

Amalgam Contact Allergy in Oral Lichenoid Lesions

Apichaya Thanyavuthi, MD, Waranya Boonchai, MD, and Pranee Kasemsarn, MD

Background: Oral lichenoid lesions (OLLs) cannot be distinguished from oral lichen planus (OLP) except that causative factors can be identified. Amalgam is one of the causative allergens, and replacement may lead to resolution.

Objectives: The aim of this study was to determine the prevalence, prognosis, and aggravating factors of amalgam contact allergy in patients with OLLs.

Methods: A clinical retrospective and prospective cohort study was carried out at the Dermatology Department, Siriraj Hospital, Mahidol University. In cases with patch test positive for an amalgam component, patients were suggested to replace their amalgam restorations.

Results: Of 53 patients with OLLs, 39 (73.6%) had positive patch test results, and 31 (58.5%) reacted to at least one amalgam component. The most common causative allergen was mercury (35.8%). Lesions on bilateral buccal mucosa and gingiva tended to have negative patch test results ($P < 0.05$). Spicy food was the main aggravating factor. Amalgam replacements were performed in 10 patients. Clinical improvement was observed in all cases with complete healing in 3 cases.

Conclusions: The prevalence of amalgam contact allergy in patients with OLLs was 58.5%. Mercury was the most common allergen, followed by copper sulfate. An association between clinical, topographic relation, and positive patch test results would be a useful predictor for favorable outcome after amalgam removal.

Oral lichenoid lesions (OLLs) are chronic inflammatory lesions of the oral cavity, which can hardly be distinguished from oral lichen planus (OLP). Various terms have been used in the literature, including lichenoid contact lesions, lichenoid contact stomatitis, and oral lichenoid reactions. Although the exact cause and pathogenesis of OLP is unknown, OLLs have several clinical subtypes depending on triggering factors and proposed pathogenesis.¹ In our study, we concentrated on OLLs that related to hypersensitivity reaction to dental restorative materials.^{1–3} The concept of contact allergy to dental restorative materials in OLLs has been widely recognized but somewhat controversial. The most

common causative allergen is mercury in dental amalgam, with few reported cases from other materials.^{1,3–8} Other proposed pathogenesis includes the toxic/irritant reaction to plaque accumulation on the filling surface.⁹ Electrochemical reaction between dissimilar metal or “galvanic effect” is also mentioned.¹⁰ Because OLLs and OLP share the same clinical and histological findings, making the diagnosis is challenging but critical, for once diagnosed, there would be a chance for complete recovery. Several authors have reported resolution of OLLs symptoms after replacement, particularly if there were positive patch test results to mercury.^{2,3,11,12} However, other studies present conflicting results.^{13,14} Resolution or improvement of the lesion after removing dental restoration helps confirm the OLLs diagnosis.¹

Although nowadays silver amalgams are being less used in some countries, many adult patients are still wearing amalgam restoration. In Thailand, amalgam remains popular for its strength, durability, and relative inexpensiveness. There has been no previous trial carried out on the relationship between clinical patch test results and clinical outcome of OLLs in the Thai population. The objectives of our study were to address the prevalence of amalgam contact allergy in patients with OLLs and its contribution to clinical prognosis, including common aggravating factors in Thailand.

MATERIALS AND METHODS

The study was approved by Siriraj Institutional Review Board, Mahidol University. Fifty-three patients with OLLs who were referred to the Contact Clinic, Dermatology Department, Siriraj

From the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Address reprint requests to Pranee Kasemsarn, MD, Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand. E-mail: doctorpranee@gmail.com.

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Dr(s) Thanyavuthi, Kasemsarn, and Boonchai had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design, Boonchai and Kasemsarn; acquisition of data, Thanyavuthi and Kasemsarn; analysis and interpretation of data, Thanyavuthi and Kasemsarn; draft of the manuscript, Thanyavuthi and Kasemsarn; critical revision of the manuscript for important intellectual content, Kasemsarn and Boonchai; administrative, technical, or material support, Thanyavuthi; study supervision, Boonchai.

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Hospital, Mahidol University from January 2002 to July 2014 were recruited. There are 10 prospective cases from July 2012 to July 2014 and 43 retrospective cases from January 2002 to June 2012.

Inclusion criteria required that all patients older than 18 years have at least 1 silver amalgam restoration in their teeth. In addition, the patients had oral lesions clinically and/or histologically compatible with OLP or OLLs and agreed to perform patch testing. These lesions included (1) reticular (net/plaque-like white patches), (2) erosive/atrophic (including desquamative gingivitis), and (3) ulcerative lesions. Patients who were given a diagnosis of lichen planus of the skin and/or nail were excluded from our study.

Lichenoid lesions of the oral mucosa were diagnosed clinically and histologically based on the previously established criteria.¹⁵ Topographic relation between lesions was classified as (1) close contact with amalgam fillings, (2) no contact, and (3) exceeding contact, which means the lesion extended by 1 cm beyond the area of contact with amalgam fillings.

Patch tests were placed on the upper back of all patients for 2 days with dental series allergens (Chemotechnique Diagnostics AB, Vellinge, Sweden) in aluminium Finn Chambers (SmartPractice, Phoenix, Ariz) (Table 1). The results were evaluated on D2, D4, and/or D7 according to International Contact Dermatitis Research Group guidelines.¹⁶ Positive reactions included those with 1+ to 3+ score. Doubtful, irritant, or negative reactions were considered as negative. Patients were suggested to replace their amalgam with composite resin if they had positive patch test to amalgam components or dental material and lesions were adjacent to the dental restoration. Patients were subsequently monitored at 1, 3, and 6 months after being diagnosed. Chart review and telephone interview were performed on retrospective cases.

The data were analyzed using descriptive analysis. Fisher exact tests were compared using SPSS v18.0 software (SPSS Inc, Chicago,

Ill). The difference was considered significant for *P* values less than 0.05.

RESULTS

The demographic data, such as sex, age, duration of the lesions, history of atopy, duration of the lesions in patch-test-positive (PT pos) and patch-test-negative (PT neg) groups, showed no statistically significant difference, *P* > 0.05 (Table 2). In both groups, most lesions were in close contact or in partial contact with amalgam restorations (90.5%), and the most commonly affected areas were the buccal mucosa (90.6%), tongue (20.8%), and lips (18.9%), gingiva (11.3%), with palate in only 2 cases (3.8%). Bilateral buccal mucosal lesions were more common in the PT neg group (92.9%) compared with the PT pos group (56.4%), with statistical significance *P* = 0.020. None of the PT neg patients had a unilateral buccal mucosal lesion. Gingival lesions, less frequently found, were more common in the PT neg group (28.6% vs 5.1%), *P* = 0.036.

Reticulated white patch lesions were most commonly reported, in 79.2% of patients, followed by erosive or atrophic lesions (18.9%) and ulcerative lesions in only 1 patient. Forty-one patients reported burning sensation; 12 patients had pain, and 7 patients were asymptomatic. We found that only 1 patient experienced metallic taste. Spicy foods were reported as aggravating factors (59.2%); hot and sour food also worsened symptoms in 14.8% and 12.9%, accordingly.

Histopathologic examination of OLP and OLLs are characterized by a bandlike cellular infiltration with mainly lymphocytes and liquefactive degeneration of the basal cell layer.¹⁵ In our study, histopathology led to the diagnosis of OLP in most cases in both PT pos (74.4%) and PT neg (78.6%) groups. Direct immunofluorescence (DIF) in performed cases showed results suggestive of lichen planus in greater than 50% of cases in both groups (64% vs 50%). Histopathology and DIF results were not significantly different between the 2 groups.

Patch Test Results

Patch testing results were positive in 39 patients (73.6%) and were found clinically relevant in 30 patients (76.9%). Patch tests were positive for a single allergen in 11 (28.2%), with 54.5% clinical relevance, and 28 patients (71.8%) reacted to more than 1 allergen, with 85.7% of them having clinical relevance. Mercury had the highest rate of positive reactions (35.8%), followed by copper sulfate (32%), nickel (28.3%), and gold sodium thiosulfate (28.3%). Positive patch test results are shown in Figure 1. The number of patients having a positive reaction to at least 1 metal that is an amalgam component (including mercury, tin, zinc, and copper sulfate) was 31 (58.5%) of 58.

Patients with a positive patch test for amalgam component or other dental materials as well as lesions that were adjacent to dental restorations were suggested to have their restoration replaced. Ten patients from our study underwent restoration removal, and all were replaced with composite resin. Among these patients, PT pos result for mercury alone was found in 3 patients,

TABLE 1. Patch Test Allergens in Dental Series

Metal	Flavoring agents
Aluminum chloride hexahydrate 2%	Myroxylon pereirae resin 25%
Potassium dichromate 0.5%	Eugenol 2%
Cobalt chloride 1%	Isoeugenol 2%
Nickel sulfate 5%	Cinnamic aldehyde 1%
Copper sulfate 2%	L-(+)-carvone (DMP-100) 5%
Gold sodium thiosulfate 2%	Menthol 2%
Palladium chloride 2%	Others
Mercury 0.5%	N,N-dimethyl-4-toluidine 5%
Tin 50%	Colophony 20%
Zinc 2.5%	Benzophenone-3 10%
Acrylate	Formaldehyde 1%
BIS-GMA 2%	Dichlorophene 1%
Methyl methacrylate 2%	
Ethylene glycol dimethacrylate 2%	
BIS-EMA 2%	
Triethylene glycol dimethacrylate 2%	
2-Hydroxyethyl methacrylate 2%	

TABLE 2. Clinical Characteristics of Patients With OLLs

	Positive Patch Test Results (N = 39)	Negative Patch Test Results (N = 14)	<i>P</i>
	n (%)	n (%)	
Age, mean (SD), y	50.8 (11.6)	47.6 (13.9)	0.402, <i>t</i> test
Female-male ratio	3.9:1	1.8:1	0.292
History of atopy	13 (33.3)	4 (28.6)	1
Duration of lesion, median (range), mo	12 (1–60)	6.5 (1–120)	0.371, Mann-Whitney <i>U</i> test
Aggravating factors			
Sour food	6 (15.4)	1 (7.1)	0.660
Spicy food	24 (61.5)	8 (57.1)	1
Hot food	4 (10.3)	4 (28.6)	1
Symptoms			
Asymptomatic	5 (12.8)	2 (14.3)	1
Burning sensation	31 (79.5)	10 (71.4)	0.711
Pain	10 (25.6)	2 (14.3)	0.480
Metallic taste	0	1 (7.1)	0.264
Type of lesions			
Reticulated white patches	31 (79.5)	11 (78.6)	1
Erosive or atrophic	7 (17.9)	3 (21.4)	
Ulcerative	1 (2.6)	0	
Location of oral lesions			
Buccal mucosa	35 (89.7)	13 (92.9)	
Bilateral	22 (56.4)	13 (92.9)	0.020*
Unilateral	13 (33.3)	0	
Tongue			
Lateral	6 (15.4)	1 (7.1)	0.254
Dorsal/ventral	4 (10.3)	0	0.333
Palate	1 (2.6)	1 (7.1)	0.462
Gingiva	2 (5.1)	4 (28.6)	0.036*
Lips	9 (18.9)	1 (7.1)	0.581
Relation to dental fillings			
Close contact	13 (33.3)	2 (14.3)	0.366
Exceeding contact	22 (56.4)	11 (78.6)	
No contact	4 (10.3)	1 (7.1)	
Contact with area of dental fillings	35 (89.7)	13 (92.9)	1
No contact	4 (10.3)	1 (7.1)	
Histopathology suggestive or compatible with lichen planus	29 (74.4)	11 (78.6)	0.531
DIF (in performed case): c/w lichen planus	16 (64)	3 (50)	0.653

*Statistical significance.

copper alone was found in 2 patients, and both mercury and copper were found in 4 patients, but one was positive to palladium. All cases had clinical improvement after dental restoration removal. Complete remission and marked improvement (more than 50% improvement from patient's visual analogue scale) were achieved in 30% and 70% of patients, respectively. Improvements were observed within 3 months after replacing amalgam restorations and complete healing in 3 cases after 6 months of follow-up. In the completely healed group, 2 patients had positive patch test results to mercury, and 1 patient had positive patch test results to copper, which is also an amalgam component. Topographic relation of the lesion in the restoration removed group was close contact (3/30%), exceeding contact (6/60%), and no contact (1/10%). A patient whose lesion was not in contact with amalgam restoration still insisted to remove

his restorations because of severe pain and recalcitrance to both topical and systemic treatments. In the completely healed group, 2 patients had a close contact lesion, which means the lesion was confined to the area of amalgam restorations, whereas 1 patient had a lesion exceeding the area of amalgam contact. We found that 36.8% of patients who had PT pos results for mercury completed the diagnostic criteria for OLLs¹⁷ (lesions in contact with amalgam, histopathologic finding and/or DIF compatible with OLP, clinical improvement after dental restoration removal).

DISCUSSION

The contact of oral mucosa with dental restorative materials or their corrosive by-products is thought to induce a sensitivity

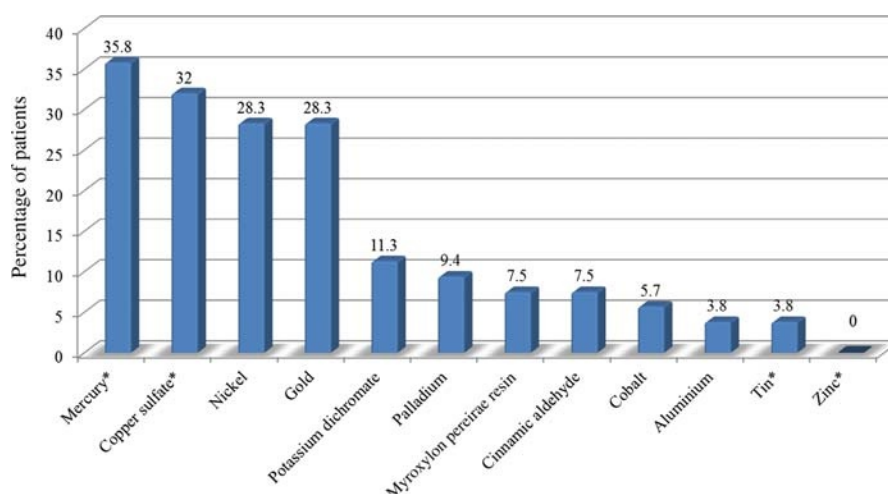


Figure 1. Patch test results in patients with OLLs. *Amalgam-containing alloy.

response, and lichenoid reaction is the most common manifestation of contact sensitization of mucosa.^{2,17} Clinically, OLLs can produce heterogeneous clinical presentations, from most commonly found white reticular patches and plaques to atrophic or ulcerated lesions similar to those found in OLP. Oral lichenoid lesions are usually unilateral and have an anatomical relationship to dental amalgam restorations.^{2,17,18} Diagnosis of OLLs related to contact with dental materials based on clinical, histopathological, and patch testing results to identify their causative allergens may also help in determining what alternative material should be used.

In our study, demographic data of patients in both PT pos and PT neg groups were not significantly different. Prevalence of OLLs among women is higher than that of men; the age of onset is 40s to 50s, similar to previous studies.^{17,19} Reticular white patch lesions and location on buccal mucosa are the most common manifestations as in other studies (Table 3).^{2,13,20,21} However, the lateral edge of the tongue, which is also common in other studies, was found only in 13%. Burning is the most prevalent symptom of OLLs, and generally, pain is more severe in atrophic or erosive

lesions. Because, in our countries, most traditional foods are spicy, such foods seemed to be the most common aggravating factor in our study and affected the patients' quality of life.

It has been stated in the diagnostic criteria that oral lichenoid contact lesions should be asymmetrical and/or unilateral lesions,^{1,2,17,18} but most of the lesions found in our patients were bilateral. This could be explained by the presence of bilateral silver amalgam fillings.²² We found no unilateral lesion in the PT neg group, which might be because of chronic inflammatory process in OLP more than contact sensitization in the PT neg group. Likewise, gingival lesions, which are less likely to contact dental restorations, were more common in the PT neg group, with statistical significance. Histopathologic and DIF study results do not differentiate well between OLLs and OLP^{2,23}; clinical examination and patch testing are usually required to distinguish these 2 conditions.¹⁸ However, a recent study found more eosinophils, plasma cells, and granulocytes in OLLs than in OLP.²⁴

Dental amalgam, which has been widely used in dental restorations before composite resin was introduced, is an alloy composed of equal part of liquid mercury and powdered alloy consisting of

TABLE 3. Clinical Characteristics of Patients With OLLs in Different Countries

Author, Year	Country	Case No.	Location, %		Contact With Amalgam, %	PT Pos, %	
			Buccal	Tongue		Amalgam-Containing Alloy*	Mercury
Skoglund and Egelrud ²⁰ , 1991	Sweden	24	100	25	N/A	0	33.3
Laine et al ¹³ , 1997	Finland	118	98.3	79.7	100	4.2	64.4
Wong and Freeman ²¹ , 2003	Australia	84	95.2	27.3	100	N/A	39.3
Thornhill et al ² , 2003	United States	81	77.8	56.8	63	11.1	27.2
Laeijendecker et al ³ , 2004	The Netherlands	60	N/A	N/A	66.7	N/A	38.3
Lynch et al ⁴ , 2015	Ireland	31	N/A	N/A	100	6.5	32
Our study	Thailand	53	90.5	20.7	90.5	33.9	35.8

*Amalgam-containing alloy includes copper, silver, zinc, tin, and amalgam powder. Mercury was discussed separately.

silver, tin, copper, and other trace metals, including zinc.^{5,19} A previous study found positive patch test results for mercury compounds varying from 16% to 91%.^{19,25,26} In our study, 35.8% had positive patch test results for mercury which is not different from previous studies (Table 3). However, we found positive patch tests to other amalgam elements (copper sulfate, tin), with copper sulfate as the most frequent element with PT pos results besides mercury (32%), with 64.7% clinical relevance, which is much higher than in other studies.^{2,4,13} Lynch et al⁴ reported positive reaction to copper sulfate in 6.5% of patients. Copper hypersensitivity reaction is rare in a recent review; nevertheless, clinical significance could be identified in selected cases.²⁷ On the other hand, irritant reaction from metal allergens is common and could be the cause of a false-positive patch test reaction. From a systematic review, few patients showed a positive reaction to other metals in dental amalgam, ranging from 4% to 64%, with the highest percentage from amalgam powder.¹⁹ However, it was not included in our dental series. Oral lichenoid lesions related to nonmetallic dental materials such as acrylate are quite rare because it is infrequent to find free molecules after the curing process, suggesting that it would rather be because of local irritation.^{28,29}

The third most common PT pos allergens in our study were gold and nickel. Gold was the component of dental crowns in close contact with OLLs in 2 patients; however, both of them denied changing the restoration, and their symptoms still persisted. Most gold PT pos patients obviously tolerate gold metal jewelry contact to the skin because metallic gold is inert and difficult to dissolve.³⁰ Nickel was positive in the same proportion as gold. Nitinol alloy of nickel and titanium is a part of orthodontic wire; however, there were no nickel-positive patch test patients who currently wore an orthodontic brace. Nickel clinical relevance was concluded by positive dimethylglyoxime spot test on their personal jewelry.

Amalgams have been suggested to be replaced in those cases in which lesions are in direct contact with amalgam and whenever patch test is positive.^{2,19,21} The percentage of complete healing achieved in patients who received replacements for their amalgam restorations was 30% (3/10), lower than those of previous studies, which ranged from 37% to 100%.^{31,32} This might be due to our shorter follow-up period (3–6 months), whereas some articles have an average follow-up period of up to 72 months.^{14,19,31–33}

From other studies, healing correlated with the topographic relationship of the amalgam and the OLLs; the greatest improvements were noted when there was close contact between the OLLs and the restoration, and the least improvements were noted when there was no contact.^{14,19} The healing and topographic relations from various studies are shown in Table 4. From our study, topographic relation between the 2 groups did not significantly differ, and lesions were in contact with restorations in most cases. In patients with lesions that exceeded the area of contact with the amalgam restorations, complete healing was 16.7% (1/6) compared with 66.7% (2/3) when there was close contact between the OLLs and the restoration. So we might conclude that, besides a

TABLE 4. Healing After Replacement of Restorations and Topographic Relation in Patients With OLLs

Author, Year	Healing and Topographic Relation, n (%)									
	Complete			Marked			No improvement			
	Close Contact	Exceeding	No Contact	Close Contact	Exceeding	No Contact	Close Contact	Exceeding	No Contact	No Contact
Skoglund and Egelrud ²⁰ , 1991	15/33 (45.5%)	6/14 (42.9%)	1/1 (100%)	16/33 (48.5%)	6/14 (42.9%)	0/1	2/33 (6.1%)	2/14 (14.3%)	0/1	0/1
Laine et al ¹³ , 1997	29/54 (53.7%)	2/23 (8.7%)	—	Contacted 36/77 (46.8%)	—	—	Contacted 10/77 (13%)	—	—	—
Wang and Freeman ²¹ , 2003	Contacted 27/30 (90%)	—	—	Contacted 1/30 (3.3%)	—	—	Contacted 2/30 (6.7%)	—	—	—
Thornhill et al ² , 2003	20/28 (71.4%)	N/A	0/5	6/28 (21.4%)	N/A	0/5	2/28 (7.2%)	N/A	5/5 (100%)	1/2 (50%)
Laeijendecker et al ³ , 2004	11/13 (84.6%)	5/8 (62.5%)	0/2	2/13 (15.4%)	3/8 (37.5%)	1/2 (50%)	0/13	0/8	—	—
Lynch et al ⁴ , 2015	Contacted 6/8 (75%)	—	—	Contacted 2/8 (25%)	—	—	Contacted 0/8	0/6	—	0/1
Our study, $P = 0.458$	2/3 (66.7%)	1/6 (16.7%)	0/1	1/3 (33.3%)	5/6 (83.3%)	1/1 (100%)	0/3	0/6	—	0/1

positive patch test, the patients with OLLs that have close contact with amalgam fillings should have a favorable outcome after removal. Similar to previous studies, the anatomical relationship seems to be a powerful predictor of OLL prognosis.^{2,9}

Some authors found a good response to the replacement of amalgams in patients with the patch test reactions to mercury,^{21,25,26,33,34} whereas others did not.¹⁴ In our study, 7 of 10 patients who had their amalgam removed had PT pos results to mercury either alone or with other metal allergens. All patients had clinical improvement, and two of them were completely healed. Previous studies showed that relief of symptoms was reported as early as 2 to 3 days after amalgam removal³⁵ or could take up to months or longer.^{13,25} In our study, clinical improvement was observed within 1 to 3 months.

Another reason why it is important to diagnose OLLs correctly, as other authors have noted, is that patients with OLLs have an increased risk of oral cancer development more than patients with OLP.^{36,37} Hence, it has been suggested to monitor only the subgroup of patients with OLLs twice a year for early detection of possible malignant transformation.³⁶

During our 6 months of follow-up, most cases had chronic and relapsing courses with no or partial clinical response to topical or systemic therapy (mostly short-term systemic corticosteroids). However, significant improvement was noticed in PT pos patients who underwent amalgam restoration replacement. Therefore, patch test together with lesion topographic relation may be useful in determining which patients will benefit from the replacement of amalgam fillings.

Limitations of our study are the retrospective methods, some data such as location of lesions, correlation with restorations, and missing surface of dental restorations. Follow-up period was too short in some cases, which might explain the lower rate of complete healing in our study. We did not perform late patch test readings, which was mentioned in some articles as potentially useful for gold sodium thiosulfate, palladium chloride, and mercury compound.¹² Moreover, we performed patch test only with metallic mercury, whereas a previous study by Laine et al¹³ recommended using other mercuric compounds including mercuric chloride and ammoniated mercury. This might have decreased the rate of positive patch test reaction to dental restorative materials in our study.

CONCLUSIONS

Contact allergy to metal in dental restorations can be an important pathogenesis of OLLs. The prevalence of positive reaction to amalgam component was 58.5% and 35.8% to mercury compound. One third of our patients had a positive patch test reaction to copper sulfate, suggesting that other amalgam-containing alloys also have an important role in OLLs. The replacement of amalgam restorations can result in clinical improvement and resolution of OLLs in most cases. Patch test results and topographic relationship between the OLLs and amalgam restoration seem to be the

strongest prognostic markers for the improvement of the lesion after amalgam replacement.

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REFERENCES

1. Al-Hashimi I, Schifter M, Lockhart PB, et al. Oral lichen planus and oral lichenoid lesions: diagnostic and therapeutic considerations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;103(suppl):S25.e21–S25.e12.
2. Thornhill MH, Pemberton MN, Simmons RK, et al. Amalgam-contact hypersensitivity lesions and oral lichen planus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003;95:291–299.
3. Laeijendecker R, Dekker SK, Burger PM, et al. Oral lichen planus and allergy to dental amalgam restorations. *Arch Dermatol* 2004;140:1434–1438.
4. Lynch M, Ryan A, Galvin S, et al. Patch testing in oral lichenoid lesions of uncertain etiology. *Dermatitis* 2015;26:89–93.
5. McParland H, Warnakulasuriya S. Oral lichenoid contact lesions to mercury and dental amalgam—a review. *J Biomed Biotechnol* 2012;2012:1–8. doi:10.1155/2012/589569.
6. McGivern B, Pemberton M, Theaker ED, et al. Delayed and immediate hypersensitivity reactions associated with the use of amalgam. *Br Dent J* 2000;188:73–76.
7. Athavale PN, Shum KW, Yeoman CM, et al. Oral lichenoid lesions and contact allergy to dental mercury and gold. *Contact Dermatitis* 2003;49:264–265.
8. Ahlgren C, Axell T, Möller H, et al. Contact allergies to potential allergens in patients with oral lichen lesions. *Clin Oral Investig* 2014;18:227–237.
9. Holmstrup P. Oral mucosa and skin reactions related to amalgam. *Adv Dent Res* 1992;6:120–124.
10. Martin MD, Broughton S, Drangsholt M. Oral lichen planus and dental materials: a case-control study. *Contact Dermatitis* 2003;48:331–336.
11. Yiannias JA, el-Azhary RA, Hand JH, et al. Relevant contact sensitivities in patients with the diagnosis of oral lichen planus. *J Am Acad Dermatol* 2000;42:177–182.
12. Koch P, Bahmer FA. Oral lesions and symptoms related to metals used in dental restorations: a clinical, allergological, and histologic study. *J Am Acad Dermatol* 1999;41:422–430.
13. Laine J, Kalimo K, Happonen RP. Contact allergy to dental restorative materials in patients with oral lichenoid lesions. *Contact Dermatitis* 1997;36:141–146.
14. Ostman PO, Anneroth G, Skoglund A. Amalgam-associated oral lichenoid reactions. Clinical and histologic changes after removal of amalgam fillings. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;81:459–465.
15. van der Meij EH, van der Waal I. Lack of clinicopathologic correlation in the diagnosis of oral lichen planus based on the presently available diagnostic criteria and suggestions for modifications. *J Oral Pathol Med* 2003;32:507–512.
16. Practical aspects of patch testing. In: Rietschel RL, Fowler JF Jr, eds. *Fisher's Contact Dermatitis*. 6th ed. Ontario, Canada: BC Decker Inc; 2008:11–29.
17. Cobos-Fuentes MJ, Martínez-Sahuquillo-Márquez A, Gallardo-Castillo I, et al. Oral lichenoid lesions related to contact with dental materials: a literature review. *Med Oral Patol Oral Cir Bucal* 2009;14:e514–e520.

18. Thornhill MH, Sankar V, Xu XJ, et al. The role of histopathological characteristics in distinguishing amalgam-associated oral lichenoid reactions and oral lichen planus. *J Oral Pathol Med* 2006;35:233–240.
19. Issa Y, Brunton PA, Glenney AM, et al. Healing of oral lichenoid lesions after replacing amalgam restorations: a systematic review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004;98:553–565.
20. Skoglund A, Egelrud T. Hypersensitivity reactions to dental materials in patients with lichenoid oral mucosal lesions and in patients with burning mouth syndrome. *Scand J Dent Res* 1991;99:320–328.
21. Wong L, Freeman S. Oral lichenoid lesions (OLL) and mercury in amalgam fillings. *Contact Dermatitis* 2003;48:74–79.
22. Aggarwal V, Jain A, Kabi D. Oral lichenoid reaction associated with tin component of amalgam restorations: a case report. *Am J Dermatopathol* 2010;32:46–48.
23. van der Waal I. Oral lichen planus and oral lichenoid lesions; a critical appraisal with emphasis on the diagnostic aspects. *Med Oral Patol Oral Cir Bucal* 2009;14:E310–E314.
24. Mravak-Stipetić M, Lončar-Brzak B, Bakale-Hodak I, et al. Clinicopathologic correlation of oral lichen planus and oral lichenoid lesions: a preliminary study. *Scientific World Journal* 2014;2014:746874.
25. Ibbotson SH, Speight EL, Macleod RI, et al. The relevance and effect of amalgam replacement in subjects with oral lichenoid reactions. *Br J Dermatol* 1996;134:420–423.
26. Koch P, Bahmer FA. Oral lichenoid lesions, mercury hypersensitivity and combined hypersensitivity to mercury and other metals: histologically-proven reproduction of the reaction by patch testing with metal salts. *Contact Dermatitis* 1995;33:323–328.
27. Fage SW, Faurschou A, Thyssen JP. Copper hypersensitivity. *Contact Dermatitis* 2014;71:191–201.
28. Cumming CG, Wight C, Blackwell CL, et al. Denture stomatitis in the elderly. *Oral Microbiol Immunol* 1990;5:82–85.
29. Kanerva L, Estlander T, Jolanki R. Allergic contact dermatitis from dental composite resins due to aromatic epoxy acrylates and aliphatic acrylates. *Contact Dermatitis* 1989;20:201–211.
30. Fowler JF Jr. Gold. *Am J Contact Dermat* 2001;12:1–2.
31. Laine J, Konttinen YT, Beliaev N, et al. Immunocompetent cells in amalgam-associated oral lichenoid contact lesions. *J Oral Pathol Med* 1999;28:117–121.
32. Skoglund A. Value of epicutaneous patch testing in patients with oral, mucosal lesions of lichenoid character. *Scand J Dent Res* 1994;102:216–222.
33. Laine J, Kalimo K, Forssell H, et al. Resolution of oral lichenoid lesions after replacement of amalgam restorations in patients allergic to mercury compounds. *Br J Dermatol* 1992;126:10–15.
34. Pang BK, Freeman S. Oral lichenoid lesions caused by allergy to mercury in amalgam fillings. *Contact Dermatitis* 1995;33:423–427.
35. Smart ER, Macleod RI, Lawrence CM. Resolution of lichen planus following removal of amalgam restorations in patients with proven allergy to mercury salts: a pilot study. *Br Dent J* 1995;178:108–112.
36. van der Meij EH, Mast H, van der Waal I. The possible premalignant character of oral lichen planus and oral lichenoid lesions: a prospective five-year follow-up study of 192 patients. *Oral Oncol* 2007;43:742–748.
37. Fitzpatrick SG, Hirsch SA, Gordon SC. The malignant transformation of oral lichen planus and oral lichenoid lesions: a systematic review. *J Am Dent Assoc* 2014;145:45–56.