Republic of Iraq
Ministry of Higher Education
and Scientific Research
Ashur University
College of Dentistry

Infective endocarditis associated with periodontal disease

A project submitted to the periodontal department to obtain a bachelor's degree in the College of Dentistry

By
Haitham Diaa Ali
Ali Mohammad Maseer

Supervised By:
Lecture
Dr. Ali Sabah Makky

Certification of the Supervisor

I certify that the research project entitled **"Infective endocarditis associated with periodontal disease"** was prepared by **Haitham Diaa Ali, and Ali Mohammad Maseer** under my supervision at the College of Dentistry, Ashur University. This work is submitted in partial fulfilment of the requirements for the award of the **Bachelor's Degree in Dentistry**.

Supervisor's Name: Dr. Ali Sabah Makky

College of Dentistry
Ashur University
Date: _____

Dedication

To my parents, who stayed awake with me through endless nights of textbooks and clinic reports—your belief in me outshone every moment of doubt. Today, as I stand here with ink on these pages, I carry not just my diploma, but the weight of your sacrifices. To every person battling diabetes and gum disease: this research is my promise to turn your pain into hope. May these words be more than science—may they be a bridge to healing.

For you, I wrote this. For us, I fought.

Acknowledgment

My foremost gratitude goes to **Dr. Ali Sabah Makky**, whose meticulous guidance and profound knowledge in metabolic dentistry helped me navigate the complexities of this interdisciplinary research. Without your willingness to answer my endless “what if?” questions, this thesis would have remained a mere concept.

To the College of Dentistry at Ashur University—thank you for fostering an environment where oral health is never seen in isolation. The countless hours spent in your clinics and libraries shaped my understanding of the diabetes-periodontal nexus.

To my parents, who supported me with daily calls that always began with “Have you eaten?” and ended with “We believe in you.” Physical distance never diluted your presence in this journey.

To researchers worldwide battling the silent epidemic of diabetes may this work add one brick to the fortress of solutions we’re building together.

Table of Content

Chapter One

Introduction and Review of literature

Infective endocarditis (IE) is an inflammatory disease usually caused by bacteria that enter the bloodstream and establish infections in the inner linings or valves of the heart, including blood vessels. Despite the availability of modern antimicrobial and surgical treatments, IE continues to cause substantial morbidity and mortality **(Gomes, Brenda PFA, et al., 2023)**. Infective endocarditis is a devastating disease with high morbidity and mortality. The link to oral bacteria has been known for many decades and has caused ongoing concern for dentists, patients and Cardiologists Factors involved in the development of a bacterial endocarditis are difficult to define but a vulnerable Surface (i.e. a damaged endocardium) and a high bacterial load in the blood seems to be decisive **(Carinci, F., et al (2018) .**Periodontitis is one of the most common inflammatory diseases worldwide, with an incidence rate of 20–50% **(Kassebaum, N.J. et al., 2014) .**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 **(Sanz, M. et al.,2020).** Several studies have established that periodontitis is a risk factor for infective endocarditis (IE)، periodontitis are among the most common human infections **(Dhotre, Shree, et al. 2018)**. 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 and associated with elevated inflammation that may contribute to bacteremia associated with IE risk **(Dhotre, Shree, et al. 2018).** Research has shown that patients withmoderate to severe periodontitis have a higher risk of an initial cerebrovascular event than Patients without periodontitis or with mild periodontitis **(Sen, S. et al., 2018).** Historically, 20% to 54% of IE cases are caused by bacterial species common to the oral Cavity. 11-13 Gingivitis, caused by the accumulation of dental plaque on the teeth, affects 50 to 90% of the world-wide population **(Lockhart, P., Chu, V., Zhao, J. et al. 2023).**

Two hundred and seventy articles were identified, of which twenty-three met the inclusion criteria. Bacteraemia rates after periodontal treatment ranged from 10-94% in the investigated patients. Mainly oral pathogens related to infective endocarditis, such as viridans group streptococci (up to 70%) and HACEK group pathogens (e.g., Aggregatibacter actinomycetemcomitans), were detected. But typical oral and periodontopathogenic species, such as Porphyromonas spp. (P.s gingivalis) (up to 50%), Actinomyces spp. (up to 30%) and Fusobacterium spp. (up to 30%), which do not usually cause infective endocarditis, were also found. Infective endocarditis episodes that might have been in association with a dental treatment were mainly caused by viridans group streptococci. Prophylactic measures like rinse application of chlorhexidine, povidone-iodine or essential oils, diode laser or systemic antibiotic prescription were described as decreasing the bacteraemia rate after periodontal interventions to 5-70% **(Hatz, Christian R., et al 2021).**

Aim of the Study

This study aims to explore the relationship between periodontal disease and infective endocarditis and to understand the mechanisms through which periodontal disease may increase the risk of infective endocarditis.

Through this study, better preventive strategies can be developed to reduce the risk of infective endocarditis, especially in individuals with heart conditions or artificial heart valve.

Risk factors

IE is associated with many risk factors of which a health care Practitioner must be aware, both cardiac and non-cardiac. Cardiac risk factors include: prosthetic valves, congenital heart defects, rheumatic heart disease, mitral valve prolapse, aortic valve stenosis And the presence of an Implantable electroniccardiac device. Non-cardiac risk Factors include: diabetes mellitus, hemodialysis, IV drug use immunosuppression and poor oral hygiene **(Martico, Michael, et al (2024).** The risk factors can be subdivided into modifiable risk factors,including smoking tobacco, poor Oral hygiene, diabetes mellitus, and pregnancy, and non-modifiable risk factors, like age and Heredity, including genetic diseases**(Albandar JM. Et al., 2000).** Additional risk factors include genetic susceptibility, tobacco smoke, alcohol use and Systemic conditions such as diabetes, osteoporosis, Malnutrition and stress **(Azzi L., Carinci F., et al 2017).** Effective treatment of Periodontal infections is important to reduce local Inflammation and bacteraemia **(Roncati M., Lauritano D., et al (2015) .** In addition, poor periodontal health appears to increase the risk of cardiovascular disease, pulmonary disease, and Preterm and low birth weight **(Di Girolamo M, Calcaterra R., et al (2016)**. Although antibiotic prophylaxis against infective endocarditis is recommended, the true risk factors for infective endocarditis are unclear **(Strom, Brian L., et al (1998) .**Infective endocarditis (IE) often is caused by bacteria that colonize teeth. The authors conducted a study to determine if poor oral hygiene or dental disease are risk factors for developing bacteremia after toothbrushing or single-tooth extraction **(Lockhart, Peter B., et al.,(2009).**

Epidemiology

Periodontal diseases can be seen in up to 90% of the global population, making it the most Common oral disease. In the United States alone, cross-sectional studies show that approximately 50% of adults currently have some form of gingivitis, and up to 80% have experienced some Form of periodontal disease in their life. Certain groups have been shown to have an increased Incidence of periodontal diseases. These groups include older individuals, males, and African-Americans. Lower-income and education levels were also associated with severe periodontitis **(BorrellLN. Et al., 2006).** Numerous studies have shown a relationship between periodontal disease and increased risk of bacteremia, which may contribute to endocarditis. A large-scale study found a higher Rate of bacteremia in individuals with periodontal Disease, particularly following dental interventions . confirmed that periodontal disease increases the risk of systemic conditions like infective endocarditis. Highlighted that untreated periodontal disease can increase the incidence of bacteremia, emphasizing the need for effective periodontal care to reduce the risk of systemic infections like endocarditis. Additionally, showed that periodontal pathogens identified in Blood samples were closely linked to the development Of infective endocarditis, particularly among patients With pre-existing heart conditions **(Solmaz V.,Mehdi H. et al (2024) .** A total of 1,082 patients with definite IE were included. Of these, 753 (69.6 %) patients had infection on a native valve, 277 (25.6 %) on a prosthetic valve, and 52 (4.8 %) on an implantable electronic device. Overall, community-acquired (69.2 %) was more common than nosocomial (6.2 %) or non-nosocomial (24.6 %) health care-associated IE. Staphylococcus aureus was the most common pathogen (22.0 %). In-hospital mortality was 15.1 %. From the multivariate analysis, congestive heart failure (CHF), stroke, prosthetic valve infection, S. aureus, and health care-associated acquisition were independently associated with increased in-hospital mortality, while surgery was associated with decreased mortality **(Leone, Sebastiano, et al (2012).** Sixteen studies were included, reporting over 1.3 million cases of IE. The crude incidence of IE following guideline updates has increased globally. Adjusted incidence increased in one study after European guideline updates, while North American rates did not increase. Cases of IE with a causative pathogen identified

ranged from 62% to 91%. Rates of streptococcal IE varied across adult and pediatric populations, while the relative proportion of staphylococcal IE increased (range pre-guidelines 16–24.8%, range post-guidelines 26–43%). AP prescription trends were reduced in both moderate and high-risk patients following guideline updates **(Williams, Michael L., et al (2021) .** 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 **(Sanz, Mariano, et al (2020) .**

Pathophysiology

Periodontal disease is caused by an imbalance between the host's immune response and the oral microbiome, with pathogenic bacteria such as Porphyromonas gingivalis, Streptococcus sanguinis, and Streptococcus mutans contributing to the Inflammation and tissue destruction. As the disease progresses, these pathogens can enter the bloodstream (bacteremia), particularly during routine oral hygiene activities such as tooth brushing or dental procedures. Once in the bloodstream, bacteria may attach to the heart valves, especially in individuals with pre-existing cardiac conditions like valvular heart disease, congenital Defects, or prosthetic heart valves. This attachment Facilitates bacterial growth and biofilm formation, Which can protect the bacteria from immune responses And antimicrobial treatments, leading to infectiv endocarditis **(Solmaz V.,Mehdi H. et al (2024).** The role of oral bacteria In the pathogenesis of infective endocarditis is a Various micro-organisms have been implicated as causative agents for bacterial endocarditis, including lactobacilli and in particular the viridans streptococci which are more commonly associated with dental caries. Of these, the most frequently isolated one has the descriptive name Streptococcus sanguis **(Knox, K. W., Hunter. Et al.(1991).**

The disease is characterized by growth of microorganisms within a platelet-fibrin thrombus protruding from a valve leaflet. An understanding of the pathogenesis involves knowledge of the mechanisms of conversion of the normal vascular surface to a thrombogenic one and the adhesion of micro-organisms to such surfaces. Model systems to study this interaction include experimental animals, mammalian epithelial cells and platelets, and proteins such as fibronectin and fibrinogen. Microbial protein surface components (adhesins) and lipoteichoic acid have also been implicated. Capsular polysaccharides may be involved, but the role of dextrans formed from sucrose has been overemphasized as the polymers are not formed in situ. Antibiotic prophylaxis for patients at risk is based on bacteriostatic or bactericidal action. However, bacterial cell surface components involved in adhesion may also be affected, and knowledge of such reactions could provide a more rational basis for antibiotic prophylaxis **(Knox, K. W., Hunter. Et al.(1991).** The microbiota of the mouth is extremely diverse and more than 700 bacterial species have been detected. Half of them are uncultivable so far. Oral Microbiota is not uniform,

specific sites exist in The mouth such as tongue, palate, cheek, teeth and periodontal pockets that have their own microbiota.The Cause of microorganisms, in 90% of cases, are Staphylococcus, streptococcus and Enterococcus. Oral Streptococci belong to viridans group (streptococcus mutans and streptococcus sanguis). As they are Part of dental plaque, they could enter the bloodstream causing bacteraemia through daily habits like chewing or tooth brushing **(Carinci, F., et al (2018) .**

Diagnosis and prognosis

The diagnosis of bacterial endocarditis is based On four factors: changing murmurs, ECG diagnosing abnormal rhythms of the heart, echocardiography Identifying adenoids and evaluating valve and Heart functions and blood culture. It is essential to Perform blood culture before antibiotic treatment Begins, at half hourly intervals in order to increase The prospects of positive blood cultures. Without Treatment, bacterial endocarditis is a fatal disease in 30% of the cases. Patient should be sent to a hospital For intravenous antibiotic therapy (benzylpenicillinAnd gentamicin are normally used) **(Thuny F, Grisoli D., et al (2012).**

Generally, An extended treatment is needed. For this reason, Programs of home hospitalization service have been progressively adopted administering antibiotics Intravenously. If staphylococcal endocarditis is suspected, penicillin could be replaced for Vancomycin. In severe cases like prosthetic valve Endocarditis patients, it might be necessary to replace The infected valve with a new valve **(Werdan K, Dietz S., et al (2014).**

Prevention and Management

Given the increasing evidence linking periodontal disease to infective endocarditis, Preventive measures Are critical, particularly for those at risk for heart disease. The American Heart Association (AHA) Recommends prophylactic antibiotics for patients with Specific heart conditions, such as prosthetic heart valves Or a history of endocarditis, before dental procedures That could induce bacteremia. This recommendation Underscores the importance of maintaining oral health To prevent heart-related infections. In addition to Antibiotic prophylaxis, maintaining good oral hygiene, including regular tooth brushing, flossing, and Professional dental cleanings, is vital for reducing the Bacterial load in the mouth. For individuals with existing periodontal disease, treatments such as scaling Or surgical interventions can effectively control bacterial populations and mitigate the risk of endocardial infection .The association between periodontal disease and Infective endocarditis highlights the importance of Good oral health practices, especially for individuals With cardiovascular risk factors. Oral infections can Introduce harmful bacteria into the bloodstream, which May then settle on heart valves, leading to endocarditis. Preventive measures, including regular oral care and Early intervention in periodontal disease, are essentialto reduce the risk of systemic complications such asinfective endocarditis **(Solmaz V.,Mehdi H. et al (2024).**

Relationship between Periodontal Disease and Infective endocarditis

Dental treatment does not seem to be a risk factor for infective endocarditis, even in patients with valvular abnormalities, but cardiac valvular abnormalities are strong risk factors. Few cases of infective endocarditis would be preventable with antibiotic prophylaxis,even with 100% effectiveness assumed. Current policies for prophylaxis should be reconsidered **(Strom, Brian L., et al. 1998)** .The associations from observational studies may be explained by shared risk factors and comorbidities instead of direct consequences. This also suggests that addressing the common risk factors—such as reducing obesity and improving glucose tolerance—could benefit both conditions **(Zhou, Mengchen, et al.2022**).periodontitis with inflamed and ulcerated crevicular or pocket epithelium surrounding the teeth may be a portal of entry for bacteria into the bloodstream. A newly proposed causal model predicts that an early bacteremia may affect the endothelial surface of the heart over many years and promote valve thickening rendering the heart valve susceptible to vegetation by a later bacteremia that would culminate over a few weeks into fulminant infection. Evidence Acquisition: In this review, various published sources of information pertaining to periodontitis, bacteremia and infective endocarditis were reviewed. This review is focused on the role of the viridans group streptococci (VGS) in periodontitis, bacteremia and infective endocarditis **(Dhotre, Shree V.,et al.2017)** .The patients with IE had fewer remaining teeth, more advanced bone resorption compared with those of patients without IE. These findings suggest a possible association between the occurrence of IE and periodontal infection **(Ninomiya, Masami, et al.2020)**Infective endocarditis (IE) is a serious disease that is associated with dental diseases and treatment(Spahr, Axel, et al. 2006).

Inflammation, Infective endocarditis and Periodontal Disease

Inflammation is a well-organized protective response to pathogens and consists of immune cell recruitment into areas of infection. Inflammation either clears pathogens and gets resolved leading to tissue healing or remains predominantly unresolved triggering pathological processes in organs **(Paul, Oindrila, et al. 2021)**

Infective endocarditis is a focus of infection within the heart and is a feared disease across the field of cardiology. It is frequently acquired in the health care setting, and more than one-half of cases now occur in patients without known heart disease. Despite optimal care, mortality approaches 30% at 1 year. The challenges posed by infective endocarditis are significant. It is heterogeneous in etiology, clinical manifestations, and course. Staphylococcus aureus, which has become the predominant causative organism in the developed world, leads to an aggressive form of the disease, often in vulnerable or elderly patient populations **(Cahill, Thomas J., et al.2017).**

Periodontal disease (PD) that is initiated by specific bacteria also triggers production of inflammatory mediators. These processes lead to loss of tissue structure and function. Reactive oxygen species and oxidative stress play a role in susceptibility to periodontal pathogenic bacterial infections **(Paul, Oindrila, et al. 2021)** .

Evidence suggests that patients with higher levels of circulating C reactive protein (CRP) have a greater risk of suffering an AMI or CVE; also, it has been demonstrated that treatment with aspirin diminishes the risk of AMI by almost 55% in patients with high levels of CRP compared with only a 13% reduction in those with low or normal levels of CRP, suggesting that aspirin's protecting effects are mediated partially by its anti-inflammatory properties. **(Ridker PM. Et al., 1997)**. Inflammation plays a major role in the genesis and progression of Atherosclerosis. **(Libby P. et al., 2009).** Periodontal disease and Infective endocarditis are both major health issues. Poor oral health has long been associated with the development of systemic diseases, with the typical example being the risk of endocarditis posterior

to dental procedures. Through the years, the association of periodontal disease with other non-infectious systemic diseases has been brought to attentione **(Carrizales-Sepúlveda, Edgar Francisco, et al,. 2018)** .

In support of this hypothesis, it has been shown that brachial artery reactivity as measured by flow-mediated dilatation is decreased in patients with severe periodontal disease and that this is associated with high levels of C-reactive protein **(Amar S , GokceN,et al,2003)** . Furthermore, Tonetti et al. demonstrated that at 60 and 180 days after intensive periodontal therapy, brachial artery reactivity was significantly greater compared with controls **(Wick G , PerschinkaH, et al ,1999)**.

This degree of improvement in the intensive periodontal therapy group was associated with a significant improvement in periodontal health, suggesting that periodontal disease, per se, may affect endothelial cell dysfunction either directly or indirectly **(Seymour, Gregory J., et al.2009)**Also, other studies have shown that patients with PD have higher levels of other inflammatory markers such as, tumor necrosis factor and Interleukin-1, 6 and 8. **(Smalley JW. Et al. 2016).**

Association between periodontal disease and ischemic heart disease

Over the past few decades, oral diseases, particularl Periodontitis, have been discussed as possible risk Factors for ischemic heart disease (IHD) **(Buhlin K,Gustafsson A,et al. 2002)**. The Prevalence of moderate periodontitis or gingivitis in The Swedish population is about 60%, and between 10% and 15% suffer from severe periodontitis Leading to loss of teeth if untreated **(Hugoson A, Norderyd O,et al.1998)**. In the Western industrialized world, IHD is one of the leading causes of death **(The World Health Report 1995)** . Since the prevalences of these two chronic inflammatory diseases are high, any possible association between them would con-cern many people. Well-known risk factors in common for the two diseases include smoking, diabetes, and low socio-economic status. Some studies suggest that these risk factors have not been fully taken into account and that therefore the association between periodontitis and IHD has been overestimated

(Hujoel PP, Drangsholt M,et al.2000). On the other hand, some authors explain the Connection between periodontitis and IHD as the Result of an invasion of periodontal pathogens into The endothelial and smooth muscle cells of the arteries that in turn stimulate platelet aggregation **(Herzberg MC,et al ,1998)**.

This may lead to a systemic inflammatory response favoring an atherosclerotic process. A correlation between oral infectious lesions, as found on radiographs, and coronary atheromatosis has been shown in a predomi- nantly male population **(Stenman, Ulrika, et al. 2009)** . In patients with type 1 DM, duration of PD Has a significant relationship with the development and progression of coronary artery calcium. Also, Other studies have found a relationship between severity of PD and presence of cardiac calcifications (i.e. Valvular calcification), which are markers of subclinical atherosclerosis **(Pressman GS. Et al., 2013).**

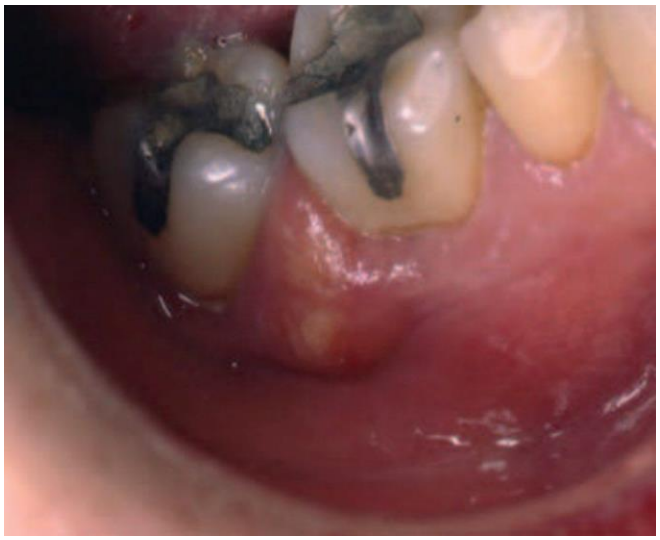
Congestive heart failure coexistent with periodontal disease

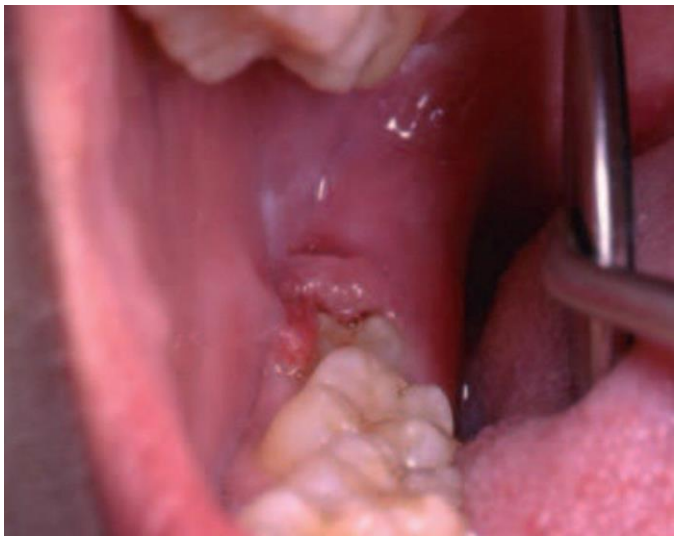
Congestive heart failure (CHF) is a clinical syndrome, most Commonly with a coronary and/or hypertension-related aetiol-ogy. This condition is linked to a high morbidity and mortality. Due to the ageing population and the increasing morbidity of coronary heart disease and arterial hypertension, which ac-cording to Framingham's study are the most common causes of CHF, early and effective treatment of heart failure (HF) is becoming increasingly important **(Czerniuk, Maciej R., et al. 2017)** . Heart Failure is a clinical syndrome involving cardiac structural and functional alterations that result in diminished cardiac output and / or increased ventricular filling pressures at rest or During stress, and may feature reduced or preserved left ventricular ejection fraction (LVEF) **(Ponikowski P. et al., 2016)**. Despite differences in demographics, aetiology, pathophysiology, clinical presentation and function, heart failure features a chronic and dysregulated inflammatory state that contributes to the progression of myocardial damage, decline in functional capacity and Poor outcomes **(Dick SA. Et al., 2016 & Shirazi LF. Et**

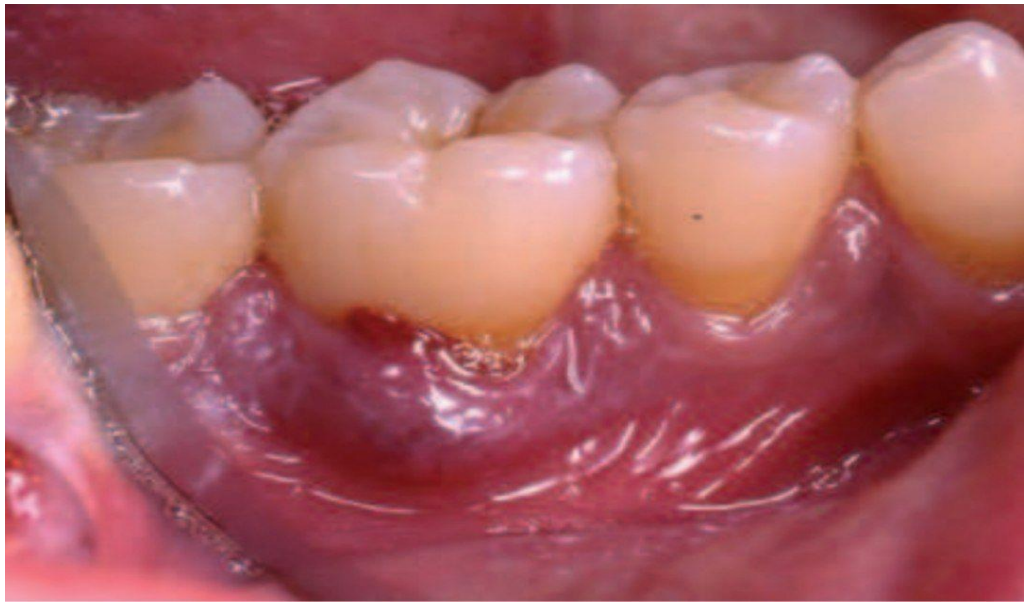
al., 2017). Recently, oxidative stress has been described as another mechanism that favours the development and progression of HF **(Tsutsui H. et al., 2011).** Presence of reactive oxygen species (ROS) causes cellular dysfunction, oxidation of proteins and lipids, and damage to the Deoxyribonucleic acid (DNA), which translate in cellular death; also, ROS alter the contractile function by modifying proteins that are crucial for the Excitation-contraction coupling, and stimulate fibroblast proliferation and metal-loproteinases activation favouring cardiac remodelling **(Tsutsui H. et al., 2011).** Congestive heart failure morbidity has been increasing in recent decades, especially within the older population, spe-cifically patients above 65 years of age. In the United States, around 6–10% of the population are diagnosed with CHF, accounting for around 20 million patients. A similar number of patients have asymptomatic myocardial damage, and they will develop symptomatic HF within next five years. Currently, it is estimated that in Poland there are over 10 million patients Diagnosed with CHF. The Average age of patients with CHF in Europe is 74 years. It has to be noted that, despite the further development in cardiology and cardiac surgery, the increasing longevity of the population will lead to an increased Prevalence of HF cases over time**(Tonetti MS, Eickholz P, Loos BG et al. 2015).**

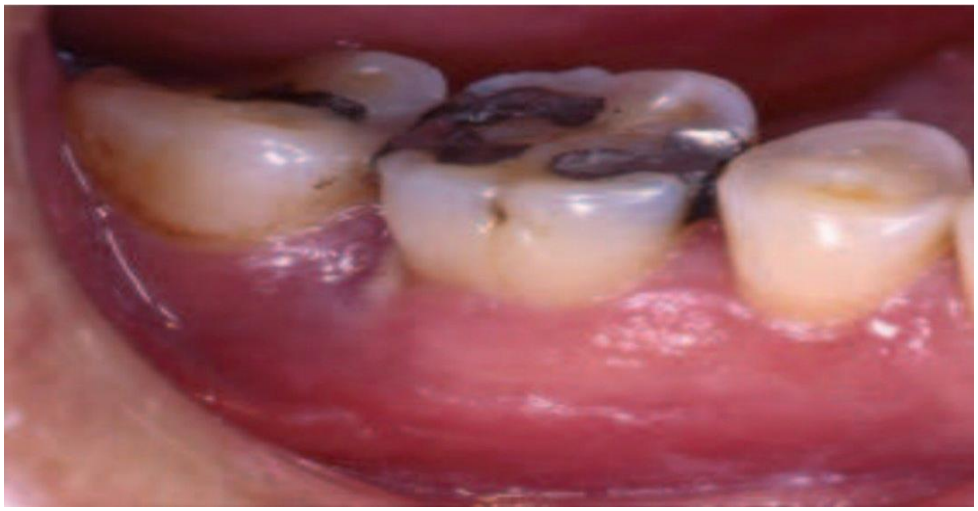
Oral lesions

Acute lesions in the periodontium, such as abscesses and necrotizing periodontal diseases, are among the few clinical situations in periodontics where patients May seek urgent care, mostly because of the associated pain. In addition, and in contrast to most other Periodontal conditions, rapid destruction of periodontal tissues may occur during the course of these Lesions, thus stressing the importance of prompt diagNosis and treatment **(Herrera, David, et al 2014)** .Other gingival and periodontal lesions may also show An acute presentation, including different infectious Processes not related to oral bacterial biofilms, mucocutaneous disorders, or traumatic and allergic lesions **(Herrera, David, et al 2014)** .Abscesses in the periodontium are odontogenic infections that may be caused by pulp necrosis, periodontal infections, pericoronitis, trauma or surgery . Odontogenic or dental abscesses are classified, According to the source of infection, into periapical (dentoalveolar) abscess, periodontal abscess and peRicoronal abscess (**Herrera, David, et al 2014)** .Abscesses can be classiffied agingival or periodontal Abscesses A gingival abscess is a localized painful swelling that affects only the marginal and interdental gingiva and is normally associated with Subgingivally impacted foreign objects. These conditions may occur in a previously healthy gingiva . A Periodontal abscess is a localized painful swelling that Affects deeper periodontal structures, including deep Pockets, furcations and vertical osseous defects, and Is usually located beyond the mucogingival line. Histologically, both lesions are identical, but a gingival Abscess affects only the marginal soft tissues of previously healthy sites, whilst a periodontal abscess Occurs in a periodontal pocket associated with a periodontitis lesion (**Herrera, David, et al 2014) .**

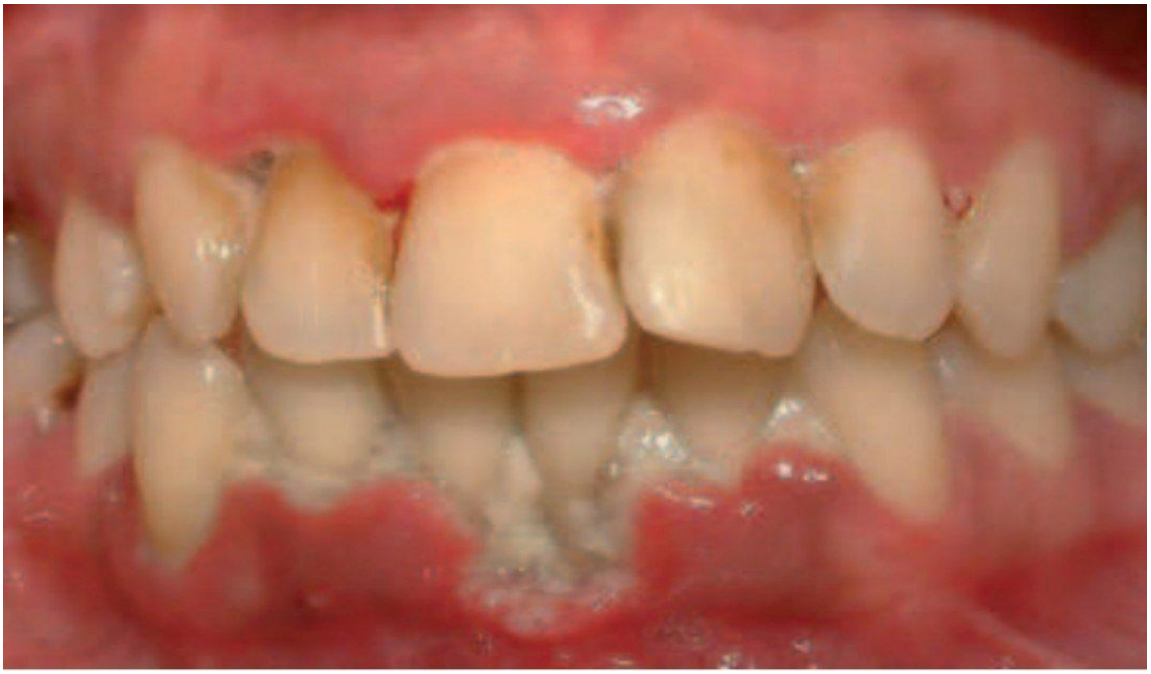




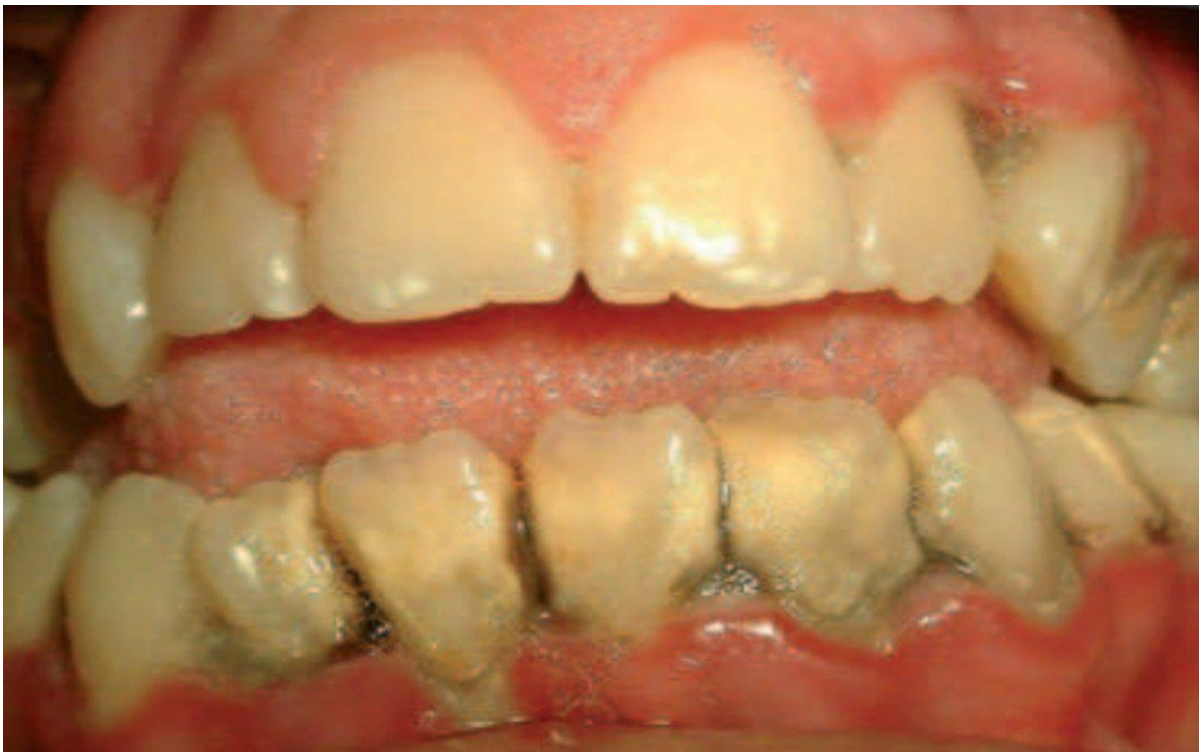




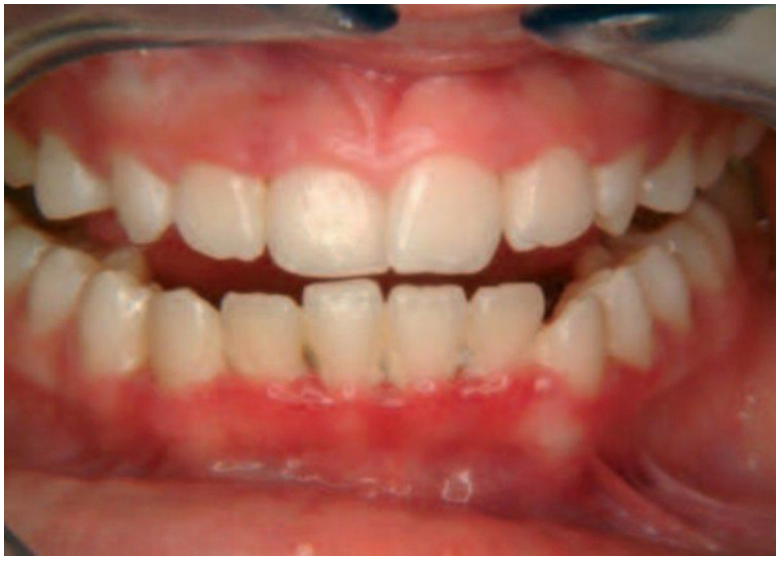
Necrotizing periodontal diseases are considered to be Among the most severe inflammatory conditions Associated with oral biofilm bacteria . Therefore, It is important to control predisposing factors, and Once the disease has developed, to act quickly in Order to limit its progression and exacerbation.Necrotizing periodontal diseases can progress rapidly and cause severe tissue destruction. It is therefore important for these conditions to be managed Promptly because there is evidence proving that necrotizing periodontal diseases can be controlled by Adequate periodontal treatment combined with effective oral-hygiene measures and control of predisposing factors (**Herrera D, et al (2000)**. However, patients with necrotizing gingivitis are frequently susceptible to future disease Recurrence, mostly as a result of the difficulties in controlling predisposing factors as well as the difficulty in achieving proper supragingival biofilm control, in part because of the sequelae of these diseases, Including the presence of gingival craters (**MacCarthy D, et al 1991**).Necrotizing periodontal diseases can also become chronic, with a slow reduction in theirSymptomatology and progression, and ensuing destruction, Although at a slower rate (**Holmstrup P, Westergaard et al . (2008)** . Some authors Believe that these conditions remain acute and may Be 'recurrent' (**Herrera, David, et al 2014)** .

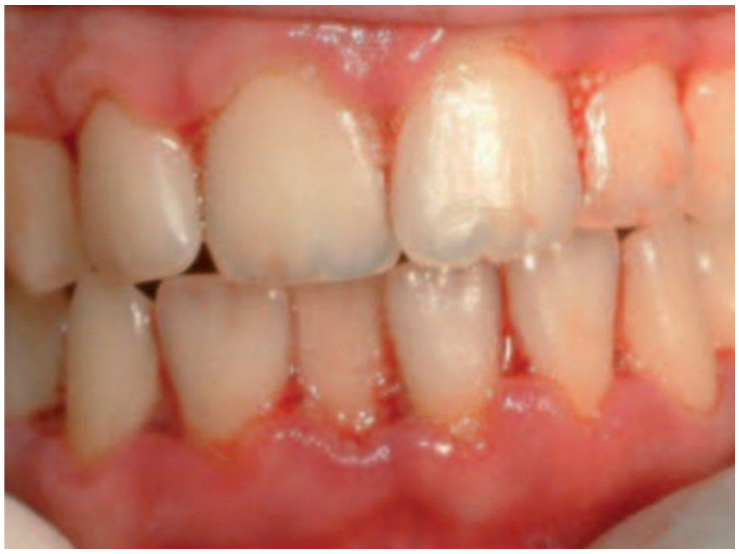


Plaque accumulation has been considered a predisposing factor for necrotizing periodontal disease (**Horning GM, Cohen et al 1995**) although it may also be a consequence of the Presence of ulcers and crater lesions that may limit Toothbrushing as a result of pain. Necrotizing periodontal disease usually occurs over a pre-existing Periodontal disease, usually chronic gingivitis (**Herrera, David, et al 2014)** . In one study, 28% of the patients with necrotizing periodontal disease reported a history of Painful gingival inflammation and 21% showed Lesions compatible with previous necrotizing peri- Odontal disease (**Horning GM, Cohen et al 1995)** .Smoking is a risk factor for necrotizing periodontal Disease (**Johnson GK, Guthmiller et al 2007)** and, in fact, most HIV-negative Patients diagnosed with necrotizing periodontal dis- Ease were smokers (**Herrera D, et al (2000)**. The mechanisms Explaining this association are probably related to the Effect of smoking on inflammation and the tissue Response, because smoking interferes with both polymorphonuclear leukocyte and lymphocyte function And nicotine induces vasoconstriction in gingival Blood vessels. Alcohol consumption has also been associated with The physiological and psychological factors favoring Necrotizing periodontal disease (**Horning GM et al 1996**) .



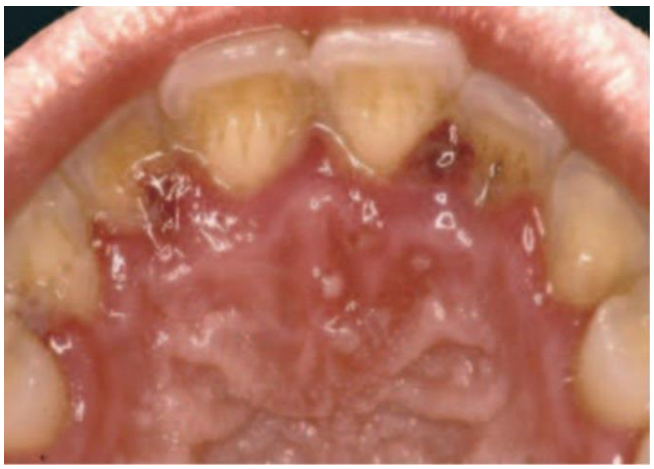
Necrotizing gingivitis The diagnosis is based on the presence of necrosis And ulcers in the free gingiva. These lesions usually Start at the interdental papilla and have a typical 'punched-out' appearance. In addition, a marginal Erythema, named 'lineal erythema', may be present, Separating the healthy and the diseased gingiva. These necrotic lesions can progress to the marginal Gingiva. The most typical location is the anterior Teeth, especially in the mandible . In necroTizing gingivitis, gingival bleeding is a frequent findIng, and it is usually spontaneous or occurs after Minimal contact . Pain normally has a rapid Onset and occurs with different degrees of severity, Depending on the severity and extent of the lesions. The bouts of pain increase with eating and with oral Hygiene practices and is normally the reason for the Patient's consultation.Other less common findings include the presence Of: pseudomembrane over the necrotic area. The Pseudomembrane consists of a whitish/yellowcolored meshwork, composed of necrotic tissue, Fibrin, erythrocytes, leukocytes and bacterial cells. When this 'membrane' is removed, the underlying Connective tissue becomes exposed and bleeds. Halitosis, although this is not an exclusive sign of Necrotizing gingivitis. Adenopathies, which are usually found in the most Severe cases of disease. If present, submandibular Lymph nodes are more affected than those in the Cervical area (**Jimenez LM, Duque et al.2005**) . Fever and a general feeling of discomfort.This group of acute gingival lesions includes lesions manifesting initially as acute conditions or as acute Episodes of a chronic condition. They can appear as Isolated lesions or as part of complex clinical pictures And they are frequently responsible for emergency Consultations. The clinical lesion is usually an ulcer or erosion (**Herrera, David, et al 2014**) .Specific bacterial infections localized in the oral mucosa are uncommon. They may be caused by bacteria normally present in the oral cavity that eventually become pathogenic, and also by bacteria Exogenous to the oral cavity, such as gonococci, tularemia or anthrax. In addition, the lesions present in The oral cavity may be a secondary location of generAlized infectious disease, as in scarlatina, diphtheria, Syphilis or tuberculosis. Both staphylococci and streptococci may cause oral Infections with gingival involvement, leading to a Lesion with a nonspecific appearance (**Herrera, David, et al 2014) .**

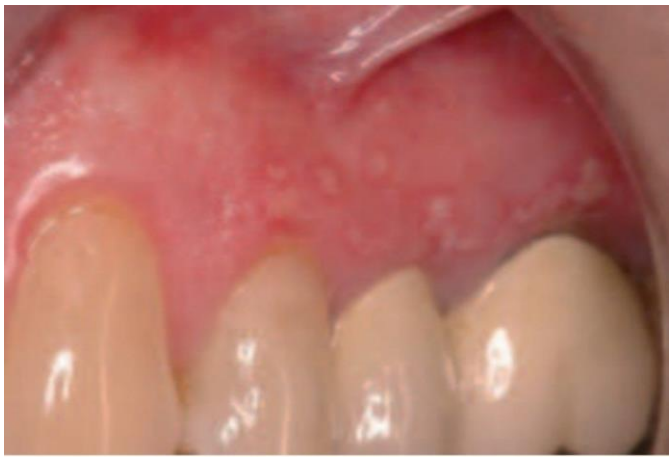




Viral infections Different viruses may cause lesions in the oral cavity, With or without concomitant skin involvement (**Miller CS et al 1996**). The most frequently associated viruses causing gingival and periodontal lesions are from the Herpesviri-Dae family (herpes simplex virus type 1, the causal Agent of oral and labial herpes lesions; herpes simplex Virus type 2, associated with genital herpes; and vari- Cella-zoster virus, responsible for varicella and herpesZoster) (**Contreras A, Slots J et al . 2000).** Herpesviruses Adapt easily to the host, and after the primary infecTion they remain inside the infected cells in a latent or Silent state; they show tropism for epithelial and neural cells, and the preferred site for latency of herpes Simplex viruses and varicella-zoster virus is ganglions In the nervous system Varicella is the outcome of an infection with varicella-zoster virus and occurs after the initial contact With the virus. It results in a generalized condition, Especially in children, with vesicle eruptions in skin After an incubation period of 1–3 weeks. Before or After appearance of the skin lesions, vesicles can be Evident in the oral cavity, including the gingiva, and They break easily, forming ulcers surrounded by an Erythematous halo. The result of the re-activation of The varicella-zoster virus from the regional sensitive Ganglia is herpes zoster, which occurs especially in The elderly or associated with immunedepression. It May affect the trigeminal ganglion, with clinical Manifestation preceded by pain or an itching feeling.

Clinical lesions are vesicles surrounded by an erythematous halo, with a unilateral distribution; the Vesicles break easily, forming erosive areas (**Herrera, David, et al 2014)** . Primary herpetic infection with herpes simplex Virus type-1 is normally asymptomatic, but it is some-times very evident in the form of generalized gingivostomatitis, with dysphagia, fever, malaise and Submandibular adenopathy. It is more frequently Observed in children 2–5 years of age, with oral Lesions in the form of ulcers or erosions, after the vesicles have broken . Treatment may include antiviral agents and adequate nutritional support, mostly when pain compromises eating (**Contreras A, Slots J et al . 2000**) Recurrent herpetic infection with herpes simplex Virus type-1 may be either intraoral or labial. Initial Symptoms include local discomfort in the form of Itching or stinging. The lesions develop as an erythema, and then a variable numbeof grouped vesicles break, forming an erosion in the oral mucosae, Gingiva or the lip . Lesions normally last for 7 –10 days and heal without scarring. Differential diag- Nosis with other conditions showing ulcers, such as Recurrent aphthous stomatitis, is important, although The latter lesions will not affect keratinized tissues As the condition is self-limitIng, no treatment is usually required, although if present in immunecompromised patients, antiviral Agents should be prescribed (**Herrera, David, et al 2014**) Other viruses, such as EpsteinBarr virus, cytomegalovirus and Coxsackie virus, are frequently transmitted Via saliva and may result in specific oral manifesta

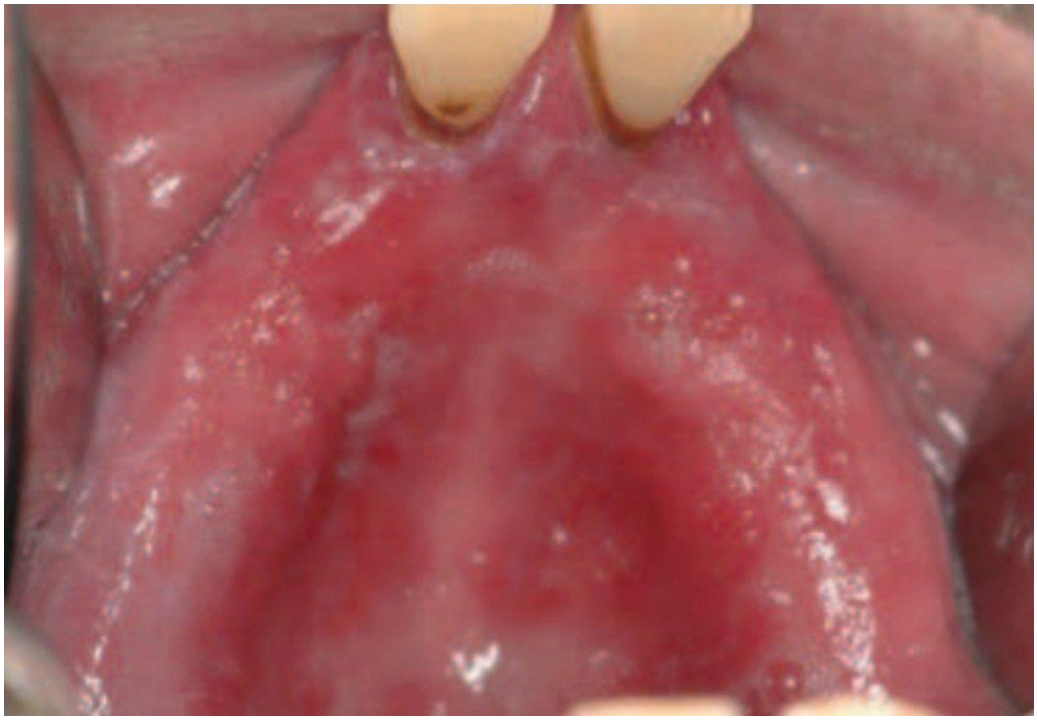




Fungal infections Many fungal species are part of the resident flora of The mouth, but they may cause pathology when local Or systemic factors trigger their overgrowth. Among these opportunistic fungal infections, candidiasis is the most frequent, normally affecting immune-compromised subjects, especially HIV-posi-Tive patients, or during infancy and in the elderly Although their localized forms Are usually not severe, it may spread and lead to more Severe infections, such as esophagic or systemic (**Herrera, David, et al 2014)**Candidiasis. Among Candida spp., C. albicans is the Most relevant for oral infections . Multiple factors are associated with the pathogenesis of oral candidiasis , and these may be Divided into host-related factors and local and environmental factors (**Herrera, David, et al 2014**). Among the Host-related factors are the presence of concomitant Systemic diseases (such as diabetes) or debilitating Conditions leading to a reduced host response. The Most common local and environmental factors Include removable prostheses, systemic antimicrobi- Als, corticosteroids and tobacco smoking . Acute candidiasis can present as pseudomembranous or erythematous candidiasis, with itching or Stinging being. The diagnosis is mainly clinical . Treatment includes antifungal agents, such as nystatin, amphotericin B or miconazole, in solutions Or gels. In severe cases, or in immune-compromised Patients, the treatment of choice is systemic fluconazole. It is also mandatory to evaluate and control the Associated predisposing/adjunctive local and/or systemic factors (**Herrera, David, et al 2014)** .Lichen planus is a chronic inflammatory disease Affecting the skin and the mucosae, and is the most Common noninfectious disease of the oral cavity. The Oral manifestation is very common, mostly in adult Women (30–50 years) of Caucasian ethnicity (**Herrera, David, et al 2014)**. The oral lesions usually precede the skin lesions or are the only lesion . Clinical mani- Festations range from the typical reticular form, Affecting the buccal and cheek mucosae, to erosive Forms, usually located in the tongue and gingiva, that Cause pain and tenderness, as well as bleeding.Pemphigus is a severe, autoimmune mucocutane- Ous disease, with a chronic and aggressive progres- Sion, characterized by the destruction of the intercellular adhesion systems between keratinocytes, Leading to intra-epithelial bulla formation . Among the different clinical forms, only the vulgaris and the vegetans can affect the oral mucosae, Although the latter is very infrequent. Pemphigus vul- Garis is more frequent in women, 40–60 years of age, With a Mediterranean or Jewish background. Skin Lesions are more common, but in 50%

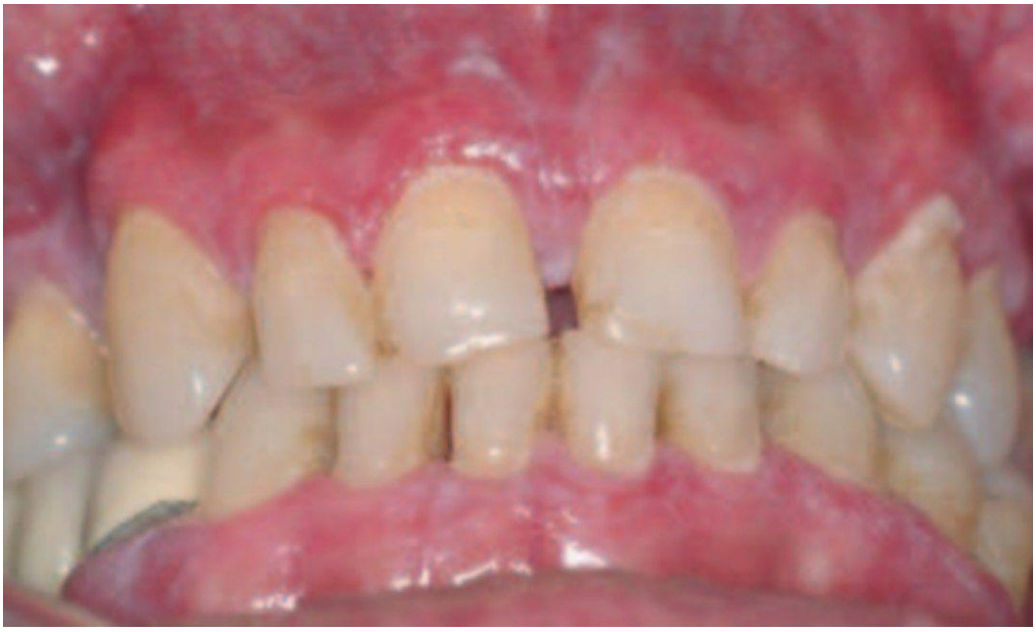
of the cases Oral lesions may precede the skin lesions . Intra- Oral lesions, if affecting the, appear as desqua- Mative gingivitis .

Diagnosis may be difficult and Will be based on histology and immune-fluorescence Pemphigoid includes a group of autoimmune Mucocutaneous diseases that affect either the skin (bullous pemphigoid and gestational herpes) or the Mucosae (mucous membrane pemphigoid or cicatricial pemphigoid) (**Herrera, David, et al 2014**)

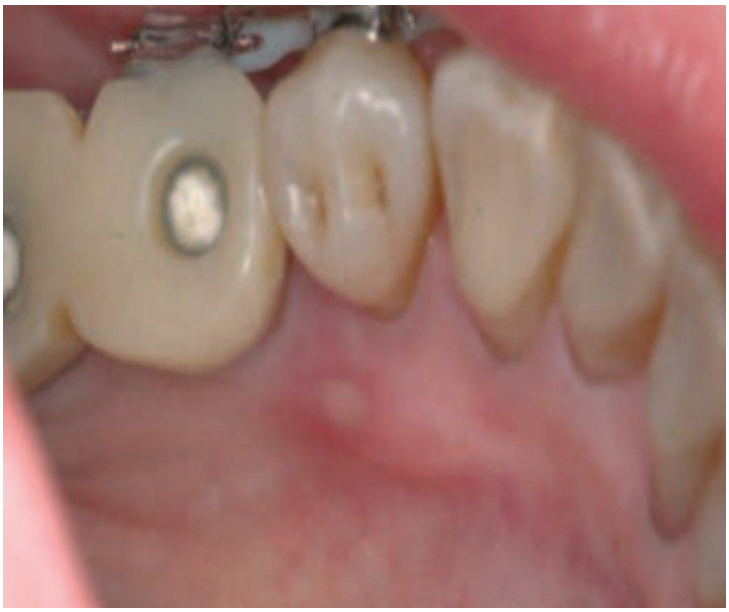


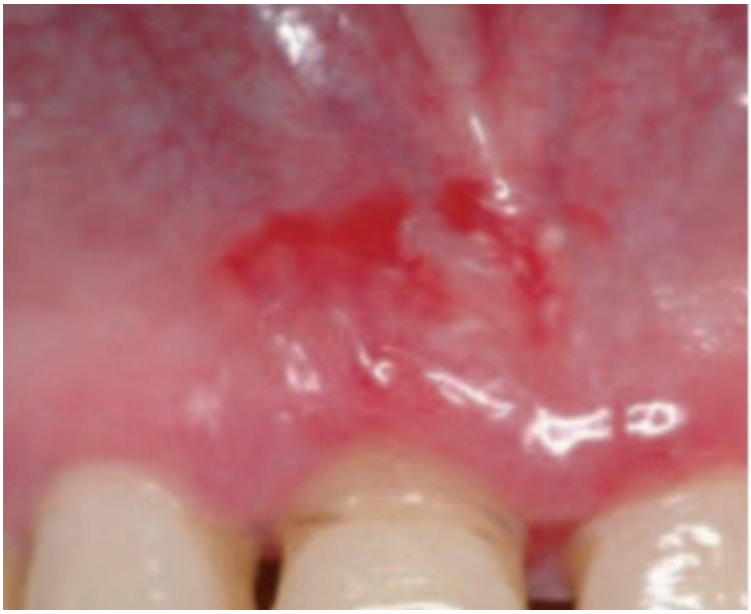
Allergy is an abnormal reaction of the human body: An exaggerated response to a contact with a foreign Substance or product (allergen) that does not neces- Sarily induce a similar reaction in other indiv (Abdollahi M, Radfar M et al.(2003). Food products, including Fruits, seafood, nuts or some vegetables, induce Most allergic reactions; however, some medicines, Including antibiotics (e.g. penicillin) or nonsteroidal Anti-inflammatory drugs (e.g. acetylsalicylic acid) Can also be responsible for allergic reactions (Herrera, David, et al 2014) .

Physical mechanical injuries may appear as erosions Or ulcers, associated with gingival recession. How- Ever, they can also present as hyperkeratosis, vesicles Or bullae, sometimes in combination with other oral Lesions on the lips, tongue or teeth; they may be Asymptomatic, but they can also induce intense, Localized pain at the



area of the lesion. The correct Diagnosis is based not only on the clinical aspect, but Also in the identification of the noxious agent, and for That, patient collaboration is crucial (Litonjua LA, Andreana S,et al. 2003) .





Chapter Two

Conclusions and Suggestions

Prevention of infective endocarditis in patients with periodontal disease disease in the context of dental treatment Requires timely administration of antibiotic therapy The Use of antibiotics should be justified, taking into account Individual indications and risks, to avoid overuse of anti-Biotics and the development of antibiotic resistance.

Educating patients with cardiovascular disease is an imPortant tool for preventing infective endocarditis and other complications following dental procedures. Patients Should understand the risks associated with bacteremia And follow oral care guidelines to help prevent inflammation of the gums and teeth. It is also important to explain To patients how to properly follow medication recommendations and adhere to preventive measures.

References

1-Gomes, Brenda PFA, et al. "Microbiota present in combined endodontic-periodontal diseases and its risks for endocarditis." Clinical Oral Investigations 27.8 (2023): 4757-477.

2-Lockhart, Peter B., et al. "Oral hygiene and infective endocarditis: a case control study." Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology 136.3 (2023): 333-342.

3-Bokhari, S. Akhtar Hussain, and Ayyaz A. Khan. "The relationship of periodontal disease to cardiovascular disease-review of literature." Journal-Pakistan Medical Association 56.4 (2006): 177.

4-"Hatz, Christian R., et al. "Antibiotic prophylaxis with amoxicillin to prevent infective endocarditis in periodontitis patients reconsidered: a narrative review." Swiss medical weekly 151 (2021): w30078.

5-Dhotre, Shree, et al. "Assessment of periodontitis and its role in viridans streptococcal bacteremia and infective endocarditis." Indian heart journal 70.2 (2018): 225-232.

6-Lockhart, P., Chu, V., Zhao, J. et al. (12 more authors) (2023) Oral hygiene and infective endocarditis: a case control study. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 136 (3). Pp. 333-342. ISSN 2212-4403.

7-Carinci, F., et al. "Focus on periodontal disease and development of endocarditis." J Biol Regul Homeost Agents 32.2 Suppl 1 (2018): 143-7.

8-Lockhart, Peter B., et al. "Poor oral hygiene as a risk factor for infective endocarditis–related bacteremia." The Journal of the American Dental Association 140.10 (2009): 1238-1244.

9-Strom, Brian L., et al. "Dental and cardiac risk factors for infective endocarditis: a Population-based, case-control study." Annals of internal medicine 129.10 (1998): 761-769.

10-Azzi L., Carinci F., et al. "pylori in periodontal pockets and saliva: A possible Role in gastric infection relapses." J Biol Regul Homeost Agents 2017; 31(1):257-62.

11-Roncati M., Lauritano D., et al. "Nonsurgical periodontal management of iatrogenic Peri-implantitis: A clinical report." J Biol Regul Homeost Agents 2015; 29(3):164-69.

12-Di Girolamo M, Calcaterra R., et al. "Bone level changes around platform switching and platform matching implants: A systematic review with meta-analysis." ORAL and Implantology 2016; 9(1):1-10.

13-Thuny F, Grisoli D., et al. "Management of infective endocarditis: challenges And perspectives." Lancet 2012; 379(9819):965-75.

14-Werdan K, Dietz S., et al. "Mechanisms of infective endocarditis: pathogen-host interaction and risk states." Nat Rev Cardiol 2014; 11(1):35-50.

15-Leone, Sebastiano, et al. "Epidemiology, characteristics, and outcome of infective endocarditis in Italy: the Italian Study on Endocarditis." Infection 40 (2012): 527-535.

16-Williams, Michael L., et al. "Epidemiology of infective endocarditis before versus after change of international guidelines: a systematic review." Therapeutic Advances in Cardiovascular Disease 15 (2021): 17539447211002687.

17-Martico, Michael, et al. "Infective endocarditis: etiology, epidemiology and current recommendations for the dental practitioner." J. Can. Dent. Assoc 90 (2024): o4.

18-Sanz, Mariano, et al. "Periodontitis and cardiovascular diseases: Consensus report." Journal of clinical periodontology 47.3 (2020): 268-288.

19-Knox, K. W., Hunter. Et al. "The role of oral bacteria in the pathogenesis of infective endocarditis." Australian dental journal 36.4 (1991): 286-292.

20-Dhotre, Shree V.,et al. "Periodontitis, bacteremia and infective endocarditis: a review study." Arch Pediatr Infect Dis 5.3 (2017): e41067.

21-Ninomiya, Masami, et al. "Relationship of oral conditions to the incidence of infective endocarditis in periodontitis patients with valvular heart disease: a cross-sectional study." Clinical Oral Investigations 24 (2020): 833-840.

22-Strom, Brian L., et al. "Dental and cardiac risk factors for infective endocarditis: a population-based, case-control study." Annals of internal medicine 129.10 (1998): 761-769.

23-Carrizales-Sepúlveda, Edgar Francisco, et al. "Periodontal disease, systemic inflammation and the risk of cardiovascular disease." Heart, Lung and Circulation 27.11 (2018): 1327-1334.

24-Campbell JH , et al,."The cell biology of atherosclerosis-new developments."Aust. NZ J. Med., 27, 497–500 (1997).

25-Amar S , GokceN,et al . "Periodontal disease is associated with brachial artery endothelial dysfunction and systemic inflammation." Arterioscler. Thromb. Vasc. Biol., 23, 1245–1249 (2003).

26-Mercanoglu F , OflazH, OzO et al. Endothelial dysfunction in patients with chronic periodontitis and its improvement after initial periodontal therapy.J. Periodontol., 75, 1694–1700 (2004).

27-Wick G , PerschinkaH, et al. Autoimmunity and atherosclerosis.Am. Heart J., 138, S444–S449 (1999).

28-Seymour, Gregory J., et al. "Infection or inflammation: the link between periodontal and cardiovascular diseases." Future cardiology 5.1 (2009): 5-9.

29-Paul, Oindrila, et al. "Inflammation in periodontal disease: possible link to vascular disease." Frontiers in physiology 11 (2021): 609614.

30-Beck JD, Garcia RG, at el. "Periodontal disease and cardiovascular disease". J Periodontol(1996);67:1123 37.

31-Arbes SJ Jr, Slade GD,et al. "Association between extent Of periodontal attachment loss and self-reported history of heart attack".an analysis of NHANES III data. J Dent Res (1999);78:1777 82.

32-Buhlin K, Gustafsson A,et al. "Oral health and cardiovascular disease in Sweden". J Clin Periodontol (2002);29:254 9.

33-Hugoson A, Norderyd O,et al. "Distribution of periodontal disease in a Swedish adult Population 1973, 1983 and 1993". J Clin Periodontol (1998); 25:542 8.

34-World Health Organization. The World Health Report 1995: bridging the gaps. Geneva: World Health Organization; 1995.

35-Hujoel PP, Drangsholt M,et al. "Periodontal disease and coronary heart disease risk". J AM Med Assoc(2000);284:1406.

36-Herzberg MC,et al . "Dental plaque, platelets, and Cardiovascular diseases". Ann Periodontol (1998);3:151 60.

37-Dorn BR, Dunn WA Jr,et al. Invasion of human Coronary artery cells by periodontal pathogens. Infect Immun (1999);67:5792 8.

38-Stenman, Ulrika, et al. "Association between periodontal disease and ischemic heart disease among Swedish women. A cross-sectional study." Acta Odontologica Scandinavica 67.4 (2009): 193-199.

39-Arsiwala, Lubaina T., et al. "Periodontal disease measures and risk of incident peripheral artery disease: The Atherosclerosis Risk in Communities (ARIC) Study." Journal of periodontology 93.7 (2022): 943-953.

40-Czerniuk, Maciej R., et al. "Plasmatic NT-proBNP concentrations in patients with coexistent periodontal disease and congestive heart failure: pilot studies." Polish Heart Journal (Kardiologia Polska) 75.2 (2017): 135-142.

41-Tonetti MS, Eickholz P, Loos BG et al. Principles in prevention of periodontal diseases: Consensus report of group 1 of the 11(th) European Workshop on Periodontology on effective prevention of periodontal and peri–implant diseases. J Clin Periodontol, 2015; 42 (suppl. 16): 5–11.

42-Saffi MA, Furtado MV, Polanczyk CA, et al. Relationship between Vascular endothelium and periodontal disease in atheroscle- rotic lesions: Review article. World J Cardiol. 2015; 7(1): 26–30,

43-Elangovan S, Nalliah R, Allareddy V, et al. Outcomes in patients visiting hospital emergency departments in the United States because of periodontal conditions. J Periodontol. 2011; 82(6): 809–819.

44-Friedewald VE, Kornman KS, Beck JD, et al. American Journal of Cardiology, Journal of Periodontology. The American Journal of Cardiology and Journal of Periodontology Editors' Consensus: periodontitis and atherosclerotic cardiovascular disease. Am J Cardiol. 2009; 104(1): 59–68

45-Pearson TA, Mensah GA, Alexander RW, et al. Centers for Disease Control and Prevention, American Heart Association. Markers of Inflammation and cardiovascular disease: application to clinical And public health practice: A statement for healthcare profes- sionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003; 107(3): 499–511

46-Kassebaum, N.J.; Bernabe, E.; Dahiya, M.; Bhandari, B.; Murray, C.J.; Marcenes, W. Global burden of severe periodontitis in 1990–2010: A systematic review and meta- Regression. J. Dent. Res. 2014, 93, 1045–1053

47-Sen, S.; Giamberardino, L.D.; Moss, K.; Morelli, T.; Rosamond, W.D.; Gottesman, R.F.; Beck, J.; Offenbacher, S. Periodontal Disease, Regular Dental Care Use, and Incident Ischemic Stroke. Stroke 2018, 49, 355–362.

48-Tsutsui H, Kinugawa S, Matsushima S. Oxidative stress and heart failure. 657 Am J Physiol Heart Circ Physiol 2011; 301:H2181–90.

49-Shirazi LF, Bissett J, Romeo F, Mehta JL. Role of inflammation in heart 655 failure. Curr Atheroscler Rep 2017; 19:27.

50-Dick SA, Epelman S. Chronic heart failure and inflammation: what do we 650 really know Circ Res 2016;119:159–76.

51-Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 644 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic 645 heart failure: The Task Force for the diagnosis and treatment of acute and 646 chronic heart failure of the European Society of Cardiology (ESC)Devel- 647 oped with the special contribution Of the Heart Failure Association (HFA) 648 of the ESC. Eur Heart J 2016; 37:2129–200.

52-Spahr, Axel, et al. "Periodontal infections and coronary heart disease: role of periodontal bacteria and importance of total pathogen burden in the Coronary Event

and Periodontal Disease (CORODONT) study." Archives of internal medicine 166.5 (2006): 554-559.

53-Zhou, Mengchen, et al. "Causal association between periodontal diseases and cardiovascular diseases." Genes 13.1 (2022): 13.

54-Pressman GS, Qasim A, Verma N, Miyamae M, Arishiro K, Notohara Y,et al. Periodontal disease is an independent predictor of intracardiac calcification. Biomed Res Int 2013;2013:854340.

55-Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflam mation, Aspirin, and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 1997; 336:973–9

56-Cahill, Thomas J., et al. "Challenges in infective endocarditis." Journal of the american college of cardiology 69.3 (2017): 325-344.

57-Herrera, David, et al. "Acute periodontal lesions." Periodontology 2000 65.1 (2014): 149-177.

58-Herrera D, Roldan et al . The periodontal abscess: a Review. J Clin Periodontol 2000: 27: 377–386.

59-MacCarthy D, Claffey et al. Acute necrotizing ulcerative gingivitis is associated with attachment loss. J Clin Periodon- Tol 1991: 18: 776–779.

60-Holmstrup P, Westergaard et al . Necrotizing periodontal disease. In: Lindhe J, Lang NP, Karring T, editors. Clinical Periodontology and implant dentistry, 5th edn. Oxford: Wi-ley-Blackwell, 2008: 459–474.

61-Horning GM, Cohen et al. Necrotizing ulcerative gingivitis, Periodontitis, and stomatitis: clinical staging and predis- Posing factors. J Periodontol 1995: 66: 990–998.

62-Johnson GK, Guthmiller et al. The impact of cigarette smoking on periodontal disease and treatment. Periodontol 2000 2007: 44: 178–194.

63-Horning GM et al. Necotizing gingivostomatitis: NUG to noma.Compend Contin Educ Dent 1996: 17: 951–954

64-Jimenez LM, Duque et al. NecrotizingUlcerative periodontal diseases in children and young adults in Medellin, Colombia, 1965–2000. J Int Acad Peri-Odontol 2005: 7: 55–63.

65-Miller CS et al . Viral infections in the immunocompetentPatient. Dermatol Clin 1996: 14: 225–241.

66-Contreras A, Slots J et al. Herpesviruses in human periodontal Disease. J Periodontal Res 2000: 35: 3–16.

67-Litonjua LA, Andreana S,et al. Toothbrushing and gingival recession. Int Dent J 2003: 53:67–72.

68-Abdollahi M, Radfar M et al. A review of drug-induced oralreactions. J Contemp Dent Pract 2003: 4: 10–31.