

Oral lichen planus and dental materials: a case-control study

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The purpose of this study was to examine the association of dental materials with oral lichen planus (OLP) and, particularly, the effects of amalgam, amalgam corrosion status, gold and dissimilar metals in continuous contact. A case-control study was performed with 43 OLP cases from the Oral Medicine Clinic at the School of Dentistry, University of Washington and 78 controls from a general dental care-screening clinic, also at the School of Dentistry, University of Washington. Health histories and oral examinations were obtained. Current metal or metal-based restorations were charted, along with corrosion status of amalgams and the presence of dissimilar metals in continuous contact. Adjusted odds ratios (ORs) and 95% confidence intervals for the following potential risk factors were found to be: (1) number of teeth with amalgam, OR = 1.02 (0.92, 1.13); (2) total surfaces of amalgam, OR = 0.96 (0.92, 1.0); (3) number of teeth with gold, OR = 1.12 (0.95, 1.31); (4) mean amalgam corrosion score, OR = 5.74 (2.34, 14.1); (5) presence of dissimilar metals in contact (per quadrant), OR = 1.25 (0.81, 1.92). These findings suggest that although the presence of amalgam or gold themselves is not associated with increased risk of OLP, corrosion of amalgams and the presence of a 'galvanic effect' from dissimilar dental materials in continuous contact (bimetallism) are associated with an increased risk of OLP.

Key words: bimetallism; case-control studies; dental amalgam; dental materials; lichen planus.

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Oral lichen planus (OLP) is a relatively common mucocutaneous disease affecting about 0.1–4% of population, depending on the study population (1, 2). OLP is primarily a disease of adults (3) and is more common in women, with a female to male prevalence of about 2:1 (4). OLP is most often present on the buccal mucosa, gingiva and tongue. It presents as a number of forms including reticular, erosive, atrophic, plaque type, papular or bullous. More than one form may be present at the same time and in the same location.

Known aetiologies for OLP include drug exposures (2, 4, 5), hepatitis C or chronic liver disease (6, 7), other systemic diseases such as diabetes (8) and psychosocial factors such as stress (9). Associations of OLP with dental material exposures, particularly dental metals, have been investigated by assessing allergic responses in patients via cutaneous patch testing (10–18). Most researchers have found increased incidence of allergic response to commonly used dental materials in patients with OLP over patients without mucosal disease.

Other investigators have attempted to explore the contribution of dental materials to oral lichenoid reactions or OLP lesions by removing dental restorations and following the course of the lesions following removal (18–23). In most cases, a positive patch test to the material, which was removed, and/or with immediate proximity of the oral lesion to the metal, was associated with improvement of the lesion following removal.

A few reports have investigated the potential associations of corrosion (oxidation) and oxidation by-products of dental materials with OLP as well as those of intraoral galvanic effects (24–28). These few studies have been primarily non-clinical or case-based, and no actual clinical trials have been reported which primarily examine these associations.

Likewise, to date, there are no reports of investigations of the effect on OLP or oral lichenoid lesions and of the removal, specifically, of restorations in which dissimilar metals are in contact (bimetallism). Thus, multiple 'before–after' case series show the resolution of lichenoid lesions

after amalgam restoration removal; however, when using this type of uncontrolled study design, one cannot tell how many lesions would have resolved without restoration removal. To our knowledge, no other controlled studies have quantitatively and systematically evaluated these potential associations.

The specific aims of this study were to use case-control methodology to:

- (1) assess the association of OLP with the number of amalgam surfaces and restorations present in the mouth;
- (2) assess the association of OLP with the presence and quality of 'corroded' (oxidized) amalgams;
- (3) assess the association of OLP with the presence of other dental materials in the mouth including the effect of 'bimetallic' contact;
- (4) determine what role demographic factors, including stress levels, may play in the presence of OLP.

Patients and Methods

Patients attending the University of Washington Oral Medicine Clinics for the treatment of OLP during a 3-month period were recruited. All patients for whom records were considered 'active' were asked to participate. Patients who had been examined and/or treated within the last 2 years were considered 'active'. These patients were initially contacted by telephone and invited to participate. The study protocol was reviewed and approved by the Human Subjects Review Board of the University of Washington, and all participants were recruited through approved informed consent procedures. A free examination was the only incentive for participation. One known aetiology for OLP is drug-induced lesions. Each subject case had been evaluated and treated for his/her OLP and was being managed by oral medicine specialists. As a routine part of their treatment, the possibility of drug-induced lesions had been considered and managed. Therefore, the patients in this study may be considered to have cases of OLP that were not drug induced. Control subjects were recruited from amongst patients who were screened through the Oral Medicine Service, for inclusion in the School of Dentistry predoctoral clinic patient pool. Controls were limited to those patients at least 30 years of age, as the onset of OLP rarely occurs before this age. Age matching was not utilized as a strategy, because the intention was to control for age in the analyses. Each subject completed a questionnaire for demographic and health information. Because stress is thought to play a role in the development, maintenance and flaring of OLP, a simple assessment of psychosocial distress was

utilized, with 5 questions asking for self-report on unhappiness, irritation, nervousness, nervous exhaustion and being upset. This score was constructed for this study and is intended to be only a simple estimate of recent and currently perceived stress. Each positive response was scored as a single point, and the summed stress score could range from 0 to 5. The dentition of each subject was charted via a clinical oral examination, with all metal or metal-containing restorations recorded for type, location and surfaces involved. Mucosal lesions were charted by quadrant. The corrosion status of all amalgam restorations was recorded according to a 'corrosion state' scale. A scale with only 3 'corrosion states' was utilized to maximize reliability and minimize misclassification. Corrosion status was scored 0–2, based on the following descriptors: 0 – amalgam is not corroded, surface is silver in colour and shiny; 1 – amalgam appears grey or slightly darkened, not shiny and may show slight pitting or marginal breakdown; 2 – amalgam is dark, discoloured, surface appears rough and/or pitted and may show severe marginal breakdown. No attempt was made to score each surface of an amalgam for corrosion status. We based the determination of corrosion status on the most affected visible surface of a restoration. All oral examinations were performed by 1 of 2 examiners. Although these examiners were (by clinical practicality) not blinded to the OLP status of the subject, no attempt was made by the examiner to determine the OLP status of the subject until the status of the dentition was charted. Both examiners were oral medicine specialists who were trained with a standardized set of clinical photographs to score the presence of 1 of the 3 corrosion states of the dental amalgam restorations. Prior to the restoration evaluations, triangular paper saliva shields (Dri Aids®, Young Dental Co., Earth City, MO, USA) were placed bilaterally against the buccal mucosa to further 'blind' the examiners to the presence of buccal OLP lesions.

2 examiners performed all examinations and restoration evaluations. An evaluation of inter-rater reliability was performed for amalgam corrosion score using 85 amalgam restorations in 12 subjects. The weighted κ was 0.81 (SE = 0.08), indicating a high level of concordance for this measure.

Scores for number of amalgams, amount of gold present, corrosion status of amalgams and the degree of bimetallic contact were calculated for each subject. Definitions for these variables are as follows: bimetallic – 2 dissimilar metals in proximal contact, e.g. amalgam and gold; opposing contact is not considered to fit the definition and this variable was measured as number of

quadrants in which the condition existed; mean corrosion score = corrosion score for each amalgam divided by number of amalgams; mean weighted corrosion score = corrosion score for each amalgam multiplied by the number of surfaces divided by number of amalgams; stress score = sum of yes answers to 5 questions utilized to assess current stress (yes = 1).

An attempt was made for each case to determine whether or not the case had been 'biopsy-confirmed' by a pathology service. Analyses were conducted separately for all cases and for the biopsy-confirmed cases only.

Analyses were conducted utilizing SPSS-PC software. *t*-tests, ANOVA and regression analyses were performed as appropriate.

Results

43 of 85 cases invited to participate chose to participate for a response rate of 51%. The predominant reasons given for non-participation were 'no time' and 'difficulty in travelling to the clinic'. The participation rate for controls (who were already present in the clinic at the time of recruitment) was 86%. The predominant reason given by controls for non-participation was 'no time'. The mean age of the controls (53.5 years) was significantly younger than that of the cases (61.0 years) and of the biopsy-confirmed cases (58.8 years), but the mean age of cases was not significantly different from biopsy-confirmed cases. Significantly, more cases (72.1%) were female than controls (51.3%), as were biopsy-confirmed cases (70.0%). No significant differences between cases and controls were seen for occupation classification or for self-described health status. No significant differences were found between cases and controls for diabetes, hypertension or other systemic diseases. Cases scored significantly higher on the simplified stress measure than controls (mean, 0.90 versus 0.46) but both showed low mean stress scores, with values <1 on a scale of 0–5. Biopsy-confirmed cases scored even higher (0.96).

In univariate analyses, the mean corrosion score was significantly higher for all cases (1.1) than for controls (0.6) and slightly higher yet for biopsy-confirmed cases (1.2) (Table 1). The mean weighted corrosion score showed similar results

(Table 1). The mean number of quadrants in which bimetallicism occurred was significantly higher amongst cases (1.2) than in controls (0.74) and, again, higher yet in biopsy-confirmed cases (1.5) (Table 1). The mean number of teeth with amalgam was not significantly different in controls and all cases (Table 2) or in biopsy-confirmed cases. Likewise, the mean number of total surfaces of amalgam was not significantly different in controls and either all cases or biopsy-confirmed cases alone (Table 2). The mean number of teeth with gold, however, was different between controls (1.6) and all cases (3.5) and also in biopsy-confirmed cases alone (2.8) (Table 2).

Because age, sex and stress scores were found to be different between controls and cases, and may have introduced confounding in the univariate analyses, multivariate analyses were conducted using these factors as covariates (to adjust for their potential effects) and resulting in adjusted odds ratios (ORs) for *a priori* factors of interest. These are presented in Table 3. No increase in risk of OLP is seen for number of teeth with amalgam or for total surfaces of amalgam. A small increase in risk is seen for number of teeth with gold present, but this increase does not reach statistical significance. The mean corrosion score of amalgams shows significant increases in risk of OLP, both for all cases and biopsy-confirmed cases only, with increases in risk of between 6 and 10 times than that of controls. The mean weighted corrosion score, which attempts to 'even out' the effect of isolated severely corroded amalgams and avoid overestimation of the potential contribution of amalgam corrosion to OLP, still showed significant increases in risk of about 50–60% for all cases and biopsy-confirmed cases, respectively. The presence of bimetallicism in a quadrant was found to be associated with an increase in risk of OLP by 25–60% per quadrant, although the confidence intervals for these ORs included 1.0.

Discussion

We believe this is the first controlled study to demonstrate a strong association between corroded dental amalgams and OLP, although controlling for the potentially confounding effects of age,

Table 1. Comparison of mean scores for corrosion: all cases and biopsy-confirmed cases only

Variable	Controls (<i>n</i> = 78)	All cases (<i>n</i> = 43)	<i>P</i> value	Biopsy-confirmed cases (<i>n</i> = 23)	<i>P</i> value
Mean corrosion score (SD), <i>t</i> -test	0.60 (0.51)	1.1 (0.55)	0.000	1.2 (0.50)	0.000
Mean weighted corrosion score (SD), <i>t</i> -test	1.3 (1.5)	2.3 (1.3)	0.001	2.4 (1.1)	0.001
Bimetallicism: number of quadrants (SD), <i>t</i> -test	0.74 (0.97)	1.2 (1.1)	0.03	1.5 (1.2)	0.01

Table 2. Comparison of mean scores for number of teeth and surfaces with amalgam and gold: all cases and biopsy-confirmed cases only

Variable	Controls (<i>n</i> = 78)	All cases (<i>n</i> = 43)	<i>P</i> value	Biopsy-confirmed cases (<i>n</i> = 23)	<i>P</i> value
Number of teeth with amalgam (SD), <i>t</i> -test	6.9 (4.9)	6.3 (3.5)	0.48	7.2 (3.6)	0.72
Total surfaces amalgam (SD), <i>t</i> -test	15.9 (13.9)	13.2 (9.2)	0.24	15.4 (10.7)	0.88
Number of teeth with gold (SD), <i>t</i> -test	1.6 (2.6)	3.5 (3.6)	0.003	2.8 (2.6)	0.06

sex and psychosocial distress. As in other studies of OLP, positive associations between OLP and increased age, female sex and increased stress were found. In addition, there appeared to be an increased risk of OLP associated with the presence of continuous bimetallic or dissimilar metal contact, although the confidence interval included 1.0, indicating that this finding may have occurred by chance. There is also an indication that there is an increased risk of OLP associated with the presence of gold restorations. When biopsy-confirmed cases alone were compared with all cases, the risks of OLP associated with amalgam corrosion and bimetallicism increased. The simple presence or quantity of amalgam, however, did not appear to make a contribution to increased risk of OLP with either all cases or biopsy-confirmed cases alone. The only other epidemiological study of which we are aware, which evaluated the association of corroded dental amalgams with increased risk for OLP, found a similarly strong association. Using their data, we calculated the crude OR to be 6.8, close to our finding of 5.7 (26).

Although other studies have reported 'local associations' between individual lesions and fillings, we have chosen not to analyse the data in this way for this study. It is important to realize that the 'cases' in this study were all patients with OLP and not isolated lichenoid lesions. As such, essentially all of the cases had tissue changes that were widespread throughout the oral mucosa. Additionally, most of the cases had a substantial number of teeth with either gold or amalgam, and these teeth were spread throughout most quadrants of the mouth. Many of the OLP lesions were in the region of the buccal mucosa, making an

assessment of the proximity to restorations more difficult. These factors would render any attempt determining a local association between the filling materials and the lesions highly questionable. Finally, case-control studies are not designed to evaluate associations within cases only. That is, with this type of study design, we cannot assess the association between OLP location and restoration location, as the controls do not have lesions.

Some of the strengths of this study should be noted. An analysis of only biopsy-confirmed cases in a subset of the subjects was possible, and this plausibly increased the observed associations. In addition, our exposure measure of corrosion was shown to be highly reliable. Furthermore, we were able to control the potentially confounding effects of age, sex and perceived stress in the analyses. Finally, because our study had controls, we are more certain than uncontrolled studies that the lesions were associated with corroded restorations and that the relationships were not due to the natural history of lichenoid lesions resolving without specific treatment.

It is important to realize that these findings of associated increased risk of OLP with the various risk factors are only that: an association. This association does not imply causation without certain other criteria being met. Biological rationale and temporal association, amongst others, are needed to increase our confidence that there is a cause and effect relationship between OLP and these factors. In this study, one weakness is the lack of temporal information. It is not known how long the various metals were present, or, in many cases, whether they predated the onset of

Table 3. Association of dental metal variables and oral lichen planus: odds ratios* and 95% confidence intervals

Variable	All cases (<i>n</i> = 43)	Biopsy-confirmed cases (<i>n</i> = 23)
Number of teeth with amalgam	1.02 (0.92, 1.13)	1.05 (0.93, 1.18)
Total surfaces amalgam	0.96 (0.92, 1.0)	0.59 (0.90, 1.02)
Number of teeth with gold	1.12 (0.95, 1.31)	1.10 (0.92, 1.30)
Mean corrosion score	5.74 (2.34, 141.0)	9.60 (2.94, 31.2)
Mean weighted corrosion score	1.52 (1.06, 2.18)	1.59 (1.03, 2.43)
Bimetallicism	1.25 (0.81, 1.92)	1.60 (0.98, 2.61)

*Adjusted for age, sex, stress score and number of teeth with metal restorations.

OLP. Hence, cause and effect relationships remain unclear. In the case of the association of amalgam corrosion status with OLP, for example, it is possible that some currently unknown factor may be at work that causes both OLP and the oxidation of amalgams.

In the case of bimetallic contact, the galvanic process itself is probably facilitating the progress of restoration corrosion as well as causing the release of increased numbers of metal ions. It is unknown whether this increased presence of metal ions itself produces the localized tissue effects and/or perhaps the increased allergic sensitization found by authors referenced in the introduction, but there is a biological rationale for increased sensitization with increased exposure. It is additionally possible that the low-level current produced by the galvanic effect itself causes localized tissue changes. However, in the case of isolated restorations with no dissimilar metallic contact, this effect would not explain localized tissue effects.

To address these questions, further case-control studies are needed which have dental treatment histories for each subject. If funding is available, large cohort studies could be performed to evaluate definitively the temporal association between OLP and dental restorations. We conclude that there are apparent associations between OLP, the corrosion status of amalgams, the presence of bimetallic contact and the presence of gold in the mouth, all of which warrant further investigation.

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References

1. Axell T, Rundquist L. Oral lichen planus: a demographic study. *Community Dent Oral Epidemiol* 1987; 15: 52–56.
2. Scully C, Beyli M, Ferreiro M C et al. Update on oral lichen planus: etiopathogenesis and management. *Crit Rev Oral Biol Med* 1998; 9: 86–122.
3. Scully C, Almeida O P D, Welbury T. Oral lichen planus in children. *Br J Dermatol* 1994; 130: 131–133.
4. Mollaoglu N. Oral lichen planus: a review. *Br J Oral Maxillofac Surg* 2000; 38: 370–377.
5. Sugerman P B, Savage N W, Zhou X, Walsh L J, Bigby M. Oral lichen planus. *Clin Dermatol* 2000; 18: 533–539.
6. del Olmo J A, Pascual I, Bagan J V, Serr M A, Escudero A, Rodriguez F, Rodrigo J M. Prevalence of hepatitis C virus in patients with lichen planus of the oral cavity and chronic liver disease. *Eur J Oral Sci* 2000; 108: 378–382.
7. Ayala F, Balato N, Tranfaglia A, Guadagnino V, Orlando R. Oral erosive lichen planus and chronic liver disease. *J Am Acad Dermatol* 1986; 14: 139–140.
8. Petrou-Amerikanou C, Markopoulos A K, Belazi M, Karamitsos D, Papanayotou P. Prevalence of oral lichen planus in diabetes mellitus according to the type of diabetes. *Oral Dis* 1998; 4: 37–40.
9. Rojo-Moreno J L, Bagan J V, Rojo-Moreno J, Conat J S, Milian M A, Jimenez Y. Psychologic factors and oral lichen planus. A psychometric evaluation of 100 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998; 86: 687–691.
10. Finne K A J, Goransson K, Winckler L. Oral lichen planus and contact allergy to mercury. *Int J Oral Surg* 1982; 11: 236–239.
11. Mobacken H, Hersle K, Sloberg K, Thilander H. Oral lichen planus: Hypersensitivity to dental restoration material. *Contact Dermatitis* 1984; 10: 11–15.
12. Koch P, Bahmer F A. Oral lichenoid lesions, mercury hypersensitivity and combined hypersensitivity to mercury and other metals: histologically-proven reproduction of the redaction by patch testing with metal salts. *Contact Dermatitis* 1995; 33: 323–328.
13. Alanko K, Kanerva L, Jolanki R, Kannas L, Estlander T. Oral mucosal diseases investigated by patch testing with a dental screening series. *Contact Dermatitis* 1996; 34: 263–267.
14. Laine J, Kalimo K, Happnen R P. Contact allergy to dental restorative materials in patients with oral lichenoid lesions. *Contact Dermatitis* 1997; 36: 141–146.
15. Koch P, Bahmer F A. 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.
16. Yiannias J A, el-Azhary R A, Hand J H, Pakzad S Y, Rogers R S III. Relevant contact sensitivities in patients with the diagnosis of oral lichen planus. *J Am Acad Dermatol* 2000; 42: 177–182.
17. Scalf L A, Fowler J F Jr, Morgan K W, Looney S W. Dental metal allergy in patients with oral, cutaneous, and genital lichenoid lesions. *Am J Contact Dermat* 2001; 12: 146–150.
18. Thornhill M H, Pemberton M N, Simmons R K, Theaker E D. Amalgam-contact hypersensitivity lesions and oral lichen planus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003; 95: 291–299.
19. Smart E R, Macleod R I, Lawrence C M. 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.
20. Ostman P O, 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.
21. Bratel J, Hakeberg M, Jontell M. Effect of replacement of dental amalgam on oral lichenoid reactions. *J Dent* 1996; 24: 41–45.
22. Ibbotson S H, Speight E L, Macleod R I, Smart E R, Lawrence C M. The relevance and effect of amalgam replacement in subjects with oral lichenoid reactions. *Br J Dermatol* 1996; 134: 420–423.
23. Dunsche A, Kastel I, Terheyden H, Springer I N, Christophers E, Brasch J. Oral lichenoid reactions associated with amalgam: improvement after amalgam removal. *Br J Dermatol* 2003; 148: 70–76.
24. Holland R. Galvanic currents between gold and amalgam. *Scand J Dent Res* 1980; 88: 269–272.
25. Lind P O, Hurlen B, Koppang H S. Electrogalvanically-induced contact allergy of the oral mucosa: report of a case. *Int J Oral Surg* 1984; 13: 339–345.
26. Lundstrom I M. Allergy and corrosion of dental materials in patients with oral lichen planus. *Int J Oral Surg* 1984; 13: 16–24.
27. Olsson S, Berglund A, Bergman M. Release of elements due to electrochemical corrosion of dental amalgam. *J Dent Res* 1994; 73: 33–43.
28. Muller A W, Van Loon L A, Davidson C L. Electrical potentials of restorations in subjects without oral complaints. *J Oral Rehabil* 1990; 17: 419–424.

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