

Assessment of allergic hypersensitivity to dental materials

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Abstract. Some metallic materials in dental prostheses may cause allergic hypersensitivity. Symptoms appear not only in the oral cavity, but also on hands, feet or the entire body. Release of metal ions is thought to cause the allergic reactions; micro-particles of the corrosion products of the metal and/or ionic metal hydroxides/oxides may be the allergens. The study purpose was to review clinical surveillance of dental allergic hypersensitivity in our dental hospital. From July 2000 to June 2005, 212 patients with suspected dental metal allergy were patch tested with 26 reagents, including 19 ready-made patch test reagents (Patch test reagents™, Torii Pharmaceutical Corporation, Tokyo, Japan) and 9 custom-made reagents. One-hundred-and-sixty-seven patients were females (78.8%) and 45 patients were males (21.2%). A total of 148 patients (69.8%) had one or more positive patch test reactions. The most common allergens were nickel (25.0%), palladium (24.4%), chromium (16.7%), cobalt (15.9%) and stannum (12.5%). Typical allergic symptoms and diagnoses were Pustulosis palmaris et plantaris, lichen planus, stomatitis and contact dermatitis. This study indicates that dentists and dental researchers should be concerned about the allergenic potential of dental metal materials.

Keywords: Allergic reactions, dental materials, patch test

1. Introduction

An increase in allergic diseases in Japan has recently been reported [1–3]; 3–4% of the population have symptoms of asthma, about 30% suffer from allergic rhinitis, and 20% of schoolchildren or junior high-school students have atopic dermatitis. In general, allergic disease is benign, but quality of life decreases remarkably due to cough, mucus and pruritus. It is not an overstatement to say that prevention of allergic disease is a public health issue.

Metal materials are used in dental treatment, but these materials have been reported to also cause allergy. Fleischmann was the first to report allergies to mercury in a dental material in 1928 [4], followed

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by Blumenthal one year later [5]. Various symptoms associated with different metals have been reported in many countries [6–9]. Nickel, chromium, mercury, palladium and cobalt are typical metal materials used in dentistry that caused allergies; reaction to these materials appeared not only in the mucosa of the oral cavity, but also on the skin of hands, feet and/or the entire body [10–12]. In general, allergic reactions to metal are mostly type-IV [13]. Elution of ultra-micro metals causes allergic symptoms, but the pathogenesis is not fully understood. Identification of the allergenic metal with a patch test is commonly utilized for diagnosis of dental metal allergy [14].

Epidemiologic surveillance is an important tool for monitoring trends in sensitization rates and for investigating the mechanism of pathogenesis in a population. The purpose of this study was to: (i) review clinical surveillance of dental allergic hypersensitivity at Tokushima University Dental Hospital; (ii) evaluate the extent and severity of adverse reactions to dental materials in Japanese patients; (iii) define the association between different allergens and the relevant clinical presentations.

2. Patients and methods

We studied the medical records of 212 patients (45 males, 167 females) who visited Tokushima University Dental Hospital for five years (July 2000–June 2005) with suspected dental metal allergy.

Patients underwent oral examination. A skin patch test was done with 26 reagents, including 19 ready-made patch test reagents (Patch test reagentsTM, Torii Pharmaceutical Corporation, Tokyo, Japan) and 9 custom-made reagents (Table 1) [15,16]. These reagents include most of metallic elements that are chief ingredients of alloys used for dental treatment in Japan. An adhesive plaster (MiniplasterTM, Torii Pharmaceutical Corporation) [17] containing these 26 reagents was attached to the upper back [18] and removed after 2 days. Skin reactions were classified at 2 days, 4 days and 7 days using criteria from the International Contact Dermatitis Research Group [19]. Medical records, including demographics and allergic symptoms, were evaluated and compared with our previous epidemiologic survey for five years and before (from 1995 to 2000 and from 1987 to 1995) [20,21].

Table 1
Patch-test reagents

No.	Allergen	% Vehicle	No.	Allergen	% Vehicle
1	CuSO ₄	2aq	14	InCl ₃	1aq
2	PdCl ₂	1aq	15	IrCl ₄	1aq
3	K ₂ Cr ₂ O ₇	0.4aq	16*	MoCl ₅	1aq
4	NiSO ₄	5aq	17	AgBr	2pet
5*	NiSO ₄	2aq	18*	SbCl ₃	1pet
6	CoCl ₂	2aq	19	ZnCl ₂	2pet
7*	HgCl ₂	0.1aq	20	MnCl ₂	2pet
8	HgCl ₂	0.05aq	21*	TiO ₂	30pet
9	SnCl ₄	1aq	22*	TiO ₂	10pet
10*	CdSO ₄	1aq	23*	BaCl ₂	0.5aq
11	HAuCl ₄	0.2aq	24*	BaCl ₂	0.1aq
12	H ₂ PtCl ₆	0.5aq	25	CrSO ₄	2aq
13	FeCl ₃	2aq	26	Al ₂ O ₃	2aq

No mark: Patch-test reagentsTM; *: Custom-made reagents.

Prosthetic appliances that we removed for treatment were analyzed using energy dispersive X-ray analysis (EDAX) (EDX-900™, Shimadzu Corporation, Kyoto, Japan).

This survey was conducted according to the ethical guidelines for epidemiologic research under the Helsinki accord and the results analyzed using SPSS 15.0J (SPSS Incorporated, Chicago, IL, USA).

3. Results

The number of dental metal allergy patients, as well as all the patients that came to Tokushima Dental University Hospital from 1987 to 2005, is shown in Fig. 1.

Two-hundred-and-twelve patients (45 males, 167 females) visited the hospital from July 2000 to June 2005, approximately two-times the number of allergy patients for the previous five years. Of these 212 patients, there was a larger population of female patients compared with previous years. Age distribution of patients in these five years is shown in Fig. 2. There were many female patients aged ≥ 50 years, whereas males were distributed equally. Proportional changes of the patch-test positive rate among year groups were statistically significant (Pearson chi-square test, $p = 0.007$). The positive rate of the July 2000–June 2005 group was high, and that of the July 1995–June 2000 group was low according to the adjusted residual of each cell (Table 2).

The positive reaction rate for all patch-test reagents is shown in Fig. 3. The high positive rate was observed in the order nickel, palladium, chromium, cobalt and stannum. Titanium, barium, antimony, aluminum and silver exhibited a low positive reaction rate. Positive reaction rate to nickel, palladium, chromium and molybdenum was increased compared with before. Spearman rank-order correlation coefficient exhibited significant correlation between the reaction rate in palladium and nickel (NiSO_4 (5%), $\rho = 0.442$, $p < 0.05$; NiSO_4 (2%), $\rho = 0.496$, $p < 0.05$), iron and iridium ($\rho = 0.456$, $p < 0.05$) and zinc and manganese ($\rho = 0.46$, $p < 0.05$).

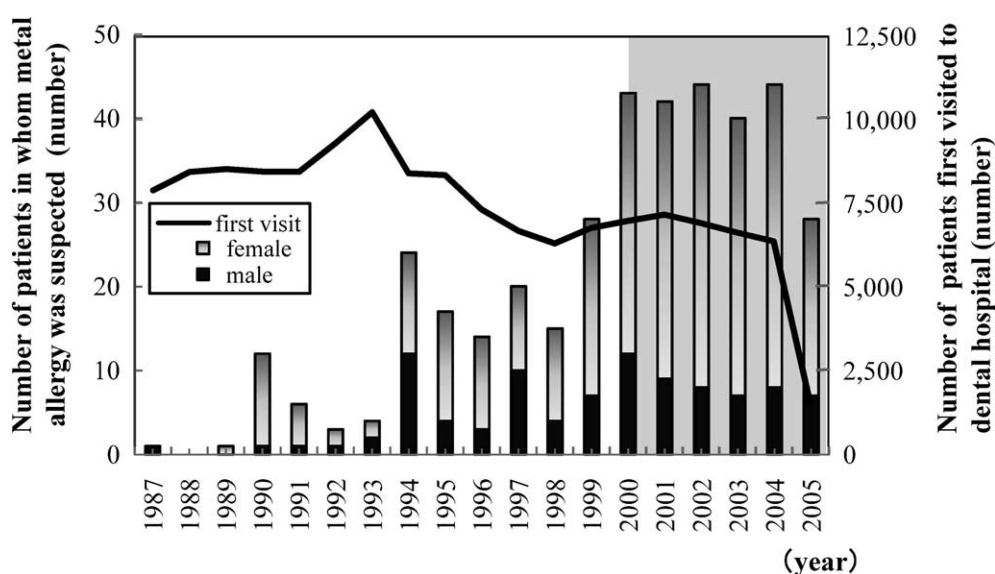


Fig. 1. Number of patients with dental metal allergy. The total number of cases from July 2000 to June 2005 was 212.

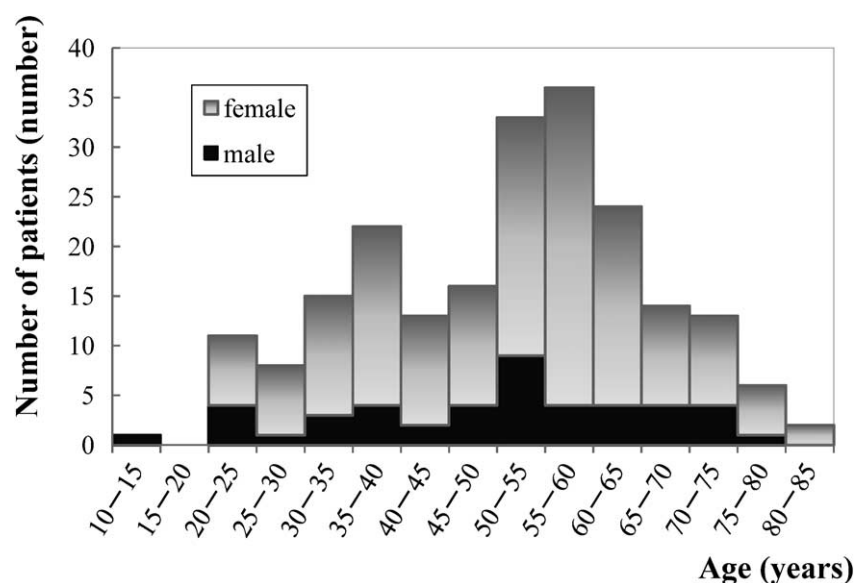


Fig. 2. Demographic characteristics of patients. Mean age was 50.8 years (S.D. 14.4 years). Female age peaked in the fifties; male age was distributed equally.

Table 2
Positive rate of patch-test

Period	July 2000–June 2005	July 1995–June 2000	July 1987–June 1995
Patient number			
Positive	148	60	41
(adjusted residual)	(+2.4)	(−3.2)	(+0.7)
Negative	64	54	19
(adjusted residual)	(−2.4)	(+3.2)	(−0.7)
Positive rate (%)	69.80	52.60	68.90

Note: Pearson chi-square test, $p = 0.007$.

Typical allergic symptoms and diagnoses of these 212 patients are shown in Table 3. Pustulosis palmaris et plantaris, lichen planus, stomatitis and contact dermatitis were frequently observed. The number of patients with pustulosis palmoplantaris was increased compared with before. Pustulosis palmaris et plantaris and contact dermatitis have only cutaneous symptoms, and concomitant intraoral symptoms were not observed in most cases.

Chi-square analysis was done to evaluate the relationship between each symptom and the allergenic metal. Contact dermatitis exhibited significantly high prevalence with positive reaction to nickel reagent (NiSO_4 (5%), $p = 0.011$, $p < 0.05$; NiSO_4 (2%), $p = 0.003$, $p < 0.05$), whereas pustulosis palmoplantaris, lichen planus, stomatitis and allergic rhinitis did not show a significant relationship to each reagent.

The progress of patients who underwent dental metal allergy treatment at our hospital is shown in Table 4. Allergic symptomatic progress was not recorded in the clinical records of some patients. About 60% of patients showed good progress.

EDAX analysis of a patient with contact dermatitis and symptomatic progress are shown in Figs 4 and 5, respectively. Improvement of systemic eruption was achieved by removing the intraoral pros-

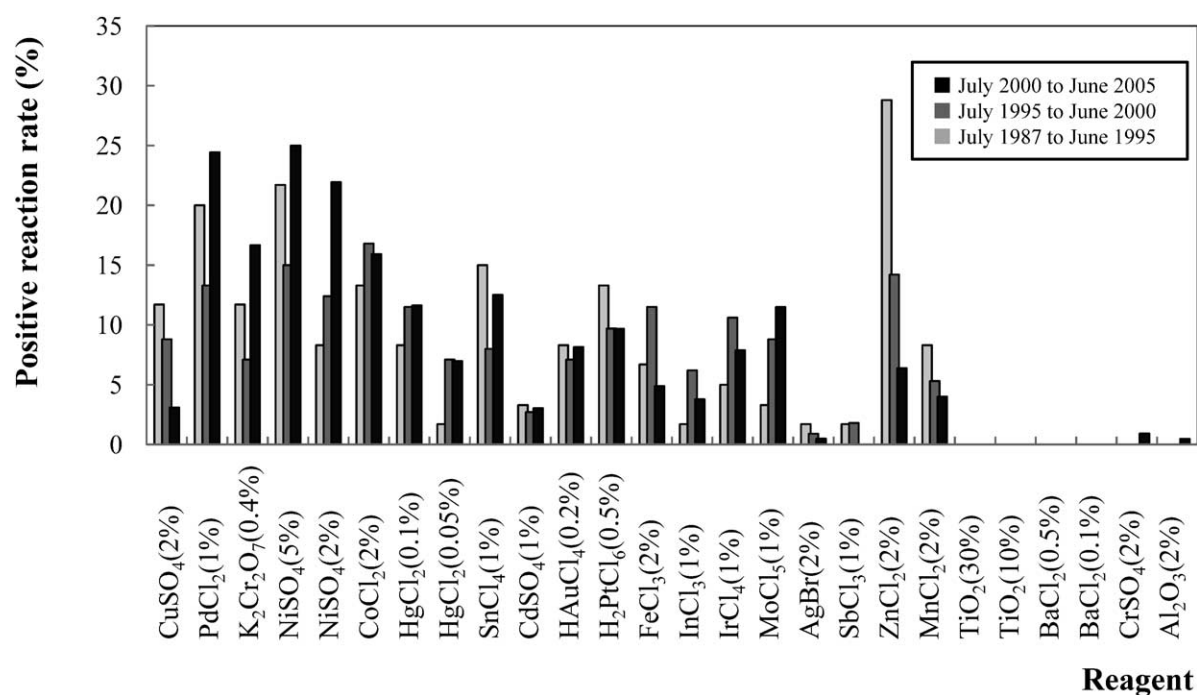


Fig. 3. Positive reaction rates for all patch-test reagents.

thetic appliance (including the positive elements (Pd, Cr, Ni, Co, Hg, Sn, Cd, Au, Pt, Fe, In, Ir, Mo, Zn)).

4. Discussion

Patch test reagents™ have been developed particularly for diagnoses of dental metal allergies [15,16]. Our study showed a higher positive reaction rate than other reports using identical [11] or other patch-test methods [22–24]. The background of our patients may have been different from previous studies that evaluated the general patient population because 86% of our patients were referred from the dental department or dermatology department with a diagnosis (or suspected diagnosis) of metal allergy.

Lifestyle factors could be one factor causing the high prevalence of dental metal allergy [24]. Nickel hypersensitivity is one of the most common metal allergies, and we found a high positive reaction rate to nickel reagents. In Japan, ear/body piercing since the 1990s has been postulated among females especially as the cause of nickel allergy. Larsson-Stymne et al. [25] reported a relationship between pierced earrings and nickel allergy. Sivertsen et al. [24] reported that nickel allergy is associated with pierced earrings rather than local pollution or atopic dermatitis. Jensen et al. [26] reported a decrease in nickel sensitization in Danish schoolgirls whose ears had been pierced after implementation of nickel-exposure regulations in 1992. Other European countries follow this regulation, and such regulations may be required in Japan. One study reported that hypersensitivity reactions to nickel are likely to occur only with prior sensitization from non-dental contacts, and even these are rare [27,28]. Nickel allergens from sources other than dental material should be considered, because use of nickel alloy for dental materials in Japan is on the wane. Patients with inflammatory swelling due to several types of pierced earrings

Table 3
Typical symptoms and diagnoses

Symptoms	Number of patients					
	July 2000–June 2005		July 1995–June 2000		July 1987–June 1995	
	Number	%	Number	%	Number	%
Pustulosis palmaris et plantaris/dyshidrotic eczema	51	24.1	19	21.7	9	15.0
Lichen planus	24	11.3	15	17.1	4	6.7
Stomatitis/cheilitis/gingivitis	21	9.9	13	14.8	8	13.3
Contact dermatitis	18	8.5	37	42.2	17	28.3
Allergic rhinitis	10	4.7			1	1.7
Anthema in hands and plantae	10	4.7	2	2.3		
Glossalgia	8	3.8			8	13.3
Asthma	8	3.8			1	1.7
Urticaria	8	3.8	1	1.1		
Atopic dermatitis	7	3.3	12	13.7		
Candidiasis	7	3.3				
Redness and eczema in one hand	7	3.3	2	2.3	3	5.0
Anthema	7	3.3				
Generalized eczema	7	3.3				
Contact dermatitis and redness with pierced earring, ring and necklaces	6	2.8				
Redness (hands and feet/face)	5	2.4				
Intraoral white lesion	4	1.9				
Glossitis/lingual nervous feeling	4	1.9	2	2.3	4	6.7
Solar dermatitis	4	1.9			2	3.3
Other	40	18.9	11	12.5	3	5.0

Table 4
Patient progress

Progress of patients treated in our department	Number of cases	Ratio (%)
Amelioration	12	31.6
Some amelioration	12	31.6
Unknown	6	15.8
No change	3	7.9
Treatment is underway	2	5.3
Patients did not wish to remove prosthetic appliances	2	5.3
There was no positive element	1	2.6
Total	38	100

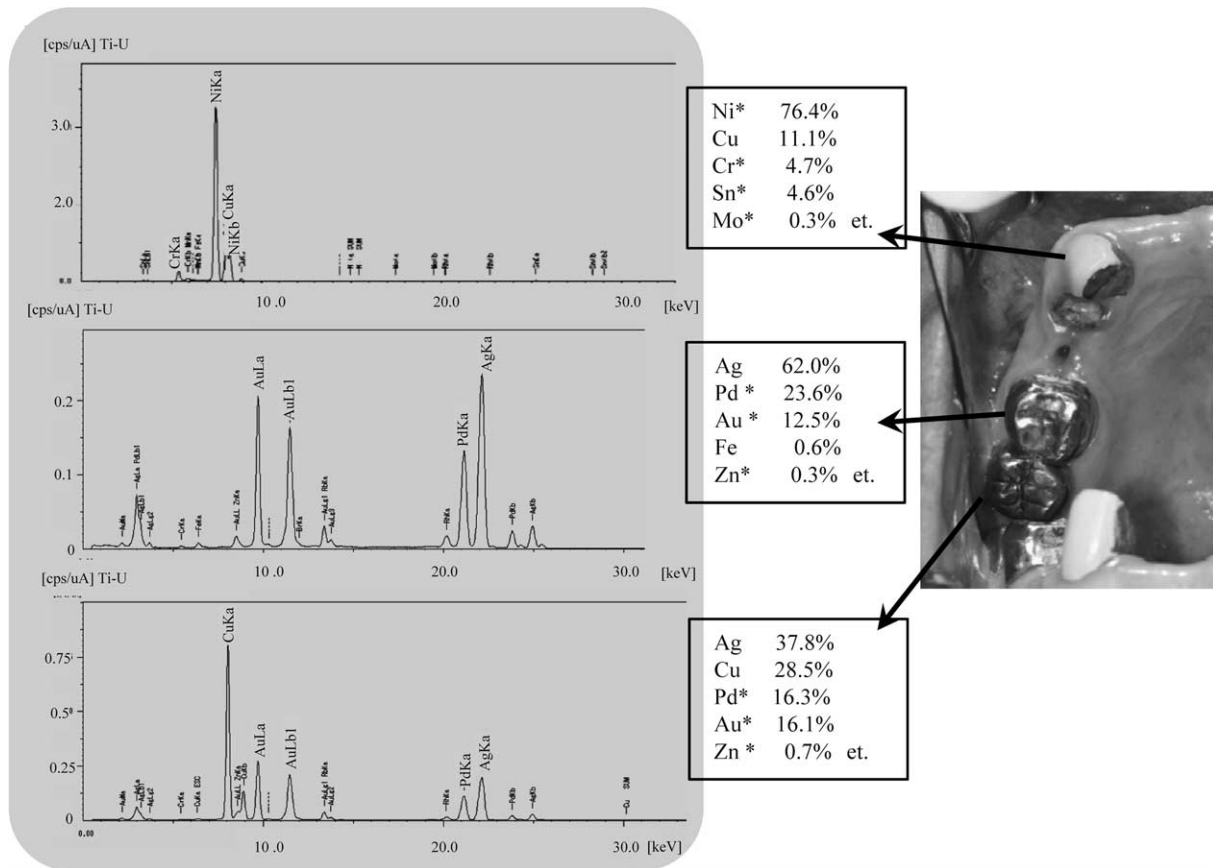


Fig. 4. EDAX analysis of patient with contact dermatitis. Prosthetic appliances included positive elements. * Positive element.

tended to show positive reactions to gold and platinum, as well as nickel and palladium. Nickel allergy is known as an important causative factor of atopic dermatitis [29]. In this study, the positive reaction rate for nickel reagents had a significant relationship with contact dermatitis, yet no relationship with atopic dermatitis. Care should be taken in the use of this material, because nickel allergy often causes serious allergic symptoms.

An important finding was the high positive reaction rate to palladium, because it is indispensable to dental practice. Inoue [18] reported that palladium is unstable in the oral cavity, releasing metal content into the saliva that could cause a serious allergic reaction. In the Japanese health insurance system, gold-and-silver palladium alloy is the primary choice for metallic restorations and fixed prostheses, so many Japanese could be exposed to palladium. A significant correlation between the reaction rates of palladium and nickel was observed, which corresponded with a report about the cross-reaction between nickel and palladium [30]. Palladium and nickel belong to the same group in the periodic table, which suggests cross-sensitization. As well as dentistry, palladium is increasingly used in industry and in the manufacture of fine jewelry, so sensitivities to palladium must be carefully considered.

It is possible that females were sensitized due to wearing pierced earring(s), males were sensitized due to occupational factors, and that an intraoral elution metal subsequently caused symptoms. A dental



Fig. 5. Symptomatic progress. The anthema was reduced by a treatment.

prosthesis would be an unlikely source of sensitization due to gastrointestinal immunologic tolerance. Addition of titanium or platinum to cosmetics using nanotechnology has been highlighted in recent years; and in at least one case, such a cosmetic was considered to be a cause of sensitization. Examination of the vital reaction of a nanomaterial seems to be an immediate requirement. Elution of a metallic ion causes metal allergy. Some studies reported *in-vitro* quantitative evaluation for elution of metallic ions. There are few *in-vivo* studies [31] because evaluation is affected by eating habits, dentifrice and saliva. The kinetics of the ionized metal *in vivo* is incompletely understood (e.g., why some react and others do not; why some react to some antigens and not others). The detailed mechanism of allergy and hypersensitivity with dental metal materials is unknown, but we speculate that the total amount of exposure for specific metallic ions reflects significant trends of dental metal allergy.

5. Conclusion

Two-hundred-and-twelve patients visited the hospital from July 2000 to June 2005, and the positive reaction rate was 69.8%. The high positive reaction rate was observed in the order nickel, palladium, chromium, cobalt and stannum. About 30% patients had only cutaneous symptoms, and concomitant intraoral symptoms were not observed. This study indicates that dentists and dental researchers should be concerned about the allergenic potential of dental metal materials.

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