

ORIGINAL ARTICLE

Metal patch test results from 1990–2009

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ABSTRACT

Although metals are common contact allergens, clinical findings of metal contact dermatitis have varied. Such patients have subsequently become rare in Japan as gold dermatitis caused by ear piercing or baboon syndrome by broken thermometers. To evaluate such clinical findings and to determine the frequency of metal allergy, we analyzed the results of patch testing with 18 metals from 1990–2009. Nine hundred and thirty-one patients (189 men and 742 women, mean age 39.0 years [standard deviation $\pm$ 17.8]) were tested. Metals were applied on the back for 2 days, and the results read with the International Contact Dermatitis Research Group (ICDRG) scoring system 3 days after application. Reactions of + to +++ were regarded as positive. Differences of positive rates between men and women, and patients from 1990–1999 and those from 2000–2009 were analyzed with the χ^2 -test. Differences were considered significant at $P < 0.05$. The metal to which the most patients reacted was 5% nickel sulfate (27.2%), irrespective of sex and phase. Significantly more women reacted to nickel sulfate ($P < 0.01$), mercuric chloride ($P < 0.05$) and gold chloride ($P < 0.01$) than men. Significantly more patients in the 1990s reacted to palladium chloride, mercuric chloride and gold chloride (all $P < 0.01$) than from 2000–2009. Nickel has been the most common metal allergen and mercury-sensitivity has decreased over 19 years in Japan.

Key words: allergic contact dermatitis, gold chloride, mercuric chloride, metal, nickel sulfate, patch test.

INTRODUCTION

Although metals are common contact allergens, clinical findings of metal contact dermatitis have varied. Gold dermatitis caused by ear piercing causing recurrent earlobe redness and swelling, and later intra-cutaneous nodules,^{1,2} and baboon syndrome from broken thermometers^{3–6} have become rare in Japan.

METHODS

The subjects were 931 patients (189 men and 742 women, mean age 39.0 years [standard deviation $\pm$ 17.8], Table 1) at the Department of Dermatology, Showa University Hospital, tested from April 1990 to March 2009. Of these, 550 patients were tested in the 1990s and 381 were tested after 2000

(Table 1). Table 2 shows the frequency of dermatological disease of tested patients. The number of those with eczema, including a clinical diagnosis of contact dermatitis, was 524 (56.3%). No patients had other overt significant health problems.

Patch tests with a metal series, which included 18 metals (Table 3), were applied on the back for 2 days, with vinyl plaster (Mini-plaster or Patch tester Torii; Torii Pharmaceutical, Tokyo, Japan) to avoid chemical reaction between aluminum and mercuric chloride.⁷ The results were read with the International Contact Dermatitis Research Group (ICDRG) scoring system 3 days after application.⁸ Day 7 reading was performed for patients revealing doubtful or vague reactions 3 days after application. Gold sodium thio-sulfate 0.5% (Japanese Society for Contact Dermatitis; or Brial Allergen, Greven, Germany) was added

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Table 1. Patient characteristics

		1990–1999	2000–2009	Total
Men	No.	100	89	189
	Average age (years)	43.0 (SD $\pm$ 17.4)	48.1 (SD $\pm$ 18.9)	45.5 (SD $\pm$ 18.2)
Women	No.	450	292	742
	Average age (years)	35.0 (SD $\pm$ 15.7)	42.1 (SD $\pm$ 18.8)	37.6 (SD $\pm$ 17.3)
Total	No.	550	381	931
	Average age (years)	36.0 (SD $\pm$ 16.3)	43.5 (SD $\pm$ 19.0)	39.0 (SD $\pm$ 17.8)

SD, standard deviation.

Table 2. Incidence of dermatological disease

Disease	
Eczema	524
Contact dermatitis	354
Dyshidrotic eczema	49
Atopic dermatitis	46
Hand eczema	20
Other eczema	55
Palmoplantar pustulosis	140
Lichen planus	46
Mucosal disorder	15
Others	206

after 2003. Reactions of + to +++ were regarded as positive. Results difficult to judge because of technical limitations were excluded. Differences of positive rates between men and women, and patients in the

1990s and those from 2000–2009 were analyzed with the χ^2 -test. Differences were considered significant at $P < 0.05$.

RESULTS

Figures 1 and 2 contrast the positive rates to metals between men and women, and between patients from 1990–1999 and 2000–2009. This study indicates that the metal to which most patients reacted was 5% nickel sulfate, irrespective of sex and phase (the positive rates were 16.4% [31/189] in men, 30.0% [222/741] in women, 28.4% [156/549] in the 1990s and 25.5% [97/381] after 2000; Figs 1,2). The second and third highest positive rates, in that order, were cobalt (10.1%; 19/181) and palladium (7.2%; 8/189)

Table 3. Metals, concentration, vehicle and laboratory

Metals	Concentration	Base	Laboratory
CuSO ₄	2	aq.	Torii Pharmaceutical (Tokyo, Japan)
PdCl ₂	1	aq.	Torii Pharmaceutical
K ₂ Cr ₂ O ₇	0.5	aq.	Torii Pharmaceutical
NiSO ₄	5	aq.	Torii Pharmaceutical
CoCl ₂	2	aq.	Torii Pharmaceutical
HgCl ₂	0.05	aq.	Torii Pharmaceutical
SnCl ₄	1	aq.	Torii Pharmaceutical
CdSO ₄	1	aq.	Torii Pharmaceutical
HAuCl ₄	0.2	aq.	Torii Pharmaceutical
Na ₃ Au(S ₂ O ₃) ₂	0.5	pet.	The Japanese Society for Contact Dermatitis or Brial Allergen (Greven, Germany)
H ₂ PtCl ₆	0.5	aq.	Torii Pharmaceutical
FeCl ₃	2	aq.	Torii Pharmaceutical
InCl ₃	1	aq.	Torii Pharmaceutical
IrCl ₄	1	aq.	Torii Pharmaceutical
MoCl ₅	1	aq.	Provided by Dr Nakayama or Manufacturing Laboratory, Showa University Hospital Pharmacy (Showa, Japan)
AgBr	2	pet.	Torii Pharmaceutical
SbCl ₃	1	pet.	Provided by Dr Nakayama or Manufacturing Laboratory, Showa University Hospital Pharmacy
ZnCl ₂	2	pet.	Torii Pharmaceutical
MnCl ₂	2	pet.	Torii Pharmaceutical

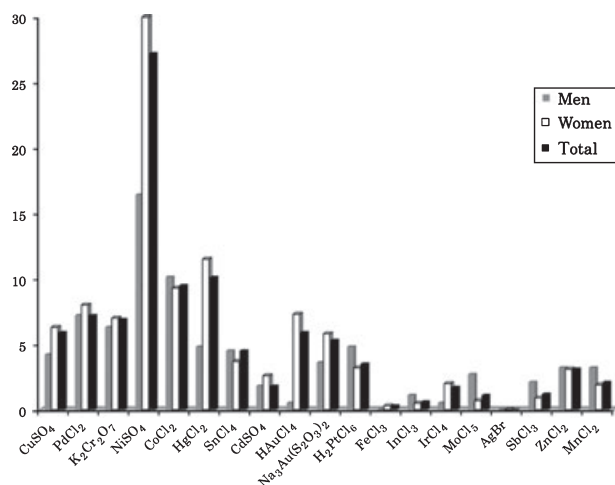


Figure 1. Positive rates to metals between men and women.

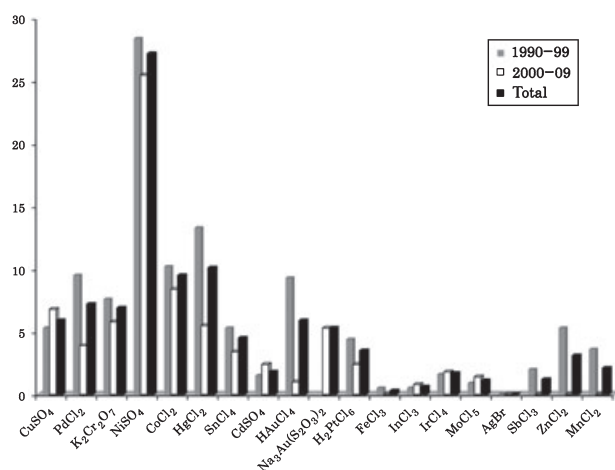


Figure 2. Positive rates to metals between patients from 1990–1999 and those from 2000–2009.

in men, mercury (11.5%; 85/741) and cobalt (9.3%; 69/742) in women, mercury (13.3%; 73/550) and cobalt (10.2%; 56/550) in patients in the 1990s and cobalt (8.4%; 32/381) and copper (6.8%; 26/381) in those after 2000. The second and third highest positive rates were to mercuric chloride (10.1%; 94/930) and to cobalt chloride (9.5%; 88/931) in all subjects.

There were significantly more women reacting to the following metals than men: nickel sulfate (16.4% [31/189] vs 30.0% [222/741], $P < 0.01$), mercuric chloride (4.8% [9/189] vs 11.5% [85/741], $P < 0.05$) and gold chloride (0.5% [1/189] vs 7.3% [54/742], $P < 0.01$). Metals to which significantly more patients reacted to earlier than later were palladium chloride (9.5% [52/549] vs 3.9% [15/381], $P < 0.01$), mercuric

Table 4. Positive rates to 5% nickel sulfate by age group

Age group (years)	No.	Ni-positive	Positive rates
≤19	85	35	41.2
20–29	291	117	40.2
30–39	152	34	22.3
40–49	116	24	20.7
50–59	119	23	19.3
60≤	167	20	12.0
Total	930	253	27.2

chloride (13.3% [73/550] vs 5.5% [21/380], $P < 0.01$) and gold chloride (9.3% [51/550] vs 1.0% [4/380], $P < 0.01$).

A limitation of our study is that our data do not predict the positive rates in the general population because all subjects were patients.

DISCUSSION

The positive rates to nickel sulfate were the highest irrespective of sex and year among 18 metals. Although these data do not predict the positive rates in the general population because all subjects were patients, our results suggest that nickel has been the most common allergen among metals for 19 years. Although the positive rate to nickel sulfate after 2000 was less than in the 1990s (25.5% vs 28.4%; Fig. 2), it does not mean a decrease of nickel allergy. The reason for this is that there were no significant differences between the earlier and later occurrences and that the average age of the later is higher than the earlier. Table 4 shows positive rates to nickel sulfate in each age group: in teenagers 41.2%, and 40.2% in those in their 20s. Although immune regulatory systems may play a role in this phenomenon, there was an overt tendency towards a higher rate in the younger age group. The Danish government has regulated the release of nickel from consumer products since 1990,^{9,10} and the German Ministry of Health declared labeling mandatory in 1992.¹¹ As a result, the prevalence of nickel allergy was reduced, particularly among the younger generation.^{10,11} To reduce nickel-sensitives, we have to consider such regulatory systems.

There were significantly more women reacting to nickel, mercury and gold than men. The positive rate to nickel in women was 30.0%, respectively. In nickel

and gold, this was caused by sex difference of life-style, in particular wearing accessories. Accessories such as ear piercing must play an important role in sensitization as previously reported.^{1,12–17} It was unclear why significantly more women reacted to mercury than men. Mercury-positive patients included 21 women of gold dermatitis caused by ear piercing, and only three of these had a history of sensitization to mercury: breaking thermometers.⁶ We speculated that those sensitized by gold had a tendency to react positively to ionized mercury because only two of 19 gold dermatitis patients were positive to non-ionized mercury (0.5% Hg pet.).⁶ Except for the 18 gold dermatitis patients without a history of mercury sensitization, there were no significant differences of positive rates to mercury between men and women (9/189 [4.8%] vs 67/723 [9.3%]).

There were significantly more patients in the 1990s who reacted to palladium chloride, mercuric chloride and gold chloride than those from 2000–2009. In these metals, the positive rate to mercuric chloride was 13.3% in the earlier 10 years compared to that of 5.5% in the later 9 years ($P < 0.01$). We speculate that the reason for this was decrease of opportunity for mercury sensitization. Although mercury was present in dental filling amalgams, thermometers and Mercurochrome,^{4,18,19} these exposures have been subsequently uncommon. In addition, thimerosal has been decreased or removed from vaccines: for example, to 0.004–0.008 mg/mL in influenza vaccine in Japan (10% of 1990s).²⁰ It is consistent with the clinical finding that baboon syndrome patients have become rare as described above.

The positive rates to gold chloride showed significant differences between the earlier 10 and later 9 years (9.3% vs 1.0%, $P < 0.01$). We speculated that it was caused by changes in ear-piercing materials. Although many wore gold earrings immediately after ear piercing from the 1980s to early 1990s in Japan, stainless or titanium earrings have been subsequently widely used as the “first pierce”.² However, another possibility should be considered: the patch test material of gold chloride could have a problem in the later 9 years because the positive rate to it was lower than gold sodium thiosulfate (1.0% vs 5.3%). Gold sodium thiosulfate is more reliable than gold chloride for patch testing as Fowler Jr. suggested.²¹ If compared between the positive rate to

gold chloride in the earlier group and that to gold sodium thiosulfate, a more reliable material, in the later group, there were no significant differences as we previously reported: gold allergy has changed from being clinically overt to occult in Japan.²

Although we applied 2% zinc chloride and 2% manganese chloride, Suzuki suggested that optimal patch test concentrations of both were 0.5%.²² In the earlier 10 years, most positive reactions to them were considered as irritant; reactions were weaker after 3 than 2 days and pustules were common. Although the reason why such reactions disappeared in the later 9 years were unclear, change of patch test unit may play some role to reduce irritant reactions. It was unclear why significantly more patients in the 1990s reacted to palladium than the later 9 years because it has been commonly used in dental materials.

In regard of clinical relevance, positive patch tests were relevant to clinical symptoms and/or past medical history in 148 nickel-positive (58.5%), 21 gold-positive (38.1%) and 11 mercury-positive patients (20.4%). Although its significance was unclear, significantly more palmoplantar pustulosis than other patients reacted to platinum (7.1% [10/140] vs 2.9% [23/791], $P < 0.05$).

In conclusion, our results suggest that nickel has been the most common metal allergen and mercury-sensitivity has decreased over the past 19 years.

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