The Management of Oral Lichen Planus

A Peer-Reviewed Publication
Written by Kimberly M. Parsons, EdD, CDA, EFDA, RDH

Abstract
Oral lichen planus is an immune-mediated and chronic inflammatory condition that can cause erosion of the oral mucosa. The disease is described as reticular, erosive, atrophic, or bullous in nature, and it typically develops in women in their fifth and sixth decades. Reticular oral lichen planus, absent erythema, is asymptomatic and does not usually need intervention. However, as there is potential for conversion to carcinoma, reticular oral lichen planus associated with erythema or erosion needs treatment and periodic re-evaluation. The literature suggests that erosive and ulcerated oral lichen planus is best managed with topical corticosteroid preparations and, in refractory cases, systemic steroids. Several other immunosuppressive medications and non-medication based interventions are also available, but at greater cost and with greater potential for adverse reactions and side effects. This educational review article focuses on best practices in the management of oral lichen planus.

Educational Objectives
At the conclusion of this educational activity, participants will be able to:
1. Describe interventions used to manage oral lichen planus
2. Identify the appropriate medications to be prescribed for managing erosive and ulcerative oral lesions
3. Implement treatment strategies for managing oral ulcers associated with the disease
4. Identify interventions discussed in the literature that are supported by limited evidence

Author Profile
Kimberly M. Parsons, EdD, CDA, EFDA, RDH, is the Program Chair of the Dental Assisting and Dental Hygiene Programs and an Assistant Professor of Dental Assisting/Dental Hygiene at the University of Southern Indiana. Her scholarly activities include research in the areas of educational technology, treatment of special needs patients, and allied dental education. Dr. Parsons has been a dental hygienist for 15 years, practicing in Arizona, Indiana, Kentucky, and Michigan. She has also worked as a dental educator in Arizona and Indiana.

Author Disclosure
Kimberly M. Parsons, EdD, CDA, EFDA, RDH, has no commercial ties with the sponsors or the providers of the unrestricted educational grant for this course.
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Introduction
Oral lichen planus (“lichen planus,” “OLP,” “oral LP,” or simply “LP”) is an immune-mediated and chronic inflammatory condition that can cause erosion of the oral mucosa. Based primarily on clinical presentation, it can be characterized as reticular, erosive, atrophic, and/or bullous. Rare in children, this condition typically develops in the fifth or sixth decade of life and is more common in women. Prevalence of LP ranges from 1% to 6.3%.

While the occurrence of reticular LP is higher, other types of LP that cause mucosal erosion or erosive/bullous lesions are more frequently reported due to the severity of the symptoms associated with these types. Reticular LP without adjacent erythema is usually asymptomatic. Erosive/ulcerative LP (ELP) is associated with significant inflammation, tissue erosion, and sometimes bullous oral lesions. Patients with ELP are likely to experience a continuous moderate to severe aching pain that may be accompanied by burning. This pain worsens when eating, particularly when hot or spicy foods are consumed, and when lesions contact alcohol. Generalized distribution of oral lesions can be debilitating. LP fluctuates between periods of remission and episodes of recurrence.

The cause of LP is unknown, but considerable research suggests the primary disease mechanism to be immune mediated. It is believed that in most cases mucosal pathology is triggered by keratinocytes or modified Langerhans cells in either antigen-specific reactivity involving keratinocyte killing by CD8 cytotoxic cells or antigen non-specific reactivity involving mast cell degranulation and matrix metalloproteinase activation. It has also been proposed that in some cases of LP refractory to immunologic intervention, the underlying cause may be partly neurogenic.

Other factors or conditions reported in relation to the development of mucosal LP include the following: genetics, infection such as the hepatitis C virus even though magnitude of the association may be minimal; effects of medication termed lichenoid drug reaction; vitamin or mineral deficiencies, such as B-12 deficiency or iron deficient anemia; systemic disease, such as the autoimmune disease Sjogren’s syndrome, rheumatoid disease, pemphigus, or graft versus host disease; and amalgam hypersensitivity. (See also Table 1.) The origination of LP stemming from an immune system abnormality informs most treatment considerations related to patient care. If underlying disease or a lichenoid drug reaction is strongly suspected as the cause of LP, the patient should be referred for additional medical evaluation or consultation. However, regardless of the association of LP with a number of medical problems, the treating clinician should not assume that the patient with LP has one of these conditions. It has been proposed that patients with LP should not be routinely screened for systemic disease without a strong indication of possible disease.

Table 1: Factors/conditions reported in mucosal lichen planus development

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<td>Genetics</td>
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<td>Vitamin/mineral deficiencies</td>
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<td>Systemic disease</td>
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<td>Amalgam hypersensitivity</td>
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Reticular LP
Reticular LP is typically asymptomatic and does not routinely require intervention. However, due to the white striations and plaques associated with reticular LP and their similar appearance to oral cancer, all lesions should be documented in the patient chart, including recording of the the location(s), taking photographs, and other pertinent descriptions of the lesions. In addition, lesions associated with reticular LP should be monitored for changes, such as size, thickness, coloration of mucosa, ulceration or erosion, and emergent symptoms such as pain, that may be indicative of potential dysplastic
Erosive/Ulcerative Lichen Planus

Similar to other forms of lichen planus, erosive/ulcerative lichen planus (ELP) is a chronic disease with no known cure. Regardless of therapy, complete resolution of lesions is difficult to achieve. Future research may identify cellular and genetic mechanisms that prove useful in the development of effective long-term treatment strategies and a possible cure. Until that time, the clinician treating ELP must utilize either pharmacotherapy known to suppress immune function and pain and promote healing or non-pharmacological interventions that have previously shown promise in managing the disease. Most medication strategies used to treat ELP have limited supportive evidence, as few of these are supported by studies using rigorous scientific methodology. There is even less evidence-based support for non-pharmacological interventions such as photochemotherapy, photodynamic therapy, or laser therapy, which have also been suggested as treatment for ELP.

Pharmacotherapy

In a Cochrane Database Systematic Review published in 2012, Cheng et al. reviewed studies up to September 2009 from multiple databases. These databases included the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, and LILACS, as well as the registries for ongoing trials. Cheng et al. selected a randomized control trial to report results of treatment of lichen planus with topical or systemic medication. They identified 15 randomized control trials with 473 total participants having erosive LP. However, they were not able to pool data due to the small number of subjects, heterogeneity of the interventions, design methods, and different outcome variables found between the studies. Meta-analysis could not be performed. Nonetheless, the authors reported that in one study with 50 subjects, 0.025% clobetasol propionate administered as a liquid microsphere significantly reduced pain when compared to the delivery of a placebo ointment. In another study, significant pain reduction occurred with a cyclosporine solution, when contrasted to a 0.1% triamcinolone acetonide in orabase formulation. In a third study, aloe vera gel was shown to be six times more likely to result in at least a 50% reduction in pain when compared with a placebo. Additionally, it was noted that pimecrolimus cream was more effective in improving ELP than a vehicle cream.

Another Cochrane Database Systematic Review assessed 28 clinical ELP trials that used “pain-report” as an outcome variable following medication application. Similar results to those found in the aforementioned review were reported, and authors from both reviews asserted that evidence on the effectiveness of treatment for ELP is weak.

Regardless, topical corticosteroids continue to be widely utilized as a first-line therapy for erosive/ulcerative LP in both medicine and dentistry. Additionally, high-potency topical steroids are thought to be the most effective strategy for reducing symptoms and minimizing disease in patients with severe pathology. One example of this is a double-blind placebo-controlled clinical study where a 75% improvement was reported following the application of fluocinonide in an adhesive base.

High-potency topical treatments include clobetasol (Temo-vate®), fluocinonide (Lidex®), and halobetasol (Ultravate®), all three of which are dispensed as 0.05% creams or ointments. Clo-
betasol propionate and fluocinonide are also provided in a 0.05% solution, but the FDA has recommended that these products only be used externally because of the possibility of hypothalamus-pituitary-adrenal inhibition. Gels can be mixed with equal parts orabase to make an adhesive paste for application to small- or medium-sized lesions. It is recommended that lesions should be coated with the gel or cream after each meal and at bedtime. Broader coverage can sometimes be achieved through the use of an acrylic appliance that holds the gel or cream against the mucosa.

Dexamethasone, another potent corticosteroid, is effective in treating generalized erosive or ulcerative lesions. It is prescribed as a rinse that is held in the mouth for a short time. When used three or four times daily, maximum coverage is provided. Two prescriptions are presented: Rx: Dexamethasone (Decadron) elixir 0.5mg/5ml (Disp 320 mls; Sig [1] For 3 days, rinse with 1 tablespoonful (15ml) qid and swallow. Then [2], for 3 days, rinse with 1 teaspoonful (5ml) qid and swallow. Then [3], for 3 days, rinse with 1 teaspoonful (5ml) qid and swallow every other time. Then [4], rinse with 1 teaspoonful (5ml) qid and expectorate). Another prescription is: Rx: Dexamethasone elixir 0.5mg/5ml (Disp 100mls; Sig: Rinse with 1 teaspoonful (5ml) for 3-4 minutes qid and spit out); discontinue when lesions become asymptomatic. Either approach may be considered as published research comparing these two prescriptions of dexamethasone is not available. Even with topical application of corticosteroid to mucosa, there is potential for systemic, as well as local side effects. Close collaboration with the patient’s physician is recommended, particularly when these medications are prescribed for a prolonged period of time. Systemic prednisone can also be prescribed, but its use should be considered only in cases involving severe recalcitrant lesions where topical approaches to therapy have failed. If systemic corticosteroid is considered, it should be prescribed at the lowest possible dosage and only for a short time. There are a number of prescribing regimens that are effective such as: Rx: Prednisone tablets 5mg (Disp: 40 tabs; Sig: Take 5 tablets in the morning for five days, then 5 tablets in the morning every other day until gone.) Medrol dose packs are also available.

Any patient using corticosteroids should be monitored for the emergence of fungal infection (candidiasis), that can occur with application of this class of drugs. If the LP patient is prone to fungal infections or has experienced candida infection in the past following steroid administration, prophylactic antifungal therapy should be pursued as concurrent therapy.

Additional immunosuppressant medications and immuno-modulatory agents that may be considered to manage severe recalcitrant erosive/ulcerative LP include calcineurin inhibitors such as cyclosporine, tacrolimus, and pimecrolimus. However, these drugs are expensive and there are few studies supporting the use of cyclosporine. Further, local and systemic side effects can be problematic.

Pimecrolimus and tacrolimus, indicated for the treatment of atopic dermatitis, have a number of studies supporting their use in treating LP. These drugs inhibit T-cell activation and cytokine release from mast cells. Systematic review of five double-blind studies and ten prospective studies, as well as numerous case reports, suggest that topical tacrolimus ointment 1% may be equal to topical betasol propionate 0.05% ointment and topical triamcinolone acetonide 0.1% paste, in terms of treatment outcome. Treatment with topical tacrolimus appears to result in measurable blood levels but, according to Swift et al., this medication has not been associated with significant adverse effects. However, prolonged use of tacrolimus may increase cancer risk, and therefore, should only be applied for a short period of time. The FDA recommends against oral application of this medication to mucosa.

Other medications, such as retinoids, dapsone, azathioprine, mycophenolate mofetil, acitretin, and enoxaparin, that have been recommended for use with ELP have limited scientific support and should not be routinely utilized. The use, particularly long term, of some of the aforementioned drugs may result in adverse reactions. For example, two common side effects of dapsone use are hemolysis and hypersensitivity reactions in the form of fever and jaundice, typically occurring within the first six weeks of therapy. Finally, all of the abovementioned drugs are more expensive relative to the cost of corticosteroids.

Non-pharmacological Treatment Modalities

There are several non-pharmacological interventions suggested for treatment of ELP. These include PUVA therapy, where uses are application of the sensitizing drug psoralen followed by ultraviolet light; photodynamic therapy, which includes a photosensitizer, light source, and tissue oxygen; and laser therapy. Only the latter is likely to be utilized in the dental office. These strategies have limited supportive evidence for treating LP but might be considered for severe recalcitrant cases. When 21 atrophic/erosive LP patients who were treated with laser phototherapy (LPT) three times a week for three months were compared to 21 atrophic/erosive LP patients who used betasol propionate 0.05% applied three times a day for three months. The LPT group was found to have a higher percentage of complete lesion resolution at 60 and 90 days with no recurrence of lesions. In contrast, the betasol group was reported to have experienced worsening of all the variables analyzed. Although this suggests that LPT may be quite effective in the treatment of recalcitrant ELP, an in-office application three times a week might be difficult for some patients to manage. PUVA therapy has been associated with adverse events, including nausea, dizziness, and 24-hour photosensitivity.

Although not considered “treatment,” patients with LP should be advised to maintain good oral hygiene and instructions in appropriate care should be considered to reduce injury to involved tissues. Dietary recommendations should include instructions to eat soft nutritious food during outbreaks, the avoidance of caffeine, and cessation of smoking and alcohol. Since ELP may be aggravated by stress and can be associated
with depression, activities that reduce stress and modify depression should be suggested. Another novel approach to treatment that has not been extensively studied but may be useful is antioxidant application (e.g., AO ProVantageGel). In one case study, the gel was applied three times daily for eight weeks with symptom improvement continuing for over a year. There is also published evidence that the saliva of a patient with LP exhibits increased levels of oxidative stress and lower antioxidant capacity compared to the saliva of healthy patients.37–39

Conclusion
Dental professionals are likely to encounter one or more cases of LP during clinical practice. Since it is probable that they will encounter reticular LP, the importance for the clinician to differentiate between this disease and other more serious problems, such as dysplasia, is high.36 However, it is the erosive/ulcerative LP that will require direct clinical intervention and careful monitoring. This course has presented several pharmacologic approaches to treatment that are evidence-based or common practice for managing erosive/ulcerative LP. In addition, the course provided suggestions for non-pharmacologic interventions, which may have limited use. Although a number of new drugs have been suggested for the treatment of ELP, at the present time, topical application of corticosteroid medication followed by systemic administration in severe refractory cases remains the standard of care.

Bibliography
Questions

1. Which of the following statements most accurately characterizes lichen planus:
   a. The condition develops in the third and forth decade
   b. Men are most likely to express the disease
   c. It is most prevalent in children
   d. It is an immune mediated condition

2. Which of the following statements is accurate:
   a. Reticular lichen planus occurs more frequently than other forms of the disease
   b. The prevalence rate for all forms of oral LP range from 1 to 6.3 percent
   c. Both a and b
   d. Neither a or b

3. Oral lichen planus is characterized as:
   a. Reticular
   b. Erosive
   c. Atrophic
   d. All of the above

4. Which of the following statements is not accurate:
   a. Lichen planus is curable
   b. Lichen planus is chronic with episodes of remission and reoccurrence
   c. Erosive LP is associated with significant inflammation
   d. Patients with erosive LP often say their mucosal is painful

5. Identify the correct statement regarding erosive lichen planus:
   a. Lichen planus associated with erosive lesions is not debilitating for the patient
   b. Erosive lichen planus is associated with moderate to severe aching pain
   c. Eating does not worsen pain experienced with erosive lichen planus
   d. Medications containing alcohol are not likely to exacerbate erosive lichen planus lesions

6. The mucosal pathology of LP is thought to include:
   a. Antigen specific activity involving keratinocyte killing by CD8 cytotoxic cells
   b. Antigen non-specific activity involving mast cell degranulation and matrix metalloproteinase activation
   c. Both a and b
   d. Neither a or b

7. Which of the following statements is most accurate:
   a. A neurogenic etiology has been proposed to explain pathology in LP
   b. Langerhans cells have little to do with disease
   c. Both a and b
   d. Neither a or b

8. Which of the following factors has been linked with lichen planus:
   a. Vitamin A deficiency
   b. Hepatitis C virus
   c. Both a and b
   d. Neither a or b

9. When medications cause lichen planus the condition is termed:
   a. Medication lichen planus
   b. Medicamentosa
   c. Erosive LP disease
   d. Lichenoid drug reaction

10. Medical conditions that have been associated with oral lichen planus include:
    a. Pemphigus
    b. Graft versus host disease
    c. Rheumatoid disease
    d. All of the above

11. If a drug reaction is strongly suspected as the cause of oral LP the patient should be:
    a. Immediately removed from the drug
    b. Referred for medical consultation prior to withdrawal from the drug
    c. Both a and b
    d. Neither a or b

12. Which of the following statements is accurate:
    a. If a patient has lichen planus he/she is likely to have one of the medical conditions associated with the disease.
    b. As a general rule patients with LP should not be routinely screened for systemic disease
    c. Both a and b
    d. Neither a or b

13. If a patient is found to have oral reticular LP a dentist should:
    a. Aggressively treat the condition
    b. Chart the condition for location and follow
    c. Immediately biopsy
    d. Assume that every lesion is precancerous

14. Dysplastic transformation of lichen planus, while rare, may occur in what percent of cases per reported research:
    a. 3.7
    b. 5.1
    c. 12.2
    d. 1.0

15. Which of the following statements accurately describes dysplastic conversion:
    a. It occurs more frequently in female patients
    b. The most common site of conversion is the tongue
    c. The average age at conversion is around 60
    d. All of the above

16. Which of the following statements is most accurate:
    a. Non-medication interventions used to treat erosive/ulcerative LP have been extensively researched
    b. Few studies involving medication treatment are supported by rigorous science
    c. Both a and b
    d. Neither a or b

17. Which class of medication is the most useful for treating erosive/ulcerative LP:
    a. The antifungals
    b. The anxiolytics
    c. The corticosteroids
    d. None of the above

18. The clinician treating erosive/ulcerative LP should consider which of the following as first line therapy:
    a. High potency corticosteroids
    b. Low potency corticosteroids
    c. An immunosuppressive such as Cyclosporine
    d. None of the above

19. A dentist treating erosive/ulcerative LP should not use which type of corticosteroid preparation:
    a. Clebetalos (Temovate®) ointment
    b. Fluocinomide (Lidex®) ointment
    c. Halobetasol (Ultravate®) cream
    d. Fluocinomide (Lidex®) solution

20. What is the percentage of corticosteroids in high-potency topicals used to treat LP:
    a. 0.20%
    b. 0.05%
    c. 0.10%
    d. 0.75%

21. When corticosteroid gels are used it is recommended that they be:
    a. Applied four times a day
    b. Applied before each meal
    c. Applied twice a day after meals
    d. None of the above

22. The correct way to prescribe dexamethasone is:
    a. 0.5 mg/5mls Disp 320 mls Sig – for 3 days rinse with 1 tablespoonful (or 15mls) qid and swallowing; then for 3 days rinse with 1 teaspoonful (or 5mls) qid and swallowing; then for 3 days rinse with 1 tsp qid and swallowing; then rinse with 1 tsp qid with expectorator
    b. 0.75mg/5mls Disp 198 ml; Sig – Rinse with 1 teaspoonful (5mls) for 3-4 minutes qid and spit out; Discontinue when lesions are asymptomatic
    c. Both a and b
    d. Neither a or a

23. When should systemic prednisone be prescribed:
    a. Immediately after lesions are diagnosed
    b. Only in cases involving severe recalcitrant lesions where topical therapy has failed
    c. When the patient has both reticular as well as erosive/ulcerative lesions
    d. None of the above

24. What is the most accurate approach to prescribing systemic prednisone:
    a. It should be prescribed at the lowest possible dosage
    b. It should be prescribed for a long period of time
    c. It should be prescribed using an increasing dose strategy
    d. None of the above

25. Adverse reactions to prescribed systemic prednisone include:
    a. Hypothalamic-pituitary-adrenal inhibition
    b. Fungal infection (candidiasis)
    c. Both a and b
    d. Neither a or b

26. Additional immunosuppressant medications and immunomodulatory agents that can be considered to manage recalcitrant erosive/ulcerative LP include:
    a. Cyclosporine
    b. Tacrolimus
    c. Pimecrolimus
    d. All of the above

27. Which statement is accurate regarding Tacrolimus use for erosive/ulcerative LP:
    a. The US Food and Drug Administration recommends against oral application of this medication
    b. Tacrolimus may increase cancer risk
    c. Tacrolimus treatment can result in measurable blood levels
    d. All of the above

28. Which statement accurately reflects medications such as the retinoids, dapsone, azathioprine, mycophenolate, mofetil, and acitretin:
    a. There is limited scientific support for their use
    b. These drugs have few side effects or adverse reactions
    c. Dapsone has not been associated with hemolysis and hypersensitivity reactions
    d. All of the above

29. Of the following non-pharmacological interventions suggested as treatment of erosive/ulcerative LP, which therapy has been contrasted with Clebetalos:
    a. PUVA therapy
    b. Photodynamic therapy
    c. Laser phototherapy
    d. None of the above

30. PUVA therapy has been associated with which of the following:
    a. Nausea
    b. Dizziness
    c. Photosensitivity
    d. All of the above
The Management of Oral Lichen Planus

Educational Objectives

1. Describe interventions used to manage oral lichen planus.
2. Identify the appropriate medications to be prescribed for managing erosive and ulcerative oral lesions.
3. Implement treatment strategies for managing oral lichen planus.
4. Identify the appropriate medications to be prescribed for managing erosive and ulcerative oral lesions.
5. How do you rate the author's grasp of the topic? Yes No
6. Rate the instructor's effectiveness. Yes No
7. Was the overall administration of the course effective? 5 4 3 2 1
8. Please rate the usefulness and clinical applicability of this course. 5 4 3 2 1
9. Please rate the usefulness of the supplemental website. 5 4 3 2 1
10. Do you feel that the references were adequate? Yes No
11. Would you participate in a similar program on a different topic? Yes No
12. If any of the continuing education questions were unclear or ambiguous, please list them.

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