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## A Review of Oral Lichen Planus for the Dental Professional

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#### Abstract

Oral lichen planus (OLP) is an inflammatory, autoimmune disorder related to an aberrant T-cell mediated response. It is a chronic, recurrent condition of unknown etiology that typically affects middle-aged, Caucasian women. It can be asymptomatic or range from mild to severe in its presentation. At its worst, patients have difficulty eating, speaking and maintaining the level of oral hygiene necessary to keep the condition quiescent. Quality of life and mental outlook may be adversely affected, especially for those with extra-oral involvement or who worry about lesions becoming cancerous. This article provides a brief overview of basic histopathology, common clinical subtypes, and OLP's potential for malignant transformation. Precipitating factors of OLP are reviewed along with clinical management strategies. Also discussed are the significant side effects of commonly used modalities and medications in OLP management, particularly corticosteroids in their various forms. Lycopene, curcumin, aloe vera, and green tea, natural treatments noted for their anti-inflammatory, anti-oxidant, and anticarcinogenic properties, have demonstrated efficacy in mitigating OLP symptoms while bypassing serious side effects. ClōSYS oral health care products, presented here *via* anecdotal experiences, offer a safe, effective way of minimizing OLP lesions while maximizing oral health. Helping patients overcome the pain, discomfort and impediment to well being posed by this challenging condition is paramount to the treatment of OLP.

**Keywords:** Oral lichen planus; Wickham's striae; Extra-oral lesions; Basal epithelium; Hyperkeratosis; Erosive subtype; Malignant transformation; Oral cancer; Lichenoid reactions; Intralesional corticosteroids; Natural treatments for OLP; ClōSYS

"The patient presented with painful oral sores. She was beside herself and said she was ready to cut her head off. A biopsy revealed oral lichen planus." Dr. Nakata, periodontist.

Lichen planus is a common dermatological condition of unknown etiology. Originally identified in 1869 as an inflammatory disorder of the stratified squamous epithelium, it was named from the Greek *lichen*, meaning moss, and *planus*, for flat [1]. The general appearance of lichen planus on the skin, referred to as cutaneous lichen planus, or CLP, is easily recognized as per the 6 P's for pruritic, papular or plaque-like lesions, purple color, polygonal shape, and a planar surface. Bilaterally symmetrical, CLP commonly affects the flexor surface of the extremities [1].

In addition to the skin, lichen planus can affect the hair and nails as well as any mucosal surface of the body. The mouth and vulvovaginal mucosa, and less frequently the esophageal, laryngeal and conjunctival linings, may be affected [1]. Its presentation in the mouth as oral lichen planus, or OLP, can range from asymptomatic keratotic spots to painful ulcerations that make it difficult to eat, speak and maintain oral hygiene [2,3]. Autoimmune and inflammatory in nature, lichen planus in all its manifestations is associated with a T-cell mediated reaction to a yet undetermined antigen [1,2].

### **Basic Histopathology**

The detailed histopathology of OLP is well known but is beyond

the scope of this article. Stated simply, OLP is a T-cell mediated autoimmune disease [1]. Langerhans cells, with both macrophagic and dendritic cell properties, obtain peripheral antigens and present them to T cells in the lymph nodes [10]. Once activated, cytotoxic T cells, accompanied by pro-inflammatory, cytokine-secreting natural killer (NK) cells, enter the basal epithelium to orchestrate apoptosis of basal keratinocytes. Lymphocytes infiltrate at the interface between the epithelium and connective tissue resulting in focal areas of hyperkeratosis that manifest clinically as Wickham's striae [1,2]. Entire liquefaction of the basal epithelium may ensue [1]. Once the basement membrane is compromised, it can no longer render a survival signal to area keratinocytes and a cycle of destruction is perpetuated [2]. Although the cause of this auto-destructive immune response is unknown, gene polymorphisms interacting with inflammatory and environmental triggers may play a role [1].

### Overview of OLP

OLP is prevalent in 1-2% of the US population and is most likely to affect Caucasian women in their 50s and 60s. Its incidence worldwide is approximately 5%, with smokers and tobacco chewers more commonly affected. Lesions can occur suddenly or emerge gradually anywhere within the oral cavity. Typically, bilaterally symmetrical lesions arise along the buccal mucosa, gingiva, and the sides of the tongue [2-4].

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OLP can exist on its own or present with extra-oral lesions. Studies show that approximately 15% of all OLP patients have lesions of the skin. While these predominantly affect the flexor surface of the arms and legs, the nails, scalp, and genital mucosa are other common sites [1]. It is estimated that 25% of women with OLP present with lesions of the vulvovaginal mucosa. The resulting adhesions, pain, burning, itching, discharge, and bleeding can make life miserable and sexual intimacy a near impossibility [1,5]. Dental professionals encountering OLP must conduct a detailed history that includes asking about extraoral lesions. The presence, location and severity of extra-oral lesions may warrant a referral to the appropriate medical professional.

A chronic condition that fluctuates in presentation over time, OLP rarely resolves spontaneously. The average duration of the disease is 3.6 years, but cases lasting nearly two decades have been reported. Longstanding cases, unresponsive to treatment, have been associated with a poor mental outlook, especially in those with extra-oral involvement, demonstrating the negative impact of OLP on quality of life [3]. The dental or medical professional assisting the patient can take affirmative action's to decrease patient suffering. While many clinicians believe little can be done to relieve OLP discomfort, emergent therapies are available to effectively address symptoms.

OLP, which can exist unbeknownst to patient or practitioner, often has distinct features that make it readily identifiable. While a thorough case history and the presence of typical oral lesions with skin or nail involvement alerts the clinician, biopsy for histopathology is the gold standard for definitive diagnosis [6]. The condition must be differentially diagnosed from those with similar presentation such as cheek chewing, discoid lupus erythematosus, bullous pemphigus, ulcerative stomatitis, chronic candidiasis, lichenoid reactions to amalgam or drugs; graft *vs* host disease, leukoplakia and epidermoid carcinoma. Immunofluorescence may be used when differentiating OLP from other autoimmune diseases [2,5-7].

### Malignant potential

OLP is often associated with oral squamous cell carcinoma (SCC) by clinicians. This is a topic of controversy and debate in the literature. While unequivocal data proving OLP lesions undergo malignant transformation is lacking, most believe that any likelihood warrants both an initial biopsy and long-term follow-up with these patients [2,5].

It is unclear whether it is the nature of OLP lesions themselves, the patient's genetic constitution, the drugs used in treatment, or the status of the patient's immune system that creates a vulnerability towards cancer development [1,6]. The approximate range of malignant transformation is 0.4%-5% over a period spanning 0.5 to 20 years [8]. In some scientific circles, OLP stands as a proposed model of inflammation-induced cancer, possibly *via* NF-kappa B-related cytokines [9]. Continued research is needed to evaluate the malignant potential and mechanism of OLP.

## **OLP** subtypes

OLP presents as 6 clinical subtypes. The classic reticular subtype, the most common, is asymptomatic and often found incidentally upon routine oral examination. Delicate white lacy streaks, known as Wickham's striae, intertwine and fan outward toward erythematous borders, most often on the posterior buccal mucosa. Although benign, the reticular subtype may progress to more serious forms of the disease [1,2,5]. The papular subtype exists as a rarely-observed, transient, asymptomatic phase characterized by pinpoint papules surrounded by fine striae [1,2]. A plaque-like form of OLP presents as large,

homogeneous white patches on the dorsum of the tongue or buccal mucosa that may resemble leukoplakia, necessitating a thorough differential diagnosis [1,9].

The erosive subtype, the most painful form of OLP, presents as ulcerative erosions throughout the oral mucosa, often accompanied by white striae in a network formation or covered by a pseudo membrane. It is the form of OLP with the greatest malignant potential. Another painful variant, the atrophic subtype, can result in desquamative gingivitis while a rare bullous subtype exhibits blisters that enlarge and rupture, leaving behind a painful, ulcerated area of mucosa [1,2,6,8,9].

### **Precipitating factors**

While the cause of immune system aberrations initiating OLP is currently unknown, precipitating factors have been identified. One is emotional stress and anxiety. Although a causal relationship has yet to be shown, the connection between psychological status and oral health is well-known [5]. Studies show OLP lesions develop in healthy individuals following stressful life events [1-3]. Other studies reveal a higher incidence of depression, anxiety, and stress associated with OLP patients [3]. It is not clear if depression and anxiety precipitate OLP, or if individuals suffering from OLP succumb to depression and anxiety due to a diminished quality of life, or both. Clinically, patients with OLP demonstrate higher cortisol levels along with increased erythema, ulceration, and pain following periods of emotional stress [5].

Mechanical trauma may also precipitate OLP. Dental procedures, cheek chewing, faulty restorations, and sharp cusps can lead to OLP sores *via* a Koebner response [1]. OLP is also associated with various viral diseases including human papilloma virus (HPV), Epstein Barr virus (EBV), human immunodeficiency virus (HIV), and hepatitis C virus (HCV) [2]. In the United Kingdom, 20% of patients with hepatitis C have OLP although a direct association between HCV and OLP has yet to be established [5].

Several commonly used medications can cause lichenoid reactions in sensitive individuals. The resulting lesions resemble those of OLP in appearance and histopathology but disappear when the offending medication is withdrawn [11]. Common culprits include antibacterials, anti-hypertensives, oral hypoglycemics, NSAIDs, and proton pump inhibitors [1,11]. It is important to review the patient's medical history when OLP is manifest.

Lichenoid contact reactions may result from amalgam restorations or from the gold, cobalt, nickel, and palladium released from the corrosion of those restorations [12]. Even crowns and composite restorations can cause a reaction in sensitive individuals. Flavoring agents can also precipitate lichenoid contact reactions, especially cinnamon and spearmint flavoring used in candies, toothpaste, and some mouthwashes. Unlike true OLP, these reactive lesions disappear when restorations are removed or repaired, and chemical irritants discontinued. While simple in theory, differential diagnosis of true OLP from lichenoid reactions is often difficult due to a time delay between the removal of the offending irritant and the healing of related mouth sores [1,2,12,13].

### **Traditional OLP management**

The management of OLP centers on the use of corticosteroids, either applied topically, injected intralesionally or administered systemically [6]. Topical steroids are the first line of treatment for mild to moderate OLP. Gels, creams, ointments, and pastes are applied to localized lesions, while rinses and aerosols are used when lesions are more diffuse. Relatively safe and effective, prolonged use



of topical steroids may cause mucosal thinning and candidiasis, and an antifungal may be needed concomitantly. Adrenal suppression and other serious complications can occur when topical steroids are absorbed systemically through thinned areas of mucosa [6,14].

When localized OLP lesions are more severe, steroids are injected intralesionally, minimizing systemic absorption and allowing for precise drug delivery. While momentarily painful, local anesthetics can be used to minimize discomfort upon injection. Disadvantages of intralesional injections include localized tissue atrophy and secondary candidiasis [6,14].

Severe OLP lesions that don't respond to topical agents warrant treatment with prednisone, a systemic steroid, where even short-term use can cause insomnia, anxiety, edema, diarrhea, generalized muscle weakness and susceptibility to infection [14]. Once lesions begin to heal, systemic steroids may be tapered off, and a trial of topical treatments initiated [6].

Calcineurin inhibitors are immunosuppressant drugs also used in the treatment of OLP [6]. One such drug, cyclosporine, can effectively decrease T-cell activation, but may do so at the cost of damage to liver and kidney functions. It can also cause hypertension, enlargement of gingival tissue, electrolyte and mineral imbalances and pancreatitis, although some patients using a cyclosporine rinse report only transient mouth burning [14,15]. Tacrolimus, and a similar immunosuppressant drug, Pimecrolimus, appear in the literature as safer alternatives [14]. Other authors suggest that these drugs may increase the risk for malignant transformation when used for extended periods of time [5,6].

OLP treatment may include other medications such as retinoids, thalidomide, metronidazole, griseofulvin and hydroxychloroquine, all carrying risk of significant side effects [2,14]. Further concerns with these agents are the high frequency of lesion recurrence and the need for more clinical trials [6,14]. While local drug delivery remains a safer, more targeted approach, these delivery systems are still being researched and developed [2].

Light therapy, administered as UV phototherapy, photodynamic therapy and lasers, is used as an alternative treatment for managing severe OLP. One form of UV therapy, called PUVA, requires the use of psoralen as a sensitizing substance. Multiple side effects and a potential link to cancer warrant it being investigated further. Photodynamic therapy may show promise as a safe OLP treatment since its only reported side effect to date is photosensitivity. Lasers, as with all types of phototherapy, require additional clinical trials to determine safety and efficacy. Lastly, cryosurgery remains an option for the most intractable of OLP cases, although recurrences are common [6].

### Natural treatments

In light of the well-documented risks associated with standard drug treatments for OLP, it may be prudent to investigate natural alternatives. OLP is, in part, an inflammatory disease with neoplastic potential. Recent research shows that oxidative stress may play a role in its pathogenesis [16,17]. The plant kingdom offers an array of compounds with anti-oxidant, anti-inflammatory, and anti-carcinogenic properties that may prove helpful in addressing OLP.

Lycopene, a fat-soluble plant pigment (carotenoid) found in tomatoes and other red fruits, is known for its potent anti-oxidant activity and has been shown to reduce OLP symptoms [6,14]. It can, however, interact with many common prescription medications including anticoagulants, antihypertensives, and statin drugs. These reactions may be mitigated by obtaining lycopene from the diet in favor of ingesting it in supplement form [18].

Curcumin is a phytochemical found in the rhizomes of the *Curcuma longa* herb. Nontoxic and safe at high doses, curcumin is sought out primarily for its anti-inflammatory properties. A randomized double-blind study has shown curcumin to be effective at relieving OLP symptoms at a dosage of 6,000 mg/day in divided doses [14]. A second study using only 2,000 mg/day failed to yield a statistical difference, demonstrating that further research is needed [19].

Aloe vera, or Aloe barbadensis, is a cactus-like plant whose gel has been revered for thousands of years for its medicinal and aesthetic benefits. Its antioxidant and antimicrobial properties have made it a popular remedy for burns, wounds, and assorted gastrointestinal issues. It has also been found to reduce the pain and expedite healing of OLP lesions [14,20]. Reported side effects include burning and itching of the lesion limited to the first week of treatment, making it a viable alternative for addressing OLP [20].

Green tea, consisting of several polyphenols with anti-inflammatory and chemo preventive properties, has been shown to inhibit T-cell activation, suppress nuclear factor-kappa B, and impede apoptosis of keratinocytes. Research shows green tea may be a safe and cost-effective treatment for minimizing the symptoms of OLP while reducing its potential for malignant transformation [14,21,22].

### ClōSYS products: anecdotal observations

As a freelance health writer working intermittently with Rowpar Pharmaceuticals, this author had the opportunity to interview Dr. Nakata, DDS, a periodontist for over 50 years, regarding his clinical experiences with ClōSYS products and OLP. Dr. Nakata was familiar with ClōSYS unflavored mouth rinse from several years of use in his periodontal practice. He discussed a case of a patient having multiple, diffuse OLP sores that substantially cleared after 10 consecutive days of using the ClōSYS unflavored oral rinse. Dr. Nakata shared the before-and-after photos of this patient with dental professionals at conventions and seminars throughout the country.

According to Dr. Nakata, two years later, the same patient was treated with antibiotics for sinusitis, which triggered a recurrence of OLP sores. Once again, the patient resumed using the ClōSYS unflavored mouth rinse and has remained free of OLP lesions for over 5 years. Dr. Nakata went on to treat several cases of OLP. In many instances, patients consistently using the ClōSYS oral rinse experienced remissions of lesions relatively quickly and without side effects. He witnessed multiple positive outcomes in diabetic patients with OLP using ClōSYS as well as in patients with sores resulting from chemotherapy.

Dr. Nakata's success with ClōSYS resulted in his becoming an investor and board member for Rowpar Pharmaceuticals, makers of the ClōSYS line of oral health products. ClōSYS, a recipient of the American Dental Association (ADA) Seal for combating oral malodor, has also proven effective at ameliorating symptoms of xerostomia and oral mucositis [23,24].

The active ingredient in ClōSYS is Cloralstan\*, a patented form of stabilized chlorine dioxide. Recognized as safe, stabilized chlorine dioxide is registered with the Environmental Protection Agency (EPA) as an innocuous, effective antimicrobial agent. It is employed in critical care areas of hospitals, in food production plants, and by the military for water purification purposes [25]. In the dental industry, Cloralstan\*, unique to ClōSYS products, destroys pathogens that cause gum disease, eliminates volatile sulfur compounds (VSC's) that lead to oral malodor, and effectively disrupts biofilms. ClōSYS products are well-tolerated by patients, and no adverse effects have been reported



since Rowpar Pharmaceuticals released ClōSYS into the marketplace in 1991 [26].Dr. Nakata readily discloses his bias to patients when telling them about the products. He notes that most patients who have kept their teeth through the years have been ClōSYS users, while observing that those who haven't used the products generally don't fare as well.

Sheilah E, a long-time manager and consultant to the dental profession, contacted Rowpar Pharmaceuticals to share her mom Janet's experience with CloSYS and OLP. This author conducted personal interviews with both women to obtain the details presented here. Janet E, a 75-year-old retired nurse, suffered with dry mouth for most of her adult life. No stranger to the tooth decay and cracked teeth that often accompany xerostomia, she was unprepared for the sudden onset of OLP that besieged her just over a year ago. Plagued with painful sores, Janet found it difficult to eat, and at 5"6", her weight dropped to 108 pounds. The mouthwash Janet routinely used for her dry mouth burned the OLP sores, and she discontinued using it. As Janet's xerostomia worsened, so too did her OLP lesions. Sheilah worried incessantly about her mother being so thin and frail.

When Janet was introduced to the ClōSYS products, she immediately noticed how gentle they were, allowing her to use them consistently. The ClōSYS toothpaste improved her dry mouth and relieved her OLP symptoms. As the sores lessened in severity, Janet was able to eat foods with some texture and spice. Sheilah was relieved to see her mom enjoying food again, gaining weight, and looking well. While ClōSYS did not cure OLP in any of the cases presented, it reduced pain, stabilized the condition, and improved patient wellbeing.

### **Discussion and Conclusion**

Oral lichen planus is an inflammatory, autoimmune disorder of unknown etiology. Subject to remissions and exacerbations, it can adversely affect quality of life. Due to its potential for malignant transformation, early diagnosis and long-term follow up is imperative regardless of clinical subtype. Any dental issues, medications, or flavorings provoking symptoms or lichenoid reactions must be addressed. Since OLP is exacerbated by emotional stress, it is prudent to implement stress reduction strategies that patients can readily employ for chronic anxiety and acute, triggering events. Due to significant side effects of commonly used medications in OLP management, it may be advisable to explore natural treatments that safely address inflammatory, oxidative and neoplastic components of OLP pathogenesis. Lycopene, curcumin, aloe vera, and green tea show promise, although further research may be needed before they are integrated into a mainstream protocol for treating OLP. ClōSYS products offer a safe, effective over-the-counter option for optimizing oral health while reducing the incidence and severity of OLP sores. The plight of an OLP patient is not without alternatives for treating, managing and potentially remediating its symptoms. Armed with knowledge of the disease and its manifestations, the dental professional can help mitigate the pain, discomfort and interruption of daily activities, vastly improving the OLP patient's quality of life.

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