

ORAL LICHENOID LESIONS AND ALLERGY TO DENTAL MATERIALS

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Background: Dental materials, oral hygiene products and food additives may cause contact allergic reactions in the mouth with varied clinical presentation. Oral lichenoid lesions (lichen planus-like lesions) can be induced by hypersensitivity to dental restorative metals, acrylates, flavorings and other substances.

Aim: The aim of this study was to demonstrate contact allergy to dental materials in patients with oral lichenoid lesions using patch tests.

Patients and methods: Routine patch tests with two sets of allergens – “European Standard“ and „Dental Screening“ (Chemotechnique Diagnostics, Sweden) supplemented with pulverized amalgam, iridium, indium, menthol, sorbic acid and platinum were done on a set of 25 patients with lichenoid lesions located on the buccal mucosa, tongue and lips. Application and interpretation of the tests were conducted according to ICDRG (International Contact Dermatitis Research Group).

Results: 15 (60 %) patients showed sensitization to 1 or more allergens, with a total of 31 positive reactions. The greatest frequency of positive reactions was to dental metals, with a total of 27 positive reactions. The order of tested metals according to frequency of positive reactions was mercury (6/25/24 %), amalgam (6/25/24 %), nickel (4/25/16 %), palladium (4/25/16 %), cobalt (3/25/12 %), gold (2/25/8 %), chrome (1/25/4 %), indium (1/25/4 %). The clinical relevance of the results with regard to the material’s presence in the mouth was demonstrated in 11 (44 %) patients. In 9 patients, replacement of the positively tested materials led to healing or to significant regression of mucosal changes.

Conclusions: The results of the patch tests showed the possible contribution of contact sensitization in the pathogenesis of lichenoid manifestations in the oral cavity. Due to the premalignant character of these lesions, replacement of positively tested materials and follow up of these patients is advised.

INTRODUCTION

The oral cavity, including the lips, is constantly exposed to a large number of potentially irritating and sensitizing substances. About 10–15 different metals, as well as synthetic resin, topical treatments, disinfectants and other dental materials may act on the buccal mucosa during routine dental treatment¹. Most dental materials used for dental fillings, fixed and removable replacements, orthodontic instruments etc. are intended for long-term use in the oral cavity and must satisfy strict biocompatibility specifications. Abroad, especially in Scandinavian countries, national registries have existed since the 1990’s. These monitor the adverse effects of dental biomaterials on the oral mucosa and they study the occurrence of contact irritation and allergic reactions to specific materials^{2,3}. This issue has not yet been addressed in the Czech Republic.

The clinical manifestations of contact hypersensitivity in the mouth vary from subjective difficulties such as

burning, pain and dryness of the mucosa (burning mouth syndrome) to objective changes in the form of nonspecific stomatitis and cheilitis with reddish, edematous mucosae, erosions and ulcers^{4–7}. A more distinctive manifestation are lichenoid reactions usually localised on the buccal mucosa, tongue and lips^{8,9}. These chronic changes are most often associated with long-term exposure of the oral mucosa to dental metals, and also to acrylates, composite materials, additives and other substances, which lead to the development of a delayed hypersensitivity reaction^{10,11}. The premalignant character of these lesions is a more recent finding^{12–14}.

The aim of this work was to investigate the proportion of contact allergies to dental materials in the etiopathogenesis of lichenoid changes in the oral cavity in a set of patients. Routine examination methods include patch tests, which consist of controlled exposure of an area of skin to a small amount of tested allergen in a non-toxic concentration¹⁵.

PATIENTS AND METHODS

Between the years 2005–2006, and in co-operation with local dentists, 183 patients with various manifestations of oral discomfort were examined and they underwent epicutaneous testing. Based on history, clinical and histopathological examination, a diagnosis of lichenoid changes in the oral cavity was made in 25 (13.6 %) patients (23 women and 2 men, aged 41–74, average age 53.5 years). None of these patients exhibited skin manifestations of lichen planus. The average duration of the lesions prior to testing was 32 months (ranging from 4–72 months). The oral lesions were most often located on the buccal mucosa (19 patients), 4 patients also had concurrent lesions located on the lateral and dorsal tongue surface, 2 patients also had lesions on the lips. Most patients had reticular and plaque-like types of lesions, in 8 patients in combination with erosive type.

Standard testing substances (Chemotechnique Diagnostics, Sweden) authorized by the ICDRG (International Contact Dermatitis Research Group) were used to demonstrate contact hypersensitivity to dental materials and to other dental products¹⁶. As testing sets for contact hypersensitivity in the mouth, 2 basic allergen series are recommended: "European Standard", which includes 25 of the most frequent European allergens, and "Dental screening" with 25 of the most common oral allergens. After consultation with dentists, these sets were expanded to include pulverized amalgam, iridium, indium, platinum, menthol and sorbic acid. Concentrations and used vehicles (petrolatum, water) are shown in Table 1 and 2. The tested substances were applied on the skin of the back over a period of 48 hours and fixated by Lohmann-Rauscher plaster to ensure occlusive conditions (Fig. 1). The results were recorded 30 minutes after plaster removal and again on the 3rd and 7th day as recommended by the ICDRG^{15, 16}. A skin reaction with erythema and effusion, possibly papulovesicles (eczema reaction), was considered a positive reaction (Fig. 2).

RESULTS

In a set of 25 patients with lichenoid oral manifestations, patch tests showed a positive reaction to one or more tested substances in 15 patients (60 %), with a total of 31 positive reactions. Negative reactions were found in 10 patients.

The most frequent positive tests were observed in dental metals, especially mercury (19.3 %) and amalgam (19.3 % of all positive reactions). Nickel exhibited 12.9 %, palladium 12.9 %, cobalt 9.7 %, gold 6.4 % positive reactions. An overview of positive reactions is shown in Table 3.

Table 4 shows the individual positively tested substances and their association with materials present in the oral cavity. Clinically relevant allergens were found in 11 patients (44 %): mercury 6x, nickel 2x, palladium 2x, gold 2x, chrome 1x, EGDMA 1x. Indeterminate relevance

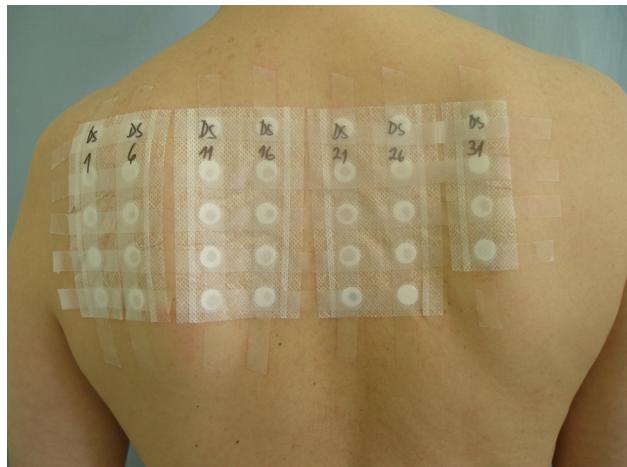


Fig. 1. Patch tests.



Fig. 2. Positive patch test for amalgam.

was found for colophony, balsam Peru, epoxy resin and certain metals.

Positive allergic reactions were observed after 48 hours of exposure in 12 patients, in 2 patients with positive mercury and amalgam the reaction was positive on the 3rd day of exposure and 1 patient exhibited a positive test for gold with a 7 day latency.

DISCUSSION

Lichenoid manifestations are a fairly common finding in the oral cavity. Their etiopathogenesis is not quite clear, however, they are most commonly considered an immunopathological reaction to various etiological factors such as pharmaceuticals, graft vs host disease reaction and contact reaction to dental materials^{10, 17, 18}. A number of studies have confirmed the frequent association between lichenoid reaction and contact hypersensitivity to dental metals. Healing or significant reduction in mucosal changes has been described in a large number of patients with a verified allergy to mercury once the amalgam fillings have

Table 1. The list of tested allergens - European Standard series.

	Compound	Concentration (%) / Vehiculum
1.	Potassium dichromate	0.5 pet
2.	4-Phenylenediamine base	1.0 pet
3.	Thiuram mix	1.0 pet
4.	Neomycin sulfate	20.0 pet
5.	Cobalt chloride	1.0 pet
6.	Benzocaine	5.0 pet
7.	Nickel sulfate	5.0 pet
8.	Clioquinol	5.0 pet
9.	Colophony	20.0 pet
10.	Paraben mix	16.0 pet
11.	N-Isopropyl-N-phenyl-4-phenylenediamine	0.1 pet
12.	Wool alcohols	30.0 pet
13.	Mercapto mix	2.0 pet
14.	Epoxy resin	1.0 pet
15.	Balsam Peru	25.0 pet
16.	4-tert-Butylphenolformaldehyde resin PTBP	1.0 pet
17.	2-Mercaptobenzothiazole	2.0 pet
18.	Formaldehyde	1.0 aq
19.	Fragrance mix	8.0 pet
20.	Sesquiterpenelactone mix	0.1 pet
21.	Quaternium 15	1.0 pet
22.	Primin	0.01 pet
23.	Kathon CG	0.01 aq
24.	Budesonide	0.01 pet
25.	Tixocortol-21-pivalate	0.1 pet

Pet = petrolatum, Aq = aqua

Table 2. The list of tested allergens - Dental Screening and additional substances.

	Compound	Concentration (%) / Vehiculum
1	Methyl methacrylate MMA	2.0 pet
2	Triethyleneglycol dimethacrylate TREGDMA	2.0 pet
3	Urethane dimethacrylate UEDMA	2.0 pet
4	Ethyleneglycol dimethacrylate EGDMA	2.0 pet
5	2,2-bis(4-(2-Hydroxy-3-methacryloxypropoxy)phenyl) propane BIS-GMA	2.0 pet
6	N,N-Dimethyl-4-toluidine	5.0 pet
7	2-Hydroxy-4-methoxybenzophenone	10.0 pet
8	1,4-Butanedioldimethacrylate BUDMA	2.0 pet
9	2,2-bis(4-Methacryloxy)phenyl propane BIS-MA	2.0 pet
10	Mercury	0.5 pet
11	2-Hydroxyethylmethacrylate 2-HEMA	2.0 pet
12	Goldsodiumthiosulfate	2.0 pet
13	Eugenol	2.0 pet
14	N-Ethyl-4-toluenesulfonamide	0.1 pet
15	4-Tolyldiethanolamine	2.0 pet
16	Copper sulfate	2.0 pet
17	Methylhydroquinone	1.0 pet
18	Palladium chloride	2.0 pet
19	Aluminum chloride	2.0 pet
20	Camphoroquinone	1.0 pet
21	N,N-Dimethylaminoethyl methacrylate DMAEMA	0.2 pet
22	1,6-Hexanediol diacrylate HDDA	0.1 pet
23	2(2-Hydroxy-5-methyl-phenyl)benzotriazol (Tinuvin P)	1.0 pet
24	Tetrahydrofurfuryl methacrylate THFMA	2.0 pet
25	Tin	50.0 pet
26	Amalgam pulv.	5.0 pet
27	Sorbic acid	2.0 pet
28	Menthol	2.0 pet
29	Iridium chloride	1.0 pet
30	Indium chloride	10.0 aq
31	Amonium tetrachloroplatinate	0.25 aq

been removed^{8, 9, 19}. Dunsche described a regression in the manifestation of lichenoid changes after amalgam substitution in 97 % of 134 patients, independent of results of epicutaneous testing²⁰. He also experimentally confirmed the possible locally toxic effect of amalgam and the significance between a close topographical relationship between artificial material and pathological manifestation on the mucosa²¹.

The oral cavity is a specific environment where chemical and electrochemical corrosion with saliva acts as an electrolyte. The resulting galvanic currents and corrosion processes may lead to the release of ions and their complexes even from stable dental metals, and these may act as haptens in the process of sensitization^{6, 22}. Other significant corrosive products in amalgam include copper and tin, which may also be a cause of lichenoid mucosal

changes^{6, 20}. Aside from amalgam, other metals, such as gold, palladium, nickel, chrome and cobalt may induce oral lichenoid mucositis²³⁻²⁵.

In our set of patients, the greatest frequency of sensitization was to dental metals. 6 patients tested positively for mercury and amalgam and the clinical relevance was confirmed by the healing of lichenoid manifestations upon removal of amalgam fillings in 4 patients and significant improvement after 4 months in 1 patient. One patient (no. 15) refused to exchange the amalgam, and was advised to limit contact with the also positively tested balsam Peru. One patient (no. 12) with crowns of gold alloy (Aurix) improved significantly after replacing the gold crowns with non-metal ceramic materials. Another patient refused to replace the gold material. One patient (no. 4) with a fixed replacement of white metal and one patient (no. 5) with crowns and dental bridges of white metal (Remanium) significantly improved 6 months following the replacement. The remaining patients with positive tests for nickel, palladium, cobalt and colophony with epoxy resin, the actual source of sensitization was not demonstrated in the mouth, although patients were informed about their latent allergy and told to limit contact with these substances. Patient no. 13 with a positive reaction to monomer EGDMA (ethyleneglycoldimethacrylate) improved significantly 3 months after replacing crowns made of composite resin.

There is currently little information on the relationship between lichenoid reactions and synthetic resins^{18, 26}. These modern so-called esthetic materials have only lately come to the forefront; although in some countries they have almost completely replaced amalgam and are currently the primary dental restoration material^{27, 28}. In a set of 1322 dental patients in Sweden, epicutaneous tests were positive for (meth)acrylates in 2.3 % and in a set of dental personnel they were positive in 5.8 %, which shows the significant sensitizing potential of these substances²⁸.

Table 3. Positive reactions of patch tests in oral lichenoid lesions.

Allergens	positive reactions	%
Mercury	6	19.3
Amalgam	6	19.3
Nickel	4	12.9
Palladium	4	12.9
Cobalt	3	9.7
Gold	2	6.4
Chromium	1	3.2
Indium	1	3.2
EGDMA	1	3.2
Balsam Peru	1	3.2
Colophony	1	3.2
Epoxy resin	1	3.2
Total	31	100

Table 4. Patients with positive patch tests, the sources of sensitization.

Patient	Positive allergens	Sources of sensitization, materials
1.	Mercury, Amalgam	amalgam fillings
2.	Mercury, Amalgam	amalgam fillings
3.	Mercury, Amalgam	amalgam fillings
4.	Nickel, Palladium	fixed replacement, white metal
5.	Nickel, Chromium	white metal crowns and bridges, Remanium
6.	Mercury, Amalgam	amalgam fillings
7.	Nickel, Palladium, Cobalt	uncertain
8.	Gold, Indium	Gold crowns, indium – uncertain
9.	Mercury, Amalgam	amalgam fillings
10.	Nickel, Cobalt	uncertain
11.	Cobalt, Palladium	uncertain
12.	Gold, Palladium	Gold crowns, Aurix
13.	EGDMA	composite resin crowns
14.	Colophony, Epoxy resin	uncertain
15.	Mercury, Amalgam, Balsam Peru	amalgam fillings, Balsam Peru – uncertain

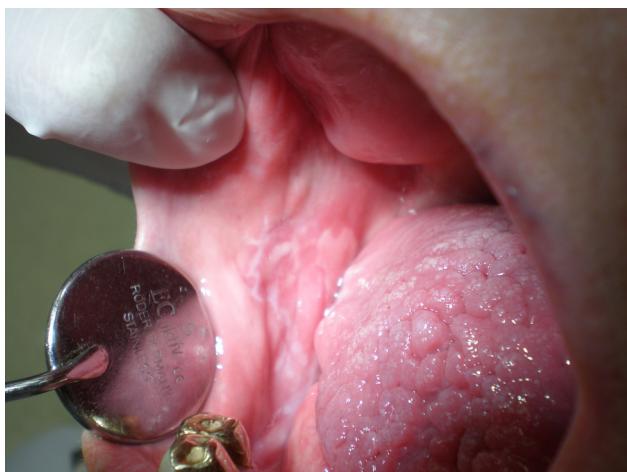


Fig. 3. Oral lichenoid lesions on the buccal mucosa



Fig. 4. Oral lichenoid lesions on the tongue

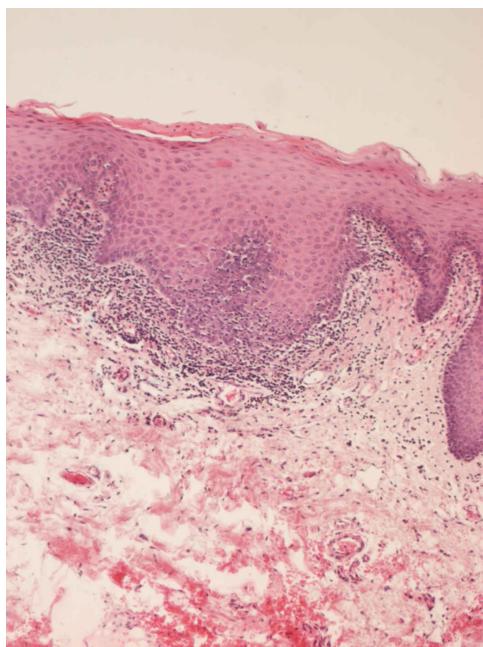


Fig. 5. Hematoxylin-eosin staining (x100). Oral lichenoid reaction

2-HEMA, EGDMA and BIS-GMA were recommended as screening allergens and correctly performed testing with an examination of the skin reaction after 1 week was emphasized. 16 % of the positive results were not noted until the 7th day after test application²⁹.

Besides dental materials, a number of topical substances including phytotherapy, oral cosmetics, various food products and beverages along with additives may trigger an adverse reaction on the oral mucosa. Aside from non-specific contact stomatitis and cheilitis, these substances may also be the source of lichenoid manifestations^{15, 30}. While an undisturbed oral mucosa with normal salivation is characterized by a certain resistance and regeneration ability, decreased saliva production, microbial mucosal colonization, mechanical trauma and long-term exposure to irritation and allergen-like substances disrupt its barrier

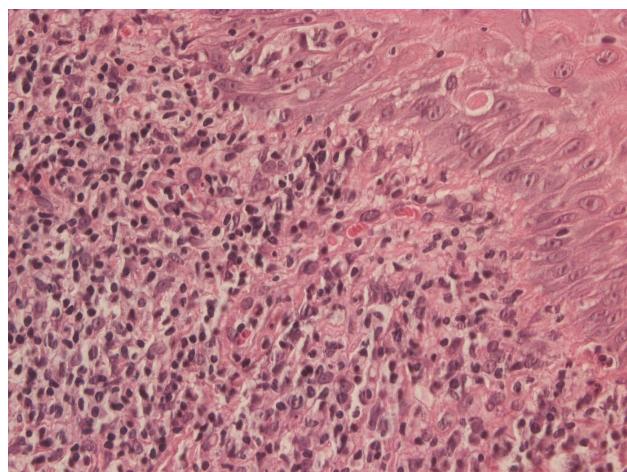


Fig. 6. Hematoxylin-eosin staining (x400). Detail of oral lichenoid lesion with Civatte body in the basal layer of the epidermis

function and create conditions for the development of a delayed hypersensitivity reaction¹⁵. Exposure to derivatives of cinnamon acid contained in toothpaste, chewing gum and sweets leads to lichenoid changes on the buccal mucosa and tongue¹¹. Menthol and peppermint found in oral hygiene products, as well as in teas, liquors, gum, etc may induce intraoral erosions and lichenoid changes³¹. Eugenol from clove oil, popular in stomatology for its disinfecting and aromatizing qualities may have a similar effect on the mucosa³². Balsam Peru is a screening allergen for aromatizing substances and may cause undetected sensitization to common non-alcoholic beverages, vermouths, teas, spices, in oral cosmetics, etc³⁰. In patient no. 15 with amalgam fillings, tests were positive for mercury, amalgam and balsam Peru. It was difficult to establish the test relevance of balsam Peru owing to its ubiquity. Removal of

the amalgam fillings was recommended, as well as limited contact with this natural resin.

Diagnosis of oral lichenoid changes is based on detailed history, clinical examination and histopathological identification. A number of clinical forms have been described. The most common consists of reticular lesions followed by plaque-like, papulous, atrophic, bullous and erosive forms^{33, 34}. Manifestation is usually asymptomatic, pain is a result of atrophic and erosive changes. Most patients in our sample had distinct whitish-grey reticular focuses on the buccal mucosa, on the dorsal and lateral tongue surfaces, also on the lips in 2 patients (Fig. 3, 4). In one-third of patients, these were combined with the erosive form.

Performing a histopathological examination is important to exclude other mucosal diseases such as bullous diseases, leukoplakia, lupus erythematosus, tumours, etc. Micromorphological changes typically include focal hyperkeratosis or parakeratosis, irregular acanthosis and liquefaction degeneration of the basal layer with a band-like lymphocytic infiltrate high in the lamina propria. Eosinophilic Civatte bodies representing degenerated basal layer cells are characteristic (ref.^{8, 34}) (Fig. 5, 6) . However, it is impossible to differentiate between idiopathic lichen planus and lichenoid contact allergic manifestations based solely on these histopathological criteria^{9, 10, 13, 35, 36}. A correctly performed biopsy in the oral cavity, sufficient sample size and its proper orientation, material fragmentation or collection from an area of chronic ulceration with mycotic and microbial superposition is a common problem⁹. In our sample of 25 patients, histopathological examination was compatible with clinical diagnosis of oral lichenoid manifestation in 18 cases. In the remaining 7 patients with a clinically typical form, biopsy described only non-specific inflammatory changes.

Skin tests should follow clinical and microscopic examination. In case of positivity, it is recommended that the tested materials be removed from the oral cavity, or at least partially replaced in areas of close contact between dental material and oral mucosa.

Close interdisciplinary co-operation with dentists is necessary for the proper identification of potential allergens in the used dental materials. The ensuing replacement of suspect dental materials and other substances in the oral cavity is often not easy and is not always accepted by the patient. On the other hand, oral lichenoid lesions associated with contact hypersensitivity, especially to dental metals, are a possible risk factor for the development of squamous cell carcinoma of the mouth^{12, 14}. In ten out 11 patients with intraoral carcinoma, patch tests revealed hypersensitivity to gold, mercury, silver and copper¹².

CONCLUSIONS

Skin tests are the only relevant examination method for the detection of a contact hypersensitivity reaction, valid even from a forensic viewpoint. They are irreplaceable in excluding pre-existing allergies to restoration mate-

rials, especially prior to an extensive procedure in the oral cavity. In the case of lichenoid mucosal manifestations, epicutaneous tests to confirm suspect intraoral allergens, which may play a role in the pathogenesis of these chronic mucosal changes, are a stress-free examination method for the patients. In some cases, a locally toxic effect of dental materials on the oral mucosa cannot be excluded, and therefore in severe, especially erosive forms, where there is close contact between mucosa and dental metals, their replacement with other materials is recommended.

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