

ORAL LICHEN PLANUS & MERCURY AMALGAM

THE ASSOCIATION IS CLEAR

Compiled by Robert Gammal March 2013

At the time of writing in March 2013, the oral surgery department at Sydney University is still teaching dentists and dental students to place mercury amalgam in patients with compromised immune systems. The blanket denial by the teachers, that they do not know of a problem, is an insult to the patients and their colleagues. The teachers of oral surgery, who deal with cancer patients on a daily basis, do not have the right to plead ignorance of one of the most toxic substances known to man, let alone one that has received so much bad publicity. I personally brought this matter to their professors in 1999, and yet they still suppress the published scientific associations between Lichen Planus and mercury amalgam. They still teach that there is no known cause of Lichen Planus and the best treatment is to use immunosuppressive drugs. They still recommend placing mercury amalgam in immunosuppressed patients. They still do NOT recommend removing the amalgams even though the literature supports this approach. Much of this research is not new. Too many people are suffering because of this emu mentality. There is only one treatment in the literature that demonstrates complete remission of OLP in the majority of cases and that is replacing the amalgams.

Although my comments must be considered anecdotal, I have personally witnessed many cases of Oral Lichen Planus, completely resolve after safe amalgam removal. This to me seems a whole lot easier than living on immunosuppressive drugs.

The references below can speak for themselves.

1. Frykholm KO, Frithiof L, Fernström ÅIB, Moberger G, Blohm SG, Björn E Allergy to copper derived from dental alloys as a possible cause of oral lesions of lichen planus *Acta Derm-Venerol* 49 1969 268-81 (G23)
2. 2 cases of lichen planus apparently caused by allergy to dental metals Nakayama H; Oshiro A; Sato S; Nakano N (Jpn) *Jibiinkoka* 1972 Apr;44(4):239- 47
3. Lichenoid tattoo hypersensitivity. Taaffe A; Knight AG; Marks R *Br Med J* 1978 Mar 11;1(6113):616-8

Four patients are described who developed granulomatous reactions in the red portions of their tattoos. Histopathological and immunofluorescence studies showed features of lichen planus. Mercury was identified in only one patient's lesion, and hypersensitivity to mercury was shown by patch testing in one other patient. Tattooing may provide a localised antigenic challenge resulting in spontaneously occurring lichen planus.

4. The red tattoo and lichen planus. Taaffe A; Wyatt EH *Int J Dermatol* 1980 Sep;19(7):394-6
5. Toxicity of metal ions to alveolar macrophages. Castranova V; Bowman L; Miles PR; Reasor MJ *Am J Ind Med* 1980;1(3-4):349-57

Significant concentrations of metals are found in the respirable particulate effluents associated with metallurgical smelters. In this investigation the effects of the metallic ions lead, cadmium, iron, mercury, aluminum, chromium, and nickel on various aspects of alveolar macrophage function were studied. The production of antibacterial substances (ie, reactive forms of oxygen) by these cells and oxygen consumption are very sensitive to the metals. Particle uptake displays moderate sensitivity, while lysosomal enzyme activity and membrane integrity are fairly resistant

to metals. In addition, the effects of the organic solvents carbon tetrachloride, toluene, and xylene on alveolar macrophage function were tested. These solvents were found to inhibit oxygen consumption and the release of antibacterial substances while not greatly affecting membrane integrity. The results of these experiments indicate that some metals and some organic substances are toxic to alveolar macrophage function.

6. Oral lichen planus and contact allergy to mercury. Finne K; Goransson K; Winckler L *Int J Oral Surg* 1982 Aug;11(4):236-9

29 patients with oral lichen planus and amalgam fillings were patch tested for contact allergy to dental materials. 18 of these patients (62%) had a contact allergy to mercury. In a control material, the frequency of mercury allergy was 3.2%. In 3 of the patients the lesions healed completely after removal of the amalgam fillings. On the basis of these findings it is recommended that all amalgam fillings be removed after a positive patch test to mercury, as a step in the treatment of oral lichen planus.

7. Salivary gland function and changes in patients with oral lichen planus. Lundström I.M.C. *Scand J Dent Res* 90:443-458 1982
8. Finne K, Göransson K, Winckler L Oral lichen planus and contact allergy to mercury *Int J Oral Surg* 11 1982 236-9
9. Allergy to the mercury in dental amalgam Allergie au mercure dans l'amalgame dentaire. Duxbury AJ; Watts DC; Wastell EA (Review) (*Fre*) *Med Hyg (Geneve)* 1982 Oct 13;40(1487):3416-8
10. Eversole LR, Ringer M The role of dental restorative metals in the pathogenesis of oral lichen planus *Oral Surg* 57 1984 383-387 (AD48)
11. Allergy and corrosion of dental materials in patients with oral lichen planus. Lundstrom IM *Int J Oral Surg* 1984 Feb;13(1):16-24

Patients with histologically verified oral lichen planus (OLP) were studied regarding allergic reactions to substances in dental materials, presence of clinical corrosion orally and factors influencing corrosion, such as mixed gold and amalgam therapy, non-precious pin- constructions or complete dentures. The material consisted of 48 OLP patients (33 female, 15 male) and the results were compared with those of a control group (40 patients) and/or general population samples. When patch tested, 39% of the OLP patients reacted to one or more components in dental materials. Reaction to mercury was most common, being noted in 26%. Clinical signs of corrosion were significantly more frequent in the OLP group (72%) than in the control cases (28%). Patients with atrophic-erosive OLP exhibited a significantly higher frequency of corrosion (83%) than those with reticular type (46%). Mixed gold and amalgam therapy and screwposts were equally present in both the OLP and control group and the frequency of complete dentures corresponded to that reported for general populations. A change of dental materials in 8 patients with positive patch tests led to marked oral improvement in 6 cases, 2 of which became completely cured. The frequencies recorded for allergic reactions and corrosion as well as the result of treatment indicate that substances in dental materials may be of significance in cases of OLP.

12. Electrogalvanically-induced contact allergy of the oral mucosa. Report of a case. Lind PO; Hurlen B; Stromme Koppang H *Int J Oral Surg* 1984 Aug;13(4): 339-45

A 69-year-old white female presented bilateral lesions of the oral mucosa possibly related to electrogalvanism. The lesions were histologically characterized as lichen planus and as mild epithelial dysplasia on the left and right sides, respectively. They disappeared after removing amalgam restorations opposing the lesions. Epicutaneous patch tests and lymphocyte-

transformation tests showed that the patient suffered from a contact allergy to mercury compounds, indicating this as a mechanism by which electrogalvanism may induce lesions of the oral mucosa.

13. Oral lichen planus: hypersensitivity to dental restoration material. Mobacken H; Hersle K; Sloberg K; Thilander H *Contact Dermatitis* 1984 Jan; 10(1):11-5

67 patients with oral lichen planus of the atrophic-erosive or reticular plaque type were examined. Dental amalgam in contact with mucosal lesions was present in 64 patients, and gold fillings in 33. Patch testing with a standard procedure was performed with components of dental fillings. 11 patients (16%) reacted to at least one of the mercury compounds compared to 8% in a reference group. Most positive reactions were caused by elemental mercury and ammoniated mercury. No patient reacted to gold or copper. Readings at days 10-14 did not increase the number of responders. 13 patients were patch tested with palladium; all were negative. It is not clear whether in the mercury- positive patients allergy to dental amalgam is a causative or aggravating factor, or merely an epiphenomenon.

14. Amalgam-related oral lichenoid reaction. Lind PO; Hurlen B; Lyberg T; Aas E *Scand J Dent Res* 1986 Oct;94(5):448-51

In 52 patients with oral lichen planus topographically related to amalgam restorations, the fillings were replaced by other materials in 18, 16 of whom experienced complete remission of the lesions within 1- 12 months. These results are discussed in relation to the results of epicutaneous patch tests for possible allergy to a number of mercury compounds. The term "oral lichenoid reaction", is suggested to describe these lesions.

15. Oral lichenoid reactions related to mercury sensitivity. James J; Ferguson MM; Forsyth A; Tulloch N; Lamey PJ *Br J Oral Maxillofac Surg* 1987 Dec;25(6): 474-80

Lichen planus is a common disorder of unknown aetiology. It has been proposed that in some cases it represents a form of allergic reaction to the metals contained in dental amalgam, particularly mercury. Twenty- nine consecutive dentate patients who had lichen planus of the oral mucosa were patch-tested to the range of metals contained in dental amalgam. Ten out of 29 (34%) showed an allergic reaction to mercury and all of these patients had amalgams greater than 5 years old. The amalgams were poorly contoured and had corroded, resulting in continued release of mercury ions. Six patients had their amalgams replaced with composite or glass ionomer materials resulting in resolution of ulcerated lesions. In a follow-up of 3-24 months, one patient had a recurrence of ulcerated areas and another, despite resolution of the oral lesions had persistent discomfort.

16. Oral lichenoid reactions related to mercury sensitivity James J, Ferguson MM, Forsyth A, Tulloch N & Lamey P-J *Br J Oral Maxillofac Surg* 25, 1987 474-480

Lichen planus is a common disorder of unknown etiology. It has been proposed that in some cases it represents a form of allergic reaction to the metals contained in dental amalgam, particularly mercury. Twenty-nine consecutive dental patients who had lichen planus of the oral mucosa were patch-tested to the range of metals contained in dental amalgam. Ten out of 29 (34%) showed an allergic reaction to mercury and all of these patients had amalgams greater than 5 years old. The amalgams were poorly contoured and had corroded, resulting in continued release of mercury ions. Six patients had their amalgams replaced with composite or glass ionomer materials resulting in resolution of ulcerated lesions. In a follow-up of 3-4 months, one

patient had a recurrence of ulcerated areas and another, despite resolution of the oral lesions had persistent discomfort.

17. Bolewska J Reibel J T lymphocytes, Langerhans cells and HLA-DR expression on keratinocytes in oral lesions associated with amalgam restorations. *J Oral Pathol Med* (1989 Oct) 18(9):525-8

It has been shown recently that patients with mucosal lesions confined to areas opposing amalgam restorations (contact lesions) show a high rate of allergic reaction towards mercury. These lesions may, therefore, represent a contact hypersensitivity reaction.

Contact lesions often have a lichenoid appearance. From a pathogenetic and differential diagnostic point of view we therefore evaluated the presence of lymphocyte subpopulations, Langerhans cells (LC) and the expression of HLA-DR antigens on mucosal keratinocytes in biopsies of contact lesions (Group 1) and in lichen planus lesions with (Group 2) and without (Group 3) partial contact with amalgam restorations. T lymphocytes dominated in all three groups and LC counts were similar. HLA-DR positive keratinocytes were found in 18- 36% of lesions in all three groups. Thus, the immunologic parameters examined are not of value in discriminating between the types of lesions studied. Rather, it seems that the pattern observed is a common reaction of the oral mucosa to known (amalgam restorations) and unknown factors

18. Amalgam associated mercury accumulations in normal oral mucosa, oral mucosal lesions of lichen planus and contact lesions associated with amalgam. Bolewska J; Holmstrup P; Moller-Madsen B; Kenrad B Danscher G *J Oral Pathol Med* 1990 Jan;19(1):39-42

Forty-three patients with oral mucosal lesions were divided into 3 groups based on the relationship between lesions and amalgam restorations. Group I consisted of patients with contact lesions confined to mucosal areas in contact with amalgam fillings. Group II patients had lichen planus lesions exceeding the area of contact with an amalgam filling and Group III comprised patients with lichen planus lesions without relation to amalgam fillings. Biopsies were embedded in epon and subjected to autometallography in order to demonstrate a possible accumulation of mercury in the affected mucosa. In 20 out of 21 patients in Group I, 4 of 11 patients in Group II and 4 of 11 patients in Group III, mercury was found in the lysosomes of macrophages and fibroblasts. In Group I the number of cells loaded with mercury was much higher than in Group II and in particular Group III. In the latter groups autometallographically demonstrated mercury was found almost exclusively in macrophages. Nineteen biopsies taken from patients with normal mucosa served as controls. Ten had occlusal (Group IV) and seven buccal fillings (Group V). The biopsies from the latter group were taken from areas opposing amalgam restorations. Two patients had no amalgam fillings (Group VI). The histochemical technique showed that three biopsies in Group IV (occlusal fillings only) and two in Group V (opposing buccal fillings) contained traces of mercury in the juxtaepithelial connective tissue. The silver enhanced mercury was found in macrophages. The two controls (Group VI) without amalgam fillings were devoid of precipitates.

19. Lichen ruber exanthematicus et pigmentosus in mercury poisoning. A contribution to individual pathology in occupational medicine Marsch WC, Groebe G *Z Hautkr* 65(11) 1990 1013-8; 1021

We report on a 21-year-old man professionally exposed to mercury, who developed lichen planus. This case must be regarded as a dispositional reaction and is in Germany entitled to indemnification in terms of a "quasi-occupational disease". The clinical signs and the probably non- allergic pathomechanism are comparable with those of lichen planus induced by gold. In

diseases due to occupational intoxication, we face an individual disposition regarding the degree of clinical symptoms, which has to underly any expert opinion on indemnity.

20. Oral mucosal lesions related to silver amalgam restorations Bolewska J, Hansen HJ, Holmstrup P, Pindborg JJ, Stangerup M *Oral Surg Oral Med Oral Pathol* 70(1) 1990 55-8

A total of 49 consecutive patients with lesions of the oral mucosa that were in contact with corroding dental amalgam restorations were subdivided into two groups. In group 1 the lesions were restricted to the contact area opposing the dental restoration, whereas the extent of the lesions in group 2 exceeded that of the contact areas. Epicutaneous test for mercury allergy showed that a significantly greater proportion of the patients in group 1 had positive reactions to mercury than in group 2 ($p=0.019$). The amalgam restorations were replaced by composite resin or porcelain fused to gold crowns, or contact between amalgam fillings and oral mucosa was prevented by an acrylic splint. After this treatment regression of lesions was far more pronounced in group 1 than in group 2 ($p<0.001$). On the basis of these findings, contact allergy to mercury is suggested as a possible etiologic factor of the mucosal changes in group 1, and the designation contact lesion is proposed for such lesions. The lesions of patients in group 2 seem unrelated to a contact allergy to mercury, and other causes such as lichen planus should be considered.

21. Stomatitis and systemic dermatitis from mercury in amalgam dental restorations. Veien NK *Dermatol Clin* 1990 Jan;8(1):157-60

Patients who are hypersensitive to mercury may develop stomatitis on mucosa adjacent to amalgam dental restorations. This reaction, an allergic contact dermatitis, often resembles lichen planus but is distinguished by its location adjacent to restorations. Widespread dermatitis and urticaria are also possible.

22. Patch testing in lichenoid reactions of the mouth and oral lichen planus Todd P et al *Contact Dermatitis* 23 1990 300

23. The Possible Relationship Between Mercury from Dental Amalgam and Diseases . 1. Effects Within the Oral Cavity. Swartzendruber DE *Medical Hypotheses*; 41 (1) 31-34 1993

Mercury is released from dental amalgams, and therefore it is necessary to consider the biological and clinical consequences of such exposure. Intraorally, it would appear as though mercury can cause hypersensitivity/toxic reactions resulting in lichen planus lesions, and may play a major role in the pathogenesis of gingivitis, periodontitis and periodontal disease.

24. Oral Lichen Planus Lesions in Contact with Amalgam Fillings - A Clinical, Histologic, and Immunohistochemical Study. Ostman PO; Anneroth G; Skoglund A *Scandinavian Journal of Dental Research*; 102 (3) p172-179 1994

Fifty-one consecutive patients had clinically diagnosed oral lichen planus (OLP) lesions in total or partial contact with amalgam fillings. The clinical features of the OLP lesions were characterized and registered, and biopsies were obtained from each OLP lesion. Histologic and immunohistochemical studies were performed, as well as tests for allergy to dental materials. The clinical diagnosis of OLP corresponded to the World Health Organization (WHO) morphologic OLP criteria in 31 (61%) cases. The remaining lesions were histologically diagnosed as mild OLP in 11 (22%) or as benign oral keratosis in nine (17%) cases. The immunohistochemical examination showed a positive reaction to fibrinogen in the basement membrane zone (BMZ) in 10 (20%) patients and to complement C3 in one (2%) patient. No positive reactions in the BMZ were found for IgA, IgG, and IgM. In 17 (33%) patients, an allergic reaction to mercury was found, and

candidiasis was diagnosed in 13 (25%) patients. The true nature of OLP- like lesions in contact with amalgam fillings still remains to be explained. For that matter, we do not know whether OLP is one disease or a number of similar immunologic or other responses to various interacting stimuli. One such stimulus might be mercury from corroding amalgam fillings.

25. Resolution of lichen planus following removal of amalgam restorations in patients with proven allergy to mercury salts: a pilot study. *Br Dent J*, 1995 Feb 11 178(3): 108-12. Smart E R., Macleod R I., Lawrence C M.

Thirteen patients with symptomatic oral lichen planus had been shown by patch testing to be allergic to ammoniated mercuric chloride. Replacement of amalgam restorations in these patients effected an improvement in all but one case. In some cases the resolution of symptoms was dramatic following the replacement of one or two fillings. The authors feel that the removal of all amalgam fillings need not be necessary except in the most intractable case.

26. Oral lichenoid lesions caused by allergy to mercury in amalgam fillings see comments published erratum appears in *Contact Dermatitis* 1996 Jul;35(1): 70 Pang BK; Freeman S Comment in: *Contact Dermatitis* 1996 Jul;35(1):69 *Contact Dermatitis* 1995 Dec;33(6):423-7

Oral lichenoid lesions (OLL) or lichen-planus-like lesions are often idiopathic. Our aim was to determine whether OLL can be caused by allergy to mercury in amalgam fillings, and whether resolution of OLL occurs after replacement of amalgam with other dental fillings. Patients with only OLL (except for 1 case with cutaneous lichen planus) referred for patch testing during 1985-1994 to the Contact and Occupational Dermatitis Clinic of the Skin & Cancer Foundation, Darlinghurst, were reviewed. Patch tests were performed with 1% mercury, 1% ammoniated mercury, 0.1% thimerosal, 0.1% mercuric chloride, 0.05% phenylmercuric nitrate and an amalgam disc, using Finn Chambers occluded for 2 days, 19 patients (17 women and 2 men; age range: 28-72 years) had OLL in close contact with amalgam fillings and showed positive patch test reactions to mercury compounds, 16 out of 19 patients had their amalgam fillings replaced. In 13 patients, the OLL healed. 1 patient had marked improvement. 1 patient had no improvement and developed multiple oral squamous cell carcinoma. In conclusion, OLL can be caused by allergy to mercury in amalgam fillings. Replacement of amalgam with other dental fillings usually results in resolution of OLL and is recommended for cases with positive patch test reactions to mercury compounds.

27. 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 Koch P, Babmer FA *Contact Dermatitis*, 33: 5, 1995 Nov, 323- 8

We report 11 patients seen between 1991 and 1994 with oral lichenoid lesions (OLL). In 10 cases, there was contact with dental amalgam fillings, and in patient no. 10 with both amalgam restorations and a gold crown. The last patient had, in addition to her OLL, lichen planus of the skin and genital mucosa. In 5 cases, combined sensitization to mercury and other metal salts, particularly gold sodium thiosulfate (GST) and palladium chloride (PDC), was observed. In 10 patients the lesions considerably improved or totally cleared within 1 to 9 months of replacement of restoration materials. Histological examination of biopsies from the test sites of amalgam, mercuric chloride, GST and PDC, taken 10 or 17 days after application of patch tests, showed lichenoid changes in 7 patients with at least 1 of the allergens. At least 2 patients had inflammatory lesions of the oral mucosa related to both amalgam and gold restorations, combined sensitization to inorganic and organic mercury derivatives, GST and, in 1 case, PDC a "dental restoration metal intolerance syndrome" is proposed.

28. A case of systemic lichen planus with nail deformity due to mercury in dental amalgam. Higashi N; Sano S; Kume A *Skin Research*; 37 (2). 1995. 252- 256. (Jpn)

A 44-year-old Japanese man developed white plaques on the tongue and buccal mucosa, scaly erythemas on the lower legs, hyperkeratotic lesions on the soles and pitting with scales on the proximal a third portion of all toe nails a few months ago. Biopsy specimens were taken from the buccal mucosa, shin and sole. Histology of three specimens were compatible with lichen planus. He had metal denture and plugged carious tooth with amalgam. Patch tests with the dental metal series showed positive reaction to mercuric chloride at 2, 3 and 7 days. The white plaques on the tongue and buccal mucosa, scaly erythema on the lower legs, hyperkeratotic lesions on the soles and pitting and scaling on the toe nails had become less distinct during 3 months after removing amalgam of his carious tooth. On the basis of above mentioned findings, we diagnosed as lichen planus due to mercury allergy. It seemed that nail deformity was also caused by allergic reaction due to mercury allergy.

29. Mercury-specific lymphocytes: An indication of mercury allergy in man. Stejskal VDM; Forsbeck M; Cederbrant KE; Asteman O *Journal of Clinical Immunology*; 16 (1) p31-40 JAN 1996

In this study, 18 patients with oral lichen planus (OLP), adjacent to amalgam fillings, were tested in vitro with an optimized lymphocyte proliferation test, MELISA (memory lymphocyte immunostimulation assay) and with a patch test. Twenty subjects with amalgam fillings but without oral discomfort and 12 amalgam-free subjects served as controls. The results show that patients with OLP have significantly higher lymphocyte reactivity to inorganic mercury, a corrosion product of amalgam, compared to control groups. Removal of amalgam fillings resulted in the disappearance of oral mucosal changes, thus indicating a causal relationship. Positive responses to phenylmercury (phenyl-Hg), a bactericidal agent in rootfillings and in pharmaceutical preparations, were also noted in the oral lichen group but not in the control groups. Thus, low- grade chronic exposure to mercury may induce a state of systemic sensitization as verified by Hg- specific lymphocyte reactivity in vitro.

30. The relevance and effect of amalgam replacement in subjects with oral lichenoid reactions. Ibbotson SH; Speight EL; Macleod RI; Smart ER; Lawrence CM *British Journal of Dermatology*; 134 (3) p420-423 MAR 1996

In this study we examined the prevalence of mercury hypersensitivity in patients with oral lichenoid reactions (OLR) and the effect of amalgam replacement in subjects with amalgams adjacent to OLR irrespective of their mercury sensitivity status. One hundred and ninety-seven patients with oral problems were examined: 109 with OLR, 22 with oral and generalized lichen planus, and 66 with other oral diagnoses. including aphthous ulcers and orofacial granulomatosis. Nineteen per cent of patients with OLR reacted to mercury on patch testing, significantly more than in those with generalized lichen planus (0%) and in those with other oral diagnoses (3%). Twenty-two patients with OLR and adjacent amalgams had amalgam replacement and, in 16 of 17 mercury-positive subjects and three of four mercury-negative subjects, the OLR resolved after amalgam removal. In conclusion, we found a significantly increased prevalence of mercury hypersensitivity in patients with localized OLR in comparison to subjects with other oral problems. Amalgam replacement resulted in resolution of OLR in the majority of patients with amalgams adjacent to OLR irrespective of their mercury sensitivity status.

31. Amalgam-associated oral lichenoid reactions. Clinical and histologic changes after removal of amalgam fillings. Ostman PO, Anneroth G; Skoglund A . Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996 81(4) 459-465

OBJECTIVE AND STUDY DESIGN. Forty-nine consecutive patients with clinically diagnosed oral lichenoid reactions in contact with amalgam fillings were studied clinically and histologically. The long-term effect of replacement of these fillings was also examined. RESULTS. Seventeen (35 %) patients showed positive reactions to mercury at the epicutaneous patch test that was carried out before treatment. After treatment, total regression of the lesions was found clinically in 33 (69%) and histologically in 26 (55%) patients. Most of the remaining lesions changed clinically and histologically to a less pronounced tissue reaction. Lesions in direct contact with amalgam fillings (group I) showed significantly better healing results than lesions that exceeded the contact area (group II). No difference in healing capacity was noted in the two groups between patients with positive patch reactions to mercury compared with those with negative reactions. Lesions that histologically were classified as benign oral keratosis showed a similar healing pattern as those classified as oral lichen planus. CONCLUSION. In group I all lesions changed histologically and clinically to a normal mucosa or to a less affected tissue reaction. In group II this change was less pronounced, which suggests that the fillings themselves were not the only factor involved in the cause of these lesions. The results suggest that various etiologic factors are involved in lichenoid reactions and that the effect of removal of amalgam fillings cannot be predicted by epicutaneous patch testing and biopsies.

32. Three cases of linear lichen planus caused by dental metal compounds. Sasaki G; Yokozeki H; Katayama I; Nishioka K J Dermatol 1996 Dec;23(12): 890-2

Three cases of linear lichen planus on the lower extremities unaccompanied by mucous lesions are described. Dental metal compounds were thought to be the precipitating factor in all cases. Skin lesions did not respond to topical steroid ointment or antihistamines. Two cases showed a positive patch test reaction to gold (HAuCl₄) and a positive lymphocyte stimulation test to gold compound (Gold sodium thiomalate). One case showed a positive patch test reaction to mercury (HgCl₂), but a negative lymphocyte stimulation test. Suspected metal compounds were demonstrated in their dental materials. Removal of gold materials in one case gradually improved the lesions within 6 months with a transient erythematous swelling of the face shortly after removal of the metal. Both of these cases responded to oral disodium chromoglycate therapy. These results suggest that metal compound specific T cells might be responsible for the development of linear lichen planus.

33. Bratel J, Hakeberg M, Jontell M: Three cases of linear lichen planus caused by dental metal compounds. Sasaki G; Yokozeki H; Katayama I; Nishioka K J Dermatol 1996 Dec;23(12): 890-2 (CL100) Journal of Dentistry. Jan- Mar 1996; 24(1-2):41-45

Effect of Replacement of Dental Amalgam on Oral Lichenoid Reactions.

Objectives: The objectives of this study were to investigate (i) healing of oral lichenoid reactions (OLR) following the selective replacement of restorations of dental amalgam, (ii) whether there were differences in healing between contact lesions (CL) and oral lichen planus (OLP), and (iii) whether there was a difference in healing potential when different

materials were selected as a substitute for dental amalgam. Methods:

Patients included in the study presented with OLR confined to areas of the oral mucosa in close contact with amalgam restorations (CL; n = 142) or with OLR which involved other parts of the oral mucosa as well (OLP; n = 19). After examination, restorations of dental amalgam which were in contact with OLR in both patient groups were replaced. The effect of replacement was evaluated at a follow up after 6-12 months. Results: In the CL group, the lesions showed a

considerable improvement or had totally disappeared in 95% of the patients after replacement of the restorations of dental amalgam (n = 474). This effect was paralleled by a disappearance of symptoms, in contrast to patients with persisting CL (5%) who did not report any significant improvement. The healing response was not found to correlate with age, gender, smoking habits, subjective dryness of the mouth or current medication. However, the healing effect in patients who received gold crowns was superior compared to that of patients treated with metal ceramic crowns (MC; $P < 0.05$). In the OLP

group (n = 19), 63% of the patients with amalgam associated erosive and atrophic lesions showed an improvement following selective replacement. OLP lesions in sites not in contact with amalgams were not affected. Most of the patients (53%) with OLP reported symptoms also after replacement.

Conclusion: From these data it can be concluded that the vast majority of OL resolve following selective replacement of restorations of dental amalgam, provided that a correct clinical diagnosis is established. It is also noteworthy that MC crowns did not facilitate healing of CL to the same extent as gold crowns.

34. Oral mucosal diseases investigated by patch testing with a dental screening series. Alanko K; Kanerva L; Jolanki R; Kannas L Estlander T *Contact Dermatitis* 1996 Apr;34(4):263-7

The role of contact allergies in oral mucosal diseases was studied. The subjects were 24 patients out of 479 tested, who had oral mucosal symptoms and positive patch test reactions in a dental series during 1987-1994 at the Department of Dermatology, Helsinki University Hospital. The clinical diagnoses were oral lichen planus (LPO, 13 patients), leukoplakia (2), glossodynia, i.e., 'burning mouth syndrome' (4), stomatitis (3) and recurrent angioedema (2). Only 1 patient had symptoms in relation to dental care. All but 2 patients had allergic reactions to mercury (Hg) (12 patients), gold sodium thiosulfate (Au) (13 patients) or both. A clinical connection between oral symptoms and contact allergy was seen in 10 patients. 9 patients (7 LPO, 2 leukoplakia) had Hg allergy. In these cases, the oral lesions disappeared after the amalgam fillings had been removed. 1 patient had recurrent stomatitis and perioral eczema after dental care and 2,2-bis(4-(2-hydroxy-3-methacryloxypropoxy)phenyl)propane (BIS-GMA) allergy. Her symptoms were caused by drilling of acrylic fillings. In addition, a connection between localized stomatitis and contact allergy was considered probable in 2 cases. 1 patient had stomatitis from contact with an orthodontic device and nickel allergy. The other had stomatitis from contact with a dental gold crown and gold allergy. No clinical connection was found between gold allergy and the oral symptoms of other patients.

35. The frequency of different T-cell receptor V-families in oral lichen planus and lichenoid contact lesions: An immunohistochemical study. Bratel J; Dahlgren U; Mattsson CS; Jontell M *Journal of Oral Pathology & Medicine*; 27 (9) p415-419 OCT 1998

Oral lichen planus (OLP) and lichenoid contact lesions (CL) are recognized as different pathological conditions of the oral mucosa. Cutaneous delayed-type hypersensitivity to mercury displayed by patients with CL but not by OLP patients supports the concept of different etiological mechanisms behind the two lesions. It is not possible to reveal this difference by histopathological assessments, and differences in clinical appearances are at present the only way to discriminate between the two conditions. It has recently been observed that T cells in OLP lesions express T-cell receptors (TCR) belonging to the V beta 3 family in a higher frequency than expected from a random distribution, suggesting an involvement of superantigens as an etiologic factor behind this condition. In an effort to discriminate more clearly between OLP and CL, and to provide clues to the etiological mechanisms behind the two lesions, the TCR V- family distributions in the inflammatory infiltrates of OLP and CL were compared. Biopsies were taken

from 10 patients with manifest OLP and 10 patients with CL. Frozen sections were incubated with antibodies against TCR V beta 3, V alpha 2 and V beta 5a utilizing a standard immunoperoxidase technique. The frequency of V3.1 (clone 8F10) was calculated as 7%, and for V alpha 2 less than 3%, and the results did not reveal any differences between OLP and CL regarding the frequencies of T- cell V-families. Thus, it was not possible to discriminate between OLP and CL by immunohistochemistry staining for different V families.

36. Metals and Kidney Autoimmunity. Bigazzi PE *Environ Health Perspect* 1999 Oct;107(Suppl 5):753-765

The causes of autoimmune responses leading to human kidney pathology remain unknown. However, environmental agents such as microorganisms and/or xenobiotics are good candidates for that role. Metals, either present in the environment or administered for therapeutic reasons, are prototypical xenobiotics that cause decreases or enhancements of immune responses. In particular, exposure to gold and mercury may result in autoimmune responses to various self-antigens as well as autoimmune disease of the kidney and other tissues. Gold compounds, currently used in the treatment of patients with progressive polyarticular rheumatoid arthritis, can cause a nephrotic syndrome. Similarly, an immune-mediated membranous nephropathy frequently occurred when drugs containing mercury were commonly used. Recent epidemiologic studies have shown that occupational exposure to mercury does not usually result in autoimmunity. However, mercury induces antinuclear antibodies, scleroderma-like disease, lichen planus, or membranous nephropathy in some individuals. Laboratory investigations have confirmed that the administration of gold or mercury to experimental animals leads to autoimmune disease quite similar to that observed in human subjects exposed to these metals. In addition, studies of inbred mice and rats have revealed that a few strains are susceptible to the autoimmune effects of gold and mercury, whereas the majority of inbred strains are resistant. These findings have emphasized the importance of genetic (immunogenetic and pharmacogenetic) factors in the induction of metal-associated autoimmunity. (italic) *In vitro* (italic) and (italic) *in vivo* (italic) research of autoimmune disease caused by mercury and gold has already yielded valuable information and answered a number of important questions. At the same time it has raised new issues about possible immunostimulatory or immunosuppressive mechanisms of xenobiotic activity. Thus it is evident that investigations of metal-induced renal autoimmunity have the potential to produce new knowledge with relevance to autoimmune disease caused by xenobiotics in general as well as to idiopathic autoimmunity.

37. *In vitro* lymphoproliferative assays with HgCl₂ cannot identify patients with systemic symptoms attributed to dental amalgam. Cederbrant K; Gunnarsson LG; Hultman P; Norda R Tibbling-Grahn L *J Dent Res* 1999 Aug;78(8):1450-8

Dental amalgam is suspected, by some exposed individuals, to cause various systemic psychological, sensory, and neurological symptoms. Since not all amalgam-bearers experience such reactions, an individual characteristic--for example, a susceptible immune system--might explain these conditions. *In vitro* lymphocyte proliferation is a valuable tool in the diagnosis of allergy. With HgCl₂ as the antigen, however, the test is hampered, because Hg²⁺ can cause unspecific lymphocyte proliferation, optimal at 1.4 to 9.5 micrograms HgCl₂/mL. Recently, the use of suboptimal HgCl₂ concentrations (< or = 0.5 microgram/mL) has been suggested to circumvent these problems. The main aim of this study was to investigate whether patients with systemic symptoms alleged to result from the presence of dental amalgam differ from healthy controls, with reference to *in vitro* lymphoproliferative responses to HgCl₂ < or = 0.5 microgram/mL. Three different test protocols-- lymphocyte transformation test (LTT) in micro- and macro-cultures, and the memory lymphocyte immunostimulation assay (MELISA)--were

used. Other immune parameters--such as a standard patch test for dental materials, the number of T- and B-lymphocytes, monocytes, granulocytes, and NK cells in peripheral blood, allergic symptoms, and predisposition--were also investigated. Twenty-three amalgam patients, 30 healthy blood donors with amalgam, ten healthy subjects without amalgam, and nine patients with oral lichen planus (OLP) adjacent to dental amalgam and a positive patch test to Hg₀ were tested. None of the investigated immune parameters revealed any significant differences between amalgam patients and controls. The sensitivity of in vitro lymphocyte proliferation ranged from 33 to 67%, with the OLP patients as a positive control group, and the specificity from 0 to 70% for healthy controls with a negative patch test to Hg₀. Thus, despite the use of HgCl₂ < or = 0.5 microgram/mL, a high frequency of positive results was obtained among healthy subjects with or without dental amalgam. Consequently, in vitro lymphocyte proliferation with HgCl₂ cannot be used as an objective marker for mercury allergy in dental amalgam-bearers.

38. Oral lichen planus versus oral lichenoid eruption as a manifestation of contact allergy. Pecegueiro M; Sachse MF; Amaro J; Farinha P Fonseca I *Contact Dermatitis* 1999 Jun;40(6):333-4
39. No evidence for specific in vitro lymphocyte reactivity to HgCl₂ in patients with dental amalgam-related contact lesions Loftenius A; Skoglund A; Ekstrand J; Hovmark A Moller E *J Oral Pathol Med* 1999 Sep;28(8):364-70

Blood lymphocytes from 20 patients with oral contact lesions to dental amalgam and 10 healthy individuals were analyzed for HgCl₂-induced proliferation in vitro, using both a modified assay and a conventional assay. The release of interferon-gamma (IFN- gamma) was measured in cell supernatants. Six patients displayed positive reactions in patch tests to mercuric compounds. No significant differences were recorded in HgCl₂- induced proliferation in cells from patients and controls, since only few in the whole material responded to submitogenic concentrations. IFN-gamma was detectable in cell supernatants from some patients but also from controls and is not predictive of mercury allergy. Neither the phenotypes of peripheral lymphocyte subsets, the frequency of circulating cells expressing the interleukin-2 (IL- 2) receptor, spontaneous lymphocyte proliferation nor concentrations of serum interleukin-6 differed between patient and control samples. In contrast to what has been claimed before, we did not find any evidence for specific in vitro lymphocyte reactivity in patients with oral contact lesions.

40. Oral lesions and symptoms related to metals used in dental restorations: A clinical, allergological, and histologic study. Koch P; Bahmer FA *J Am Acad Dermatol* 1999 Sep;41(3):422-430

BACKGROUND: Allergy to mercury as a cause of oral lichenoid lesions (OLL) remains controversial. Some authors reported high frequency of sensitization to mercury and beneficial effect from removal of amalgam fillings in such patients, whereas others state that this procedure affects favorably all OLL, whether patients are sensitized to inorganic mercury or not. **OBJECTIVE:** Our purpose was to determine the frequency of sensitization to metal salts in 194 patients (patients with OLL partly adjacent to amalgam fillings: 19, oral lichen planus (OLP) without close contact to amalgam: 42, other oral diseases: 28, oral complaints: 46, control group: 59). We further studied the histologic changes of biopsy specimens from positive patch tests to metal salts, and investigated the effect of removal of amalgam in OLL, to clarify whether it is possible to identify patients who will benefit from this procedure. **METHODS:** Patch testing was performed with the German standard series, a dental prosthesis series, and a metal salt series including gold, mercury, and palladium salts as well as other salts of metals used in dental restorations. Late readings (10 and 17 days after application of the patch tests) were performed in all patients. **RESULTS:** Of 19 patients with OLL adjacent to amalgam fillings, 15 (78.9%) were sensitized to inorganic mercury (INM), significantly more than those with OLL not adjacent to amalgam, other

oral diseases or complaints, and the control group. In 5 of 15 (33.3%) of the patients with OLL, a positive patch test to INM was observed only at D10 or D17. Amalgam was removed in 18 patients with OLL (sensitization to INM: 15), and in 11 patients with OLP (sensitization to INM: 2). After removal, the lesions of 13 of 15 of the INM-sensitized patients with OLL (86.7%) and 2 with OLP healed or improved significantly, but this was not observed with the INM negative patients. Frequency of sensitization to gold sodium thiosulfate (GST) and palladium chloride 1% pet (PDC) was high in all groups. This was partly because readings were performed late. Lesions of 2 patients with allergic contact stomatitis caused by gold and 1 caused by palladium healed completely after removal of these restorations. Histologically, lichenoid changes were observed in 14 of 36 biopsy specimens of positive patch tests from INM (9/21), GST (2/10), and PDC (3/5) in all patient groups, mainly in persistent patch tests at D10 or D17. This was not observed in 12 biopsy specimens taken from persistent patch tests from other substances, including nickel sulfate. CONCLUSION: Our results suggest that sensitization to mercury is an important cause of OLL, whether all lesions or only a part of them are adjacent to amalgam fillings. Sensitization to GST may reflect true gold allergy and should be considered as a cause of oral diseases in some patients. Sensitization to PDC is frequent but has yet only little clinical relevance. Patch tests may be positive only at D10 or D17. This suggests the importance of additional readings of GST, PDC, and mercury salts at this time.

41. Contact hypersensitivity to mercury in amalgam restorations may mimic oral lichen planus Camisa C; Taylor JS; Bernat JR Jr; Helm TN *Cutis* 1999 Mar;63(3):189-92

Oral lichenoid lesions caused by hypersensitivity to mercury in amalgam fillings may mimic oral lichen planus on clinical and histologic examination. A positive patch test reaction to more than one mercurial allergen increases confidence in the diagnosis and justifies the removal and replacement of all amalgam fillings with those made of other materials. A complete remission may be expected about 3 months after the last amalgam filling is removed.

42. Robinson NA Lichenoid tissue reactions of the oral mucosa. *Singapore Dent J* (2000 Dec) 23(1 Suppl):56-63

The lichenoid tissue reaction (LTR) is characterised by epidermal basal cell damage and a variable subepithelial inflammatory infiltrate. There is a range of mucosal lesions exhibiting the LTR, chief of which is Oral Lichen Planus (OLP). The other oral lichenoid lesions resemble OLP clinically and histologically and at times it can be difficult to differentiate between the lesions. The important oral lichenoid lesions are reviewed in this paper.

43. Schuurs AH van Joost T [Oral lichen planus, amalgam and other restorative materials]
44. Orale lichen planus, amalgaam en andere vulmaterialen. *Ned Tijdschr Tandheelkd* (2000 May) 107(5):198-202

Mucosal lesions in the oral cavity, identical to oral lichen planus (OLP), as a consequence of contact with in particular dental silver amalgam may be due to an allergic reaction to mercury or, possibly, a toxic effect on the oral mucosa. Substitution of amalgam preferably by gold--unless sensitisation to gold exists--often results in remission, which sustains a pathogenic role of amalgam in OLP. Substitution of amalgam should be considered if the mucosal lesions correspond topographically to the restorations and epicutaneous patch testing results in a positive reaction on mercury.

45. Thornhill MH Pemberton MN Simmons RK Theaker ED Amalgam-contact hypersensitivity lesions and oral lichen planus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* (2003 Mar) 95(3):291-9

OBJECTIVE: The purpose of this study was to investigate the relationship between amalgam restorations and oral lichen planus. STUDY DESIGN: Eighty-one patients with oral lichenoid lesions were characterized clinically and skin patch tested for amalgam or mercury hypersensitivity. Thirty-three of these patients had amalgam fillings in contact with oral lesions replaced and were followed to determine the outcome. RESULTS: Clinically, 2 patient groups were identified: (1) 30 patients with probable amalgam-contact hypersensitivity lesions (ACHLs) and (2) 51 patients with oral lichen planus (OLP) but no clear relationship with amalgam. Seventy percent of ACHL cases were patch test positive for amalgam or mercury compared with only 3.9% of OLP cases ($P < .0001$). Amalgam replacement resulted in lesion improvement in 93% of ACHL cases. No such improvement was observed in the OLP cases treated ($P < .001$). CONCLUSION: OLP is a heterogeneous condition within which an ACHL subgroup can be identified. ACHLs, but not other OLP lesions, respond favorably to amalgam replacement. A strong clinical association between lesions and amalgam restorations plus a positive patch test result was a good predictor of lesion improvement on amalgam replacement.

46. Magnin P Stuck M Meier E Kagi M Lussi A Braathen L Buser D [Amalgam-associated lichenoid lesions of the oral mucosa: filling replacement therapy] *Schweiz Monatsschr Zahnmed* (2003) 113(2):143-50
47. Greenberg MS Form expert panels to develop diagnosis and management protocols. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* (2003 Mar) 95(3):265
48. Wong L Freeman S Oral lichenoid lesions (OLL) and mercury in amalgam fillings. *Contact Dermatitis* (2003 Feb) 48(2):74-9

84 patients with oral lichenoid lesions (OLL) were seen in the contact dermatitis clinic. All these patients had reticulate, lacy, plaque-like or erosive lichenoid changes adjacent to amalgam fillings. Patch testing to metallic mercury, 0.1% thimerosal, 1% ammoniated mercury, 0.1% mercuric chloride, and in some cases 0.05% phenylmercuric nitrate and amalgam discs was undertaken. 33 (39%) patients had positive patch test findings. 30/33 patch test positive patients had replacement of their amalgam fillings, with 28 (87%) patients experiencing improvement of symptoms and signs within 3 months. This confirms that mercury allergy is a factor in the pathogenesis of OLL in some cases. In cases where patch test negative patients improve with amalgam replacement, mercury may be acting as an irritant in the pathogenesis of OLL.

49. Martin MD Broughton S Drangsholt M Oral lichen planus and dental materials: a case-control study. *Contact Dermatitis* (2003 Jun) 48(6):331-6

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.

50. Athavale PN Shum KW Yeoman CM Gawkrödger DJ Oral lichenoid lesions and contact allergy to dental mercury and gold. *Contact Dermatitis* (2003 Nov) 49(5):264-5
51. Little MC Griffiths CE Watson RE Pemberton MN Thornhill MH Oral mucosal keratinocytes express RANTES and ICAM-1, but not interleukin-8, in oral lichen planus and oral lichenoid reactions induced by amalgam fillings. *Clin Exp Dermatol* (2003 Jan) 28(1):64-9

Oral lichen planus (OLP) is a chronic inflammatory disease of the oral mucosa characterized by a band-like accumulation of lymphocytes in the connective tissue adjacent to the basement membrane as well as intraepithelially. Amalgam fillings can induce oral lichenoid reactions (OLR) that are similar to OLP. The adhesion molecule ICAM-1 and the chemokines interleukin-8 and RANTES all play central roles in leucocyte trafficking. The aim of this study was to investigate the possible role of these molecules in the migration of leucocytes into the oral mucosa in OLP and OLR. Standard immunoperoxidase techniques were used to visualize the expression of ICAM-1, RANTES and interleukin-8 in frozen biopsy sections. ICAM-1 was expressed by endothelial cells, but not by keratinocytes, in normal oral mucosa. ICAM-1 was expressed by keratinocytes in 11 of 12 biopsies of OLP and in six of seven biopsies of OLR. In all of these cases ICAM-1 was also expressed by endothelial cells and leucocytes. Although not present in normal oral mucosa, RANTES was expressed by keratinocytes in 21 of 24 biopsies of OLP and in seven of seven cases of OLR. Interleukin-8 was not detected in any of the samples. The expression of ICAM-1 and RANTES by epithelial keratinocytes in the oral mucosa in OLP and OLR could be a key inflammatory mechanism in these diseases.

52. Dunsche A Kastel I Terheyden H Springer IN Christophers E Brasch J Oral lichenoid reactions associated with amalgam: improvement after amalgam removal. *Br J Dermatol* (2003 Jan) 148(1):70-6

BACKGROUND: The pathogenetic relationship between oral lichenoid reactions (OLR) and dental amalgam fillings is still a matter of controversy. **OBJECTIVES:** To determine the diagnostic value of patch tests with amalgam and inorganic mercury (INM) and the effect of amalgam removal in OLR associated with amalgam fillings. **METHODS:** In 134 consecutive patients 467 OLR were classified according to clinical criteria. One hundred and fifty-nine biopsies from OLR lesions were histologically diagnosed according to the World Health Organization criteria for oral lichen planus (OLP) and compared with 47 OLP lesions from edentulous patients without amalgam exposure. One hundred and nineteen patients were patch tested with an amalgam series. In 105 patients (357 of 467 lesions) the amalgam fillings were removed regardless of the patch test results and OLR were re-examined within a follow-up period of about 3 years. Twenty-nine patients refused amalgam removal and were taken as a control group. **RESULTS:** Eleven patients with OLR (8.2%) had skin lesions of lichen planus (LP). Histologically, the lesions in the OLR group could not be distinguished from those seen in the OLP group. Thirty-three patients (27.7%) showed a positive patch test to INM or amalgam. Amalgam removal led to benefit in 102 of 105 patients (97.1%), of whom 31 (29.5%) were cured completely. Of 357 lesions, 213 (59.7%) cleared after removal of amalgam, whereas 65 (18.2%) did not improve. In the control group without amalgam removal (n = 29) only two patients (6.9%) showed an improvement (P < 0.05). Amalgam removal had the strongest impact on lesions of the tongue compared with lesions at

other sites ($P < 0.05$), but had very little impact on intraoral lesions in patients with cutaneous LP compared with patients without cutaneous lesions ($P < 0.05$). Patients with a positive patch test reaction to amalgam showed complete healing more frequently than the amalgam-negative group ($P < 0.05$). After an initial cure following amalgam removal, 13 lesions (3.6%) in eight patients (7.6%) recurred after a mean of 14.6 months. CONCLUSIONS: Of all patients with OLR associated with dental amalgam fillings, 97.1% benefited from amalgam removal regardless of patch test results with amalgam or INM. We suggest that the removal of amalgam fillings can be recommended in all patients with symptomatic OLR associated with amalgam fillings if no cutaneous LP is present.

53. Dunsche A Frank MP Luttges J Acil Y Brasch J Christophers E Springer IN Lichenoid reactions of murine mucosa associated with amalgam. *Br J Dermatol* (2003 Apr) 148(4):741-8

BACKGROUND: In 97% of all patients with oral lichenoid reactions (OLR) associated with dental amalgam a removal of the fillings leads to a decline of the lesions, as a minimum. OBJECTIVES: The aim of this study was to determine if contact allergic or local toxic effects or both may contribute to OLR using an animal model with mercury-sensitive and non-sensitive rats. METHODS: Twenty Brown Norway rats, which have a genetic predisposition for an autoimmune syndrome after exposure to mercury and 20 Lewis rats, not mercury sensitive, were treated as follows: 10 animals of each group were sensitized with a low dose of mercuric chloride. Half of all animals received local exposure of the right buccal mucosa to amalgam (left: control), the others to amalgam alloy free of mercury. All rats were patch tested with an amalgam series. RESULTS: After 20 days of exposure 96% of all animals showed white mucosal lesions restricted to the contact zone of the alloy on the treated side, but only up to 25% had a positive patch test reaction to amalgam or inorganic mercury (INM). The lesions showed no relation to species, alloy, sensitization or patch test reaction. CONCLUSIONS: While allergic mechanisms may contribute to mucosal contact lesions in Brown Norway rats, this is less probable in Lewis rats. Mercury in general appears to be irrelevant in the development of ORL in this study. If this holds true for humans as well, patch testing with an amalgam series may be helpful in a minor fraction of all patients with OLR.

54. Kato Y Hayakawa R Shiraki R Ozeki K A case of lichen planus caused by mercury allergy. *Br J Dermatol* (2003 Jun) 148(6):1268-9
55. Lopez-Jornet P Camacho-Alonso F Gomez-Garcia F Bermejo Fenoll A The clinicopathological characteristics of oral lichen planus and its relationship with dental materials. *Contact Dermatitis* (2004 Oct) 51(4):210-1

The objective of this work was to carry out a clinicopathological study to ascertain whether clinical and histopathologic differences existed between oral lichen planus OLP patients with and without metal restorations. The predominant clinical form in both groups was reticular white, with no statistically significant differences between the forms associated or not with metal. The histological variables showed no statistically significant differences between the groups.

56. Segura-Egea JJ Bullon-Fernandez P Lichenoid reaction associated to amalgam restoration. *Med Oral Patol Oral Cir Bucal* (2004 Nov-Dec) 9(5):423-4; 421-3

Hypersensitivity to mercury associated with amalgam restorations may occur and present in one of two different ways. Most commonly it presents as an oral lichenoid reaction affecting oral mucosa in direct contact with an amalgam restoration and represents a delayed, type IV, cell mediated immune response to mercury or one of the other constituents of the dental amalgam.

We report a case of oral lichenoid reaction associated to amalgam restoration. A 38 year-old woman presented a caries lesion of tooth #37. A Class I preparation was performed and filled with amalgam. After 19 months, intra-oral examination revealed atrophic lesion, lightly erythematous, affecting the left buccal mucosa. The lesion contacted directly with the amalgam restoration in the lower first molar. The right buccal mucosa was normal. Her medical history was unremarkable, she was taking no medication and had no known allergies. However, the patient had felt certain rare sensation in that zone when eating sharp meals. Biopsy showed histological changes compatible with oral lichen planus. The patient decided not to change again the restoration, because she did not have important annoyances and she did not wish to be treated again. Other restorations were performed with composite resins, and no reaction was evidenced in the mucosa.

57. Issa Y Brunton PA Glenny AM Duxbury AJ Healing of oral lichenoid lesions after replacing amalgam restorations: a systematic review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* (2004 Nov) 98(5):553-65

OBJECTIVE: We sought to systematically review the literature related to oral lichenoid lesions (OLLs) and amalgam restorations. **STUDY DESIGN:** Cohort and case-controlled studies (no randomized controlled trials or controlled clinical trials available) were reviewed with respect to inclusion criteria and data on patients with OLLs, treatment interventions, and the measurement of outcomes. **RESULTS:** Fourteen cohort and 5 case-controlled trials met the criteria. The study population consisted of 1158 patients (27% male and 73% female; age range, 23-79 years). From 16% to 91% of patients had positive patch test results for at least 1 mercury compound. Of 1158 patients, 636 had to have their restorations replaced. The follow-up period ranged from 2 months to 9 1/2 years. Complete healing ranged from 37.5% to 100%. The greatest improvements were seen in lesions in close contact with amalgam. **CONCLUSIONS:** Protocols must be standardized to obtain valid results. The replacement of amalgam restorations can result in the resolution or improvement of OLLs. Patch testing seems to be of limited value. The topographic relationship between an OLL and an amalgam restoration is a useful-- but not conclusive--marker.

58. Laeijendecker R Dekker SK Burger PM Mulder PG Van Joost T Neumann MH Oral lichen planus and allergy to dental amalgam restorations. *Arch Dermatol* (2004 Dec) 140(12):1434-8

OBJECTIVES: To determine contact allergies in patients with oral lichen planus and to monitor the effect of partial or complete replacement of amalgam fillings following a positive patch test reaction to ammoniated mercury, metallic mercury, or amalgam. **DESIGN:** In group A (20 patients), the oral lesions were confined to areas in close contact with amalgam fillings. In group B (20 patients), the lesions extended 1 cm beyond the area of contact with amalgam fillings. In group C (20 patients), the oral lesions had no topographic relationship with amalgam fillings. Partial or complete replacement of amalgam fillings was recommended if there was a positive patch test reaction to ammoniated mercury, metallic mercury, or amalgam. Control group D (20 patients) had signs of allergic contact dermatitis. **RESULTS:** Amalgam fillings were replaced in 13 patients of group A, with significant improvement. Dental amalgam was replaced in 8 patients of group B, with significant improvement. In group C, amalgam replacement in 2 patients resulted in improvement in 1 patient. These results were evaluated after 3 months. No positive patch test reactions to mercury compounds were found in patients with concomitant cutaneous lichen planus and in group D. **CONCLUSIONS:** Contact allergy to mercury compounds is important in the pathogenesis of oral lichen planus, especially if there is close contact with amalgam fillings and if no concomitant cutaneous lichen planus is present. In cases of positive patch test

reactions to mercury compounds, partial or complete replacement of amalgam fillings will lead to a significant improvement in nearly all patients.

59. Rogers RS Bruce AJ Lichenoid contact stomatitis: is inorganic mercury the culprit? Arch Dermatol (2004 Dec) 140(12):1524-5
60. Scott A Egnér W Gawkrödger DJ Hatton PV Sherriff M van Noort R Yeoman C Grummitt J The national survey of adverse reactions to dental materials in the UK: a preliminary study by the UK Adverse Reactions Reporting Project. Br Dent J (2004 Apr 24) 196(8):471-7; discussion 465

OBJECTIVE: Dental treatment involves the use of a wide range of materials. Many of the dental materials or their components pose a potential risk to the patient and member of the dental team. Pre-market biocompatibility testing cannot guarantee absolute safety, making monitoring of materials likely to cause an adverse reaction essential. The prevalence of adverse reactions to dental materials amongst dental patients and staff has not been systematically monitored in the UK. This project aims to develop a systematic approach to the evaluation and monitoring of the extent and severity of adverse reactions to dental materials in the UK. **METHOD:** Through the distribution of reporting forms to dental surgeries and laboratories in the UK, the ARRPP has received 1,075 complete reports relating to adverse reactions seen or experienced by dental staff and patients. **RESULTS:** The main findings were that different materials cause adverse reactions to different groups of people. The largest proportion of patient related adverse reactions were reported to be due to metals (n = 175). These were mainly amalgam associated oral lichenoid reactions (n = 124). Dental technicians reported acrylic resin as the causal factor of hand dermatitis in 61% (44 out of a total 72) of cases reported. Finally, dental surgery staff reported gloves as causing hand dermatitis in 75% of cases (398 out of a total 531). **CONCLUSIONS:** Different dental materials affect different person groups depending on their exposure to the material. Dental staff are most at risk from an adverse reaction to latex gloves, whereas most reported reactions for patients were due to metals. For dental technicians the biggest danger of an adverse reaction was from acrylic resins. There is a need to continue to raise the awareness among dental professionals of the existence of the Adverse Reactions Reporting Project so as to overcome problems of under-reporting.

61. Issa Y Duxbury AJ Macfarlane TV Brunton PA Oral lichenoid lesions related to dental restorative materials. Br Dent J (2005 Mar 26) 198(6):361-6; discussion 549; quiz 372

OBJECTIVES: To determine the effectiveness of replacing restorations considered to be the cause of an oral lichenoid lesion (oral lichenoid reaction)(OLL). **DESIGN:** Clinical intervention and nine-month follow up. **SETTING:** The study was carried out in the University Dental Hospital of Manchester, 1998-2002. **SUBJECTS AND METHODS:** A total of 51 patients, mean age 53 (SD 13) years, who had oral lesions or symptoms suspected to be related to their dental restorations were investigated. Baseline patch tests for a series of dental materials, biopsies and photographs were undertaken. Thirty-nine out of 51 (76%) of patients had their restorations replaced. **RESULTS:** The clinical manifestations of OLL were variable; the majority of OLL were found to be in the molar and retro molar area of the buccal mucosa and the tongue. Twenty-seven (53%) patients had positive patch test reactions to at least one material, 24 of them for one or more mercury compound. After a mean follow up period of nine months, lesions adjacent to replaced restorations completely healed in 16 (42%) patients (10 positive and 6 negative patch tests). Improvement in signs and symptoms were found in 18 (47%) patients (11 positive and 7 negative patch tests). **CONCLUSION:** OLLs may be elicited by some dental restorations. Replacing restorations adjacent to these lesions is associated with healing in the

majority of cases particularly when lesions are in close contact with restorations. A patch test seems to be of limited benefit as a predictor of such reactions.

62. Pigatto PD Guzzi G Oral lichenoid lesions: more than mercury. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* (2005 Oct) 100(4):398-400
63. Cedrola S Guzzi G Crippa R Bouquet JE La Porta CA Amalgam fillings associated with increased matrix metalloproteinase 9 levels in human saliva. *J Eur Acad Dermatol Venereol* (2005 Jul) 19(4):509-10
64. Thornhill MH Simmons RK Pemberton MN Theaker ED Patch test value. *Br Dent J* (2005 Oct 8) 199(7):445
65. Pigatto PD Guzzi G Severi G Oral lichen planus: mercury and its kin. *Arch Dermatol* (2005 Nov) 141(11):1472-3; author reply 1473
66. Thornhill MH Sankar V Xu XJ Barrett AW High AS Odell EW Speight PM Farthing PM The role of histopathological characteristics in distinguishing amalgam-associated oral lichenoid reactions and oral lichen planus. *J Oral Pathol Med* (2006 Apr) 35(4):233-40

OBJECTIVES: To identify histological features that distinguish amalgam-associated oral lichenoid reactions (AAOLR) from oral lichen planus (OLP). **METHODS:** Oral pathologists provided their opinion as to the possibility of distinguishing AAOLR and OLP histologically, the features important in distinguishing AAOLR from OLP and the diagnosis of 12 AAOLR and 12 OLP cases including the features that drew them to their conclusion. **RESULTS:** There was considerable variation between pathologists in their ability to distinguish the AAOLR and OLP cases. The sensitivity and specificity for histological diagnosis were 40% and 32% respectively. There were four features that were used most commonly to discriminate between AAOLR and OLP: an inflammatory infiltrate located deep to superficial infiltrate in some or all areas; a focal perivascular infiltrate; plasma cells in the connective tissue and neutrophils in the connective tissue. Each was independently predictive of AAOLR or OLP ($P < 0.028$). **CONCLUSIONS:** This study confirms the uncertainty of the diagnostic histological differences between AAOLR and OLP. Distinguishing these conditions should not rely on histology alone, but should be based on a synthesis of all available information including history, examination, histopathology and skin patch testing.

67. Wright J Diagnosis and management of oral lichenoid reactions. *J Calif Dent Assoc* (2007 Jun) 35(6):412-6

Lichen planus is one of the most common mucocutaneous conditions seen in dental practice. A variety of other conditions known as lichenoid reactions can simulate lichen planus either clinically or histologically. This paper will discuss the more common lichenoid reactions seen in clinical practice and review the diagnosis and management of these conditions.

68. Lopez-Jornet P Camacho-Alonso F Do metal restorations in mouth alter clinical and histological appearance of oral lichen planus? *N Y State Dent J* (2008 Nov) 74(6):40-3

The objective of our study was to determine whether clinical and histopathological differences exist between patients with oral lichen planus (OLP) with dental amalgam and those without. The study involved 213 patients with OLP. They were divided into two groups: those with OLP without dental amalgam, and those with OLP with dental amalgam. The most frequent location for both groups was the buccal mucosa and bilateral presentation. No clinical or histopathological statistically significant differences were found between OLP with or without dental amalgam.

69. McCullough MJ Tyas MJ Local adverse effects of amalgam restorations. *Int Dent J* (2008 Feb) 58(1):3-9

Amalgam has been used for the restoration of teeth for well over 100 years, and is the most successful of the direct restorative materials with respect to longevity. Despite the increasing use of tooth-coloured materials, with advantages of aesthetics and adhesion, amalgam is one of the most widely used dental restorative materials. One of the principal disadvantages of amalgam, apart from aesthetics, is that it may have adverse biological effects, both locally and systemically. Locally, it can cause an erythematous lesion on the adjacent oral soft tissues (tongue and buccal mucosa), and systemically free mercury in the amalgam may give rise to a hypersensitivity reaction. The purpose of this paper is to review the literature concerning the local adverse reactions to dental amalgam. The focus will be on the reactions of the oral mucosa, and brief consideration will be given to laboratory cytotoxicity of dental amalgam and its components, and to the 'amalgam tattoo'.

70. Evrard L Parent D Oral allergies to dental materials. *Bull Group Int Rech Sci Stomatol Odontol* (2010) 49(1):14-8

Oral allergies represent a pathological entity not well known nor diagnosed by dental health professionals. The purpose of this work is to present an information relative to the multidisciplinary steps to be done to solve allergy problems. Three clinical examples of contact oral allergies (to mercury, or gold, or methacrylates) are presented, as to illustrate signs and symptoms of an oral allergy to the more frequent dental materials implied. We discuss the problem of oral allergies from what is known from the scientific literature. We stress the importance of a multidisciplinary approach to take into account patients with an oral allergy, with participation of specialists from dental and dermatologic fields.

71. Eyeson J House I Yang YH Warnakulasuriya KA Relationship between mercury levels in blood and urine and complaints of chronic mercury toxicity from amalgam restorations. *Br Dent J* (2010 Feb 27) 208(4):E7; discussion 162-3

AIM: To determine whether patients complaining of oral and medical symptoms perceived to be associated with chronic mercury toxicity have elevated mercury levels in their blood and urine. METHODS: The study group in this audit were 56 patients presenting to an oral medicine unit with complaints perceived to be related to chronic mercury toxicity. Their symptoms and comorbidity were charted and mercury levels in blood and urine were biochemically tested by atomic absorption spectrophotometry. RESULTS: None had elevated mercury levels in blood or urine above the normal threshold level. Subgroup analysis showed subjects with oral lesions, autoimmune disorders and multiple sclerosis had relatively and significantly higher mercury levels within this cohort, but within the threshold values. When tested by multiple logistic regression adjusted for age and gender, mercury levels in blood or urine, numbers of amalgams were not significant for multiple sclerosis or previously diagnosed autoimmune disease. CONCLUSION: Mercury levels in blood and urine of this cohort of patients with perceived chronic mercury toxicity were within the normal range in accordance with a national laboratory threshold value.

72. Aggarwal V Jain A Kabi D Oral lichenoid reaction associated with tin component of amalgam restorations: a case report. *Am J Dermatopathol* (2010 Feb) 32(1):46-8

Amalgam or its components may cause type IV hypersensitivity reactions on the oral mucosa. Majority of the reported cases involved a delayed hypersensitivity to mercury. A case of bilateral oral lichenoid reaction is presented, which was present in relation to amalgam restorations. Histopathological features were compatible with lichenoid mucositis. Patch test was positive with pulverized amalgam and tin. The lesion healed up after replacement of restorations with an intermediate restorative material. The clinician should be aware of all possible pathological etiologies of white lesions. If there is any doubt about the nature or management of an unusual oral lesion, referral to appropriate specialists is mandatory.

73. Pigatto PD Bombeccari G Spadari F Guzzi G Oral lichenoid reaction, dental amalgam, and tin allergy. *Am J Dermatopathol* (2011 Jun) 33(4):414-5
74. Luiz AC Hirota SK Dal Vechio A Reis VM Spina R Migliari DA Diagnosing oral lichenoid contact reaction: clinical judgment versus skin-patch test. *Minerva Stomatol* (2012 Jul-Aug) 61(7-8):311-7

AIM: Objective of this study was to compare the skin-patch test with the clinical diagnosis of oral lichenoid contact reaction (OLCR) as indicators for amalgam replacement. METHODS: Of 53 patients (38 female and 15 male; mean age 48.7) with oral lichen planus (OLP), 26 were identified as having OLCR, and clinically graded according to the proximity of their lesions with amalgam fillings: class I (weak association), class II (moderate association), and class III (strong association). All OLCR patients were skin-patch tested for both standard (Brazilian) and specific allergens (TROLAB, Germany). Patients were considered skin-patch positive only if they developed positive skin reactions for thimerosal and/or amalgam components. Amalgam replacement was indicated in all class II and III patients. For class-I patients, amalgam replacement was indicated only if they were skin-patch test positive. Readings for the skin-patch test were made at 48h and 96h. RESULTS: Of the 26 patients with OLCR, two missed the follow-up and were excluded, leaving 24 cases. Of these, four were class-I, and all were negative for the skin-patch test. Twelve were class-II, of whom seven were skin-patch positive. Eight were class-III, of whom six were skin-patch positive. Following amalgam replacement in the 12 class-II patients, six showed improvement and six had complete resolution, while in the eight class-III patients, two showed improvement and six a complete resolution. CONCLUSION: Clinical diagnosis of OLCR lesions is a more reliable indicator for the question of amalgam replacement than is the skin-patch test.

75. Lartitegui-Sebastián MJ Martínez-Revilla B Saiz-García C Eguizabal-Saracho S Aguirre-Urizar JM Oral lichenoid lesions associated with amalgam restorations: a prospective pilot study addressing the adult population of the Basque Country. *Med Oral Patol Oral Cir Bucal* (2012 Jul) 17(4):e545-9

Oral lichenoid lesions (OLLs) are linked to a heterogeneous group of pathologies involving the oral mucosa that cannot be distinguished from the oral lichen planus excepting the fact that direct causal factors such as silver amalgam restorations (SARs) can be allocated to them. PURPOSE: To analyze the prevalence of mucosal lesions associated with SAR in a group of SAR carrying patients in the Basque Country. STUDY DESIGN: A clinical prospective study was carried out on 100 adult patients over 30 years of age at the UPV/EHU Clinical Odontology Service whose rear teeth had at least one SAR. Patients were identified and mucosal lesions and amalgam restorations were characterized. Patch tests were performed on patients with lesions and amalgams were replaced with composite material. A statistical and comparative analysis was performed with the resulting data. RESULTS: OLLs were found in 7 patients whose predominant lesion was bilateral, asymmetrical and asymptomatic white papule-macule. Lesions were related to old and corroded SARs. Patch testing was positive in two cases. SAR substitution produced an improvement in 5 cases. CONCLUSIONS: The presence of lichenoid

lesions associated with SARs is infrequent in our environment and is preferentially related to old and corroded restorations.

76. McParland H Warnakulasuriya S Oral lichenoid contact lesions to mercury and dental amalgam--a review. *J Biomed Biotechnol* (2012) 2012:589569

Human oral mucosa is subjected to many noxious stimuli. One of these substances, in those who have restorations, is dental amalgam which contains mercury. This paper focuses on the local toxic effects of amalgam and mercury from dental restorations. Components of amalgam may, in rare instances, cause local side effects or allergic reactions referred to as oral lichenoid lesions (OLLs). OLLs to amalgams are recognised as hypersensitivity reactions to low-level mercury exposure. The use of patch testing to identify those susceptible from OLL is explored, and recommendations for removing amalgam fillings, when indicated are outlined. We conclude that evidence does not show that exposure to mercury from amalgam restorations poses a serious health risk in humans, except for an exceedingly small number of hypersensitivity reactions that are discussed.

77. Chainani-Wu N Madden E Lozada-Nur F Silverman S High-dose curcuminoids are efficacious in the reduction in symptoms and signs of oral lichen planus. *J Am Acad Dermatol* (2012 May) 66(5):752-60

BACKGROUND: Curcuminoids are components of turmeric (*Curcuma longa*) that possess anti-inflammatory properties.**OBJECTIVE:** We sought to study the efficacy of curcuminoids in controlling the signs and symptoms of oral lichen planus, at doses of 6000 mg/d (3 divided doses), and their safety at this dose.**METHODS:** Twenty consecutive, eligible patients who consented were enrolled into this randomized, double-blind, placebo-controlled clinical trial in 2007 through 2008. Measurement of symptoms and signs of oral lichen planus using the Numerical Rating Scale (NRS) and the Modified Oral Mucositis Index (MOMI), respectively; complete blood counts; liver enzymes; C-reactive protein; and interleukin-6 levels was done at baseline and day 14. Two-sided P values are reported.**RESULTS:** In the placebo group, the percentage changes from baseline in NRS (median [interquartile range] = 0.00 [-29 to 16.7], $P > .99$), erythema (0.00 [-10 to 16.7], $P = .98$), ulceration (0.00 [0.00 to 26.7], $P = .63$), and total MOMI scores (-3.2 [-13 to 9.09], $P = .95$) were not statistically significant, whereas they were statistically significant in the curcuminoids group: NRS (-22 [-33 to -14], $P = .0078$); erythema (-17 [-29 to -8.3], $P = .0078$), ulceration (-14 [-60 to 0.00], $P = .063$), MOMI (-24 [-38 to -11], $P = .0039$). The curcuminoids group showed a greater reduction in clinical signs and symptoms as compared with the placebo group, measured by percentage change in erythema ($P = .05$) and total MOMI score ($P = .03$), and proportion showing improvement in NRS (0.8 vs 0.3, $P = .02$) and total MOMI score (0.9 vs 0.5, $P = .05$). Adverse effects were uncommon in both groups.**LIMITATIONS:** The small sample size resulted in limited power, particularly for multivariate analyses.**CONCLUSIONS:** Curcuminoids at doses of 6000 mg/d in 3 divided doses are well tolerated and may prove efficacious in controlling signs and symptoms of oral lichen planus.

78. Lo Muzio L Santarelli A Campisi G Lacaita M Favia G Possible link between Hashimoto's thyroiditis and oral lichen planus: a novel association found. *Clin Oral Investig* (2013 Jan) 17(1):333-6

OBJECTIVES: Hashimoto's thyroiditis as well as lichen planus has been associated to a number of disorders, generally of auto-immune origin. A novel possible association between oral lichen planus (OLP) and Hashimoto's thyroiditis (HT) is here proposed on the basis of a cross-sectional survey.**MATERIALS AND METHODS:** One hundred and five

unrelated OLP patients were considered. Diagnosis of HT was based on positive serum anti-TPO, anti-Tg, TSH levels and the typical ultrasound pattern of the thyroid gland. RESULTS: In the present survey, the prevalence of HT in the OLP group was 14.3% whereas the prevalence of HT-related hypothyroidism in the general population was reported to be equal to 1%. By Fisher's exact test, it was revealed that the difference between our data and historical prevalence of HT was found statistically significant. CONCLUSION: Actually, there is no definitive hypothesis that could explain the coexistence of OLP and HT. However, considering the onset timing of HT followed by OLP in 93.3% of our series, we suspected a causal or predisposing role for HT. Specifically, we believe that in HT patients, circulating thyroid antibodies could contribute to trigger an organ-specific auto-immune response also in the oral mucosa or skin, leading to the development of LP lesions. CLINICAL RELEVANCE: Because of the large number of cases of asymptomatic chronic auto-immune thyroiditis, it would be useful that women over 40 years of age affected by OLP were screened for thyroid dysfunction, particularly HT.