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REVIEW ARTICLE

RESEARCH ON SYSTEMIC DISEASES AND THEIR ORAL MANIFESTATIONS

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ABSTRACT

Understanding systemic disorders and their oral symptoms has shown to be beneficial in improving patient outcomes. Dental and medical practitioners may enhance patient outcomes and general health by working together to identify, diagnose, and manage systemic disorders at an earlier stage once the connection between the two is understood. My research endeavors focus on the many common and complicated instances of systemic disorders that have developed distinctive oral manifestations in recent years. The research looks into Sjogren's Syndrome, Lupus, Diabetes, Celiac Disease, Behçet's Disease, Oral Lichen Planus and Crohn's Disease. This research relies heavily on information from reliable medical sources that cover the conditions discussed. In addition to textual descriptions, the study provides helpful graphical and statistical portrayals of the various medical conditions. I also looked at ways of preventing the infections in the first place, as well as treatments for the systemic diseases they may cause. This study contributes to the reader's understanding of the clinical significance of the relationship between systemic disorders and their oral manifestations, a subject that has generated a number of studies in recent years. Any statistical claims made have been backed up by reputable sources that have been verified by experts in the medical field.

INTRODUCTION

Systemic disorders don't only impact one part of the body. Instead, they affect a number of organs and systems across the body. In addition to a vast variety of symptoms, these disorders are generally characterized by intricate pathophysiological processes. A significant amount of global mortality and morbidity may be attributed to them, and they impact people of all ages, sexes, and socioeconomic statuses. The World Health Organization estimates that these illnesses are responsible for 71% of all fatalities¹. Systemic disorders have far-reaching effects, not only on the people who suffer from them but also on the economy and society as a whole. Ongoing medical treatment, medication, and behavioral changes are typically necessary for the management of systemic disorders, but they may add up in expense and inconvenience. Many systemic disorders have oral manifestations, which means they may impact the health and the appearance of the teeth, gums, tongue, and other oral tissues. These oral manifestations often show a negative impact on a person's lifestyle by causing pain, difficulties with eating and speaking, and low self-esteem. Symptoms are often the first indicator of a systemic disease, making them fundamental to the early detection, treatment, and management of many conditions. Because of the bilateral interaction between the mouth and the rest of the body, oral infections may significantly affect the development and progression of a number of systemic disorders.

Cytokines which promote inflammation, such as the necrosis factor for tumorous growth and the eosinophil differentiation factor, are typically released in response to these illnesses and may cause systemic inflammation. Several systemic disorders, such as Sjogren's Syndrome, Lupus, Diabetes, Celiac Disease, Behçet's Disease, Oral Lichen Planus, and Crohn's Disease, have been associated to chronic inflammation and its genesis or progression. Dysregulation of immune cells including T cells, B cells, and dendritic cells is a common result of oral infections and may drastically affect the immunological response. Immune activation and inflammation caused by this imbalance have been linked to the onset and progression of several systemic illnesses. Researchers have shown that these factors lead to fewer regulatory T cells being produced, which are essential for keeping the immune system in check². Continued research and development of novel therapies and management techniques are being made to improve outcomes for people with systemic disorders, and these efforts remain a key public health priority across the globe.

Systemic Diseases and their Oral Manifestations

Sjögren's Syndrome: Sjogren's Syndrome is an autoimmune condition in which the immune system wrongly attacks the glands responsible for producing moisture in the body, including the tear and saliva glands. The condition's defining symptoms—dry eyes and a dry mouth—result from this abnormality in tear and saliva production³.

Two subtypes of this illness have been recognized, and they are:

Primary Sjögren's syndrome: Often found to occur on its own, i.e., is not dependent upon other related infections. **Secondary Sjögren's syndrome:** found to mostly develop as an accompaniment infection to other infections e.g., lupus. Causes of the condition are quite variable. However, it is said that the condition is heritable, with some people inheriting genetic material that predisposes them to the illnesses. Hormonal make-up, still, demonstrates that the illness is more common in women and is hence related to the oestrogen hormone in women³.

Extreme dryness of the mouth is the primary symptom of this illness. This symptom is also called xerostomia. Xerostomia is characterized by a variety of symptoms, such as a dry or sticky mouth, frequent thirst, cracked or dry lips, mouth ulcers, trouble speaking or swallowing, and a burning sensation in the mouth, all of which are caused by a lack of saliva or an inability to produce enough saliva³. These symptoms make it hard for the patient to eat and talk normally, reducing the patient's quality of life. Tooth decay and gum disease are also more likely to develop as a result.



Figure 1. Xerostomia or dry mouth, an oral symptom for 1. Sjögren's Syndrome (Dr. Anjali Singh)⁴

Treatment: Sjögren's syndrome therapy aims to provide symptomatic relief, reduce the risk of complications, and improve the patient's quality of life.³ In this case, we focus on relieving the discomfort associated with Xerostomia. To alleviate dry mouth symptoms, practitioners offer saliva production-stimulating products like gum with sorbitol additions and over-the-counter saliva replacements³.

Due to the increased likelihood of cavities and gum disease, patients with Sjögren's syndrome should take special care to maintain good oral hygiene. Maintaining regular dental examinations and cleanings is encouraged, with the possibility of receiving recommendations for toothpaste and mouthwash from your dentist.

Preventive measures: Due to the unclear cause the condition has no known preventive measure.

Lupus: Lupus, often called systemic lupus erythematosus (SLE), is a chronic autoimmune disease that causes inflammation and damage to many different tissues and organs.⁵ In addition to systemic lupus, various forms of the disease have been recognized, such as drug-induced lupus, neonatal lupus, and cutaneous lupus. Similar to Sjögren's Syndrome, this illness mostly affects females. Hyposalivation, cheilitis, and oral mucosal ulcers are the most common symptoms associated with this illness⁵.



Figure 2. Oral ulcers commonly evident in SLE Patients (Paul Howard)⁶

One of the most noticeable signs of lupus is oral ulcers, which show up in 78.6% of patients⁵. These ulcers are extremely painful and may impede both eating and talking. White or red lesions of varying sizes and shapes may occur. They have a particularly negative effect on the roof of the mouth, damaging the covering tissue and exposing the tissue below. However, it is believed that the immune system's attack on the cells lining the oral mucous membrane is a contributing factor in the development of canker sores within the mouth cavity in lupus patients. Oral ulcers in lupus might also be caused by other things like stress or medicine.

Preventive measures: Proper dental hygiene Keeping your teeth and gums clean is one of the best strategies to avoid painful ulcers caused by lupus. Maintaining good oral hygiene involves more than just using an antiseptic mouthwash once in a while. Smoking and excessive alcohol use both irritate the oral mucosa and should be avoided by those with lupus. Lupus flare-ups may be prevented by avoiding direct sunlight. Lupus patients should always use high-SPF sunscreen before walking outside. Regular medical visits: Regular doctor visits may help monitor lupus symptoms and spot any changes early. Oral ulcerations are a serious sign that should be reported to the doctor immediately.

Treatment: Depending on the severity of the ulcers and the patient's general condition, treatment for mouth ulcers in lupus may include either topical or systemic medications. Inflammation and soreness may be alleviated with topical therapies like steroid pills and mouthwashes⁵. In extreme situations, systemic drugs like immunosuppressants may be required.

Diabetes: Diabetes is a metabolic disease that impairs the body's capacity to handle sugar in the blood. People with diabetes have high blood glucose levels because their bodies either don't create enough insulin or don't utilize the insulin they make properly.⁹ Over time, this may damage the body's eyes, kidneys, nerves, heart, and blood vessels, among other organs and tissues. Diabetes comes in Type 1, Type 2, and gestational variant. When the pancreatic cells responsible for making insulin are attacked and destroyed by the body's immune system, type 1 diabetes results⁹.

The most prevalent kind of diabetes, known as type 2, develops when insulin stops having its usual impact on the body or when the body stops producing enough insulin. Gestational diabetes manifests throughout pregnancy but heals itself after the baby is delivered. Periodontal disease is a major oral complication of diabetes. Diabetics are more likely to develop gum disease, an infection that damages the tissues that support the teeth. Bleeding gums, foul breath, tooth loss, and bone loss may all result from this illness. High amounts of glucose in the saliva of diabetics provide a favorable habitat for the bacteria that cause gum disease.



Figure 3. Periodontal disease, a common case in Diabetes (Bixby, 2018)⁸

Preventive Measures: The development of diabetes may be controlled if the patient maintains tight monitoring of their blood sugar levels. Periodontal disease may be avoided with regular blood sugar monitoring and adherence to the treatment plan. Those with diabetes might lessen their risk of developing oral issues through quitting tobacco and cutting down on alcohol. Tobacco use is a major contributor to periodontal disease and other oral health issues. Drinking alcohol is associated with an increased risk of oral health issues and impaired glucose homeostasis.

Treatment: When treating diabetes, it is important to monitor and manage blood sugar levels as well as treat any oral symptoms that may develop. The primary focus of diabetes care is on achieving and maintaining stable blood sugar levels. Complications may be avoided via regular monitoring of blood sugar levels and adherence to the approved treatment plan. Good oral hygiene practices are crucial in managing the oral complications of diabetes. Gum disease treatment options include scaling and root planing by a dentist, antibacterial medications, and, in severe instances, surgery. Artificial saliva products and drinking enough of water may help alleviate dry mouth, another typical oral symptom of diabetes⁹⁷. Quitting smoking and cutting down on alcohol use may help alleviate dry mouth.

Celiac Disease: Celiac disease is an immunological response to gluten, a protein primarily prevalent in wheat. It is also known as celiac sprue or gluten-sensitive enteropathy.¹⁰ Celiac disease is distinct from gluten sensitivity and intolerance because the latter two conditions do not require an immune system attack on the small intestine¹⁰. People with celiac disease are unable to absorb nutrients properly because of an immunological reaction induced by gluten consumption. Celiac disease often causes symptoms that affect the mouth and adjacent tissues. These oral symptoms may appear before the gastrointestinal symptoms do, making them a possible early indicator of the illness. Symptoms of the condition include defects in the enamel of the teeth. Children with celiac disease often have these flaws in their permanent teeth since enamel is still forming at this age. Enamel hypoplasia is the most prevalent dental enamel abnormality in people with celiac disease¹⁰. Insufficient or abnormally formed tooth enamel is a hallmark of this condition. It may affect many teeth and show up as spots where enamel is missing, enamel that is excessively thin or fragile, or surface abnormalities. Enamel hypoplasia may result in greater susceptibility to dental decay and sensitivity, as well as aesthetically undesirable traits such as discolouration or inconsistencies in tooth form.

Prevention and Treatment: There are no clearly spelt-out preventative strategies for this illness. However, there are certain activities you may do to minimize the severity of the problem or to assist manage Celiac disease symptoms.



Figure 4. Enamel hypoplasia common in Celiac Disease (McKenzie, 2021)¹¹

Individuals who are sick with celiac disease, have to adopt a rigorous diet free of glutes. This includes avoiding any meals and items that contain gluten, including wheat, barley, and rye¹⁰. It is also crucial to examine food labels carefully to ensure that they do not contain hidden sources of gluten.

For individuals identified with seriously damaged intestines, the practitioner may suggest steroids which help alleviate the severity during recovery¹⁰. It is advised that patients follow up on frequent checkups to continually monitor the condition. The doctor can readily check the situation by examining blood samples. Continued symptoms may necessitate endoscopy¹⁰ to evaluate intestinal condition. The worst scenario for this problem is refractory celiac which has not yet found effective therapy. Because the illness has badly harmed the intestines, this case can only be handled.

Behçet's Disease: Behçet's disease, also known as Behçet's syndrome, is a chronic, recurring inflammatory condition that affects various organ systems, including the skin, eyes, mucous membranes, joints, blood vessels, and gastrointestinal tract. It is to be caused by an aberrant immunological response, which may be triggered by environmental stimuli in genetically predisposed people¹². Behçet's disease's specific pathogenesis is unknown, although it is considered to entail a mix of genetic, environmental, and immunological variables that result in immune cell activation and the generation of inflammatory cytokines.¹²

The condition is distinguished by periodic bouts of inflammation that may affect various regions of the body. Behçet's disease symptoms might vary greatly, although they typically include:

- Sores in the mouth that are painful (aphthous stomatitis)
- Sores in the genital area
- Skin blemishes
- Joint swelling and discomfort

Recurrent aphthous stomatitis¹², often known as canker sores, is frequently connected with the condition. Aphthous stomatitis is a frequent oral manifestation of Behçet's illness that is distinguished by the recurrence of painful, round-shaped ulcers in the mouth. These ulcers may form on the tongue, inside the cheeks, lips, or throat and can persist anywhere from a few days to a few weeks. These ulcers might be the initial sign of Behçet's illness in certain patients.

While there is no cure for Behçet's disease, treatment options are available to control symptoms and avoid complications. Here are some methods for preventing and treating Behçet's disease.

Prevention: Because the etiology of Behçet's illness is not completely understood, there is no established way for preventing it. However, avoiding stress, smoking, and some drugs that might aggravate symptoms may help prevent flare-ups.



Figure 5. Deep aphthous stomatitis on a patient with Behçet's disease (Gualtierotti et al., 2018)¹³

Treatment: Medication: Depending on the severity of the aphthous stomatitis, different drugs, such as corticosteroids, immunosuppressants, or biologic therapy, may be administered. Eye treatment: If the patient has eye irritation, an ophthalmologist is consulted, since corticosteroid and azathioprine pills or eyedrops may be prescribed to ease and avoid serious problems. Relieving joint pain: Physical therapy and exercise may help manage joint pain and stiffness. Joint replacement surgery may be required in certain circumstances. A healthy lifestyle, which includes regular exercise, a well-balanced diet, and stress management strategies, may also help control symptoms and avoid complications.

Oral Lichen Planus: Oral Lichen Planus (OLP) is a chronic inflammatory mucosal disease that affects the oral cavity. Its cause is unknown. It is distinguished by the presence of white, reticulated, erosive lesions on the buccal mucosa, tongue, gingiva, and other oral mucosal areas. OLP can occur at any age, but it is most common in adults in their forties and fifties.¹⁴ Women are more likely to be affected than men. There are three clinical forms of OLP: reticular, erosive, and atrophic.¹⁴ The most common type is reticular, which is distinguished by white, lacy, or network-like lesions on the oral mucosa. The erosive form has painful, ulcerated lesions, whereas the atrophic form has thinning of the oral mucosa and loss of papillae.¹⁴



Figure 6. Oral Lichen Planus (Gear, 2018)¹⁵

Prevention: Although the specific etiology of OLP is unknown, there are several precautions that may be taken to lessen the chance of having OLP. Brushing and flossing twice a day, as well as using mouthwash, may help prevent infections and improve overall dental health. Limit your intake of spicy or acidic meals, smoke, and alcohol to help avoid the emergence of lichen planus in the mouth. Get frequent dental check-ups to identify early indications of OLP and avoid complications like infections.

Treatment: Treatment for Oral Lichen Planus (OLP) is determined by the severity of the symptoms as well as the kind of OLP present. OLP has no cure, however there are various treatment options available to assist manage symptoms, decrease inflammation, and avoid complications. Doctors may prescribe topical or systemic corticosteroid creams, ointments, or gels for direct application to the affected region. Topical corticosteroids relieve symptoms such as pain, burning, and irritation by lowering inflammation¹⁴. Systemic corticosteroids, such as prednisone, may be used in severe instances of OLP to decrease inflammation and manage symptoms. Long-term usage of systemic corticosteroids, on the other hand, may cause negative effects and should be taken with care¹⁴. For severe instances of OLP, immunosuppressant medicines such as cyclosporine or azathioprine may be administered. They relieve inflammation by inhibiting the immune system, but they may have dangerous adverse effects and must be used under constant medical supervision.

Retinoids, such as acitretin, may be used to treat OLP by increasing skin cell shedding and lowering inflammation¹⁴. To address discomfort associated with OLP, pain relievers such as over-the-counter or prescription pain medicines may be administered.

Crohn's Disease: Crohn's disease is a slow, but long-term inflammation disease affecting majorly affecting the bowel hence affecting the gastrointestinal system, from the mouth to the anus. Abdominal discomfort, diarrhea, and weight loss are common symptoms caused by inflammation and ulceration of the intestinal lining. Clinical assessment, blood tests, imaging techniques (CT scans or MRI), and endoscopic examination of the digestive system to acquire biopsies of the affected tissue are all used together to arrive at a diagnosis of Crohn's disease¹⁶.



Figure 7. Swollen gums with small white pustules evident in Crohn's Disease (Muhvić-Urek et al., 2015)¹⁶

Swollen gums are a typical oral symptom of Crohn's disease. The inflammation caused by Crohn's disease can affect the gingival tissue, which is the gum tissue that surrounds and supports the teeth¹⁶. The swollen gums may appear red and tender, and they may bleed easily when brushing or flossing. In some cases, the swelling may be severe enough to cause discomfort or pain.

Prevention: Stopping smoking habits. Quitting smoking may help reduce the risk of developing the condition or help manage your symptoms if you have already been diagnosed. Eating a nutritious, well-balanced diet can help support overall health and lower the risk of developing the condition.

Maintaining proper oral hygiene, such as brushing and flossing frequently, and seeing your dentist for regular checks, will help prevent the illness inasmuch as its symptoms lead to dental problems.

Treatment: Since Crohn's disease has no cure its therapy is therefore oriented on obtaining and maintaining remission, so that the symptoms are under control and there is no active inflammation in the digestive system. Doctors may prescribe Crohn's disease medications such as anti-inflammatory drugs, immunosuppressants, and biologic therapies. The precise medicine or medications used will be determined by the degree and location of the condition, as well as other criteria such as age and general health. Surgical intervention may be required in severe instances to remove damaged parts of the intestine or to treat problems such as intestinal blockage or fistula development¹⁶. Complications such as fistulas, strictures, or abscesses may also be treated surgically.

CONCLUSION

Understanding oral infections sheds light on bacterial infections that enter the bloodstream and spread to other organs and tissues, causing further infections and contributing to systemic disease progression. The bidirectional relationship between the oral cavity and the rest of the body emphasizes the importance of regular dental check-ups, which can significantly aid in the management of systemic diseases. Early diagnosis and control of these oral infections' symptoms is thus critical for improving results and general well-being for those affected by systemic illnesses. Thus, the presence of oral manifestations is irrefutably an important diagnostic tool for many systemic diseases.

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