal disease (periodontitis), considered the most common cause of oral infection and tooth loss in these species (EMILY et al., 1999; GIOSO, 2003; NIEMIEC, 2008).

The periodontal disease is characterized by causing involvement in the periodontium, that is, in the structures responsible for protection (gingiva) and dental support (cementum, periodontal ligament and alveolar bone) (GIOSO, 2003; GORREL, 2010).

Because the rich vascularization of the periodontium and tooth movement in the dental alveolus, bacterium and their metabolites can enter the lymphatic and blood vessels (bacteremia) during the patient's chewing (GIOSO, 2003; SANTOS; CARLOS; ALBUQUERQUE, 2012), causing functional failure of several organs such as heart, kidneys, liver, lungs and pancreas, especially in senile patients (GOLDSTEIN, 1990, TELHADO et al., 2004; WHYTE, 2014; ALMEIDA et al., 2017; FRANÇA et al., 2017; KANG et al., 2017).

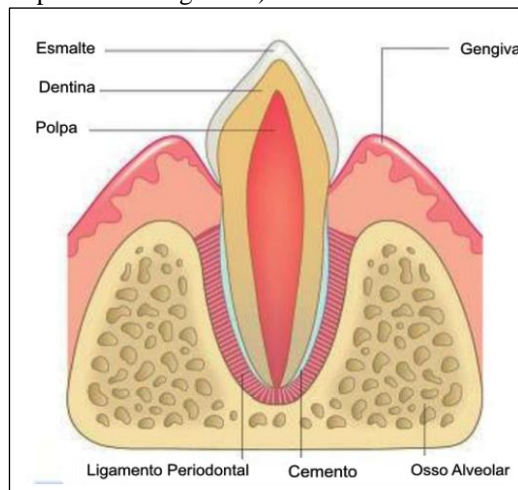
In view of the high incidence of oral disorders in small animals and their various local and systemic consequences, the purpose of this study was to perform a literature review on periodontal disease in dogs and cats and to emphasize secondary impairments in other organs in due to bacteremia, which can directly compromise the quality of life and survival of affected patients.

## **2 LITERATURE REVIEW**

### **2.1 PERIODONTAL DISEASE IN PETS**

Among the various conditions that affect the oral cavity of dogs and cats, periodontal disease stands out, considered the most common cause of oral infection and tooth loss in these species (EMILY et al., 1999; GIOSO, 2003; NIEMIEC, 2008). It is characterized by causing inflammation and destruction of periodontal tissues, that is, in the structures responsible for protection (gum) and dental support (cementum, periodontal ligament and alveolar bone) (Figure 1) (VELDEN, 2000; GIOSO, 2003; ROZA, 2004; SANTOS et al., 2012; SILVA et al., 2017).

Figure 1. Illustrative representation of the structures that make up the protective periodontal (gum) and support (cementum, alveolar bone and periodontal ligament).



Source: GIOSO, 2003.

The periodontal disease affects both pets, especially dogs and cats (GIOSO, 2003) and humans, similarly (ALMEIDA et al., 2017; GRUBBS et al., 2017; KANG et al., 2017; SHIN, 2017).

The etiologic agent of periodontitis is the bacterial plaque (soft induce or dental biofilm) supra and subgingival, formed by the association of numerous Gram + and Gram-, aerobic and anaerobic bacteria, with and without motility, food debris, leukocytes, macrophages, lipids, carbohydrates, mineral salts, metabolites and oral peeling cells (SANTOS; CARLOS; ALBUQUERQUE, 2012; SILVA et al., 2017).

With the organization and interaction of the constituents of the bacterial plaque, there is the production of by-products that contaminate the entire oral cavity and damage the periodontal and adjacent structures, by triggering an immune response, with consequent production of prostaglandins, activation of enzymes such as collagenases, proteases and osteoclast stimulation (WIGGS; LOBPRISE, 1997; SAN ROMÁN, 1999).

Plaque is constantly formed and organized (every 24-48 hours), and, if not removed, mineralizes (by precipitation of salivary mineral salts) forming the dental calculus (odontolith) that adheres to the teeth, predisposing to progression of oral disease for being rough and facilitating the adherence of more dirt and pathogenic microorganisms (SAN ROMÁN, 1999; GIOSO, 2003; HARVEY, 2005).

Several factors can influence the predisposition of the disease such as age, race, size, general health, dental occlusion, presence of retention of primary and supernumerary teeth, hypoplasia of tooth enamel, gingival hyperplasia, non-oral hygiene, consistency of the foods

offered and immunity local and systemic (GORREL, 2010; SANTOS; CARLOS; ALBUQUERQUE, 2012; SILVA et al., 2017).

The periodontitis (Figure 2) it is classified according to the degrees of involvement of the periodontium: absent (absence of oral symptoms), mild (accumulation of plaque, mild gingivitis, gingival edema and mild formation of odontoliths), moderate (gingivitis, gingival edema, odontoliths and onset formation of periodontal bag) and severe (bone loss, significant tooth mobility and tooth loss and considerable amount of odontolytes) (GIOSO, 2003).

Figure 2. Photographic image of a dog's oral cavity with severe periodontal disease.



Source: Personal Archive, 2018.

Symptoms vary according to the degree of the disease and the balance between the host and the condition (GIOSO, 2003; ROZA, 2004), being more common halitosis, hyperemia, bleeding and gingival retraction, presence of odontoliths and periodontal bag, contact gingival ulcers, bone resorption causing mobility, furcation exposure, tooth loss and oronasal communications, nasal discharge, facial swelling and tenderness, jaw fractures are more common and / or maxilla, dysphagia, sialorrhea, systemic changes, among others (GORREL, 1998; SANTOS; CARLOS; ALBUQUERQUE, 2012; CARREIRA; DIAS; AZEVEDO, 2015; WALLIS et al., 2015).

The diagnosis of periodontal disease is based on history, complete anamnesis (diet, history of oral ailments and previous treatments, habit of gnawing objects, hygiene, among others) and clinical symptoms presented by the animal, in addition to direct inspection of the oral cavity associated with extra and intraoral x-rays (VELDEN, 2000; GIOSO, 2003), whose results will establish the degrees of this disease (SANTOS; CARLOS; ALBUQUERQUE, 2012).

The treatment of periodontitis, performed with the patient under general anesthesia, aims at the elimination of the causal agent, removal of dental calculi, tooth extractions and polishing of the remaining dental elements (GORREL, 2000; ROZA, 2004).

Regular toothbrushing (with the aid of a soft veterinary or human pediatric brush, associated with veterinary toothpaste) is the best method of preventing periodontitis (WIGGS; LOBPRISE, 1997), which avoids the organization of bacterial plaque, keratinizes the gum, in addition to favoring increased local microcirculation (WIGGS; LOBPRISE, 1997; SAN ROMÁN, 1999; ROZA, 2004), in addition it is considered as a simple, fast and low cost procedure (VENTURINI, 2006).

## 2.2 SYSTEMIC DISEASES RESULTING FROM PERIODONTAL DISEASE

In general, due to the vascularization of periodontal structures and the movement of the tooth in the tooth alveolus, microorganisms and their metabolites can enter the lymphatic and blood vessels (bacteremia) during chewing of the animal (GIOSO, 2003; SANTOS; CARLOS; ALBUQUERQUE, 2012) and the secondary systemic immune response predisposes the formation of immune complexes in the bloodstream. These, can adhere internally to the walls of the endotheliums, because it is a chronic process, cause functional failure of several organs, especially heart, kidneys, liver, lungs, bones and glands, especially in elderly patients (GOLDSTEIN, 1990, TELHADO et al., 2004; WHYTE, 2014; ALMEIDA et al., 2017; FRANÇA et al., 2017; KANG et al., 2017).

### 2.2.1 Cardiopathies

In the last decades, the relationship between periodontitis with cardiovascular diseases has gained importance in human medicine, therefore, a significant number of epidemiological studies have been carried out. In this context, Lockhart et al. (2012) reported that, in humans, periodontitis has a direct association with atherosclerotic vascular disease and thromboembolism and, consequently, reduced cardiac output; on the other hand, Dietrich et al. (2013) stated that the data are scarce to confirm such an association and that further studies are essential.

According to Saffi et al. (2018), young men showed higher rates of associations between periodontitis and heart disease when compared to senile and women. In this sense, Ávila et al. (2011) stated that pregnant women with rheumatic heart disease may present obstetric

complications secondary to periodontal disease due to bacterial endocarditis (the result of bacteria adhering to the endocardium, which may progress to thromboembolic diseases).

Lockhart et al. (2012) reported that periodontitis has been associated with increased levels of pro-inflammatory markers, recognized risk indicators for cardiovascular diseases, such as C-Reactive protein, IL-6, fibrinogen and leukocyte count. They also reported that several periodontal pathogens were detected in atheromatous plaques, such as *Porphyromonas gingivalis*, *Prevotella intermedia*, *Tannerella forsythensis* and *Actinobacillus actinomycetemcomitans*.

In veterinary medicine, on the other hand, studies on the connection of periodontal disease with cardiovascular diseases are still scarce. According to Kittleson (2008), Infectious endocarditis is the most common cardiac disease in dogs, being caused by bacteria from the oral cavity that enter the circulatory current, connecting the heart valves, being associated with high mortality. However, it is difficult to diagnose in animals, with medium and large animals over the age of four, the most affected (SANTOS, 2012).

Still on this theme, Lemsaddek et al. (2016) demonstrated this association by assessing the presence of *Enterococcus spp* in the gums and hearts of dogs affected by periodontal disease, also emphasizing the importance of regular oral hygiene to avoid such secondary systemic diseases.

### **2.2.2 Nephropathy**

Although periodontitis is a risk factor for chronic kidney disease, according to Schmalz et al. (2016) and Sharma et al. (2016) there are patients who do not have any clinical symptoms, however they can manifest laboratory renal changes.

Oral microorganisms enter bloodstream, damaging the renal glomeruli due to the presence of immune complexes included in the glomerular capillaries, which generates a type III hypersensitivity response (WAKI et al., 2010; CHANG et al., 2017). This activates the coagulation cascade with the deposition of fibrin and infiltration of polymorphonuclear leukocytes; which release stimuli for the production of numerous bioactive mediators. Platelets exacerbate glomerular damage by releasing vasoactive and inflammatory substances (mainly thromboxanes), facilitating the coagulation cascade (GRUBBS et al., 2017).

Thus, the relationship between periodontitis and chronic renal stimulation can compromise tubules and glomeruli silently, contributing to chronic kidney disease, which alters the glomerular filtration rate. Also, arterial stenosis, resulting from arterosclerosis



secondary to periodontitis, can cause renal hypoxia, worsening chronic kidney disease (GRUBBS et al., 2017; RUOKONEN et al., 2017; SHIN, 2017).

In the United States, periodontal disease was found to contribute to the mortality of patients with chronic kidney disease (SHARMA et al., 2016); similar results have been described by Ruokonen et al. (2017).

Kidney disease can be assessed by the presence of proteinuria (HEIENE et al., 2007; SCHAEFER et al., 2011), glomerular filtration rate and azotemia (CHAMBRONE et al., 2013; NYLUND et al., 2017). In this theme, individuals with diabetes and periodontal disease had higher proteinuria values when compared to those without oral disease (KANG et al., 2017). França et al. (2017) also experienced severe renal changes in rodents with experimentally induced periodontitis.

It is assumed that periodontal treatment, as well as in humans, has benefits for kidney function in affected animals. However, in the studies published to date, there are flaws whose results can be biased (ARTESE et al., 2010; CHAMBRONE et al., 2013; SCHMALZ et al., 2016; GRUBBS et al., 2017).

According to Grubbs et al. (2017), 56.8% of human patients with severe periodontal disease and on dialysis, reported the effectiveness of dental treatment against kidney disease. Still in this context, in order to avoid adverse reactions after kidney transplantation, Nylund et al. (2017) reported the importance of dental treatment in pre-dialysis in humans. In a recent study, Almeida et al. (2017) concluded a statistically significant improvement in 26 human patients with renal disease with severe periodontitis who underwent dental treatment. Chambrone et al. (2013) related periodontal treatment in dogs to a 23% reduction in the risk of chronic kidney disease.

### **2.2.3 Hepatopathies**

Bacteremia due to periodontal disease can cause intrahepatic cholestasis, inflammation, fibrosis and necrosis of the liver parenchyma, progressing to increased liver enzymes (PEDDLE et al., 2009), corroborating the findings of the study by Hasegawa et al. (2015) who discussed the presence of changes in liver enzymes (bilirubin, alkaline phosphatase and albumin) in humans with periodontal disease before liver transplantation; in the same research, they found a direct correlation between this oral condition and liver cirrhosis; however, they observed that there was no relationship between periodontal disease and liver function markers in affected patients.

In the veterinary scientific literature, Peddle et al. (2009) reported that 35% of dogs with periodontitis had concomitant systemic diseases, including liver disease.

#### **2.2.4 Lung diseases**

The bacterial pneumonia starts due to the colonization of pathogens in the oral cavity and oropharynx, which can cause failure of the host's defense mechanisms. A study found that elderly patients are more sensitive to acquiring aspiration pneumonia when the bacteria *Porphyromonas gingivalis*, associated with periodontal disease was present in the bacterial plaque and saliva of these patients (ALMEIDA, 2006).

Chronic obstructive pulmonary disease may also be associated with the mechanism of aspiration, adhesion and pulmonary colonization of oral pathogens in the lower respiratory tract, in addition to the relationship with alveolar bone resorption. The cytokines produced by the periodontium, in response to bacterial aggression, modify the respiratory epithelium, making it susceptible to impairments, especially in immunosuppressed patients (ALMEIDA, 2006).

#### **2.2.5 Osteopathies**

The relationship between chronic periodontal disease and osteoporosis and the progression of bone loss has been established; Inflammatory cytokines are believed to be involved in the occurrence of osteopenia, with interleukins 1 and 6 showing synergism with the increase in bone resorption by osteoclasts (ALMEIDA, 2006).

In this sense, interleukin-1 stimulates the synthesis of prostaglandins, inducing bone resorption by osteoclasts and, in addition, it has effects on osteoblasts, inhibiting bone formation. Interleukin-6 is generated in bone tissue itself, due to hormones (parathormone) and other cytokines, such as interleukin-1 and tumor necrosis factor (ALMEIDA, 2006).

#### **2.2.6 Endocrinopathies**

Periodontal disease is considered one of the complications of some endocrinopathies, especially insulin-dependent and type II diabetes. In patients undergoing periodontal treatment, there was a decrease in the amount of daily insulin needed to maintain blood glucose levels in diabetic patients (ALMEIDA, 2006).

**3 CONCLUSIONS**

Periodontal disease is commonly diagnosed in dogs and cats, and is characterized by the involvement of periodontal structures, which protect and support dental elements.

In addition to serious local damage, periodontal disease can cause systemic changes (heart, kidneys, liver, lung, among others), especially in senile and debilitated animals, culminating in functional failure of several organs, due to the migration of oral microorganisms and their metabolites to blood and lymph vessels. In humans, this relationship is well defined and proven; in contrast, in veterinary studies are still limited, mainly due to the occurrence of conditions concomitant with periodontal disease. Thus, the importance of early diagnosis and treatment of periodontal disease is emphasized, aiming to prevent the progression of the disease with consequent systemic compromises that directly affect the quality of life and survival of those affected.

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