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## Would You Recognize Lupus?

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### Abstract

Systemic Lupus Erythematosus, or SLE, is a chronic autoimmune disease which significantly affects various organs of the body and the oral cavity. According to various studies, SLE can cause an increased risk of periodontitis, fungal infections, and dental caries within the oral cavity. Periodontitis is an inflammatory condition mediated by an infectious etiology which affects the supporting tissues of the periodontium and alveolar bone. With SLE being an inflammatory condition as well, recent studies have emerged hypothesizing the possible association between SLE and periodontitis. Other effects on the oral cavity such as fungal infections including lichen planus and angular cheilitis are occasionally seen in patients with lupus. Furthermore, SLE has been shown to increase the prevalence of dental caries due to decreased salivary flow and pH, and subsequent changes in the oral flora. On a systemic level, internal inflammation of SLE could lead to several other problems within the body and certain medications patients take for SLE treatment can cause cutaneous lesions. Therefore, as clinicians, it is imperative to adequately review patient medical histories as well as perform intraoral and extraoral examinations in order to fully understand the possible contraindications between dental treatment and SLE.

### Introduction

The purpose of this literature review is to inform clinicians on the oral and systemic aspects of SLE and how evidence-based decision making may impact dental treatment planning in order to provide patients with the best quality of care.

### SLE and the Oral Cavity

Systemic Lupus Erythematosus, or SLE, is a chronic autoimmune inflammatory disease affecting the central nervous system, the heart, lungs, kidneys and skin. Some of the most common symptoms seen with this disease include the malar, or butterfly, rash, joint pain and swelling, loss of appetite, nausea, etc. The etiology of SLE is not completely known, but this autoimmune disease is more prevalent among women of child bearing age. Since there is no cure for SLE, the goal of treatment is to relieve symptoms and protect organs by decreasing internal inflammation.<sup>1</sup>

### Review of Literature

#### SLE and Periodontitis

In a recent study, an analysis was done comparing the frequency and severity of chronic periodontitis between SLE patients and non-SLE patients. After measuring plaque index, BOP, probing depths, and attachment levels on both groups, the researchers determined the severity of periodontal disease was about the same, but chronic periodontitis occurred at an earlier age in SLE patients.<sup>2</sup>

In another study, researchers found a significant elevation in anaerobic bacteria such as *Prevotella*, *Selenomonas*, and *Treponema*, in SLE patients by extracting DNA from endodontic paper points placed in their deepest pockets. A positive correlation has been found between SLE patients and the “red complex” periodontal pathogens as well.<sup>3</sup>

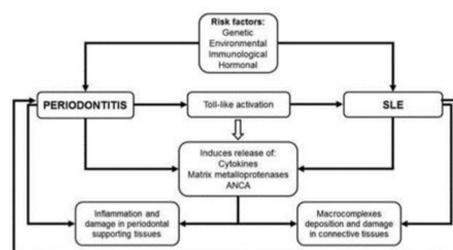


Fig. 1. Possible mechanisms associating Toll-like receptor with systemic lupus erythematosus and periodontal disease.<sup>11</sup>

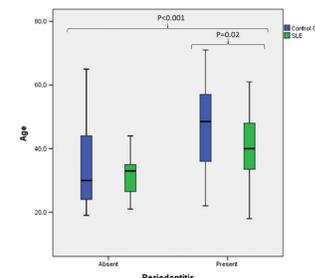


Fig 1. Distribution of 75 SLE patients and 75 control subjects with an without chronic periodontitis according to age.<sup>2</sup>

#### SLE and Fungal Infections

SLE patients may experience angular cheilitis, with severe crusting around their lips which is most often asymptomatic.<sup>4</sup> It is possible for patients to present with erosive lichen planus as well with the most common areas being the buccal mucosa, hard palate, and lower lip.<sup>5</sup> Invasive fungal infections as a whole serve as a major problem for these patients, causing an increased risk of mortality and increased hospital readmission.<sup>6</sup>



#### SLE and Dental Caries

A cross-sectional study was conducted and determined a strong correlation between SLE patients and certain risk factors for dental caries including a substantial decrease in salivary flow, a more acidic oral pH, and an increase in cariogenic bacteria including *S. mutans* and *S. sobrinus*.<sup>7</sup>

### SLE on a Systemic Level

SLE has the potential to cause serious organ inflammation throughout the body including the muscles, blood vessels, and the lining of the lungs and kidneys. In addition to internal inflammation, there is a risk of leukopenia and thrombocytopenia, causing an increased risk of infection and bleeding respectively.<sup>1</sup> There are potential adverse effects from prolonged use of a specific SLE medication Hydroxychloroquine, or HCQ, one effect being cutaneous lesions.<sup>8</sup> Along with this, another adverse effect of HCQ is hyperpigmentation of the lips and gingiva.<sup>9</sup>

### Conclusion

As clinicians it is pertinent to thoroughly review over medical histories, perform adequate extraoral and intraoral examinations, and provide the best quality of care for patients suffering with SLE. Intraoral examinations are of particular importance due to oral ulcerations being present in about 9-45% of SLE patients and xerostomia being likely if the disease affects the salivary glands.<sup>10</sup>

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## **Would You Recognize Lupus?**

Review of Literature by: Barbara Brown, Maegan Simms, and Sydney Smith  
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### **Abstract**

Systemic Lupus Erythematosus, or SLE, is a chronic autoimmune disease which significantly affects various organs of the body and the oral cavity. According to various studies, SLE can cause an increased risk of periodontitis, fungal infections, and dental caries within the oral cavity. Periodontitis is an inflammatory condition mediated by an infectious etiology which affects the supporting tissues of the periodontium and alveolar bone. With SLE being an inflammatory condition as well, recent studies have emerged hypothesizing the possible association between SLE and periodontitis. Other effects on the oral cavity such as fungal infections including lichen planus and angular cheilitis are occasionally seen in patients with lupus. Furthermore, SLE has been shown to increase the prevalence of dental caries due to decreased salivary flow and pH, and subsequent changes in the oral flora. On a systemic level, internal inflammation of SLE could lead to several other problems within the body and certain medications patients take for SLE treatment can cause cutaneous lesions. Therefore, as clinicians, it is imperative to adequately review patient medical histories as well as perform intraoral and extraoral examinations in order to fully understand the possible contraindications between dental treatment and SLE. The purpose of this literature review is to inform clinicians on the oral and systemic aspects of SLE and how evidence-based decision making may impact dental treatment planning in order to provide patients with the best quality of care.

### **Introduction**

Systemic Lupus Erythematosus, or SLE, is a chronic autoimmune inflammatory disease which significantly affects various organs of the body and the oral cavity.<sup>1</sup> SLE is the systemic form of lupus and directly affects multiple areas in the body, including the central nervous system, the heart, lungs, kidneys, and the skin. With SLE being categorized as an autoimmune disease, this complex and potentially severe condition attacks healthy cells, tissues, and organs, resulting in chronic inflammation. There is no cure for systemic lupus erythematosus at the present time. However, the goal of treatment is to relieve the symptoms of the disease and protect internal organs by decreasing the amount of inflammation within the body. Common symptoms of people suffering from SLE include joint pain and swelling, loss of appetite, nausea, muscle aches, and severe fatigue. Most people suffering from SLE will develop arthritis during the course of the disease, and this form of arthritis mimics another autoimmune disease known as rheumatoid arthritis.<sup>2</sup> However, the most notable symptom of people with lupus in general is the skin rash over the nose and cheeks termed the malar rash, otherwise known as the butterfly rash. This non painful rash can be precipitated or even worsened by a process called photosensitivity, or exposure to sunlight. Photosensitivity could even cause what's called a "flare" of SLE, which is characterized by increased inflammation throughout the body.<sup>2</sup> In addition to the malar rash, other areas of the skin exposed to sunlight can be susceptible to a rash too.<sup>3</sup>

The etiology of SLE is not completely known but some suggest it may be related to genetic, environmental, or hormonal factors. The strongest risk factor of this disease is gender, with SLE being more prevalent among women of child-bearing age between age 20 to 45, and a male to female ratio of 1:8.<sup>2</sup> Certain people are more at risk than others in developing SLE including people of African American, Hispanic, and Asian descent.<sup>3</sup> Due to the ability to detect lupus at earlier stages, the incidence of lupus has significantly increased over the past 40 years.<sup>4</sup>

On a broad scale, there are approximately 16,000 new cases of lupus are diagnosed every year and five million people suffer from this disease worldwide. Unfortunately there is no single test to diagnose SLE, so in order to diagnose someone with this condition, one has to rule out other autoimmune diseases with the same symptoms such as rheumatoid arthritis.<sup>3</sup>

Luckily, the American College of Rheumatology has developed eleven specific criteria in order to effectively diagnosis people with SLE. Along with rheumatologists, neurologists, immunologists, etc., oral health care professionals are an additional key asset to this interprofessional group due to the oral manifestations seen in patients with SLE.<sup>2</sup> Due to the numerous effects systemic lupus erythematosus can have on the body, the purpose of this literature review is to inform clinicians on the oral and systemic aspects of SLE and how evidence-based decision making may impact dental treatment planning in order to provide patients with the best quality of care. All of the studies and additional information discussed in this review of literature were primarily found on PubMed and serve to backup all of the claims regarding SLE and its effects on the oral cavity and the body as a whole.

### **SLE and Periodontitis**

In regards to SLE and its effects on the oral cavity, many studies have shown a possible association between systemic lupus erythematosus and periodontitis. Periodontitis is an inflammatory condition mediated by an infectious etiology which affects the supporting tissues of the periodontium and alveolar bone. The accumulation of dental plaque initiates gingival inflammation, leading to anaerobic bacterial colonization and loss of periodontal attachment and possible tooth loss. Certain bacteria known as the “red complex” organisms serve as the infectious etiology of periodontitis, which include *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*.<sup>1</sup> This subgingival microbiota increases the severity of the

periodontal disease as well as local inflammation.<sup>5</sup> With SLE being an inflammatory condition as well, recent studies have emerged hypothesizing the possible association between SLE and periodontitis.

In fact, the prevalence of periodontitis in patients with SLE varies, ranging from 60 to about 93.8%. In a recent study, an analysis was done to compare the frequency and severity of chronic periodontitis between seventy-five patients with SLE to seventy-five patients without SLE or any rheumatic disease. They measured plaque index of all patients and various indicators of periodontal disease including probing depth, clinical attachment level, and bleeding on probing. Out of the seventy-five patients in the group with SLE, fifty-one of them had chronic periodontitis and forty-one of the seventy-five people without SLE had chronic periodontitis. The severity of the disease in both groups was about the same, however, chronic periodontitis occurred earlier for patients with SLE. Overall, the likelihood of developing chronic periodontitis was systematically higher for the patients with SLE, especially at younger ages.<sup>6</sup>

Similar to this study, a systematic review and meta-analysis was conducted using various publications to determine another possible association between periodontitis and systemic lupus erythematosus. A total of 1,383 patients were studied, with 487 having SLE and 896 without SLE. These patients were observed in multiple observational studies of cross-sectional, case-control, or cohort design. After doing a meta-analysis, the researchers found the overall risk of contracting periodontitis in SLE patients was significantly greater than patients without SLE with a risk ratio of 1.76. However, this study did not find any significant association in regards to the specific indicators of periodontitis including pocket depth, clinical attachment loss, or bleeding on probing. From these results, the researchers concluded further longitudinal studies need to be conducted to actually confirm the association between SLE and periodontitis.<sup>1</sup>

Research has shown periodontal treatment can reduce the symptoms of SLE by reducing the expression of Toll-Like Receptors (TLRs). TLRs are sensing proteins of the innate immune system which trigger the inflammatory response to bacterial invasion.<sup>7</sup> Studies have shown significant elevations in anaerobic bacteria such as *Prevotella*, *Selenomonas*, and *Treponema* in patients with SLE. In a recent study, the subgingival microbiota was measured in both SLE patients and healthy subjects to determine if there is a link between periodontal disease and SLE. Researchers found a significant elevation in anaerobic bacteria in SLE patients while there was an increase in abundance of aerobic bacteria in non-SLE patients. This was achieved by placing endodontic paper points into sites with the deepest pockets for one minute each. DNA was then extracted from the samples and sequenced. Positive correlations were found between SLE patients and the “red complex” periodontal pathogens *T. denticola*, *P. gingivalis*, and *T. forsythia*.<sup>6</sup>

### **SLE and Fungal Infections**

In addition to an increased risk of periodontitis, patients with SLE may experience fungal infections such as angular cheilitis, lichen planus, and invasive fungal infections as a whole. SLE patients with angular cheilitis will commonly experience severe crusting around their lips, often times being painless. These mucocutaneous lesions can present themselves in a variety of ways including keratotic, bullous, or verrucous lesions.<sup>8</sup> Furthermore, about 45% of patients with SLE have oral mucosa involvement including erythema in multiple sites. Although less common than erythemic sites, it is possible for SLE patients to present cases of fungal infections such as erosive oral lichen planus.<sup>9</sup> The most common areas for lesions include the buccal mucosa, hard palate, and lower lip.<sup>8</sup>

Invasive fungal infections as a whole pose a major problem for patients with SLE, with infections of the respiratory and urinary tracts, and blood causing about 30% of deaths. With an increased risk of mortality and a higher prevalence of hospital readmission, these infections tend to worsen patient prognosis and are associated with patients who have a greater disease severity. In order to determine the commonness and risks associated between invasive fungal infections and SLE, a cross-sectional study was conducted among Colombian patients with systemic lupus erythematosus. This study included two-hundred subjects and was conducted over a six year period with 84.5% of the patients being women with the median age being thirty-six years old. There was a median diagnosis of forty-one months, with medications and comorbidities of the patients recorded in the beginning of the study. In result, fifteen patients presented with invasive fungal infections. The researchers in this study found *Candida albicans* being the most frequently isolated fungal microorganism, followed by *Candida tropicalis*, predominantly found in blood sites. Other fungal microorganisms found in this study include *Histoplasma capsullatum*, *Candida glabrata*, and *Cryptococcus neoformans*. When referring to the increased risk of mortality, patients with SLE who suffered from invasive fungal infections as well had a 9.91 times higher risk of mortality than SLE patients without these fungal infections.<sup>10</sup>

### **SLE and Dental Caries**

Not only does SLE have an association with periodontitis and fungal infections, this disease in fact has an association with an increased prevalence of dental caries as well. Dental caries is the most prevalent oral disease, affecting people from all over the world. There are several risk factors associated with dental caries, with these factors being assessed in patients with SLE in a current observational cross-sectional blind study. Some specific dental caries risk factors researchers assessed during this study included salivary flow, pH, buffer capacity, and

presence of cariogenic bacteria. The frequency of dental caries were assessed among 60 participants with SLE, either in active or inactive forms of SLE, divided equally into two groups of 30 subjects each. Two indexes were used in this study to analyze dental caries including the decayed, missing, and filled teeth, or DMFT index, and the Integrative Dental Caries Index, or IDCI.<sup>11</sup>

The researchers of this cross-sectional study found a strong positive correlation between active SLE patients and the specific risk factors for dental caries including a decrease in salivary flow, a change in oral pH, and the quantity of cariogenic bacteria, such as *Streptococcus mutans* and *Streptococcus sobrinus*. The two factors with the most vital role in the high caries activity of patients with lupus included salivary flow and pH. In active SLE, those patients had a more substantial decrease in salivary flow and a significantly more acidic salivary pH. Moreover, the researchers determined most patients who suffer with SLE suffer from certain oral complaints as well which are associated with a decrease in salivary flow, with the prevalence in this study being 85%.<sup>11</sup>

### **SLE on a Systemic Level**

On a more systemic level, with SLE being an inflammatory condition, some serious organ inflammation could occur in the brain, liver, and kidneys. There is a potential for leukopenia, or a decrease in white blood cell count, and thrombocytopenia, or low platelet count, in patients with SLE. The risk of both leukopenia and thrombocytopenia involves an increased risk of infection and an increased risk of bleeding, respectively. Other areas prone to inflammation within the body seen in SLE patients include muscles, blood vessels, the lining of the lungs, and kidneys. When lupus starts to involve the brain, this could lead to personality changes, possible seizures, and nerve damage.<sup>2</sup>

In terms of treatment for SLE, certain medications patients take can cause cutaneous lesions and possibly contribute to development of periodontal disease prematurely. Treatment of SLE is primarily directed toward decreasing the amount of inflammation or the level of autoimmune activity with certain anti-inflammatory drugs for people with mild symptoms, and corticosteroids tend to be used for people with more severe forms of SLE.<sup>2</sup> In regards to specific medications patients with SLE might take, recent studies showed a high correlation between the presence of pathogens like *Fusobacterium* and *P. gingivalis* and the dosage of prednisone.<sup>5</sup> Furthermore, in some patients cutaneous lesions could result, either from taking Hydroxychloroquine (HCQ), an antimalarial drug used to treat SLE, as a result of increased disease.<sup>12</sup> Medication cessation should be completed with a referral to a dermatologist to determine the cause of lesions. The cause of the reaction due to HCQ is unknown and may be due to the imbalance of the immune system in the early initiation of the drug. The recommendations by the dermatologist can vary depending on the severity of cutaneous lesions and whether or not the reaction has an effect on the systemic condition of the patient.<sup>12</sup> Another adverse effect of HCQ can be hyperpigmentation on the lips and gingiva after a long duration of medication intake. A cross-sectional study of forty-one patients was conducted to determine the possibility of hyperpigmentation in systemic disease. Of the forty-one cases, 73.2% of them were prescribed the hydroxychloroquine to treat SLE. After thirty-two months of hydroxychloroquine treatment pigmented lesions were noted in the lower limbs, face, lips, and gingiva of the SLE patients. Only the SLE patients who participated in this study presented with hydroxychloroquine hyperpigmentation, which suggests hydroxychloroquine pigmentation may be more frequent in SLE patients than in other diseases.<sup>13</sup>

## **Conclusion**

As clinicians, it is imperative to adequately review patient medical histories as well as perform extraoral and intraoral examinations in order to fully understand the possible contraindications between dental treatment and SLE. Upon discovering the presence of SLE in a patient, it is important to understand the increased risk of myocardial infarction to help prevent medical emergencies. According to a cross-sectional study, an increase of endothelial microparticles is found in SLE patients. Endothelial microparticles trigger neutrophil activation and coagulation which in turn triggers inflammation causing endothelial vascular issues which may lead to myocardial infarction.<sup>14</sup> It is important for a clinician to be well versed in the medications these patients are taking for SLE and whether there is a need for possible medication cessation. Equally important to adequately reviewing over SLE patient's medical history, it is obligatory to efficiently complete an extra-oral examination as well to find possible cutaneous lesions, and hyperpigmentation caused by SLE medications.<sup>12</sup> Similar to providing extra-oral examinations, intra-oral examinations are an additional necessity for these patients considering oral ulcerations may be present, and are in fact present in nine to forty-five percent of the people suffering from lupus according to the European Journal of Dermatology. However, the initial diagnosis of these oral ulcerations may require a biopsy and collaborate work with a rheumatologist to determine whether or not these ulcerations are caused from lupus itself. Another important thing to keep in mind as clinicians when it comes to lupus is some patients might experience xerostomia if it affects their salivary glands, so providing fluoride varnishes to these patients might be a necessity and they could be at a higher caries rate compared to other patients.<sup>3</sup>

A recent study investigated the oral health quality of life in patients with SLE. Researchers found patients with SLE have a lower oral health quality of life mainly due to the increased need for oral prosthesis wearing. Due to the increased periodontal bone loss in these patients, it is fairly common among patients with SLE to lose teeth and require partial dentures. Studies have shown an increase in mouth sores and ulcers due to ill-fitting dentures, thus lowering their quality of life.<sup>15</sup> It is important to recognize and understand all of the effects of SLE on the oral cavity and the entire body in order to provide the best quality care for patients living with this autoimmune inflammatory disease.

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