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go hand in hand. The oral cavity is the ingress to our entire body. Nutrition enters there, and our teeth masticate the food so that all the alimentary components we need can be released to our complete body.

Infections in the oral cavity therefore have a huge impact on general health. After all, chewing forces push intra-oral periodontal bacteria into our bloodstream. This process can cause severe collateral damage. In the first part of our article, we discussed the impact of periodontal pathogens on cardiovascular diseases, diabetes, respiratory diseases, pregnancy, rheumatoid arthritis and chronic kidney disease.

In this second article we will highlight six other key points about the relationship between periodontitis (i.e. periodontal pathogens) and systemic diseases.

7. Alzheimer's disease

Alzheimer's disease is a progressive neurodegenerative disorder characterised by cognitive decline, memory loss, and changes in behaviour. Three key aspects play a role: accumulation of amyloid-beta peptides, aggregation of hyperphosphorylated tau protein and chronic neuroinflammations in the brain.¹

Periodontitis increases the risk of Alzheimer's because periodontopathogens increase the production of the amyloid beta peptides, which occurs in the brain damage in Alzheimer's patients. Moreover, both Alzheimer's and periodontitis are associated with increased oxidative stress, which can damage tissues and cells.²

The impact of periodontitis on Alzheimer's disease is based on three mechanisms:

- 1. Bacterial translocation: periodontal pathogens, such as *P. gingivalis*, can enter the bloodstream and reach the brain, potentially contributing to the formation of amyloid plaques and neurofibrillary tangles.
- 2. Inflammatory mediators: cytokines and other inflammatory mediators produced in response to periodontal

- infection can cross the blood-brain barrier, promoting neuroinflammation.³
- 3. Immune response: chronic periodontal infection can lead to a systemic immune response that affects the central nervous system.

Recent studies have shown a higher prevalence of periodontitis in individuals with Alzheimer's disease compared to those without. Some trials indicate that treating periodontitis can reduce systemic inflammation and potentially slow cognitive decline in Alzheimer's patients.⁴

Therefore, screening and diagnosis for Alzheimer's patients is important to manage and prevent periodontitis. Screening and diagnosis for periodontitis patients could be combined with monitoring cognitive functions and evaluating for signs of cognitive decline.

8. Erectile problems

Erectile dysfunction (ED) is the inability of a man to achieve or maintain an erection sufficient for satisfactory sexual performance.

It can result from various factors, such as physical causes (cardiovascular disease, diabetes, or hormonal imbalances), psychological causes (stress, anxiety, and depression) or lifestyle factors (smoking, excessive alcohol consumption, and lack of physical activity).⁵

The relationship between erectile dysfunction and periodontitis is an emerging area of research, with growing evidence suggesting that periodontal health may influence sexual health.⁶

There are four shared mechanisms between both problems:

1. Chronic inflammation: ED and periodontitis involve chronic inflammation. Periodontal inflammation can contribute to systemic inflammation, which may affect erectile function. Periodontal infections increase levels of systemic inflammatory markers such as C-reactive protein (CRP) and interleukins. mage – stock.adobe.com

- 2. Endothelial dysfunction: inflammation from periodontitis can lead to endothelial dysfunction, impairing blood vessel function and potentially contributing to ED. Chronic inflammation and oxidative stress from periodontitis can impair endothelial function, affecting blood flow to the penis and leading to ED.
- 3. Cardiovascular health: both conditions are linked to cardiovascular health. Periodontitis can exacerbate cardiovascular diseases, which are known risk factors for ED.⁷
- **4.** Bacterial translocation: oral bacteria from periodontitis can enter the bloodstream and potentially affect vascular health, which is crucial for maintaining erectile function.

Studies have shown an association between periodontitis and an increased prevalence of erectile dysfunction. Men with periodontitis may be at higher risk for developing ED. Some trials even suggest that treating periodontitis can lead to improvements in markers of systemic inflammation and potentially improve erectile function.⁸

The same clinical recommendations are again applicable here: good oral hygiene, regular dental check-ups, interprofessional dental-medical collaboration and early screening. Also, lifestyle modifications are encouraged: healthy lifestyle changes, such as a balanced diet, regular exercise, and smoking cessation, to improve both oral and sexual health.

9. Cancer

Cancer encompasses a range of diseases characterised by uncontrolled cell growth and the ability to invade or spread to other parts of the body. Various types of cancer can affect different organs and systems.

Specific periodontitis bacteria are also associated with certain types of cancer, such as pancreatic cancer and especially colon cancer.9 As risk factors, genetic predisposition, environmental exposures (e.g. smoking, radiation), and lifestyle factors (e.g. diet, physical activity) are indicated. Furthermore, chronic inflammation as in chronic periodontitis is a known risk factor for the development and progression of many cancers. The persistent inflammation and immune system activation in periodontitis may influence cancer development and progression by their elevated levels of inflammatory cytokines and biomarkers. Increased oxidative stress is associated with both periodontitis and cancer. Oxidative stress can damage DNA and contribute to carcinogenesis.¹⁰

Certain periodontitis-associated bacteria, such as *P. gingivalis*, have been linked to the development of some cancers, potentially through these mechanisms of chronic inflammation and bacterial toxins.

Specific cancer types and evidence:

- 1. Oral cancer: there is evidence suggesting that periodontitis may be a risk factor for oral cancers. The chronic inflammatory environment in periodontitis may promote carcinogenic processes in oral tissues.¹¹
- 2. Head and neck cancer: studies have shown associations between periodontitis and an increased risk of head and

- neck cancer. Chronic inflammation and bacterial infection in periodontitis may contribute to these types of cancer.¹²
- 3. Other types: some research suggests associations between periodontitis and increased risk of other cancers, such as pancreatic cancer, though the evidence is less established.

Cancer, however, can also have an impact on periodontitis. Treatments such as chemotherapy and radiation therapy can adversely affect oral health, leading to conditions like dry mouth, mucositis, and increased susceptibility to infections, including periodontitis. Furthermore, cancer and its treatments can impair the immune system, making individuals more susceptible to periodontal infections. Finally, cancer and its treatments can affect nutritional intake and oral hygiene practices, potentially exacerbating periodontal disease.

10. Metabolic syndrome

Periodontitis and metabolic syndrome are interconnected through pathways involving inflammation, insulin resistance, and microbiome alterations. Metabolic syndrome is a cluster of conditions that increase the risk of heart disease, stroke, and type 2 diabetes. It includes several components: central obesity (excessive fat around the abdomen), hypertension (high blood pressure), dyslipidemia (abnormal cholesterol or triglyceride levels), insulin resistance (reduced ability of cells to respond to insulin, leading to high blood sugar levels) and a pro-inflammatory state (elevated levels of inflammatory markers like C-reactive protein [CRP]).¹³

There are several links between periodontitis and metabolic syndrome:

- 1. Chronic inflammation: periodontitis causes systemic inflammation, characterised by elevated inflammatory markers such as CRP and cytokines (e.g. TNF-α, IL-6). This chronic inflammation is a key feature of metabolic syndrome, contributing to insulin resistance and endothelial dysfunction.
- Insulin resistance: periodontitis-induced inflammation can exacerbate insulin resistance, a core component of metabolic syndrome. Moreover, the inflammatory cytokines from periodontitis can interfere with insulin signaling pathways.
- 3. Microbiome dysbiosis: both conditions are associated with microbial imbalances. Periodontitis involves pathogenic oral bacteria, while metabolic syndrome is linked to gut microbiome dysbiosis. The oral bacteria from periodontitis can enter the bloodstream and potentially affect the gut microbiome, contributing to metabolic disturbances.¹⁴
- 4. Adipose tissue inflammation: in metabolic syndrome, excess adipose tissue releases pro-inflammatory cytokines.

 These cytokines can worsen periodontitis by enhancing the inflammatory response in periodontal tissues.¹⁵
- 5. Oxidative stress: both conditions are associated with increased oxidative stress, which contributes to tissue damage and inflammation. Oxidative stress from metabolic syndrome can exacerbate periodontal tissue destruction.

Integrated care by addressing periodontitis may help reduce systemic inflammation and improve insulin sensitivity, positively impacting metabolic syndrome management.

Lifestyle modifications are however of utmost importance: a balanced diet rich in anti-inflammatory foods (e.g. fruits, vegetables, whole grains) can benefit both conditions and regular exercise improves insulin sensitivity and reduces inflammation, aiding in the management of both periodontitis and metabolic syndrome.

Finally, anti-inflammatory medications and treatments for insulin resistance can benefit both conditions. Probiotics and prebiotics may help restore microbial balance and reduce inflammation.¹⁶

11. Gut dysbiosis

Periodontitis and gut dysbiosis are linked through the complex interplay between oral and gut microbiomes, systemic inflammation, and the immune response. Gut dysbiosis refers to an imbalance in the gut microbiota (overgrowth of harmful bacteria, fungi, or viruses, and a decrease in beneficial bacteria), the community of microorganisms living in the intestines. This imbalance can disrupt normal digestive functions, the immune system, and even overall health.¹⁷

Dysbiosis can cause chronic inflammation in the gut, which can spread systemically. Conditions like inflammatory bowel disease, irritable bowel syndrome, and metabolic disorders can be linked to gut dysbiosis.¹⁸

Again, there is a clear link with periodontitis:

- 1. Systemic inflammation: periodontitis leads to systemic inflammation, which can affect gut health. Similarly, gut dysbiosis can lead to systemic inflammation that affects oral health.
- 2. Microbial translocation: bacteria from the oral cavity can enter the bloodstream and potentially influence the gut microbiota. For instance, *P. gingivalis*, a major pathogen in periodontitis, has been found in the gut and can contribute to dysbiosis.¹⁹

3. Immune system: both conditions involve the immune system's response to microbial imbalance and inflammation. Chronic inflammation in one site can influence inflammation in another, creating a bidirectional relationship.

4. Shared risk factors: conditions like diabetes, poor diet, and smoking can contribute to both periodontitis and gut dysbiosis. Additionally, the use of antibiotics can impact both oral and gut microbiomes.

Treating periodontitis may improve gut health and vice versa. ²⁰ A comprehensive approach to managing both conditions can involve improving oral hygiene, dietary changes, probiotics, and anti-inflammatory treatments. Furthermore, a diet rich in fiber, prebiotics, and probiotics can support a healthy gut microbiome and potentially reduce inflammation associated with periodontitis.

12. Peri-implant mucositis and peri-implantitis

Periodontitis can have a significant influence on the development and progression of peri-implant mucositis and/or peri-implantitis.²¹ These conditions are primarily driven by bacterial infections. Individuals with a history of periodontitis may have a higher microbial load and increased bacterial diversity, which can contribute to the development of peri-implant mucositis and/or peri-implantitis if implants are placed. In addition, chronic inflammation from periodontitis can affect systemic health and immune response, potentially making patients more susceptible to peri-implant mucositis and/or peri-implantitis.

Individuals with a history of periodontitis may struggle with plaque control, which is crucial for the health of both natural teeth and implants. Poor plaque control around implants can increase the risk of peri-implant mucositis and/or peri-implantitis.²²



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