

A retrospective study of 2585 patients patch tested with the European standard series in Hong Kong (1995–99)

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Abstract

Background Data on patch test findings in Hong Kong are scarce, with the last survey performed more than 10 years ago. A retrospective analysis of results from all patch tests performed on patients with suspected allergic contact dermatitis from January 1995 to December 1999 in the Social Hygiene Service, which provides a public dermatology service in Hong Kong, was undertaken. We aimed to explore the demographic data associated with positive reactions and the profile of contact sensitizing allergens in Hong Kong.

Methods A total of 2585 patients were patch tested with the European standard series during the period. Most were Chinese, with a female-to-male ratio of 3 : 2.

Results One or more positive responses were noted in 1415 patients (54.7%). The most common allergen was nickel sulfate (24.4%), followed by fragrance mix (13.7%), cobalt chloride (8.7%), *p*-phenylenediamine (6.0%), and balsam of Peru (5.7%). Nickel sensitivity was more common in female patients, and dichromate sensitivity was more common in male patients ($P < 0.001$). Female gender, an age of 40 years or below, truncal and upper limb involvement, absence of lower limb involvement, and a positive atopy history were significant risk factors for nickel sensitivity.

Conclusions This study provides a profile of allergens responsible for allergic contact dermatitis in the public dermatology service in Hong Kong. A prospective study, using a larger panel of allergens, involving patients from both the private and public sectors, would provide a more comprehensive profile of contact allergens in Hong Kong and contribute to the establishment of a local standard series.

Introduction

Patch testing is essential in the diagnosis and management of allergic contact dermatitis. It aids in the identification of etiologic allergens and subsequent instructions in allergen avoidance or protection. Contact sensitization may be influenced by genetic factors, age, sex, and atopy.¹ Information on these allergens is also important in the monitoring of epidemiologic trends and the planning of preventive and regulatory activities.

Data on patch test findings in Hong Kong are scarce. The last survey on this issue was performed more than 10 years ago, and was based on a single private dermatology practice.²

In this retrospective study, we analyzed the results from all patch tests performed on patients with suspected allergic contact dermatitis from January 1995 to December 1999 in the Social Hygiene Service, the main provider of public dermatology services in Hong Kong. We aimed to explore the demographic data associated with positive reactions and the profile of contact sensitizing allergens in the territory.

Materials and Methods

Patients

This retrospective study included all patients patch tested in nine clinics administered by the Social Hygiene Service between 1995 and 1999. The patch test reports and medical records were retrieved for analysis.

The Social Hygiene Service, under the Department of Health, has a network of nine clinics providing public dermatology services to all districts in Hong Kong. It receives referrals from public and private medical practitioners. Most patients seen are Chinese, reflecting the composition of the local population (94.9% being Chinese by ethnicity according to the 2001 census).³

Between 1995 and 1999, the total number of new dermatology cases entertained by the Service amounted to 165,908, with eczema accounting for 24.5% (40,594). It is usual practice to perform patch testing in patients with suspected allergic contact dermatitis. The total number of patients who underwent patch testing was 2585,

corresponding to 6.4% of all new cases of eczema seen in the same period.

Patch testing

After obtaining informed consent, all patients were tested with the European standard series (Hermal, Reinbek, Germany). Finn chambers (Epitest Limited Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster, Vennesla, Norway), containing the allergens, were applied to the upper back of the patient. The patients were instructed to keep the test area dry and to avoid vigorous exercise. They were requested to return after 48 h for the first reading. The tape strips were removed by the nursing staff. The result was read by the attending dermatologist 30 min later to avoid dermatographic erythema. The second reading was made at 96 h.

The patch test reactions were classified according to the International Contact Dermatitis Research Group recommendations.⁴ A reaction was classified as positive if it was of “+” or more in intensity on the second reading. The clinical relevance of a positive response was determined by considering the clinical picture at the time of presentation and possible allergen exposure. A positive reaction to the patch test had “present relevance” if it was the cause of the patient’s dermatitis at the time of presentation. The rest of the positive responses were regarded to have “unknown relevance” in this study.

Data analysis

The data were coded and analyzed using the Statistical Package for Social Sciences (SPSS 9.0, SPSS Inc., Chicago, IL, USA). Associations between patient characteristics (namely gender, age group, atopy) and a positive patch test result were evaluated using the chi-squared test. It was also used to assess the associations between patient characteristics and a positive reaction for individual allergens, as well as the association between the number of positive responses and gender. The strengths of the associations were summarized using odds ratios (ORs) and 95% confidence intervals (95% CIs). All calculated *P* values were two-sided and *P* < 0.05 was considered to be statistically significant. The level of significance α was adjusted for multiple testing using the Bonferroni correction, by dividing it (α) by the number of tests.⁵ It was applied to the univariate analysis of the associations between the patient characteristics and positive reaction for individual allergens. Multivariate analysis (logistic regression, forward stepwise conditional) was performed to evaluate the influence of individual risk factors on the outcome of patch testing. The interaction term (gender by age group) was entered into the model for testing. The criterion for entering a variable in the model was *P* ≤ 0.05.

Results

Patient characteristics

All 2585 patients patch tested during the study period were included in the analysis. Of the 1535 female patients, 1000

(65.1%) were aged 40 years or below. For the male patients, 477 (45.4%) were aged 40 years or below. Nearly all (99.1%) were Chinese. The duration of presenting skin problems was 1 year or more in 57.6%, and more than 1 month but less than 1 year in 31.1%.

Patch test results

A total of 1415 patients (54.7%) had one or more positive responses to the allergens in the European standard series. Of these, 878 (62.0%) were female. The positive reactions had present relevance in 40.8% (*n* = 578), and allergic contact dermatitis was diagnosed. The rest of the positive results (59.2%) were considered to have “unknown relevance” to the clinical picture at the time of presentation.

Table 1 shows the distribution of sensitization to the allergens according to gender. Positive responses were present to all allergens in the European standard series. For the common allergens, the positive patch test reactions were almost equally distributed between male and female patients, with the exception of nickel sulfate and potassium dichromate.

Age and gender

A positive patch test result, as defined by the presence of at least one positive patch test response, was more common in female than male patients (*P* = 0.002). The OR of having a positive patch test for female to male patients was 1.277 (95% CI, 1.09–1.50).

A positive patch test result was also more common in those aged 41 years or above than those aged 40 years or below in male patients (*P* = 0.001). The OR of having a positive patch test for males aged ≥ 41 years relative to those aged ≤ 40 years was 1.52 (95% CI, 1.19–1.94). No such difference was observed in female patients.

The patterns of sensitivity to various allergens differed by age and gender. It was found that nickel sulfate sensitivity was more common in those aged 40 years or below (when compared with those aged 41 years or above) in both genders (female: *P* < 0.001; OR, 2.01; 95% CI, 1.57–2.57; male: *P* < 0.001; OR, 2.06; 95% CI, 1.48–2.87). Cobalt chloride sensitivity was statistically more common in those aged 40 years or below in female patients, but not in male patients (female: *P* = 0.002; OR, 1.90; 95% CI, 1.26–2.87).

Thiuram mix sensitivity was more common in those aged 41 years or above in female patients only (*P* < 0.001; OR, 2.61; 95% CI, 1.69–4.04). *p*-Phenylenediamine sensitivity was more common in those aged 41 years or above in both genders (female: *P* < 0.001; OR, 4.20; 95% CI, 2.57–6.85; male: *P* < 0.001; OR, 4.96; 95% CI, 2.65–9.30). Fragrance mix sensitivity was also more common in those aged 41 years or above in both genders (female: *P* < 0.001; OR, 1.70; 95% CI, 1.27–2.27; male: *P* < 0.001; OR, 1.98; 95% CI, 1.35–2.90).

For all ages, only nickel sulfate sensitivity was more common in female patients [*P* < 0.001; OR (female/male),

Table 1 Patch test results of the European standard series

Allergens in the European Standard Series	Number of patients with positive reaction(s) (% of the total number of patients tested in each category)		
	Female (n = 1535)	Male (n = 1050)	Total (n = 2585)
Nickel sulfate* 6H ₂ O 5%	456 (29.7%)	174 (16.6%)	630 (24.4%)
Fragrance mix 8%	217 (14.1%)	137 (13.0%)	354 (13.7%)
Cobalt chloride 6H ₂ O 1%	140 (9.1%)	85 (8.1%)	225 (8.7%)
p-Phenylenediamine free base 1%	77 (5.0%)	77 (7.3%)	154 (6.0%)
Balsam of Peru 25%	87 (5.7%)	61 (5.8%)	148 (5.7%)
Thiuram mix 1%	88 (5.7%)	52 (5.0%)	140 (5.4%)
Neomycin sulfate 20%	89 (5.8%)	37 (3.5%)	126 (4.9%)
Colophony 20%	79 (5.1%)	44 (4.2%)	123 (4.8%)
Potassium dichromate* 0.5%	35 (2.3%)	75 (7.1%)	110 (4.3%)
Wool alcohols 30%	54 (3.5%)	29 (2.8%)	83 (3.2%)
Formaldehyde in water 0.01%	45 (2.9%)	26 (2.5%)	71 (2.7%)
Kathon CG in water 1%	38 (2.5%)	23 (2.2%)	61 (2.4%)
Paraben mix 16%	28 (1.8%)	24 (2.3%)	52 (2.0%)
Clioquinol 5%	24 (1.6%)	25 (2.4%)	49 (1.9%)
p-tert-Butylphenol-formaldehyde resin 1%	22 (1.4%)	19 (1.8%)	41 (1.6%)
Benzocaine 5%	18 (1.2%)	19 (1.8%)	37 (1.4%)
Quaternium-15 1%	22 (1.4%)	12 (1.1%)	34 (1.3%)
Epoxy resin 1%	16 (1.0%)	18 (1.7%)	34 (1.3%)
Mercapto mix 2%	12 (0.8%)	17 (1.6%)	29 (1.1%)
Mercaptobenzothiazole 2%	12 (0.8%)	17 (1.6%)	29 (1.1%)
Sesquiterpene lactone mix 0.1%	9 (0.6%)	8 (0.8%)	17 (0.7%)
Primin 0.01%	5 (0.3%)	6 (0.6%)	11 (0.4%)
N-Isopropyl-N'-phenyl-p-phenylenediamine 0.1%	4 (0.3%)	7 (0.7%)	11 (0.4%)

*Chi-squared test: $P < 0.001$ (two-tailed).

2.13; 95% CI, 1.75–2.59] (Table 1). By contrast, only potassium dichromate sensitivity was more common in male patients [$P < 0.001$; OR(male/female), 3.30; 95% CI, 2.19–4.96].

Site of involvement

A total of 1484 patients (57.9%) had upper limb involvement. This was followed by head and neck (1060 patients, 41.3%), lower limb (690 patients, 26.9%), trunk (608 patients, 23.7%), and genital (37 patients, 1.4%) involvement. As there may be multiple sites of involvement for some patients, the total adds up to more than 2585 (the total number of patients).

Atopy

Two hundred and fifty-eight patients (10.0%) were assessed as atopic and 1726 patients (66.8%) as nonatopic. Atopy was defined as the presence of a personal or family history of asthma, allergic rhinitis, or atopic eczema. Owing to the retrospective nature of our study, information on atopy was not available for 601 patients (23.2%), who were therefore excluded from this part of the analysis. There was a statistically significant difference in the total contact sensitization rate between atopics and nonatopics [$P = 0.01$; OR(atopic/nonatopic), 1.41; 95% CI, 1.08–1.83]. Specifically, nickel

sensitization was more common in atopic individuals [$P < 0.001$; OR(atopic/nonatopic), 1.84; 95% CI, 1.38–2.46]. Otherwise, there was no statistically significant difference between atopic and nonatopic patients in terms of sensitization to the other allergens.

Multiple sensitivity

Of the 1415 patients who had one or more positive patch test response, 714 (50.5%) had one, 416 (29.4%) had two, and 285 (20.1%) had three or more positive responses. There was no statistically significant difference between female and male patients in terms of the total numbers of sensitized allergens. As expected, nickel sensitivity was correlated with cobalt sensitivity (Spearman's rank correlation coefficient $r_s = 0.250$; $P < 0.001$). Dichromate sensitivity was correlated with cobalt sensitivity ($r_s = 0.186$; $P < 0.001$). Sensitivities to fragrance mix and balsam of Peru were also associated ($r_s = 0.284$; $P < 0.001$), as were sensitivities to balsam of Peru and paraben mix ($r_s = 0.190$; $P < 0.001$).

Multivariate analysis

Using logistic regression (forward stepwise conditional), factors favoring a positive patch test (OR > 1) and factors favoring a negative result (OR < 1) are shown in Table 2.

Table 2 Odds ratios of risk factors for a positive patch test result*

Factor	Odds ratio (95% confidence interval)	P
Age (41 years and above vs. 40 years and below)	1.23 (1.03–1.46)	0.021
Gender (female vs. male)	1.21 (1.01–1.43)	0.035
Head and neck involvement (presence vs. absence)	1.24 (1.02–1.51)	0.033
Trunk involvement (presence vs. absence)	1.53 (1.25–1.87)	< 0.001
Upper limb involvement (presence vs. absence)	1.37 (1.12–1.66)	0.002
Lower limb involvement (presence vs. absence)	0.66 (0.54–0.80)	< 0.001
History of atopy (presence vs. absence)	1.45 (1.10–1.90)	0.007
History of atopy (not assessed vs. absence)	6.06 (4.77–7.69)	< 0.001

*Derived from a logistic regression model.

Table 3 Odds ratios of risk factors for a positive patch test result for the top five allergens

Factor	Odds ratio (95% confidence interval)				
	Nickel	Fragrance mix	Cobalt	p-Phenylenediamine	Balsam of Peru
Age (41 years and above vs. 40 years and below)	0.48 (0.39–0.60)§	1.68 (1.30–2.06)§	0.59 (0.44–0.80)‡	4.77 (3.25–7.01)§	1.43 (1.02–2.00)*
Sex (female vs. male)	1.88 (1.52–2.32)§				
Head and neck involvement (presence vs. absence)				1.94 (1.39–2.72)§	
Trunk involvement (presence vs. absence)	2.99 (2.41–3.72)§		1.52 (1.11–2.07)†		
Upper limb involvement (presence vs. absence)	1.31 (1.04–1.64)*	1.40 (1.10–1.77)†			
Lower limb involvement (presence vs. absence)	0.69 (0.54–0.87)†		0.64 (0.45–0.91)*		
History of atopy (presence vs. absence)	1.44 (1.06–1.96)*				
History of atopy (not assessed vs. absence)	2.62 (2.11–3.26)§	2.27 (1.78–2.89)§	2.09 (1.56–2.80)§	2.02 (1.42–2.87)§	2.18 (1.54–3.08)§

* $P < 0.05$; † $P < 0.01$; ‡ $P < 0.005$; § $P < 0.001$.

The interaction term, gender by age group, was tested and excluded because of a lack of statistical significance. To handle the lack of data on atopy for 601 patients, two indicator variables, namely “history of atopy (presence vs. absence)” and “history of atopy (not assessed vs. absence)” were included in the model. The influence of individual risk factors on the likelihood of a positive patch test result to each of the top five allergens was also analyzed (Table 3).

Discussion

Despite the intrinsic limitations of a retrospective approach, this study was the first territory-wide investigation on allergic contact dermatitis in Hong Kong. We retrieved all the relevant clinical data from the medical records, except for information on atopy in 601 patients. Moreover, patients in our clinics did

not have to pay extra charges for patch testing. Therefore, our patients were not selected by their ability to pay, and the decision for patch testing depended entirely on clinical suspicion and the patient’s willingness. In this respect, we considered that our study sample was fairly representative of this patient group in the community. Most studies on patch testing have been patient based, with a few exceptions, such as the Copenhagen Allergy Study in Denmark^{6,7} and a population-based study in Germany.⁸ It should be noted that our study focused on the findings of the European standard series, which is the main screening tray used in patients suspected to have allergic contact dermatitis in Hong Kong. Thus, it is possible that we might have missed allergens that are not included in the European standard series.

About 55% of patients had one or more positive responses, but only 40.8% of the positive results had present relevance. This is an important limitation of our study. Owing to the

difficulty in ascertaining "past relevance" (positive reactions as the cause of a previous dermatitis) in a retrospective study, we restricted ourselves to interpreting the clinical relevance of a positive response by considering the dermatitis at the time of presentation and possible allergen exposure. Only "present relevance" was sought in this study, with the rest of the positive reactions regarded as having "unknown relevance."

The female preponderance in our positive patch test results ($P = 0.002$) was in line with most series, and could be attributed to the large number of nickel-sensitized women (456 of a total of 1415 patients with one or more positive results).¹⁹ In addition, using logistic regression, seven risk factors favoring a positive patch test were identified, with the effect of each given by its OR (Table 2). "Genital involvement" was excluded from the model because of statistical insignificance ($P = 0.053$). This may be a result of the relatively small number of patients with genital involvement ($n = 37$) in our series. The two indicator variables created for atopy showed interesting findings. A positive patch test result was more common in those with a history of atopy "not assessed" than those with no atopy history (OR, 6.06; 95% CI, 4.77–7.69). This OR was greater than that for those with atopy relative to those without (OR, 1.45; 95% CI, 1.10–1.90) (Table 2). One possible explanation is that these "not assessed" patients were clinically so typical of allergic contact dermatitis that the clinician did not ask for a history of atopy. A prospective study carried out with strict protocol adherence would help to determine the effect of atopy on patch test results.

Nickel sulfate was the most common allergen (24.4% of all patients), as with most Western and Asian series.^{7,10–12} The female predominance (29.7% of all 1535 female patients) was most probably a result of different exposure. Logistic regression of our data further showed that nickel sensitization was more likely if the patient was 40 years of age or below, female, atopic, with truncal and upper limb involvement but no lower limb involvement. Although the effect of atopy on nickel sensitization is not conclusive in the literature, atopy favored a positive response to nickel in our series (OR, 1.44; 95% CI, 1.06–1.96).^{1,8,13–15} Interestingly, a positive patch test result to nickel was more common in those with their history of atopy "not assessed" than in those with no atopy history (OR, 2.62; 95% CI, 2.11–3.26) (Table 3). As discussed in the previous paragraph, one possible explanation is that these "not assessed" patients were clinically so typical of allergic contact dermatitis to the allergen (in this case, nickel) that the clinician did not ask for a history of atopy. The same explanation can be offered for similar findings amongst the other four allergens in Table 3. To prevent nickel sensitization, the most effective means is to reduce exposure to nickel. For example, Denmark issued a statutory order limiting the release of nickel from metal items in close contact with the skin to less than 0.5 $\mu\text{g}/\text{cm}^2/\text{week}$ in 1991.¹⁶ The frequency of

nickel allergy decreased from 24.5% in 1985–86 to 9.2% in 1997–98 in children aged 0–18 years in a recent Danish study ($P < 0.0008$).¹⁷ A similar regulation was adopted in the European Union.¹⁸

Fragrance mix was the second most common allergen in our series (13.7% of all patients), as in most centres.^{10–12,19} Both fragrance mix and balsam of Peru are markers of fragrance or perfume allergy, thus explaining the correlation between their sensitivities in our study. In addition, sensitization to both was more likely if the patient was aged 41 years or above. An association between sensitivity to paraben mix and balsam mix was also noted in our study, possibly because parabens are commonly used as preservatives in cosmetics.²⁰

Fragrances accounted for 30% of identified cases of allergic contact dermatitis caused by cosmetics.²¹ A total of 423 patients in our series of 2585 were sensitized to either fragrance mix or balsam of Peru, reflecting the prevalence of fragrance allergy. The evaluation of these patients is often difficult because labeling of cosmetics with their ingredients is not yet required by law in Hong Kong. Cosmetic ingredient labeling was made compulsory in the European Union in 1997, 20 years after such a requirement was implemented in the USA.²² Such a lack of regulation in Hong Kong also makes avoidance difficult for the consumer.

Cobalt was the third most common allergen in our series. Multiple metal sensitivities are a well-known phenomenon and, as in our series, cobalt sensitivity is associated with nickel and dichromate sensitivity.¹⁵ In our series, cobalt shared some of the risk factors with nickel: 40 years of age or below, truncal involvement, and no lower limb involvement. *p*-Phenylenediamine was the fourth most common allergen. Logistic regression analysis of our data showed that sensitization to this agent was more likely if the patient was 41 years of age or over and had head and neck involvement. This is consistent with the exposure to *p*-phenylenediamine in permanent hair dyes in the middle-aged and older in Hong Kong.

Although positive responses to all allergens in the European standard series were found, the frequencies of positive reactions to sesquiterpene lactone mix, primin, and *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine were less than 1%. A modification of the European standard series by excluding these three allergens may be considered in Hong Kong.⁴ Moreover, allergens of local interest may be added. For example, topical traditional Chinese medicines (such as myrrh, mastic), which have been reported to cause allergic contact dermatitis in this locality, are suitable candidates.^{23–25}

In conclusion, this study provides a profile of the allergens responsible for allergic contact dermatitis in the public dermatology service in Hong Kong. The frequency of nickel and fragrance sensitization calls for more efforts in preventive and perhaps regulatory measures. This survey involved the retrospective analysis of data from patch testing with the European standard series in the public sector; however a

prospective study involving both public and private dermatologists, using a more comprehensive panel of allergens, including those specific to the local community and workforce, would provide more insights into the agents responsible for contact allergic dermatitis in Hong Kong. A local standard series, taking the epidemiologic data into account, can then be formulated and updated as necessary.

Disclaimer

The views expressed in this article are those of the authors and not necessarily of their respective institutions.

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