

Investigation of contact allergy to dental metals in 206 patients

ULRIKE RAAP¹, MEIKE STIESCH², HEIDI REH¹, ALEXANDER KAPP¹ AND THOMAS WERFEL^{1,3}

¹Department of Dermatology and Allergology, ²Department of Prosthetic Dentistry, and ³Department of Immunodermatology and Allergy Research, Hannover Medical School, Hannover, Germany

Background: Contact allergy to dental materials is poorly understood; clinical manifestations are heterogeneous.

Objective: To analyse positive patch test reactions to metals (as their alloys or salts) used in dentistry together with clinical symptoms and possible relevance to dental fillings.

Methods: We retrospectively analysed 206 patients who underwent patch testing with metals used in dentistry because of suspected contact allergy to them.

Results: Twenty-eight of 206 patients had positive patch test reactions to metals used in dentistry. The number of positive patch test reactions was highest for gold sodium thiosulfate, palladium chloride, and nickel sulfate ($n = 10$, respectively), followed by amalgam, ammoniated mercury, and cobalt chloride ($n = 4$, respectively) and amalgam-mixed metals (including copper, tin, zinc, and silicon), and ammonium tetrachloroplatinate ($n = 1$). Only 14 (7%) of 206 patients had a clinically relevant contact allergy with conditions of the oral mucosa ($n = 7$ with lichen planus and $n = 7$ with stomatitis) and positive patch test reactions to dental metals containing the suspected allergen. Improvement of symptoms was assessed in one patient with amalgam contact allergy 2 weeks after removal of dental fillings.

Conclusions: Clinically relevant contact allergies to dental metals are infrequent. Gold sodium thiosulfate and palladium chloride presented the most frequent contact allergens.

Key words: allergic contact dermatitis; dental metal; gold sodium thiosulfate; nickel sulfate; oral lichen planus; oral stomatitis; palladium chloride. © 2009 John Wiley & Sons A/S.

Conflicts of interest: The authors have declared no conflicts.

Accepted for publication 12 January 2009

The relevance of allergic reactions to dental materials is poorly understood (1). The oral mucosa, including the lips, is constantly exposed to a large number of potentially irritating and sensitizing substances. Exposure of allergens to the oral mucosa may have tolerizing effects, which is used therapeutically in sublingual immunotherapy. In this regard, application of dental braces (oral nickel exposure) prior to ear piercing (cutaneous nickel exposure) was associated with a significantly reduced prevalence of nickel allergy (2, 3). However, most of the dental materials used for dental fillings, plates, and dentures are intended for long-term use, and this exposure may sensitize

patients. The clinical manifestations of contact allergy to dental material are not uniform. Patients may present with subjective complaints affecting the oral mucosa, including burning, pain, and more objective conditions such as stomatitis and lichenoid reactions localized to the buccal mucosa, tongue, and lips (4, 5).

The aim of our present study was to investigate the proportion of contact allergies to a dental metal series (according to the German Contact Dermatitis Research Group) and the clinical symptoms of patients in addition to a possible clinical relevance with dental fillings containing the suspected allergen.

Methods

Patients

We performed a retrospective study analysing data collected in our department from June 2003 to March 2008. Only patients tested with dental metals (according to the German Contact Dermatitis Research Group) were included. In total, 206 patients underwent patch testing because of suspected contact allergy to dental metals. We recorded age, sex, clinical symptoms, location of lesions, indications for patch testing, atopic background, and occupation of the patients.

Patch testing

Patch testing was performed at the Department of Dermatology and Allergology, Hannover Medical School, according to the German guidelines (6). Allergens were supplied by Hermal (Rhinebeck, Germany) and Chemotechnique Diagnostics (Malmö, Sweden) (Table 1). Patients were tested with the European baseline series, which includes nickel sulfate [5% petrolatum (pet.)] and cobalt chloride (1% pet.), and amalgam (5% pet.), gold sodium thiosulfate (0.25% pet.), palladium chloride (1% pet.), amalgam-mixed metals (20% pet.), ammonium tetrachloroplatinate (0.25% pet.), and ammoniated mercury (1% pet.) as recommended by the German Contact Dermatitis Research Group. Patch testing with elemental mercury has not been recommended by the German Contact Dermatitis Research Group. In brief, contact allergens were applied with Finn Chambers[®] (Epitest Ltd Oy, Tuusula, Finland) on hypoallergenic Fixomull[®] stretch (Baiersdorf Medical GmbH, Hamburg, Germany) to the upper back. The strips were removed after 2 days. Readings were performed on D2, D3, and D4 by an allergist of the Department of Dermatology and Allergology, Hannover Medical School. Results were evaluated according to the standard scoring system recommended (6).

Histology

To support clinical diagnoses, 11 patients with symptoms affecting the oral mucosa underwent a biopsy of the oral mucosa. Three-millimetre punch biopsies were taken using local anaesthesia. Paraffin samples were stained with haematoxylin–eosin and Periodic acid/shift and reported by a dermatopathologist.

Results

Patient characteristics

Of 206 patients tested, 28 patients showed at least one positive patch test reaction to dental metals. The majority of these 28 patients were female ($n = 27$, 96%; mean age $\pm$ SD: 48.2 ± 15.8). Only one male patient (4%, aged 45 years) presented had a reaction. Seven of 27 female patients had a history of atopy, 2 of them had atopic dermatitis, 4 had allergic rhinitis, and 2 had an oral allergy syndrome to fruits and nuts. The male patient had no atopic history or oral allergy syndrome. One hundred and seventy-eight of 206 patients did not have any patch test reaction to dental metals. One hundred and thirty-seven of these patients were female (mean age $\pm$ SD: 41.5 ± 17.3), of whom 45 were atopic including 10 patients with atopic dermatitis, 37 with allergic rhinitis, and 23 with an oral allergy syndrome to birch pollen-related food allergy. Forty-one of the 178 patients were male (mean age $\pm$ SD: 47.3 ± 13.7), of whom 36 had an atopic background including 5 patients with atopic dermatitis, 32 with an allergic rhinitis, and 19 with an oral allergy syndrome to birch pollen-related fruits.

Clinical symptoms in the oral cavity

The most frequent oral manifestation of the 28 patients with positive patch test reactions to dental metals was lichen planus ($n = 9$) as assessed clinically and verified histologically in all. Furthermore, oral stomatitis was diagnosed in 8

Table 1. Number of positive patch test reactions in relation to the clinical presentation

Symptoms (number of patients)	Amalgam	Gold sodium thiosulfate	Palladium chloride	Nickel sulfate	Amalgam-mixed metals ^a	Cobalt chloride	Ammonium tetrachloroplatinate	Ammoniated mercury
Oral lichen planus (9)	1	2	4	2	1	1	0	1
Oral stomatitis (8)	2	3	3	4	0	1	1	2
Periodontitis (2)	0	1	0	0	0	0	0	1
Cheilitis (1)	1	0	0	0	0	0	0	0
Recurrent aphthosis (1)	0	1	0	0	0	0	0	0
Glossodynia (4)	0	1	2	2	0	1	0	0
Burning mouth/tongue (3)	0	2	1	2	0	1	0	0

^aCopper, tin, zinc, and silicon.

patients (2 of them histologically), glossodynia in 4, burning mouth in 3, periodontitis in 2, cheilitis in 1, and recurrent aphthosis in 1 of 28 patients with positive patch test reaction to dental metals. Those patients not having a positive patch test reaction to dental metals ($n = 178$) had clinical conditions including oral lichen planus ($n = 40$), oral stomatitis ($n = 32$), recurrent aphthosis ($n = 17$), burning mouth/tongue ($n = 11$), glossodynia ($n = 8$), leukoplakia ($n = 8$), periodontitis ($n = 7$), cheilitis ($n = 5$), lingua plicata ($n = 3$), and other complaints not affecting the oral cavity but with suspected allergy to metals used in the dental series (including $n = 15$ with atopic dermatitis, $n = 18$ with foot and hand eczema, and $n = 14$ with suspected allergy to endoprostheses).

Positive patch test reactions to dental metals

In total, the number of positive patch test reactions to dental metals was low. Only 28 of 206 patients had a positive patch test reaction to dental metals. The number of positive patch test reactions was highest for gold sodium thiosulfate ($n = 10$), palladium chloride ($n = 10$), and nickel sulfate ($n = 10$), followed by amalgam, ammoniated mercury, and cobalt chloride ($n = 4$, respectively) and amalgam-mixed metals (including copper, tin, zinc, and silicon), and ammonium tetrachloroplatinate ($n = 1$) (Table 1).

The highest number of positive patch test reactions was found in patients with stomatitis (16 positive reactions) and patients with lichen planus (12 positive reactions), followed by patients with glossodynia and burning mouth (6 positive reactions, respectively) and periodontitis (2 positive reactions) and cheilitis or recurrent aphthosis (1 positive reaction, respectively) (Table 1).

Clinical relevance of contact allergy to dental metals

The clinical relevance was defined by specific morphological symptoms in the oral cavity together with a positive patch test reaction to dental metals or dental alloys containing the suspected contact

Table 2. Clinical relevance of patients with contact allergy to dental materials

Symptoms	Number of patients	Clinical relevance ^a
Oral lichen planus	9	7
Oral stomatitis	8	7
Periodontitis	2	0
Cheilitis	1	0
Recurrent aphthosis	1	0
Glossodynia	4	0
Burning mouth/tongue	3	0

^aThe clinical relevance was defined by symptoms/signs in proximity to dental metals that were positive in the patch tests and present in dental fillings or alloys.

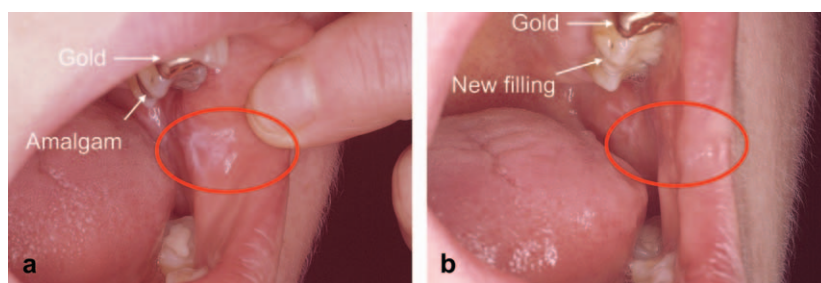
allergen in the dental fillings. Specific morphological symptoms were defined by visible inflammatory changes at the oral mucosa. A specific association between the affection of the oral mucosa, dental filling (information of chemical composition of the dental alloy received by the dental physician in cooperation with the dental technician), and positive patch test reaction to dental metals was found in 7 of 9 patients with oral lichen planus and in 7 of 8 patients with stomatitis who were encouraged to change their dental fillings (Table 2). One patient with stomatitis who had a positive patch test reaction to amalgam displayed a significant improvement of oral lesions 2 weeks after removal of the amalgam fillings (Fig. 1a and b).

Patients with conditions including periodontitis, cheilitis, recurrent aphthosis glossodynia, and burning mouth/tongue who had a positive patch test reaction were not defined for having a clinical relevant contact allergy if the positive patch test reaction did not correlate with the component of the dental alloy (information received by the dental physician in cooperation with the dental technician).

Percentage of positive patch test reactions with clinical relevance according to clinical symptoms

In total, 49 of 206 patients tested had clinical manifestations of oral lichen planus. Seven of 49 patients with oral lichen planus had a positive patch test reaction with clinical relevance; therefore, in

Fig. 1. Presentation of contact allergy at the oral mucosa of a patient with a positive patch test reaction to amalgam who had amalgam and gold fillings (a, red circle shows affection of the oral mucosa). Two weeks after removal of the amalgam filling, the lesions disappeared without other treatment (b).



<15% of the patients with oral lichen planus, there was a possible role of contact allergy.

Of 206 patients who underwent patch testing, 32 had stomatitis. Seven of these 32 (22%) patients with stomatitis had clinically relevant positive patch test reaction.

Discussion

In the present study, we present data concerning a heterogeneous group of patients with a variety of manifestations of oral contact allergy to dental metals. The most common conditions were oral lichen planus and stomatitis. The highest number of allergic contact reactions was to gold sodium thiosulfate and palladium chloride. All patients who reacted to nickel ($n = 10$) also had positive patch test reactions to palladium chloride because of cross-reactivity (7). Certain metal implants can release variable amounts of nickel and cobalt. The clinical relevance of this release is unclear (8). Therefore, the relevance of a positive patch test reaction to nickel with regard to dental alloys remains obscure.

There has been demonstration of contact allergy to mercury in relation to oral lichen planus (9–12). Khamaysi et al. recorded 1 of 17 patients with oral lichen planus as being allergic to mercury (13). In our study, one patient with oral lichen planus had contact allergy to ammoniated mercury.

Two of our patients with oral lichen planus had contact allergy to gold sodium thiosulfate similar to that reported previously (14).

Only 14 of 206 patients displayed a clinically relevant contact allergy to dental metals. These patients had a clear involvement of the oral mucosa with oral lichen planus and stomatitis and a positive patch test reaction to a dental metal present in their current dental filling according to the information available from their dentists. One patient with contact allergy to amalgam and oral stomatitis had a significant improvement of oral symptoms 2 weeks after removal of the amalgam fillings with no additional treatment (Fig. 1).

Recently, it has been shown that a patient with burning lip syndrome who had no lesions at the oral mucosa had a clinical relevant contact allergy to gold and nickel (15). As this patient's mercury dental fillings were corroded, atomic absorption spectrometry was performed after a chewing gum test, which showed twofold increased levels of total mercury released in the saliva. The authors speculated that tiny amounts of nickel and gold in amalgam metal matrix alloys were the reason for the complaints of patients. Therefore, the authors proposed to remove the patient's mercury amalgam fillings that were adjacent to her lips. After removal, the

patient recovered quickly, suggesting that patients without mucosal manifestations may have a clinical relevant allergy if carefully evaluated.

Taken together, our study shows that contact allergies to dental metals do not occur frequently but with gold sodium thiosulfate and palladium chloride being the most frequent contact allergens in our study. The clinical relevance of positive patch test reactions to nickel, however, remains questionable because of cross-reactivity with palladium chloride. Patch test reactions may be of clinical significance in association with stomatitis and lichen planus close to dental fillings containing the contact allergen.

Acknowledgements

We kindly thank our Allergy team including Simone Borges, Anne Cosse, Gisela Selle, Dorit Marzichewsky, and Andrea Gieseke for their excellent support in preparing the patch testing and Dr Bernward Völker for histological analysis.

References

1. De Rossi S S, Greenberg M S. Intraoral contact allergy: a literature review and case reports. *J Am Dent Assoc* 1998; 129: 1435–1441.
2. Van Hoogstraten I M, Andersen K E, Von Blomberg B M et al. Reduced frequency of nickel allergy upon oral nickel contact at an early age. *Clin Exp Immunol* 1991; 85: 441–445.
3. Mortz C G, Lauritsen J M, Bindslev-Jensen C, Andersen K E. Nickel sensitization in adolescents and association with ear piercing, use of dental braces and hand eczema. The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis (TOACS). *Acta Derm Venereol* 2002; 82: 359–364.
4. Ditrichova D, Kapralova S, Tichy M et al. Oral lichenoid lesions and allergy to dental materials. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2007; 151: 333–339.
5. Issa Y, Duxbury A J, Macfarlane T V, Brunton P A. Oral lichenoid lesions related to dental restorative materials. *Br Dent J* 2005; 198: 361–366.
6. Diepgen T L, Dickel H, Becker D et al. [Evidence-based evaluation of the effect of type IV allergies on the reduction of fitness for work. Survey of occupational skin diseases]. *Hautarzt* 2005; 56: 207–223.
7. Watsky K L. Occupational allergic contact dermatitis to platinum, palladium, and gold. *Contact Dermatitis* 2007; 57: 382–383.
8. Thomas P, Schuh A, Ring J, Thomsen M. [Orthopedic surgical implants and allergies. Joint statement by the Implant Allergy Working Group (AK 20) of the DGOOC (German Association of Orthopedics and Orthopedic Surgery), DKG (German Contact Dermatitis Research Group) and DGAKI (German Society for Allergology and Clinical Immunology)]. *Hautarzt* 2008; 59: 220–229.
9. Yiannias J A, el Azhary R A, Hand J H, Pakzad S Y, Rogers R S III. Relevant contact sensitivities in patients with the diagnosis of oral lichen planus. *J Am Acad Dermatol* 2000; 42: 177–182.
10. Laine J, Konttinen Y T, Beliaev N, Happonen R P. Immuno-competent cells in amalgam-associated oral lichenoid contact lesions. *J Oral Pathol Med* 1999; 28: 117–121.

11. Koch P, Bahmer F A. Oral lesions and symptoms related to metals used in dental restorations: a clinical, allergological, and histologic study. *J Am Acad Dermatol* 1999; 41: 422–430.
12. Koch P, Bahmer F A. Oral lichenoid lesions, mercury hypersensitivity and combined hypersensitivity to mercury and other metals: histologically-proven reproduction of the reaction by patch testing with metal salts. *Contact Dermatitis* 1995; 33: 323–328.
13. Khamaysi Z, Bergman R, Weltfriend S. Positive patch test reactions to allergens of the dental series and the relation to the clinical presentations. *Contact Dermatitis* 2006; 55: 216–218.
14. Athavale P N, Shum K W, Yeoman C M, Gawkrödger D J. Oral lichenoid lesions and contact allergy to dental mercury and gold. *Contact Dermatitis* 2003; 49: 264–265.
15. Pigatto P D, Brambilla L, Guzzi G, Spadari F. Burning lips syndrome. *Contact Dermatitis* 2007; 57: 344–346.

Address:

Ulrike Raap, MD

Department of Dermatology and Allergology

Hannover Medical School

Ricklinger Str. 5

30449 Hannover

Germany

Tel: +49 511 9246 232

Fax: +49 511 9246 234

e-mail: raap.ulrike@mh-hannover.de