

A retrospective study of patch tests in Chongqing, China from 2004 to 2009

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Summary

Background. There has been no previous report on allergens responsible for dermatitis in southwest China.

Objective. To investigate the prevalence of contact allergy in southwest China, we retrospectively analysed the patch testing results in our department from 2004 to 2009.

Methods. A total of 2758 patients were patch tested with the Chinese baseline series of contact allergens (Beijing Medical University), the most common baseline series used in China. The results from patch tests were collected, analysed, and compared with clinical findings.

Results. Of 2758 patients tested, 1826 (66.2%) were allergic to one or more common allergens. Five hundred (27.4%) patients had more than two contact allergies. One patient showed positive reactions to seven allergens. The most common allergens among the 1826 patients with positive reactions were nickel sulfate (39.5%), potassium dichromate (13.5%), thiomersal (11.6%), fragrance mix (6.9%), and rubber mix IV (5.8%). Nickel sensitivity was more common in female patients, and potassium dichromate sensitivity was more common in male patients ($p < 0.001$).

Conclusion. Contact allergy in southwest China has particular characteristics, and these findings should be helpful in the development of strategies to reduce contact allergy in this geographical region.

Key words: allergen; contact dermatitis; eczema; nickel sulfate; patch testing.

Allergic contact dermatitis is common. Although the diagnosis may be suggested clinically, diagnostic patch testing is required to properly investigate the dermatitis. Information on the prevalence of contact allergy is important for monitoring epidemiological trends and planning preventive and regulatory interventions.

No comparative data analysis on patch testing in Chongqing, one of the largest cities in southwest China,

has been published. In this retrospective study, we have analysed the results from all patch tests performed on patients with suspected allergic contact dermatitis in one medical centre, which is responsible for patients in the southwest China area, from January 2004 to December 2009. Our aims were to explore the demographic data associated with positive reactions and the profile of contact allergens in the territory.

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Patients and Methods

Study population

Data, including clinical history and results of patch testing, were obtained from the Department of Dermatology, Southwest Hospital (the largest military medical centre

in west China) in Chongqing, from January 2004 to December 2009. Patients on systemic steroid therapy or with acute eczema were excluded. Patch test results from 2758 patients were analysed. All patients were ethnically Chinese Han.

Patch testing

Patch testing was performed with the Chinese base-line series (Table 1), which is available from Beijing Medical University, Beijing, China, and is used in hospitals nationwide in China (1, 2). Rubber mix I is a mixture of mercaptobenzothiazole, *N*-cyclohexyl-2-benzothiazole sulfenamide, and 2, 2'-benzothiazyl disulfide. Rubber mix II contains tetramethylthiuram disulfide and tetramethylthiuram monosulfide. Rubber mix III contains *N*-phenyl-*N*'-cyclohexyl-*p*-phenylenediamine, *N*-isopropyl-*N*-phenyl-*p*-phenylenediamine, and *N*, *N*'-diphenyl-*p*-phenylenediamine. Rubber mix IV is a mixture of *N*, *N*'-diphenylguanidine, zinc diethyldithiocarbamate, and zinc dibutylthiocarbamate.

Allergens were applied to the upper back of patient for 2 days, with Finn Chambers® on Scanpor® tape (obtained from Beijing Medical University, Beijing, China). Reactions were examined on D2 and D3, following the recommendations of the International Contact Dermatitis Research Group (3). A reaction was defined as positive if it was '+' or more in intensity on the second reading. An irritant response, a doubtful reaction (+?) or a negative reaction was interpreted as a negative response (4). The clinical relevance of a positive reaction was evaluated by considering the clinical presentation and possible allergen exposure. A positive reaction to the patch test was of 'current relevance' if it was considered to have caused the patient's dermatitis at the time of presentation and the dermatitis improved with avoidance of that allergen. All other positive responses were regarded as having 'unknown relevance' in this study.

Statistical analysis

Data were recorded on a standardized computer entry form, and statistically analysed with the Statistical Package for Social Sciences (SPSS 9.0; SPSS, Chicago, IL, USA). Associations between patient characteristics (sex, age group, atopy, and location) and positive patch test results were evaluated with the chi-squared (χ^2) test. By use of the normal approximation to the binomial distribution, confidence intervals (CIs) for the 95% estimated prevalence was calculated. The χ^2 -test was used to test for possible significant differences. All results were expressed as odds ratios (ORs) with 95% CIs (4).

Results

Patient characteristics

Patch testing data from 2758 patients were included in the analysis. There were 1136 males (41.2%) and 1622 females (58.8%). Of the 1136 male patients, 629 were aged ≤ 40 years. Of the female patients, 1141 were aged ≤ 40 years. The age ranged from 17 to 68 years, with an average of 38.5 ± 12.4 years. The duration of dermatitis ranged from 3 months to 18 years (mean 2 ± 1.3 years). The duration of presenting skin problems was 1 year or more in 62.4%, and more than 1 month but less than 1 year in 37.6%.

Within the group, there were 1304 (47.3%) manual workers, 447 (16.2%) students, 416 (15.1%) office workers, 298 (10.8%) businessmen, and 293 (10.6%) who were not in gainful employment (including unemployed, retired, and housewives).

Patch testing results

A total of 1826 patients (66.2%) showed one or more positive reactions. Of these, 1052 (57.6%) were female and 774 (42.4%) were male. The positive reactions had current relevance in 40.5% ($n = 1117$), and allergic contact dermatitis was diagnosed. The rest of the positive results (59.5%) were considered to have unknown relevance. The most common diagnosis was allergic contact dermatitis, comprising 40.5% of the cases. Irritant contact dermatitis was the second most common diagnosis, with 5.1% of the total (Table 2).

Of the 1826 patients who had one or more positive patch test reactions, 1125 (61.6%) had one, 500 (27.4%) had two, 99 (5.4%) had three, 60 (3.3%) had four, 38 (2.1%) had five, 3 (0.2%) had six, and 1 (0.1%) had seven.

There were more female patients than male patients with positive patch test reactions ($p < 0.001$). The OR for having a positive patch test reaction for female relative to male patients was 1.16 (95% CI 0.99–1.36). There were also more positive patch test reactions in the ≤ 40 -year age group than in the > 41 -year age group among male patients ($p = 0.048$). The OR for having a positive patch test reaction for males aged ≤ 40 years relative to those aged > 41 years was 1.29 (95% CI 1.00–1.65). Similar results were observed in female patients ($p < 0.001$). The OR for having a positive patch test reaction for females aged ≤ 40 years relative to those aged ≥ 41 years was 1.70 (95% CI 1.37–2.12).

The most frequent allergens (Table 1) were nickel sulfate (39.5%), potassium dichromate (13.5%), thiomersal (11.6%), fragrance mix (6.9%), and rubber mix IV (5.8%).

Table 1. Patch test results with the Chinese baseline series (n = 2758)

Allergens	No. of patients with positive reaction(s) (% of the total number of patients tested in each category)	Reaction(s)			
		+, no. (%)	++, no. (%)	+++, no. (%)	Irritant or doubtful response, no. (%)
Nickel sulfate 5.0%	1090 (39.5)	351 (32.2)	374 (34.3)	209 (19.2)	156 (14.3)
Potassium dichromate 0.5%	371 (13.5)	210 (56.6)	106 (28.6)	17 (4.6)	38 (10.2)
Thiomersal 0.1%	320 (11.6)	227 (70.9)	52 (16.3)	26 (8.1)	15 (4.7)
Fragrance mix 8%	190 (6.9)	122 (64.2)	60 (31.6)	8 (4.2)	0
Rubber mix IV 0.6%	160 (5.8)	133 (83.1)	20 (12.5)	5 (3.1)	2 (1.3)
p-Phenylenediamine 0.1%	144 (5.2)	73 (50.7)	48 (33.3)	23 (16.0)	0
Colophonium 20.0%	99 (3.6)	79 (79.8)	18 (18.2)	2 (2.0)	0
Rubber mix II 0.6%	63 (2.3)	22 (34.9)	18 (28.6)	7 (11.1)	16 (25.4)
Ethylenediamine dihydrochloride 1.0%	57 (2.1)	42 (73.7)	10 (17.6)	2 (3.5)	3 (5.3)
Rubber mix III 0.6%	53 (1.9)	18 (34.0)	21 (39.6)	13 (24.5)	1 (1.9)
Formaldehyde 1.0%	37 (1.3)	25 (67.6)	7 (18.9)	2 (5.4)	3 (8.1)
Imidazolidinyl urea 2.0%	27 (1.0)	16 (59.3)	5 (18.5)	4 (14.8)	2 (7.4)
2-Bromo-2-nitropropane-1,3-diol 0.25%	27 (1.0)	21 (77.8)	2 (7.4)	2 (7.4)	2 (7.4)
Rubber mix I 0.6%	23 (0.8)	18 (78.3)	4 (17.4)	1 (4.3)	0
Benzocaine 5.0%	20 (0.7)	18 (90.0)	2 (10.0)	0	0
Neomycin sulfate 20.0%	17 (0.6)	15 (88.2)	2 (11.8)	0	0
Paraben mix 16%	15 (0.5)	8 (53.3)	7 (46.7)	0	0
Epoxy resin 1.0%	3 (0.1)	3 (100.0)	0	0	0

Table 2. Clinical diagnoses established after patch testing

Diagnosis	No. of patients	Percentage of all the patients studied (n = 2758)
Allergic contact dermatitis	1117	40.5
Occupational allergic contact dermatitis	339	12.3
Irritant contact dermatitis	141	5.1
Occupational irritant contact dermatitis	96	3.5
Eczema (not otherwise defined)	453	16.4
Atopic dermatitis	215	7.8
Dermatitis 'other' (pompholyx, nummular eczema etc)	397	14.4

The distribution of allergens differed by age and sex (Table 3). Nickel sulfate reactions were most frequent in those aged ≤ 40 years for both sexes (female, OR 1.54, 95% CI 1.38–1.75; male, OR 2.05; 95% CI 1.41–2.83), and were significantly more frequent in female patients than in males. Potassium dichromate reactions were more common in males, and particularly in males aged ≤ 40 years (OR 2.10; 95% CI 1.86–2.57). The third most frequent allergen was thiomersal, and reactions were most common in patients aged ≤ 40 years, without sex differences (female, OR 1.80, 95% CI 1.56–2.57; male, OR 2.01; 95% CI 1.53–2.67). Fragrance mix,

the fourth most common allergen, produced significantly more reactions in females aged ≤ 40 years, and reactions were less common in males. Finally, rubber mix IV induced more reactions in male patients than in female patients; there was no age-related effect.

Positive patch test reactions were observed mostly in manual workers (68.5%), and 54.3% were related to occupational exposure, especially to nickel sulfate, potassium dichromate, or rubber mix IV. Of the workers with positive patch test reactions, 44.3% were mechanics and construction workers, 24.5% were beauticians and hairdressers, 13.8% were refuse collectors, 3.6% were medical staff, and 13.8% had other occupations, including catering, sales, and cleaning. Among the non-occupational group, 24.3% had positive reactions; 82.8% were housewives, 8.5% were retired, and 8.7% were unemployed. Positive patch test reactions were observed in 7.2% of the group comprising students, office workers, and businessmen.

Factors favouring a positive patch test reaction (OR > 1) and factors favouring a negative result (OR < 1), determined with the use of logistic regression (forward stepwise conditional), are shown in Table 3. The influence of individual risk factors on the likelihood of a positive patch test reaction to each of the top five allergens was also analysed (Table 4).

Among patients with positive patch test reactions, 61.2% (1689) had upper limb involvement, 38.5%

Table 3. Odds ratio risk factors for a positive patch test result for the top five allergens

Factor	Odds ratio (95% confidence interval)				
	Nickel sulfate	Potassium dichromate	Thiomersal	Fragrance mix	Rubber mix IV
Sex (male versus female)	2.38 (2.01–2.82)***	0.69 (0.55–0.86)**	1.24 (0.97–1.592)***	0.66 (0.49–0.88)**	0.84 (0.61–1.17)***
Occupational dermatitis (presence versus absence)	0.53 (0.13–0.95)***	1.62 (1.31–1.96)***	1.31 (0.89–1.92)***	0.63 (0.38–0.95)***	2.31 (1.32–3.58)**
History of atopy (presence versus absence)	1.29 (1.01–1.65)***	2.12 (1.56–2.79)**	1.73 (1.15–2.42)**	0.51 (0.21–0.89)**	0.74 (0.12–1.25)*
Head and neck involvement (presence versus absence)	2.13 (1.83–2.32)*	—	1.52 (1.22–1.73)**	1.365 (1.01–1.51)***	—
Trunk involvement (presence versus absence)	1.845 (1.52–2.01)**	1.457 (1.13–1.88)**	—	—	—
Upper limb involvement (presence versus absence)	1.102 (0.89–1.36)**	1.314 (1.03–1.65)***	—	—	1.532 (0.35–0.73)***
Lower limb involvement (presence versus absence)	—	0.812 (0.51–1.03)***	—	—	1.23 (0.94–1.51)**
Age (≥ 41 years versus ≤ 40 years)	0.61 (0.52–0.72)***	3.72 (2.53–3.99)***	1.09 (0.86–1.39)***	0.75 (0.56–1.04)***	2.49 (1.79–3.46)***

Chi-square tests: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

(1064) had head and neck involvement, 32.5% (896) had trunk involvement, 22.1% (609) had lower limb involvement, and 0.9% (26) had genital involvement. There were 10.3% (284) with disseminated involvement. As there may be multiple sites of involvement for some patients, the total adds up to more than 2758 (the total number of patients).

In all of the 2758 tested patients, the most common clinical manifestations, in order of frequency, were chronic dermatitis (53.2%), acute dermatitis (18.3%), lichenification or hyperkeratosis (22.5%), and chronic dermatitis with fissures (3.5%). Pigmentation and hypopigmentation were rare, and accounted for 1.3% and 1.2%, respectively. Among all patients, pruritus was the most common clinical symptom (92.4%), following by stinging sensation (3.5%), burning (3.1%), and numbness (1.0%).

Discussion

Environmental exposure to allergens can vary from region to region, owing to local differences in lifestyle, therapeutic practice, and industries. These variations are also reflected in the most frequent allergens triggering sensitization. The present study was the first investigation on allergic contact dermatitis in Chongqing, China. We observed that the pattern of reaction to allergens in Chongqing was different to those in other areas in

Table 4. Odds ratios of risk factors for a positive patch test result*

Factor	Odds ratio (95% confidence interval)	p-value
Age (≥ 41 years versus ≤ 40 years)	1.457 (1.238–1.715)	0.013
Sex (male versus female)	1.158 (0.986–1.361)	0.048
Head and neck involvement (presence versus absence)	0.539 (0.315–0.742)	0.032
Trunk involvement (presence versus absence)	1.312 (1.121–1.542)	<0.001
Upper limb involvement (presence versus absence)	1.217 (1.043–1.512)	0.006
Lower limb involvement (presence versus absence)	0.934 (0.632–1.211)	<0.001
History of atopy (presence versus absence)	1.625 (1.438–1.815)	0.007
History of atopy (not assessed versus absence)	2.432 (2.217–2.632)	0.014

*Derived from a logistic regression model.

China. For example, nickel sulfate was the most common allergen (22.1%) in Beijing, followed by fragrance mix (15.5%), and *p*-phenylenediamine (12.8%) (5), whereas nickel sulfate (16%) and potassium dichromate (11%) were the most common allergens in Shanghai (6). Nickel

sulfate (24.4%), fragrance mix (13.7%) and cobalt chloride (8.7%) were the three most common allergens in Hong Kong (7).

About 66.2% of patients had one or more positive responses, but only 40.5% of the positive results had current relevance. This is an important limitation of our study. Owing to the difficulty in ascertaining the positive reactions as the cause of a previous dermatitis, we restricted ourselves to considering only 'current relevance' (dermatitis at the time of presentation and possible allergen exposure), with the rest of the positive reactions being regarded as having 'unknown relevance'.

The female preponderance in our positive patch test results was in line with most series (7), and could be attributed to the large number of nickel-sensitized women (632 of a total of 1090 patients with nickel sensitization). In addition, with the use of logistic regression, seven risk factors favouring a positive patch test reaction were identified, with the effect of each given by its OR (Table 4). Positive patch test reactions were more common in those aged ≤ 40 years than in those aged ≥ 41 years. One possible explanation for this is that young people have more opportunity to acquire contact allergy at work than older people.

Nickel sulfate is the most common allergen (59.8% of all patients) in Chongqing, as in most other areas in China (5–7) and most Western and Asian series (8, 9). Logistic regression of the data further showed that nickel sensitization was more common in female patients aged ≤ 40 years or atopic patients, who normally present with upper limb and trunk involvement instead of lower limb involvement. Susceptible groups were manual workers and students. In men, nickel dermatitis is predominantly occupational. The female predominance was most probably a result of different patterns of exposure, which could be explained by significantly more contact with costume jewellery and nickel-containing household appliances in young and middle-aged women. Nickel-allergic subjects are at higher risk of developing hand eczema (10), a disorder associated with increased healthcare costs as well as poor quality of life (11), and even systemic allergic dermatitis (12).

Potassium dichromate was the second most common allergen in our study (17.8% of all patients), similar to what has been found in other studies (6). In those aged ≥ 41 years, potassium dichromate showed more reactions in males than in females [OR (male/female) 3.30; 95% CI 2.19–4.96]. Chromate has a wide presence in our environment, particularly in cement. Exposure to chromate has significantly increased in Chongqing, owing to construction and accelerated development of the city. For most of the patients with chromate

allergy, exposure was occupationally related, especially among construction workers, mechanics, and refuse collectors. The lack of personal protective equipment in China, especially in infrastructure construction, also makes avoidance difficult for some people.

Thiomersal was the third most common allergen in our study (16.6% of all patients). In Europe, thiomersal contact allergy is seen, but it is seldom of relevance. In China, the presence of thiomersal in skin-lightening creams and prohibited tooth fillers may be relevant.

The sensitization rate for fragrance mix (13.8%) is similar to that in north China (15.5%) (9), and it was more common in patients aged ≤ 40 years. Fragrance allergy accounted for 30% of identified cases of allergic contact dermatitis caused by cosmetics (13). There is voluntary ingredient labelling of cosmetics in the United States (14) and it is mandatory in the EU (where fragrance allergens are separately identified on cosmetic products and household products such as detergents) (15). The evaluation of patients who are allergic to fragrances is difficult in China, as no comparable regulations on cosmetics labelling have been introduced; such a lack of regulation in China also makes avoidance difficult for the consumer.

Rubber mix IV was the fifth common allergen in our study (11.9% of all patients), and allergy to this was more common in male patients. Most of the patients had an occupational exposure history, with a prominent distribution among drivers, medical personnel, housewives, and rubber-manufacturing workers.

Although positive reactions to other allergens in the Chinese baseline series were found, the frequencies of positive reactions to benzocaine, neomycin sulfate, paraben mix and epoxy resin were $< 1\%$. A modification of the Chinese baseline series by excluding these allergens may be considered in China by reference to the inclusion criteria for the European baseline series.

In conclusion, this current retrospective study provides a profile of the allergens responsible for allergic contact dermatitis in the public dermatology service in Chongqing, China. To reduce the prevalence of sensitivity to nickel and chromate, efforts in preventative education and regulation are necessary. Dermatologists should remind patients to be aware of exposure to allergens in their daily life and work. This survey involved the retrospective analysis of data from patch testing in a large public hospital sector; however, a prospective study, including patients in local communities and specific occupations, would provide more insights into the agents responsible for allergic contact dermatitis in Chongqing, China. Meanwhile, the Chinese baseline series, taking

the available data into account, could be updated as necessary.

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