

Contact Sensitization in Chinese Patients with Hand Eczema

Chunya Ni, Xia Dou, Jianyou Chen, Xuejun Zhu, and Lingling Liu

Background: Contact sensitization is an important cause of hand eczema, a common disease that affects both daily and occupational life.

Objective: To describe contact allergens in Chinese patients with hand eczema and to analyze the association between allergens and occupational exposure.

Methods: Three hundred sixty-six patients with hand eczema underwent patch testing with a modified North American standard series between September 1989 and December 2009.

Results: Positive patch-test reactions were observed in 74% of patients. The most frequent allergens were p-phenylenediamine (22.7%), nickel sulfate (21.9%), fragrance mix (19.9%), ammoniated mercury (19.7%), and carba mix (17.8%). Nickel and fragrance allergy in women, and carba mix and chromate allergy in men, showed gender predilection, and 64.2% of patients developed hand eczema from occupational exposure. Positive reactions to p-phenylenediamine in hairdressers and to chromate in metalworkers and construction workers presented higher frequencies ($p < .05$).

Conclusions: p-Phenylenediamine, nickel, fragrance, mercury, and rubber chemicals are common allergens in Chinese patients with hand eczema. Gender and occupation may cause different exposures; thus, allergens may vary.

HAND ECZEMA is a common problem that affects occupational as well as private aspects of life. The prevalence of hand eczema in Swedish adults was 9.7% in 1996,¹ and the crude incidence rate was reported to be 5.5 to 8.8 cases per 1,000 person-years.^{2,3}

The development of hand eczema is often influenced by multiple factors, including exogenous and endogenous aspects. Epidemiologic studies have identified contact sensitization as one of the most important factors associated with persistent symptoms of hand eczema.⁴ Contact sensitization may be the primary cause of hand eczema or a complication of irritant or atopic hand eczema.⁵ Appropriate patch testing is helpful in identifying contact allergens, and the avoidance of exposure to allergens in cases of allergic contact dermatitis often leads to great improvement in hand eczema.

This retrospective study aimed to (1) identify the contact allergens in Chinese patients with hand eczema by

patch testing and (2) to analyze the association between contact allergy and occupational hand eczema.

Patients and Methods

Between September 1989 and December 2009, 366 patients with hand eczema were patch-tested in our contact dermatitis clinics with a modified North American standard series (Peking University Health Science Center, Beijing, China). The diagnosis of hand eczema was determined through the patient's medical history and physical examination. Patients with hand eczema who were suspected of having contact allergy were included.

All allergens were administered with modified Finn Chambers (Peking University Health Science Center) on modified Scanpor tape (Peking University Health Science Center) applied on the upper back for 2 days; results were recorded on day 2 and on day 3 or day 4. The method of procedure and the evaluation of the readings were in accordance with International Contact Dermatitis Research Group guidelines.

Statistical analysis was performed with SPSS version 11.5 software (SPSS Inc., Chicago, IL). Data were presented as mean $\pm$ standard deviation. The chi-square test was used to compare the frequency of positive reactions between groups, and $p < .05$ was considered statistically significant.

From the Department of Dermatology, Peking University First Hospital, Beijing, China, and the Department of Dermatology, Huashan Hospital of Fudan University, Shanghai, China.

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Results

Of 366 patients, 256 were females and 110 were males, for a gender ratio of 2.3:1. The mean age was 38.2 ± 13.9 years (range, 3–76 yr). Stratified with gender and age, a preponderance in females aged 20 to 39 years was observed (Fig 1). The mean duration of disease was 3.6 ± 4.7 years (range, 1 week to 33 years). Thirty patients (8.2%) had a history of atopic disease (atopic dermatitis, allergic rhinitis, or allergic asthma).

One or more positive patch-test reactions were found in 271 (74.0%) of the patients (73.4% of the 188 females and 75.5% of the 83 males). Of 30 patients with a history of atopy, 22 (73.3%) had positive patch-test reactions. p-Phenylenediamine (PPD) was the allergen with the highest positive rate (22.7%), followed by nickel sulfate (21.9%), fragrance mix (19.9%), ammoniated mercury (19.7%), carba mix (17.8%), potassium dichromate (13.1%), thiuram mix (12.0%), black rubber mix (9.8%), ethylenediamine (6.8%), formaldehyde (6.0%), and colophony (5.7%). Positive patch-test reactions in relation to gender are shown in Table 1. The number of positive reactions to nickel sulfate and fragrance mix were much higher in women whereas contact allergies to carba mix and potassium dichromate were more frequent among men ($p < .05$). No significant differences between genders were found in regard to the other allergens.

A total of 235 patients (64.2%) developed hand eczema from occupational exposure, including 26 health care workers (11.1%), 25 office workers (10.6%), 23 textile workers (9.8%), 22 rubber workers (9.4%), 18 accountants (7.7%), 18 teachers (7.7%), 17 hairdressers (7.2%), and 12 metalworkers (5.1%). Among them, 172 patients (73.2%) had one or more positive patch-test reactions. The most frequent allergens found for each occupation group are shown in Table 2. Patch-test reactions to PPD in hairdressers presented a higher positive rate, compared

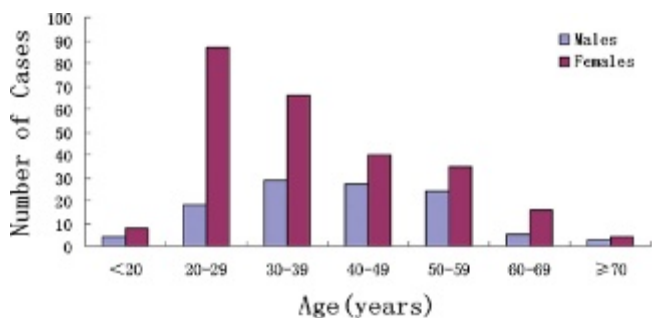


Figure 1. Distribution of hand eczema in relation to gender and age ($n = 366$). Preponderance was most pronounced in the younger female groups.

to those not in this occupation in the study sample ($p < .05$). Similar results were found in metalworkers and construction workers who were allergic to potassium dichromate.

Discussion

Although it is generally believed that irritant factors are the most common causes of hand eczema,^{5,6} contact sensitization should not be neglected because it may be the primary cause of hand eczema or a complication of irritant or atopic hand eczema. The etiology of hand eczema cannot be determined from clinical manifestations, and a carefully conducted patch test is mandatory in all cases of hand eczema lasting more than 4 weeks to determine the specific diagnosis and for qualified counseling of the patient.⁵ However, positive patch-test reactions are not always clinically relevant for patients with hand eczema. Final diagnosis of allergic contact dermatitis needs the support of a corresponding medical history.

PPD, nickel sulfate, fragrance mix, ammoniated mercury, rubber chemicals (including carba mix, thiuram mix, and black rubber mix), and potassium dichromate were found to be the most frequent contact allergens in our study, which is mostly in agreement with previous studies.^{7,8} Besides nickel, fragrance and rubber chemicals, the particularly high positive rates of PPD and ammoniated mercury in our study sample are noteworthy.

PPD is a frequent and important component of permanent hair-dye products; exposure to it may cause severe allergic contact dermatitis involving mainly the scalp, face, and hands. Consumer hair dyeing has been considered the most prominent cause of PPD sensitization, followed by occupational hair-dye exposure and cross-sensitization to textile dyes.⁹ In our study, the majority of patients with positive reactions to PPD presented a history of hair-dye exposure. Furthermore, up to 82% of positive reactions to PPD were found in hairdressers. Our findings indicate that occupational exposure may be more important for PPD allergy in patients with hand eczema.

A high frequency of positive reaction to ammoniated mercury, seldom mentioned in previous studies, was also found in our study sample. Ammoniated mercury is an inorganic mercury compound that is extensively used in medical and cosmetic products. Primary sensitization is most likely due either to inoculation with vaccines containing mercury preservatives or to dental restorations.¹⁰ Cross-sensitization to metallic mercury and mercury compounds may also increase the rate of positive

Table 1. Positive Patch-Test Reactions in Relation to Gender

<i>Allergen*</i>	<i>Positive Reactions</i>	<i>Females</i>	<i>Males</i>	<i>p Value</i>
	(<i>n</i> = 366)	(<i>n</i> = 256)	(<i>n</i> = 110)	
<i>p</i> -Phenylenediamine 1%	83 (22.7%)	61 (23.8%)	22 (20.0%)	.423
Nickel sulfate 5%	80 (21.9%)	65 (25.4%)	15 (13.6%)	.013
Fragrance mix (I/II) 8%	73 (19.9%)	59 (23.0%)	14 (12.7%)	.023
Ammoniated mercury 1%	72 (19.7%)	48 (18.8%)	24 (21.8%)	.498
Carba mix 3%	65 (17.8%)	33 (12.9%)	32 (29.1%)	< .001
Potassium dichromate 0.5%	48 (13.1%)	24 (9.4%)	24 (21.8%)	.001
Thiuram mix 1%	44 (12.0%)	30 (11.7%)	14 (12.7%)	.786
Black rubber mix 0.75%	36 (9.8%)	22 (8.6%)	14 (12.7%)	.223
Ethylenediamine 1%	25 (6.8%)	16 (6.3%)	9 (8.2%)	.502
Formaldehyde 1% aq	22 (6.0%)	15 (5.9%)	7 (6.4%)	.852
Colophony 20%	21 (5.7%)	18 (7.0%)	3 (2.7%)	.105
Epoxy resin 1%	15 (4.1%)	7 (2.7%)	8 (7.3%)	.085
Benzocaine 5%	15 (4.1%)	14 (5.5%)	1 (0.9%)	.109
Mercapto mix 2%	14 (3.8%)	7 (2.7%)	7 (6.4%)	.173
Imidazolidinylurea 2%	8 (2.2%)	3 (1.2%)	5 (4.5%)	.102
Neomycin sulfate 20%	8 (2.2%)	7 (2.7%)	1 (0.9%)	.481
Bronopol 0.5%	7 (1.9%)	4 (1.6%)	3 (2.7%)	.742
Paraben mix 16%	5 (1.4%)	3 (1.2%)	2 (1.8%)	1.000

aq = aqueous.

*Allergens are in petrolatum unless otherwise noted.

reactions to ammoniated mercury. Moreover, mercury compounds are highly irritating to the skin, which may influence the evaluation of results. In that case, a prolonged reading time may be required for distinguishing allergic reactions from irritant reactions. The high positive-reaction rate of ammoniated mercury in our study sample may be associated with the excessive addition of mercury to cosmetic products even though

the use of topical ammoniated mercury ointment was abandoned in China more than 10 years ago. A survey conducted in Beijing found that the amount of mercury in 90% of spot-removing cosmetics sold on the wholesale market exceeded the amount allowed by China's Hygienic Standard for Cosmetics (≤ 1 mg/kg) by 2 to 2×10^5 times.¹¹ Moreover, environmental mercury pollution from metal smelting, coal combustion, and miscellaneous

Table 2. Most Frequent Allergens, by Patient Occupation

<i>Occupation</i>	<i>Allergens</i>	<i>Positive Rate (%)</i>
Health care worker (<i>n</i> = 26)	Rubber chemicals [†]	34.6
Office worker (<i>n</i> = 25)	Fragrance mix	28.0
Textile worker (<i>n</i> = 23)	Nickel sulfate	30.4
Rubber worker (<i>n</i> = 22)	Rubber chemicals [†]	54.5
Accountant (<i>n</i> = 18)	Fragrance mix	33.3
Teacher (<i>n</i> = 18)	Fragrance mix	33.3
Hairdresser (<i>n</i> = 17)	<i>p</i> -Phenylenediamine	82.4*
Metalworker (<i>n</i> = 12)	Potassium dichromate	50.0*
Cleaner (<i>n</i> = 8)	Fragrance mix	50.0
Food producer (<i>n</i> = 7)	Nickel sulfate and ammoniated mercury	42.9
Construction worker (<i>n</i> = 5)	Potassium dichromate	60.0*

**p* < .05, compared to other patients without corresponding occupational exposure.[†]Carba mix, thiuram mix, black rubber mix, and mercapto mix.

activities such as battery and fluorescent lamp production may cause widespread exposure.¹²

In the past few decades, much attention was focused on allergy to nickel and fragrance,^{13–15} both of which were in many domestic and occupational products intended for hand use. Nickel allergy has been thought to be a risk factor for the development of hand eczema.^{13,16} Comparing the positive rate of nickel and fragrance among female patients with that among male patients, most previous studies showed a female predominance.^{9,17} Our study also showed a significantly higher frequency among female patients, for gender ratios of 1.95:1 for nickel and 1.8:1 for fragrance, respectively. This higher frequency for females may be attributed to the higher chance of their being exposed daily to products containing these allergens.

In our study, a pronounced male predominance was observed in regard to allergies to carba mix and potassium dichromate. The higher frequency of positive reactions in men may be related to occupational exposure because the positive rate for potassium dichromate in metalworkers and construction workers is much higher than that in others. Contact allergy to carba mix as well as other rubber chemicals is common among the rubber workers and health care workers in our study sample.

Occupational hand eczema is one of the most commonly recognized occupational diseases and has a major socioeconomic impact. High frequencies of occupational hand eczema have been found among persons in many occupations (ie, health care workers, cleaners, bakers, hairdressers, metalworkers, and construction workers).^{18–25} In our study, the patients were scattered among different occupations. Health care workers, office workers, textile workers, and rubber workers are represented. Allergies to PPD (hairdressing exposure) and chromate (metal and cement exposure) may be the significant causes of occupational allergic contact dermatitis. However, testing with standard series is rarely sufficient in occupational cases, and many contact sensitizers may be missed. It is also difficult to verify the occupationally relevant sensitizations.²⁶ Additional occupation-specific series and guidance on the appropriate patch-test dilutions for individual chemicals may be required in the future.

Study Limitations

The study sample was drawn from a selected group: referred patients at a single center who were suspected of having contact allergy. The results may therefore not be representative of the general population. The lack of

patient follow-up information makes it hard to assess the clinical relevance of positive reactions.

Conclusion

p-Phenylenediamine and ammoniated mercury, as well as nickel, fragrance, and rubber chemicals, were the most frequent contact allergens for Chinese patients with hand eczema. Female predominance in nickel and fragrance allergies and male predominance in carba mix and chromate allergies may be attributable to different daily and occupational exposures. PPD and chromate allergies may be related to occupational exposure.

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