International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

The Role of Oral Hygiene in the Prevention of Systemic Diseases: A Public Health Perspective

Ms. Nandini Banerjee

Assistant Ptofessor, SVB's College of Pharmacy

ABSTRACT:
The article examines the connection between oral hygiene and overall health, stressing the importance of public health efforts to promote better oral care practices as a preventative measure against chronic illnesses. Oral hygiene plays a crucial role in maintaining general well-being, and conditions in the mouth can have a more significant impact on the body than many healthcare providers realize. Poor oral health is not only linked to issues like cavities and gum disease but is also associated with systemic conditions such as heart disease, diabetes, respiratory infections, and complications during pregnancy.
The overlap between medicine and dentistry highlights the necessity for strong collaboration between healthcare providers and dentists, which can lead to early detection and better prevention of these health concerns. The complications resulting from these diseases contribute to substantial morbidity, mortality, and financial burdens on the healthcare system. A focus is placed on understanding how the oral microbiota supports health and how disturbances in this balance can lead to illness.

Keywords: Oral health, systemic health, noncommunicable diseases, periodontitis, public health Cardiovascular disease, diabetes, oral microorganisms, oral- systemic connection, pre-term low births

INTRODUCTION

The oral cavity is often referred to as "the window to general health," emphasizing the integral connection between oral and systemic well-being. As noted by Seymour, it is now widely accepted that "good general health cannot exist without good oral health," highlighting the mouth's role as a crucial intersection of dentistry and medicine. Over 100 systemic diseases and more than 500 medications exhibit oral manifestations, particularly prevalent among older adults. Historically, figures like Hippocrates recognized the link between oral health and systemic conditions, with reports of curing systemic ailments through dental interventions. Despite this historical perspective, the full significance of oral conditions on systemic health has only recently gained recognition[(1).]

The bidirectional relationship between oral and systemic health is increasingly understood, though further research is essential. The influence of oral health on overall well-being has garnered attention from multiple U.S. Surgeons General and the World Health Organization. The oral cavity is essential for various physiological functions, including speech, chewing, swallowing, and the initial stages of digestion, while also contributing to psychological identity.[(2,3)]

The oral cavity is home to diverse surface types, each hosting unique populations of 500-700 species of bacteria, viruses, fungi, and protozoa. Oral hygiene plays a critical role in shaping the oral microbiome; individuals with good hygiene typically have a simpler microbial composition dominated by gram-positive organisms, whereas poor hygiene leads to a more complex, diverse flora, often rich in anaerobic gram-

negative bacteria.[4] Saliva and gingival crevicular fluid create a complex environment that helps maintain oral health, supporting mineralization and protecting against dietary acids.[5]

Disruption of this oral ecosystem, known as dysbiosis, can lead to an increase in harmful bacteria, resulting in conditions such as tooth decay. Notable oral conditions with established links to systemic health include dental caries and periodontal diseases, such as gingivitis and periodontitis. Research by Garcia et al. suggests that an increase in missing teeth correlates with a decline in quality of life, as poor dental health affects chewing ability and nutritional intake.[6,7]

The relationship between oral diseases and general health is intricate. Systemic diseases can influence oral health through direct pathological processes or indirectly via behavioral changes related to the disease or its treatment. Conversely, alterations in oral health can impact systemic conditions. For instance, tooth loss is associated with increased all-cause mortality and cardiovascular disease risk, while periodontal disease has prominent links to non-communicable diseases (NCDs) such as diabetes and heart disease.[8]

Lifestyle factors like high sugar intake, unhealthy eating habits, smoking, and excessive alcohol consumption are common risk factors for both oral diseases and NCDs.[9] Improved oral hygiene has been linked to better cardiovascular health, including reduced progression of carotid artery thickening, and studies show that enhanced oral care can lower hemoglobin A1C levels in diabetic patients. Moreover, poor oral hygiene is implicated in the development of oral cancer.[10, 11, 12]

In older adults, maintaining routine oral hygiene—such as brushing teeth after meals—can significantly reduce the risk of aspiration pneumonia.[13, 14] This demographic is particularly vulnerable to dental infections and associated complications. Tooth loss can hinder the ability to chew certain foods, potentially leading to malnutrition in later life.[15]

A careful assessment of the oral cavity can reveal signs indicative of underlying systemic conditions, enabling early diagnosis and intervention. The concept of "focal infection," proposed by Dr. William Hunter in 1910, posits that oral disease can contribute to systemic conditions like anemia, gastritis, and colitis. A comprehensive examination should include an evaluation of mucosal changes, signs of periodontal inflammation, and overall dental health. For example, signs of anemia may present as pale mucosa, atrophic glossitis, or oral thrush, while conditions like lupus erythematosus and Crohn's disease may lead to specific oral lesions.

The importance of periodontal health has been highlighted in various studies, revealing its role in systemic health issues, including cardiovascular disease and diabetes management. Conversely, diabetes can exacerbate periodontal disease, creating a reciprocal relationship that requires careful monitoring and management. Emerging evidence links periodontal bone loss to an increased risk of coronary heart disease and stroke. [16,17]

In summary, the oral cavity serves not only as a gateway to digestion but also as a critical indicator of overall health. The intricate connections between oral and systemic health underscore the need for continued research and a more integrated approach to healthcare, ultimately improving outcomes for both oral and general health.

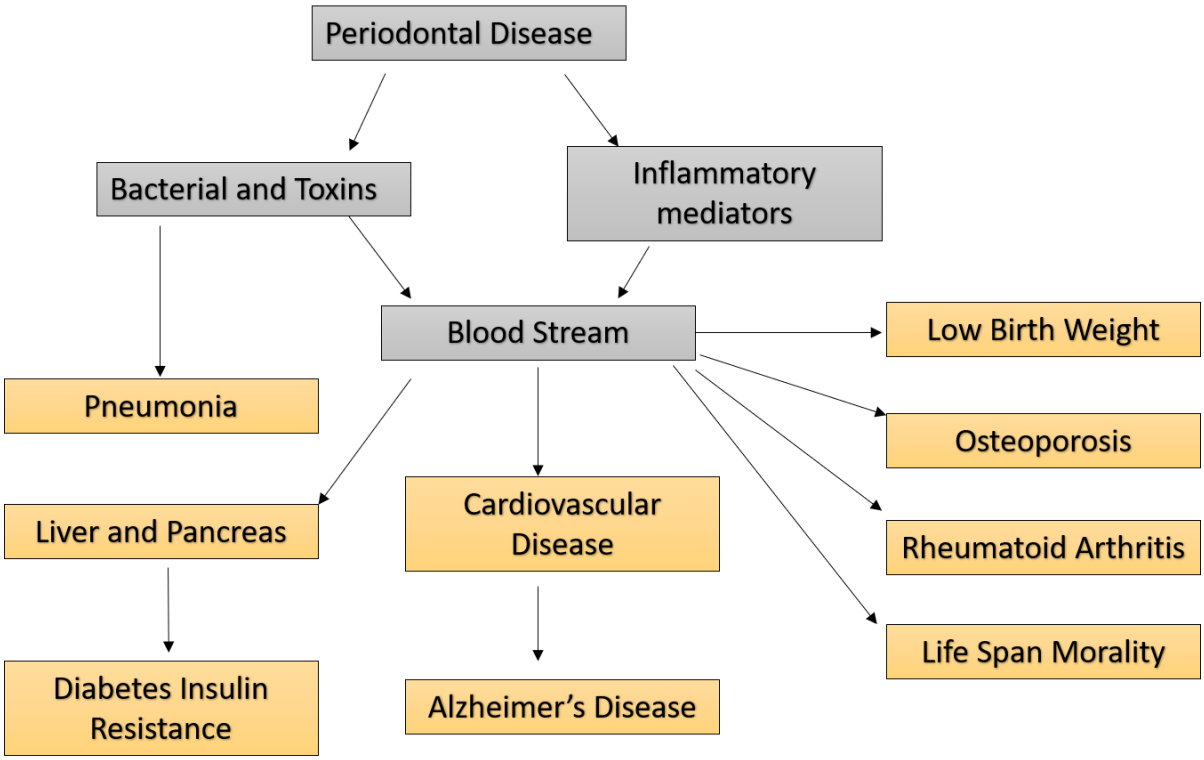

Figure 1: Oral and systemic health Link

ORAL MANIFESTATIONS OF SYSTEMIC DISEASES

Oral diseases often share common behavioral risk factors with various non-communicable diseases (NCDs), such as high sugar intake, unhealthy dietary habits, smoking, and excessive alcohol consumption. Research has shown a strong association between poor oral health and major NCDs, including cardiovascular diseases and diabetes mellitus. For example, maintaining good oral hygiene has been linked to improvements in cardiovascular health, particularly in reducing the progression of carotid artery thickening. Additionally, systematic reviews indicate that enhanced oral hygiene can lower hemoglobin A1C levels in individuals with diabetes.

Beyond chronic illnesses, poor oral hygiene has also been implicated in the development of oral cancer. In geriatric populations, consistent oral care practices, such as brushing after meals, can significantly reduce the incidence of aspiration pneumonia. Unfortunately, older adults are generally at a heightened risk for dental infections, which can lead to complex health complications. Tooth loss often results in difficulties chewing, contributing to potential malnutrition. Furthermore, untreated oral infections can escalate into systemic infections that affect endocardial implants and artificial joints.

The prevalence of dental issues in older adults with dementia further underscores the importance of maintaining good oral hygiene. As the global population ages, promoting oral health and regular dental check-ups among seniors is crucial to mitigate the risk of severe dental infections and their associated health risks.

In pediatric populations, dental caries in primary teeth remains alarmingly high worldwide. Oral diseases are often chronic and accumulate over a person's lifetime, with childhood being a critical period that influences both general and oral health. Socioeconomic factors during childhood can have a lasting impact on the prevalence of oral diseases in adulthood.

Poor oral hygiene is a significant factor in the development of various oral conditions. In young children, inadequate oral care is the primary cause of early childhood caries (ECC). Studies show that infants and toddlers with heavy plaque accumulation are at an increased risk for severe caries. Similarly, preschool-aged children with higher plaque index scores experience more caries than those with better oral hygiene. However, it is essential to note that determining the direct impact of oral hygiene on caries development is complex, especially when considering the confounding effects of fluoride in dental products.[18]

While fluoride is effective in preventing dental caries when proper plaque removal is practiced, a recent meta-analysis suggested that without fluoride, personal oral hygiene alone may not significantly reduce caries incidence. Despite this, clinicians should continue to advocate for the benefits of good oral hygiene, as it remains a practical and cost-effective strategy to support oral health. [19,20]

In terms of periodontal health, inadequate oral hygiene is a significant risk factor for periodontitis, a common and destructive oral infection. Periodontal disease results from bacterial infection in dental plaque, with several specific gram-negative bacteria identified as key pathogens. Periodontitis can lead to inflammation, bone loss, and the formation of periodontal pockets.

Research suggests that periodontal disease may increase susceptibility to systemic diseases through several mechanisms, including shared risk factors and the presence of harmful bacteria in subgingival biofilms. Factors such as smoking, stress, and advanced age contribute to both periodontal disease and systemic conditions like cardiovascular disease.

Moreover, subgingival biofilms serve as a reservoir for gram-negative bacteria, which can trigger significant inflammatory responses within the body. This bacterial load can lead to vascular changes and increased risks of clotting and inflammation, further complicating systemic health.[21]

The periodontium itself acts as a reservoir for pro-inflammatory cytokines, which can enter the bloodstream and perpetuate systemic effects. These mediators may contribute to various health issues, including cardiovascular complications and adverse pregnancy outcomes, such as preterm labor and low birth weight.

In summary, the intricate relationship between oral health and systemic diseases highlights the need for a comprehensive approach to healthcare that prioritizes oral hygiene. Understanding this connection is vital for developing effective strategies to enhance both oral and overall health, ultimately improving quality of life for individuals across all age groups.[22,23]

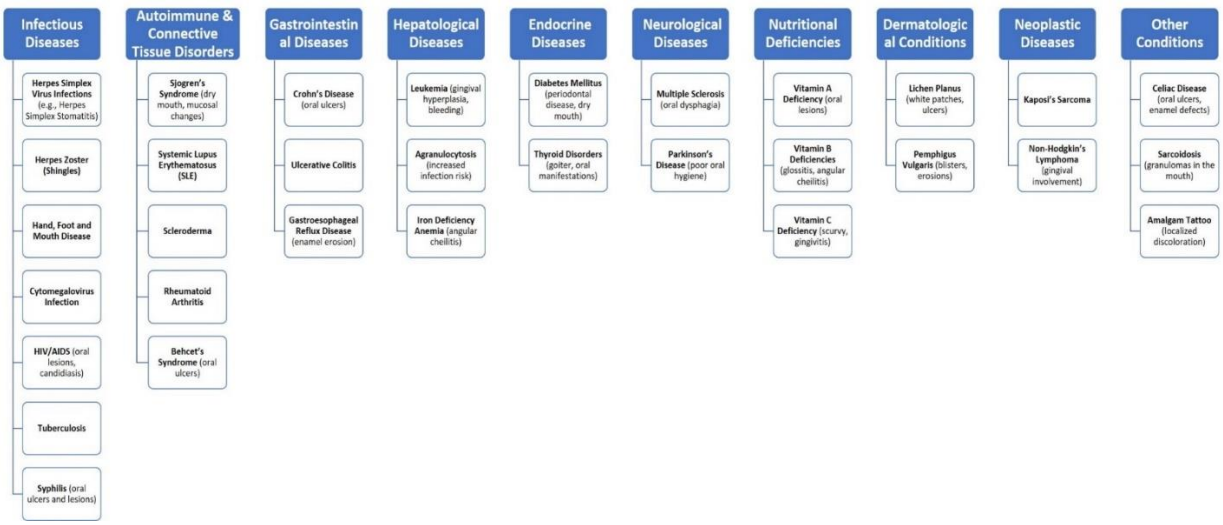

Figure 2: Different systemic conditions : Disease and Disorders linked

Here's a list of diseases that can show oral manifestations[24,25]

Infectious Diseases

1. Herpes Simplex Virus Infections (e.g., Herpes Simplex Stomatitis)
2. Herpes Zoster (Shingles)
3. Hand, Foot and Mouth Disease
4. Cytomegalovirus Infection
5. HIV/AIDS (oral lesions, candidiasis)
6. Tuberculosis
7. Syphilis (oral ulcers and lesions)

Autoimmune and Connective Tissue Disorders

1. Sjogren's Syndrome (dry mouth, mucosal changes)
2. Systemic Lupus Erythematosus (SLE)
3. Scleroderma
4. Rheumatoid Arthritis
5. Behcet's Syndrome (oral ulcers)

Gastrointestinal Diseases

1. Crohn's Disease (oral ulcers)
2. Ulcerative Colitis
3. Gastroesophageal Reflux Disease (enamel erosion)

Hematological Diseases

1. Leukemia (gingival hyperplasia, bleeding)
2. Agranulocytosis (increased infection risk)
3. Iron Deficiency Anemia (angular cheilitis)

Endocrine Diseases

1. Diabetes Mellitus (periodontal disease, dry mouth)
2. Thyroid Disorders (goiter, oral manifestations)

Neurological Diseases

1. Multiple Sclerosis (oral dysphagia)
2. Parkinson's Disease (poor oral hygiene)

Nutritional Deficiencies

1. Vitamin A Deficiency (oral lesions)
2. Vitamin B Deficiencies (glossitis, angular cheilitis)
3. Vitamin C Deficiency (scurvy, gingivitis)

Dermatological Conditions

1. Lichen Planus (white patches, ulcers)
2. Pemphigus Vulgaris (blisters, erosions)

Neoplastic Diseases

1. Kaposi's Sarcoma
2. Non-Hodgkin's Lymphoma (gingival involvement)

Other Conditions

1. Celiac Disease (oral ulcers, enamel defects)
2. Sarcoidosis (granulomas in the mouth)
3. Amalgam Tattoo (localized discoloration)

ORAL HYGIENE AND CARDIOVASCULAR DISEASES

Oral hygiene plays a significant role in the prevention of cardiovascular diseases (CVDs) due to the complex relationship between oral health and systemic health. Poor oral hygiene can lead to gum diseases, such as gingivitis and periodontitis, which are linked to an increased risk of cardiovascular issues. Here's an overview:

Periodontal disease causes inflammation in the gums, which can spread systemically, contributing to a chronic inflammatory state. This inflammation is a known risk factor for atherosclerosis (plaque buildup in arteries). Bacterial Translocation: Harmful oral bacteria can enter the bloodstream through inflamed gums, potentially leading to infections in blood vessels or the heart, such as endocarditis[26].

Atherosclerosis and Plaque Formation: Oral pathogens like *Porphyromonas gingivalis* have been found in atherosclerotic plaques, suggesting they may contribute to plaque buildup and arterial stiffness. Impact on Blood Vessels: The systemic inflammation caused by gum disease can damage endothelial cells lining the blood vessels, impairing their function and increasing the risk of hypertension and heart attack.[27,28]

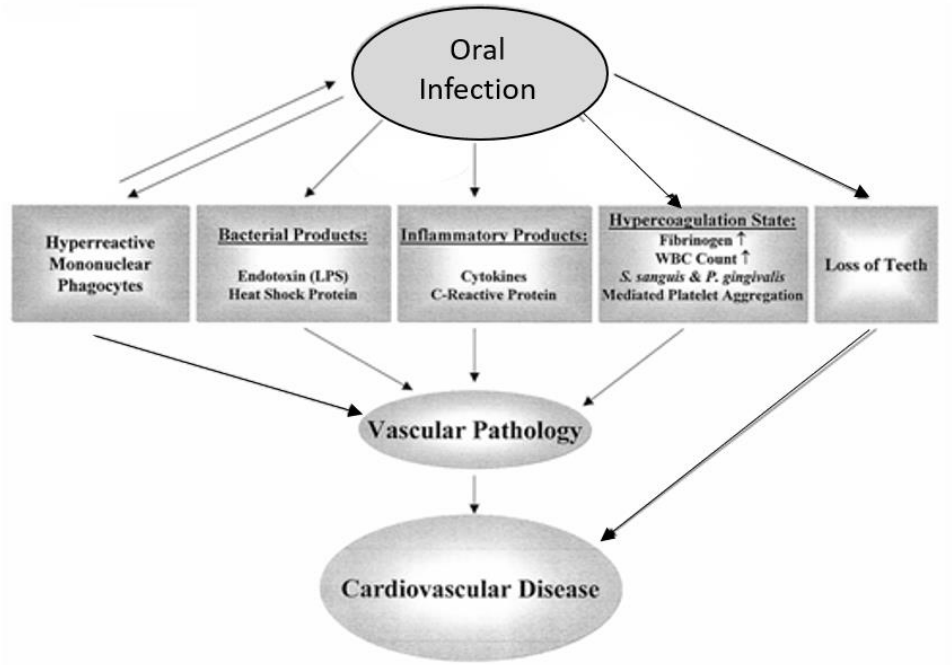

Figure 4: Proposed mechanisms linking oral infection and oral disease to CVS disease

THE BIDIRECTIONAL LINK BETWEEN DIABETES AND PERIODONTAL DISEASE[29]

Diabetes mellitus and periodontal disease are closely interconnected, with each condition influencing the other. Individuals with diabetes are more susceptible to infections, including gum diseases like periodontitis, due to weakened immune responses. At the same time, chronic inflammation from periodontitis can worsen blood sugar levels, making diabetes more challenging to manage. This mutual relationship emphasizes the importance of proper oral care for individuals with diabetes to reduce complications.

Research has shown that severe gum disease can not only result from poorly controlled diabetes but also contribute to its progression. High blood sugar levels in people with diabetes can lead to the accumulation of advanced glycation end products (AGEs), which impair immune cell function and increase

inflammation. This inflammation promotes gum tissue destruction and fosters harmful bacteria in the mouth, creating a cycle of deterioration [30,31].

On the other hand, periodontal infections can trigger insulin resistance by releasing inflammatory substances like TNF-α and IL-1. This creates a feedback loop where poor blood sugar control worsens gum disease, and the gum disease further complicates diabetes management. Clinical studies have found that treating periodontal disease through professional cleaning and other mechanical therapies can lead to slight improvements in blood sugar levels, with an average reduction of around 0.4% in HbA1c. While this effect varies among individuals, it highlights the importance of addressing gum disease as part of diabetes care.

To improve overall health outcomes, managing both diabetes and gum disease is essential. Regular dental checkups, effective oral hygiene, and professional periodontal treatment should be part of a diabetes management plan. In some cases, combining mechanical treatments with antibiotics may enhance blood sugar control and reduce the impact of gum infections.

This connection between diabetes and periodontal health calls for collaboration between healthcare providers and dental professionals. By working together, they can help patients better manage both conditions and improve their overall quality of life.[32]

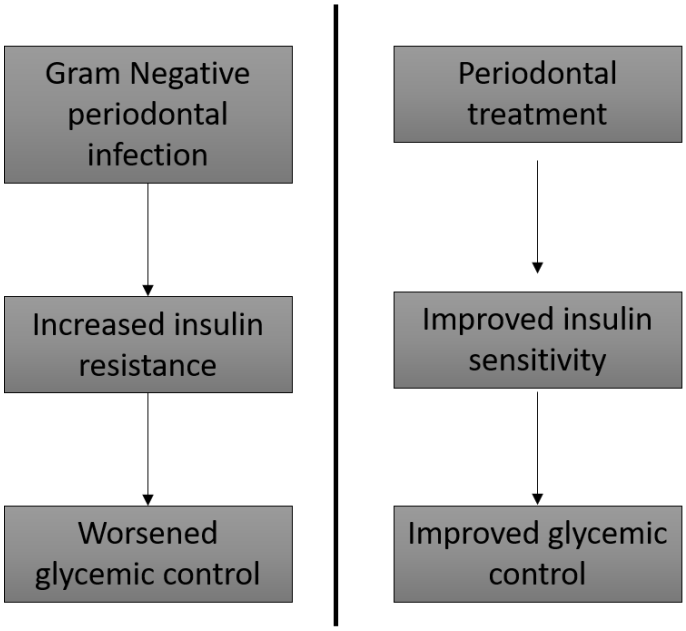

Figure 4: Potential effects of periodontal infection and therapy on glycemic diabetes patient

ORAL HYGIENE AND RESPIRATORY INFECTIONS: ETIOLOGY AND PATHOGENESIS

Oral hygiene plays a critical role in preventing respiratory infections, particularly in high-risk populations such as the elderly and those in healthcare settings. Poor oral health can lead to the colonization of the oropharyngeal region by pathogenic bacteria, which may be aspirated into the lungs, causing respiratory infections like pneumonia. This association is particularly significant in vulnerable individuals, where factors such as age, comorbidities, and compromised immune defenses exacerbate the risk.[33]

Pneumonia, a serious infection of the pulmonary parenchyma, is primarily caused by bacteria, viruses, fungi, or parasites. It poses a significant health threat, especially to elderly and immunocompromised individuals, and can be life-threatening. The etiology of pneumonia often involves the aspiration of oropharyngeal contents into the lower respiratory tract. Typically, the lower respiratory tract remains

sterile due to protective mechanisms such as mucociliary clearance, cough reflexes, and immune responses. However, these defenses can fail, especially in hospitalized or debilitated patients, leading to bacterial colonization and infection.[34]

Pathogenic bacteria associated with pneumonia often originate in the oral cavity. Potential respiratory pathogens (PRPs) such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Mycoplasma pneumoniae* commonly colonize the oropharyngeal region before being aspirated. Dental plaque, particularly in individuals with periodontal disease, provides a reservoir for these bacteria. Additionally, anaerobic species like *Porphyromonas gingivalis* and *Fusobacterium* can also be aspirated, causing pneumonia.

Risk factors for nosocomial pneumonia include advanced age, chronic diseases such as diabetes and chronic lung disease, mechanical ventilation, prolonged hospital stays, and poor oral hygiene. Poor oral health increases plaque accumulation, which may release hydrolytic enzymes that alter mucosal surfaces, making them more susceptible to bacterial adhesion. This creates a favorable environment for PRPs to colonize and potentially infect the respiratory tract.[35]

Studies demonstrate a significant link between poor oral hygiene and respiratory infections. Research indicates that individuals with higher oral hygiene index (OHI) scores are more likely to develop respiratory diseases. Elderly individuals in nursing homes with infrequent dental visits experience higher rates of pneumonia-related deaths. Furthermore, studies show that individuals with greater periodontal attachment loss are at an increased risk for chronic lung diseases, reinforcing the connection between periodontal health and respiratory conditions. [36,37]

ORAL HYGIENE AND ADVERSE PREGNANCY OUTCOMES:

Poor oral hygiene during pregnancy has been associated with adverse outcomes, including preterm birth and low birth weight. Periodontal disease, a common oral condition, can initiate an inflammatory response that impacts maternal health and fetal development. Elevated levels of inflammatory markers such as cytokines (*e.g.*, IL-1, IL-6, TNF-α) and prostaglandins (PGE2) during periodontal infections can cross the placental barrier, triggering preterm labor or other complications. Recognizing this, public health initiatives focused on oral health in pregnant women, such as routine dental visits and education on proper oral care, are essential for reducing these risks and enhancing maternal and infant well-being.[38]

Low Birth Weight and Pregnancy-Related Gingival Health

Pregnancy-induced hormonal changes often result in gingival inflammation, known as pregnancy gingivitis, even without significant increases in dental plaque. Oral contraceptives can similarly alter gingival health by influencing vascular permeability and promoting inflammation. Poor oral health during pregnancy, particularly periodontal disease, has been linked to low birth weight (defined as less than 2,500 grams) and preterm delivery, both of which are significant public health concerns. These conditions account for substantial perinatal morbidity and mortality, as low-birth-weight infants face heightened risks of neurodevelopmental disorders, respiratory issues, and behavioural abnormalities.

Multiple researches have shown the connection between maternal oral infections and pregnancy outcomes. Periodontal pathogens such as *Porphyromonas gingivalis*, *Treponema denticola*, and *Aggregatibacter actinomycetemcomitans* can produce bioactive molecules, including lipopolysaccharides (LPS), which activate inflammatory cascades. These molecules promote cytokine and prostaglandin synthesis, elevating amniotic fluid levels of PGE2 and TNF-α to thresholds that can induce preterm labor. Case-control studies reveal that mothers of preterm or low-birth-weight infants tend to have more severe periodontal disease

compared to mothers of normal-birth-weight infants. Logistic regression analyses have demonstrated that periodontal disease significantly increases the risk of adverse pregnancy outcomes, with odds ratios as high as 7.9.[39, 40]

Further studies show a dose-response relationship between periodontal disease activity and adverse outcomes. Elevated gingival crevicular fluid (GCF) levels of PGE2 in mothers correlate with decreased birth weights and gestational age, implicating periodontal inflammation as a key factor in preterm births. In fact, approximately 18.2% of preterm low-birth-weight cases may result from maternal periodontal disease. However, the host's immune-inflammatory response, which determines susceptibility to periodontitis, also appears to play a critical role. This suggests that periodontal disease may serve as both a marker of and a contributor to adverse pregnancy outcomes. [41,42]

Public Health Interventions for Maternal Oral Health

To mitigate the risks of poor pregnancy outcomes related to periodontal disease, public health measures must prioritize oral health during pregnancy. Strategies include educational campaigns to raise awareness about the importance of oral hygiene, provision of affordable dental care, and integration of oral health services into prenatal care programs. These interventions can significantly reduce the prevalence of periodontal disease and its associated risks, improving overall maternal and neonatal health outcomes.[43]

THE ROLE OF ORAL HYGIENE IN THE PREVENTION OF GASTROINTESTINAL DISEASES

Maintaining proper oral hygiene is vital not only for oral health but also for preventing gastrointestinal diseases. The oral cavity serves as the entry point to the digestive system, and poor oral hygiene can lead to the proliferation of harmful microorganisms that may influence gastrointestinal health. Conditions such as gastritis, ulcers, and even colorectal cancer have been linked to oral infections and periodontal disease due to shared inflammatory and microbial pathways.

Harmful oral bacteria, such as *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, commonly found in periodontal infections, can migrate to the gastrointestinal tract through saliva and swallowing. These bacteria can disrupt the gut microbiome, a critical regulator of gastrointestinal health, and trigger systemic inflammation. For example, *F. nucleatum* has been implicated in colorectal cancer due to its ability to adhere to gut epithelial cells, promote tumorigenesis, and suppress immune responses. Similarly, *Helicobacter pylori*, a known causative agent of peptic ulcers and gastric cancer, has been detected in dental plaque, suggesting that poor oral hygiene may facilitate its persistence and transmission.[44,45]

Periodontal inflammation contributes to the systemic inflammatory burden by releasing pro-inflammatory cytokines, including IL-6 and TNF-α, into circulation. These cytokines can exacerbate gastrointestinal conditions such as inflammatory bowel disease (IBD), gastritis, and gastroesophageal reflux disease (GERD). Chronic inflammation in the gut, driven by oral pathogens or systemic inflammatory mediators, may also compromise the integrity of the intestinal mucosal barrier, leading to increased susceptibility to gastrointestinal infections.[46,47]

Oral-Gut Axis and Gastrointestinal Disease Risk

Emerging research highlights the "oral-gut axis," emphasizing the interconnectedness of oral and gut microbiomes. Imbalances in oral microbiota caused by poor oral hygiene can influence gut microbial composition and function. Studies have shown that individuals with periodontitis are more likely to experience gastrointestinal issues, including IBD, due to altered microbial diversity and immune system activation. Moreover, dental plaque serves as a reservoir for pathogenic bacteria that can travel to the gut,

leading to increased risks of systemic diseases. Poor oral hygiene has also been associated with increased oxidative stress, which further contributes to gastrointestinal disease progression, particularly in disorders such as Crohn's disease and ulcerative colitis.[48]

Preventive Measures

Promoting oral hygiene is a critical strategy for reducing the risk of gastrointestinal diseases. Preventive measures include:

- Brushing, flossing, and the use of antimicrobial mouth rinses to reduce plaque and bacterial load.
- Professional cleanings and early detection of oral infections to prevent systemic spread.
- Avoiding sugary foods and incorporating probiotics to support a balanced oral and gut microbiome.
- Educational campaigns highlighting the link between oral health and systemic diseases, including gastrointestinal conditions.

PERIODONTAL DISEASE AND RHEUMATOID ARTHRITIS

Periodontal disease has been linked to rheumatoid arthritis (RA), a chronic autoimmune condition characterized by inflammation of the joints, leading to the destruction of cartilage, bone, and ligaments. Both conditions share similar inflammatory processes. In diseased gingival tissues and RA-affected joints, comparable cytokines and growth factors are produced, which contribute to bone resorption—a common issue in both diseases. This overlap indicates a shared inflammatory mechanism underlying these conditions.[49,50,51]

Research has shown that individuals with RA and periodontal disease exhibit significantly elevated levels of anti-cyclic citrullinated peptide (anti-CCP) antibodies. This association suggests that periodontal disease may play a role in the development or progression of RA. Notably, *Porphyromonas gingivalis*, a key pathogen in periodontal disease, produces an enzyme capable of inducing citrullination of proteins, a process implicated in the autoimmune response in RA.

Enhanced periodontal care, including regular dental cleanings and effective oral hygiene practices, may benefit individuals with RA by potentially mitigating systemic inflammation and reducing disease severity.[52,53]

HEMATOLOGIC DISORDERS AND THEIR ORAL MANIFESTATIONS

Hematologic disorders, malignancies, and blood cell dyscrasias encompass a diverse group of diseases that often exhibit systemic spread and may involve the oral cavity, as well as the hard and soft tissues of the head and neck. In some cases, oral manifestations may represent the initial clinical signs of these conditions. Additionally, immunosuppressive treatments for hematologic diseases can result in oral complications, including viral, fungal, or bacterial infections, mucositis, and candidiasis.[54]

Acute leukemia frequently presents with oral lesions, more so than chronic leukemia, and is commonly associated with gingival hypertrophy or hyperplasia characterized by edema and erythema. Thrombocytopenia often manifests as petechiae, ecchymoses on the oral mucosa, and spontaneous gingival bleeding.

In lymphomas, oral involvement varies. Hodgkin lymphoma rarely affects the oral cavity, whereas non-Hodgkin lymphoma, including mucosa-associated lymphoid tissue (MALT) lymphomas, often presents as painless, slow-growing masses in the oral cavity. These may involve areas such as the palate, gingiva, buccal mucosa, tongue, or Waldayer’s ring, sometimes with ulceration due to trauma. Neck lymph nodes are frequently affected as well.

Multiple myeloma often exhibits orofacial signs, including osteolytic lesions, primarily in the mandible, causing swelling, pain, paraesthesia, and tooth loss due to bone destruction.(55)

Langerhans cell histiocytosis (LCH), a rare hematologic disorder predominantly affecting children, involves the head and neck region in most cases of disseminated disease. Symptoms vary depending on whether the condition is unifocal or multifocal. Commonly affected areas include the skull (especially the temporal bone), lymph nodes, skin, and orbit. Oral lesions, typically in the jaws, manifest as localized or multiple gingival swellings with edema, inflammation, periodontal involvement, teeth mobility, or dislocation. Bone destruction often creates a "floating teeth" appearance on radiographs.

Rarely, LCH presents as a single bone lesion, often in the maxilla, with a characteristic punched-out radiolucent appearance, cortical bone erosion, or diffuse periodontal and mucosal involvement. Diagnosing LCH in the head and neck region can be challenging, as it may mimic more common conditions, such as periodontal diseases, leading to diagnostic delays.(56,57 58)

RENAL SYSTEM AND ORAL COMPLICATIONS

Renal transplantation can lead to several oral complications, often related to the use of immunosuppressant medications like ciclosporin, which are essential for preventing kidney rejection (BNF, 2020). Immunosuppression in these patients increases their vulnerability to various oral conditions, including gingival hyperplasia, aphthous ulcers, and infections such as herpes simplex virus (HSV) and candidiasis. Oral leukoplakia, which may undergo malignant transformation into squamous cell carcinoma, and Kaposi's sarcoma are also observed. Gingival hyperplasia, frequently associated with ciclosporin use, results from fibroblast proliferation and excessive collagen deposition in response to the drug. Candidiasis occurs due to fungal overgrowth in the immunocompromised environment, while viral lesions such as HSV manifest due to reactivation of latent infections.(59)

THE ROLE OF ORAL HYGIENE IN SYSTEMIC DISEASE IN PEDIATRIC PATIENTS (60,61,62)

Inadequate oral hygiene can lead to infections and inflammation that may have far-reaching effects beyond the oral cavity.

Cardiovascular Disease:

Research has shown a relationship between poor oral hygiene, particularly periodontal disease, and an increased risk of cardiovascular diseases. In children, periodontal disease can trigger an inflammatory response that may contribute to vascular inflammation and atherosclerosis later in life. Chronic oral infections can lead to the release of inflammatory mediators, such as cytokines, that may promote cardiovascular disease.

Respiratory Infections:

Poor oral hygiene can contribute to respiratory problems, particularly in children with pre-existing respiratory conditions such as asthma or cystic fibrosis. Infected dental tissues or the presence of oral bacteria in the throat can be aspirated into the lungs, increasing the risk of respiratory infections, pneumonia, or even exacerbating asthma symptoms.

Diabetes:

There is a well-documented link between oral health and diabetes. Children with uncontrolled diabetes are at a higher risk of developing gum disease (gingivitis and periodontitis) due to higher glucose levels in the saliva, which promotes bacterial growth. Conversely, periodontal disease may also worsen glycemic

control, creating a vicious cycle. Maintaining oral hygiene is essential for children with diabetes to help control blood sugar levels and prevent complications.

Premature Birth and Low Birth Weight:

In pregnant women, poor oral hygiene has been associated with an increased risk of preterm birth and low birth weight. Although less studied in children, early childhood oral health may influence maternal health outcomes and thus indirectly affect the child. Chronic inflammation from untreated oral diseases can influence pregnancy outcomes, impacting the child's health.

Nutritional Deficiencies:

Poor oral health in pediatric patients can make eating painful and difficult, leading to nutritional deficiencies. Untreated cavities or gum disease may affect the child's ability to chew food properly, resulting in a reduced intake of essential nutrients. Malnutrition, in turn, can have long-term consequences on a child's growth, immune function, and overall health.

Obesity:

The relationship between poor oral health and obesity in children has been observed in several studies. Children with dental issues may experience discomfort while eating, which can lead to poor eating habits and an increased preference for soft, sugary foods. Furthermore, the inflammation from oral diseases can contribute to systemic inflammation, which is often seen in obese children.

Cognitive and Behavioral Health:

Chronic oral infections, pain from untreated dental conditions, and poor oral hygiene can contribute to difficulties in focusing, irritability, and behavioral problems in children. There is also evidence linking poor oral health to developmental delays and learning difficulties, particularly in children with existing chronic health conditions.

Infective Endocarditis:

Although rare, children with certain heart conditions, such as congenital heart defects, are at risk of developing infective endocarditis, a life-threatening infection of the heart valves, which can be triggered by bacteria entering the bloodstream through oral wounds or infections. Proper oral hygiene and regular dental visits are crucial in reducing this risk.

EXTENT AND IMPACT OF ORAL DISEASE IN OLDER ADULTS

The Global Burden of Disease 2010 Study identified untreated dental caries in permanent teeth as the most prevalent condition worldwide, affecting 35% of the global population. This prevalence has remained stable from 1990 to 2010, though it varies significantly by region. For example, untreated caries are most common in Central Europe (47%) and least common in Australasia (20%). The highest prevalence of caries occurs at ages 25 and 70, likely due to the decline in school-based prevention programs and the emergence of root caries in older adults.

Globally, 11% of adults suffer from severe periodontitis, with its prevalence also remaining unchanged between 1990 and 2010. Periodontitis increases gradually with age, peaking around age 40, and remains stable in older age groups. The geographic variation in the prevalence of severe periodontitis among older adults is substantial, ranging from 51% in East Sub-Saharan Africa to just 10% in Oceania.[63]

Edentulism, or the complete loss of teeth, affects 2.3% of adults worldwide and has decreased by 45% since 1990. This decrease suggests improvements in the prevention and treatment of both caries and periodontitis. However, edentulism increases sharply with age, peaking at 65 years. The prevalence of edentulism also varies greatly across regions, with 30% of older adults in the Andean and Tropical regions

of Latin America being edentulous, compared to only 9% in East Asia. In developed countries like the U.S., where edentulism is on the decline, older adults still average 19 teeth remaining, which is below the 20 teeth needed for effective chewing and mastication.

When older adults have fewer than 20 teeth, they face difficulties with chewing, often leading to larger particle sizes being swallowed, longer chewing times, and changes in food preparation. This can lead to a diet with reduced intake of vegetables, fruits, and fiber, and higher consumption of fats, sugars, and calories, potentially causing nutrient deficiencies, including lower levels of vitamins, minerals, and serum albumin.[64]

The study also calculated the Disability-Adjusted Life Years (DALYs) for untreated caries, severe periodontitis, and edentulism. These three oral health conditions were responsible for 15 million DALYs globally in 2010, equating to an average health loss of 224 years per 100,000 people. The DALYs for oral conditions increased by 21% from 1990 to 2010, largely due to population growth and aging. The direct treatment costs of $298 billion and indirect productivity losses of $144 billion account for approximately 7% of global health expenditures, highlighting the significant burden of oral diseases.

Oral health disparities among older adults reflect the broader inequities seen in general health, with socioeconomic, environmental, and political factors influencing oral health outcomes. The elderly population accounted for 3.5 million of the DALYs, primarily due to edentulism, followed by severe periodontitis and untreated caries.

For frail older adults, the prevalence of oral diseases is often two to three times higher than in the general elderly population. For instance, a study of homebound seniors in New York City found that 79% had untreated caries, 96% had not visited a dentist since becoming homebound, and only 46% could eat comfortably. Similarly, a study of long-term care residents in Massachusetts revealed that 59% had untreated caries, 34% had urgent treatment needs, and half of the edentulous residents lacked dentures. These findings emphasize the ongoing oral health challenges faced by older adults, particularly those in vulnerable situations.[65,66]

CHALLENGES AND OPPORTUNITIES IN ORAL HEALTH

Oral diseases remain a significant public health challenge worldwide, with various factors contributing to their prevalence. These diseases are largely preventable, yet they continue to affect a large portion of the global population. Socioeconomic disparities and inadequate resources, particularly in low- and middle-income countries, play a key role in the persistence of oral health issues. Children from impoverished backgrounds and socially marginalized groups are particularly vulnerable to conditions like dental caries and often face barriers to accessing necessary dental care. In many developing nations, the majority of oral health problems go untreated due to the prohibitive cost of treatment, which exceeds the available financial and human resources. These issues not only impose a burden on families but also strain health care systems.

A more comprehensive framework is needed to understand the causes of chronic diseases, including oral diseases, and the health inequalities that exist across different populations. Factors such as behavioral, biological, psychosocial, economic, and political determinants all contribute to these disparities. Oral health inequalities are still prevalent both within and between countries, largely due to inadequate economic policies, poor governance, and insufficient health care resources. Addressing these issues, particularly the socioeconomic and commercial factors, is crucial to improving global oral health outcomes.

A paradigm shift from a surgical model to a more preventive, medical approach to oral health is gaining support. The goal is to maintain a disease-free mouth through early intervention, potentially enhancing people's quality of life and preventing the need for more invasive procedures. Minimally invasive treatments have proven to be effective and should be prioritized to reduce the need for extensive dental work.

However, while several theoretical frameworks and strategies exist for improving oral health, there is a lack of large-scale studies evaluating their effectiveness in real-world settings.[67]

High-Risk vs. Population-Based Approaches

Two main strategies for improving oral health have been proposed: the high-risk strategy and the population-based approach. The high-risk strategy focuses on providing preventive care to individuals at greater risk of dental diseases. This may include identifying children at high risk of caries through dental screenings and providing treatments like dental sealants. Studies have shown that topical applications of silver and fluoride are effective in preventing and managing caries. However, this strategy is limited as it targets individuals rather than addressing the societal factors that contribute to oral health issues. Moreover, it may inadvertently widen health inequalities, as individuals with better education and resources are more likely to engage in preventive care.[68]

In contrast, the population-based approach aims to address the root causes of oral diseases at a societal level. Measures like sugar taxation, incentives for healthy eating, and water fluoridation have been proposed to create broader, systemic changes. This approach is considered more radical and can potentially reduce overall disease rates by influencing societal norms. Ideally, oral health policies should combine both strategies, targeting both high-risk groups and the general population to maximize the benefits and reduce health disparities. However, limited resources mean that careful planning is necessary to ensure sustainability.[69]

RELATIONSHIP BETWEEN ORAL INFECTIONS AND SYSTEMIC DISEASES, AND FUTURE RESEARCH DIRECTIONS

As previously mentioned, numerous studies have suggested a link between oral infections, particularly periodontitis, and various systemic diseases. One of the most extensively studied conditions in this regard is endocarditis. Research indicates that dental procedures and oral infections meet the established epidemiological criteria for endocarditis causation. However, conclusive evidence establishing a direct causal relationship between oral infections and other systemic diseases is still lacking. While epidemiological studies (both cross-sectional and longitudinal) can identify associations, they do not establish causation. It is possible that periodontal disease could simply coexist with systemic disorders or share common risk factors, resulting in frequent comorbidity without a direct cause-and-effect relationship. Therefore, further research is essential to clarify the potential role of oral infections in triggering or exacerbating other systemic conditions.

In his work, Slots outlined criteria for establishing causal links between periodontal disease and systemic diseases. These criteria suggest future research directions, such as examining the prevalence and incidence of systemic diseases in patients with periodontitis compared to those with healthy gums. Additionally, prospective studies should investigate whether the onset of systemic diseases follows the appearance of periodontal disease and whether treating periodontitis can reduce the incidence of other medical conditions. Further research on the microorganisms involved in both oral and systemic diseases is needed, as is animal research to explore the systemic effects of periodontal infection. Only if these criteria are met

can a causal link between periodontal disease and systemic diseases be considered likely. While more studies are required, it is widely accepted that maintaining good oral health is essential not just for preventing oral disease but also for supporting overall health.[65,70]

CONTROVERSIES AND FUTURE RESEARCH

Numerous studies have attempted to validate the relationship between periodontal disease and systemic conditions like myocardial infarction and stroke. While some studies have shown a higher risk of stroke associated with periodontitis, other research has found no significant connection. This highlights the complexity of the relationship between oral health and systemic diseases and underscores the need for further research. There is growing interest in investigating whether periodontal infections contribute to the progression of cardiovascular diseases, cancer metastasis, or immune system disorders. Increased collaboration between dental professionals and other healthcare providers is essential to advancing this research.

The investigation into the connections between oral health and systemic diseases is a rapidly evolving field, and early identification of oral disease may facilitate early diagnosis and treatment of systemic conditions. More research is needed to strengthen the integration of dental and medical care, allowing for improved management of overall patient health. .[71,72]

CONCLUSION

Oral hygiene plays a crucial role in overall health, contributing significantly to the prevention of systemic diseases such as cardiovascular diseases, diabetes, respiratory infections, and adverse pregnancy outcomes. Public health initiatives aimed at improving oral hygiene, educating the public, and enhancing access to dental care can help reduce the incidence of these chronic conditions. As oral health is deeply interconnected with general health, incorporating oral hygiene into broader public health policies and preventive care programs is vital for promoting long-term well-being and reducing the global health burden.

The mouth serves as a significant source of infection and inflammation, which can impact overall health. Research highlights the interconnectedness between oral infections, inflammation, and systemic diseases. Dental professionals, including hygienists, dentists, and specialists, must recognize these connections and modify their assessment, prevention, and treatment protocols accordingly to enhance both oral and overall health.

Oral and maxillofacial manifestations often serve as early indicators of systemic diseases, with many signs and symptoms presenting in the head and neck region. Dentists and general practitioners are key to identifying these early manifestations. A thorough oral examination and detailed medical history are crucial for diagnosing potential systemic issues. Any suspicious oral lesions or changes, such as unexplained bleeding, tooth mobility, or abnormal radiological findings, should be carefully investigated. Cytological scraping, biopsies, or fine-needle aspirations may be necessary for accurate diagnosis. This article provides an overview of the common oral and maxillofacial findings that may signal the onset of systemic diseases in both adults and children, including diagnostic criteria and differential diagnoses.

REFERENCES

1. Seymour GJ. Good oral health is essential for good general health. the oral-systemic connec tion. Clin Microbiol Infect. 2007;13(Supot 4):1-2.

2. Chapple IL. The impact of oral disease upon systemic health-symposium overview. J Dent.2009:37(8)5568-5571
3. Amar S, Han X. The impact of periodontal infection on systemic diseases. Med Sci Monit 2003:9(12) RA291-RA299
4. Aas JA, Paster BJ, Stokes LN, Olsen L, Dewhirst FE. Defining the normal bacterial flora of the oral cavity. J Clin Microbiol. 2005;43(11):5721-5732
5. Haumschild MS. Haumschild R.1. The importance of oral health in long-term care. J Am Med Kaidonis J, Townsend G. The 'sialo-microbial-dental complex in oral health and disease. Ann Anat 2016:203:85-89.
6. Jin LL. Lamster 18, Greenspan JS, Pitts NC, Scully C, Warnakulasuriya S. Global burden of oral diseases: emerging concepts, management and interplay with systemic health. Oral Des 2016:22(7):609-619. Say Assoc. 2009:10(9):667-671
7. Garcia Rt, Henshaw MM, Krall EA, Relationship between periodontal disease and systemic health, Periodontol 2000 2001.25-21-36
8. Scannapieco FA. The oral microbiome: its role in health and in oral and systemic infections Clinical Microbiology News! 2013:35(20):163-169
9. Beighton, D., J. R. Radford, and M. N. Naylor. 1990. Protease activity in gingival crevicular ¯uid from discrete periodontal sites in humans with periodontitis or gingivitis. Arch. Oral Biol. 35:329±335.
10. Larsen T. Fiehn FE. Dental biofilm infections-an update. APMIS 2017:125(4):376-384. Kilian M, Chapple I. Hannig M, et al. The oral microbiome-an update for oral healthcare 12 professionals. Ar Dent / 2016;221(19)657-666
11. Boon, N. A., and K. A. A. Fox. 1995. Disease of the cardiovascular system, p. 191±312. In C. R. W. Edwards, I. A. D. Bouchier, C. Haslett, and E. R. Chilvers (ed.), Davidson's principles and practice of medicine, 17th ed. Churchill Livingstone, New York, N.Y.].
12. Byrne, J., C. Ellsworth, E. Bowering, and M. Vincer. 1993. Language de velopment in low birth weight infants: the ®rst two years of life. J. Dev. Behav. Pediatr. 14:21±27.].
13. Bonten, M. J., C. A. Gaillard, F. H. van Tiel, H. G. Smeets, S. van der Geest, and E. E. Stobberingh. 1994. The stomach is not a source for colonization of the upper respiratory tract and pneumonia in ICU patients. Chest 105: 878±884.].
14. Carroll, G. C., and R. J. Sebor. 1980. Dental ¯ossing and its relationship to transient bacteremia. J. Periodontol. 51:691±692
15. Mack F, Schwahn C, Feine JS, et al. The impact of tooth loss on general health related to quality of life among elderly Pomeranians: results from the study of health in Pomerania (SHIP-0). Int J Prosthodont 2005 18: 414–9
16. Abnet CC, Qiao Y-L, Dawsey SM et al. Tooth loss is associated with increased risk of total death and death from upper gastrointestinal cancer, heart disease, and stroke in a Chinese population-based cohort. Int J Epidemiol 2005 34: 467–474
17. Holmlund A, Holm G, Lind L. Number of teeth as a predictor of cardiovascular mortality in a cohort of 7,674 subjects fol lowed for 12 years. J Periodontol 2010 81: 870–876.
18. Heilmann, A., Tsakos, G., and Watt, R. G. (2015). “Oral health over the life course,” in A Life Course Perspective on Health Trajectories and Transitions, eds Burton-Jeangros C, Cullati S, Sacker A, and Blane D (Cham: Springer), 39–59.

19. Coll, P. P., Lindsay, A., Meng, J., Gopalakrishna, A., Raghavendra, S., Bysani, P., et al. (2020). The prevention of infections in older adults: oral health. J. Am. Geriatr. Soc. 68, 411–416. doi: 10.1111/jgs.16154
20. Chen, K. J., Gao, S. S., Duangthip, D., Lo, E. C. M., and Chu, C. H. (2019). Prevalence of early childhood caries among 5-year-old children: a systematic review. J. Investig. Clin. Dent. 10:e12376. doi: 10.1111/jicd.12376
21. Chen, K. J., Gao, S. S., Duangthip, D., Lo, E. C. M., and Chu, C. H. (2018). Managingearlychildhoodcaries for youngchildren inChina.Healthcare6:11. doi: 10.3390/healthcare6010011
22. Chanpum, P., Duangthip, D., Trairatvorakul, C., and Songsiripradubboon, S. (2020). Early childhood caries and its associated factors among 9- to 18-month old exclusively breastfed children in Thailand: a cross-sectional study. Int. J. Environ. Res. Public Health. 17:3194. doi: 10.3390/ijerph170 93194
23. Gao, S. S., Duangthip, D., Lo, E. C. M., and Chu, C. H. (2018). Risk factors of early childhood caries among young children in Hong Kong: a cross sectional study. J. Clin. Pediatr. Dent. 42, 367–372. doi: 10.17796/1053-4625 42.5.8
24. Selwitz, R. H., Ismail, A. I., and Pitts, N. B. (2007). Dental caries. Lancet 369, 51–59. doi: 10.1016/S0140-6736(07)60031-2
25. Maltz, M., Jardim, J. J., and Alves, L. S. (2010). Health promotion and dental caries. Braz. Oral Res. 24(Suppl. 1), 18–25. doi: 10.1590/S1806-83242010000500004
26. Hujoel, P. P., Hujoel, M. L. A., and Kotsakis, G. A. (2018). Personal oral hygiene and dental caries: a systematic review of randomised controlled trials. Gerodontology 35, 282–289. doi: 10.1111/ger.12331
27. Lertpimonchai, A., Rattanasiri, S., Arj-Ong Vallibhakara, S., Attia, J., and Thakkinstian, A. (2017). The association between oral hygiene and periodontitis: a systematic review and meta-analysis. Int. Dent. J. 67, 332–343. doi: 10.1111/idj.12317
28. Duangthip, D., Wong, M. C. M., Chu, C. H., and Lo, E. C. M. (2018). Caries arrest by topical fluorides in preschool children: 30-month results. J. Dent. 70: 74–79. doi: 10.1016/j.jdent.2017.12.013
29. Abnet CC, Qiao Y-L, Dawsey SM et al. Tooth loss is associated with increased risk of total death and death from upper gastrointestinal cancer, heart disease, and stroke in a Chinese population-based cohort. Int J Epidemiol 2005 34: 467–474.
30. Holmlund A, Holm G, Lind L. Number of teeth as a predictor of cardiovascular mortality in a cohort of 7,674 subjects fol lowed for 12 years. J Periodontol 2010 81: 870–876.
31. Mack F, Schwahn C, Feine JS, et al. The impact of tooth loss on general health related to quality of life among elderly Pomeranians: results from the study of health in Pomerania (SHIP-0). Int J Prosthodont 2005 18: 414–9.
32. Marik PE. Aspiration pneumonitis and aspiration pneumonia. NEngl J Med 2001 344: 665–671.
33. Ren Q, Yan X, Zhou Y et al. Periodontal therapy as adjunctive treatment for gastric Helicobacter pylori infection. Cochrane Database of Systematic Reviews 2016: CD009477. https://doi. org/10.1002/14651858.CD009477.pub2
34. Scannapieco FA, Cantos A. Oral inflammation and infection, and chronic medical diseases: implications for the elderly. Peri odontol 2000 2016 72: 153–175.
35. Schwahn C, Volzke H, Robinson DM et al. Periodontal dis ease, but not edentulism, is independently associated with increased plasma fibrinogen levels. Thromb Haemost 2004 92: 244–252.

36. Silver JG, Martin AW, McBride BC. Experimental transient bacteraemias in human subjects with varying degrees of plaque accumulation and gingival inflammation. J Clin Periodontol 1977 4: 92–99.
37. Conner HD, Haberman S, Collings CK et al. Bacteremias fol lowing periodontal scaling in patients with healthy appearing gingiva. J Periodontol 1967 38(6 Part I): 466–472.
38. Forner L, Larsen T, Kilian M et al. Incidence of bacteremia after chewing, tooth brushing and scaling in individuals with periodontal inflammation. J Clin Periodontol 2006 33: 401 407.
39. Lockhart PB, Brennan MT, Sasser HC et al. Bacteremia associ ated with toothbrushing and dental extraction. Circulation 2008 117: 3118–3125.
40. Lockhart PB, Brennan MT, Thornhill M et al. Poor oral hygiene as a risk factor for infective endocarditis–related bac teremia. J Am Dent Assoc 2009 140: 1238–1244.
41. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infec tive endocarditis: guidelines from the American Heart Associa tion: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Commit tee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Sur gery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation 2007 116: 1736–54.
42. Roberts GJ, Watts R, Longhurst P et al. Bacteremia of dental origin and antimicrobial sensitivity following oral surgical pro cedures in children. Pediatr Dent 1998 20: 28–36.
43. Rayfield EJ, Ault MJ, Keusch GT et al. Infection and diabetes: the case for glucose control. Am J Med 1982 72: 439–450.
44. Lang CH. Sepsis-induced insulin resistance in rats is mediated by a beta-adrenergic mechanism. Am J Physiol 1992 263: E703–E711.
45. Ling PR, Bistrian BR, Mendez B et al. Effects of systemic infu sions of endotoxin, tumor necrosis factor, and interleukin-1 on glucose metabolism in the rat: relationship to endogenous glu cose production and peripheral tissue glucose uptake. Metabo lism 1994 43: 279–284.
46. Tervonen T, Lamminsalo S, Hiltunen L et al. Resolution of periodontal inflammation does not guarantee improved glyce mic control in type 1 diabetic subjects. J Clin Periodontol 2009 36: 51–57.
47. Chapple IL, Genco R. Diabetes and periodontal diseases: con sensus report of the joint EFP/AAP workshop on periodontitis and systemic diseases. J Clin Periodontol 2013 40(s14): S106 12.
48. Mackenzie RS, an De Millard H. Interrelated effects of dia betes, arteriosclerosis and calculus on alveolar bone loss. JAm Dent Assoc 1963 66: 191–198
49. Beck J, Garcia R, Heiss G et al. Periodontal disease and cardio vascular disease. J Periodontol 1996 67: 1123–1137.
50. DeStefano F, Anda RF, Kahn HS et al. Dental disease and risk of coronary heart disease and mortality. BMJ 1993 306: 688 691.
51. Hujoel PP, Drangsholt M, Spiekerman C et al. Examining the link between coronary heart disease and the elimination of chronic dental infections. J Am Dent Assoc 2001 132: 883–889.
52. Hujoel PP, Drangsholt M, Spiekerman C et al. Periodontitis systemic disease associations in the presence of smoking–causal or coincidental? Periodontol 2000 2002 30: 51–60.
53. Desvarieux M, Demmer RT, Rundek T et al. Relationship between periodontal disease, tooth loss, and carotid artery pla que: the oral infections and vascular disease epidemiology study (invest). Stroke 2003 34: 2120–2125.

54. Haraszthy VI, Zambon JJ, Trevisan M et al. Identification of periodontal pathogens in atheromatous plaques. J Periodontol 2000 71: 1554–1560.
55. Li L, Messas E, Batista EL et al. Porphyromonas gingivalis infection accelerates the progression of atherosclerosis in a heterozygous apolipoprotein E–deficient murine model. Circula tion 2002 105: 861–867.
56. Offenbacher S, Madianos PN, Champagne CM et al. Periodon titis-atherosclerosis syndrome: an expanded model of pathogen esis. J Periodontal Res 1999 34: 346–352.
57. Zhang M-Z, Li C-L, Jiang Y-T et al. Porphyromonas gingivalis infection accelerates intimal thickening in iliac arteries in a bal loon-injured rabbit model. J Periodontol 2008 79: 1192–1199.
58. Schaefer AS, Richter GM, Groessner-Schreiber B et al. Identifi cation of a shared genetic susceptibility locus for coronary heart disease and periodontitis. PLoS Genet 2009 5: e1000378.
59. Schaefer AS, Bochenek G, Jochens A et al. Genetic evidence for PLASMINOGEN as a shared genetic risk factor of coronary artery disease and periodontitis: clinical perspective. Circ Car diovasc Genet 2015 8: 159–167. 18
60. Amar S, Gokce N, Morgan S et al. Periodontal disease is asso ciated with brachial artery endothelial dysfunction and systemic inflammation. Arterioscler Thromb Vasc Biol 2003 23: 1245 1249.
61. Higashi Y, Goto C, Jitsuiki D et al. Periodontal infection is associated with endothelial dysfunction in healthy subjects and hypertensive patients. Hypertension 2008 51: 446–453.
62. Tonetti MS, Dyke TE. Periodontitis and atherosclerotic cardio vascular disease: consensus report of the joint EFP/AAP work shop on periodontitis and systemic diseases. J Clin Periodontol 2013 40(s14): S24–9.
63. D'Aiuto F, Orlandi M, Gunsolley JC. Evidence that periodontal treatment improves biomarkers and CVD outcomes. J Clin Periodontol 2013 40(s14): S85–105.
64. Paraskevas S, Huizinga JD, Loos BG. A systematic review and meta-analyses on C-reactive protein in relation to periodontitis. J Clin Periodontol 2008 35: 277–290.
65. Tonetti MS, D'aiuto F, Nibali L et al. Treatment of periodonti tis and endothelial function. N Engl J Med 2007 356: 911–920.
66. Behle JH, Sedaghatfar MH, Demmer RT et al. Heterogeneity of systemic inflammatory responses to periodontal therapy. J Clin Periodontol 2009 36: 287–294.
67. Linden GJ, Lyons A, Scannapieco FA. Periodontal systemic associations: review of the evidence. J Clin Periodontol 2013 40: S8–S19.
68. Aldridge, J. P., V. Lester, T. L. Watts, A. Collins, G. Viberti, and R. F. Wilson. 1995. Single-blind studies of the effects of improved periodontal health on metabolic control in type 1 diabetes mellitus. J. Clin. Periodontol. 22:271±275..
69. Asikainen, S., and S. Alaluusua. 1993. Bacteriology of dental infections. Eur. Heart J. 14:43±50.
70. Baltch, A. L., H. L. Pressman, C. Schaffer, R. P. Smith, M. C. Hammer, M. Shayegani, and P. Michelsen. 1988. Bacteremia in patients undergoing prophylaxis as recommended by the American Heart Association, 1977. Arch. Intern. Med. 148:1084±1088.
71. Breslau, N., G. G. Brown, J. E. DelDotto, S. Kumar, S. Ezhuthachan, P. Andreski, and K. G. Hufnagle. 1996. Psychiatric sequelae of low birth weight at 6 years of age. J. Abnorm. Child Psychol. 24:385±400.
72. Cimasoni, G. 1983. Crevicular ¯uid updated. Monogr. Oral Sci. 12:1±152. 19. Clinton, S. K., J. C. Fleet, H. Loppnow, R. N. Salomon, B. D. Clark, J. G. Cannon, A. R. Shaw, C. A. Dinarello, and P.

Libby. 1991. Interleukin-1 gene expression in rabbit vascular tissue in vivo. Am. J. Pathol. 138:1005±1014.