

Time trends of contact allergy to a modified European baseline series in Beijing between 2001 and 2006

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Summary

Background. Monitoring trends of sensitivity rates in a population is useful for epidemiological surveillance. The time trends for sensitivity rates of allergens have not previously been reported in China.

Objectives. The aim of the present study was to determine the prevalence and trends of contact allergy in patients with suspected allergic contact dermatitis in Beijing, China.

Patients/Methods. A retrospective analysis of all patch test data from our database was performed. A total of 1354 patients with suspected allergic contact dermatitis between 2001 and 2006 were studied. Patch tests with 20 allergens or mixtures of allergens were performed and analysed.

Results. Sensitivity to potassium dichromate (50.1%) was most frequent, and sensitivity to imidazolidinyl urea (3.0%) was least frequent. Increasing trends in sensitivity rates for 10 allergens with significant linear regression were observed ($p < 0.05$), including mercapto mix, black rubber mix, potassium dichromate, formaldehyde, epoxy resin, benzocaine, ethylenediamine dihydrochloride, paraben mix, tixocortol-21-pivalate, and sesquiterpene lactone mix. Sensitivity rates for the other 10 allergens remained stable or showed only a trend (fragrance mix) towards an increase ($p_{\text{trend}} > 0.05$).

Conclusions. High sensitivity rates were observed in the study. Significant increasing trends in sensitivity rates for 10 allergens, probably reflecting increasing changes in exposure, were found.

Key words: allergic contact dermatitis; epidemiology; exposure analysis; patch test.

Allergic contact dermatitis is considered to be a significant public health problem. The first step in preventing allergic contact dermatitis is to determine contact allergens,

and the second is to decrease exposure. The patch test not only provides clinical epidemiological data for identifying contact allergens, but also assesses the effects of interventions, such as regulation (1, 2). Monitoring trends in sensitization rates in a population is a useful way of evaluating interventions (3). In Europe, the European Surveillance System on Contact Allergies (www.essca-dc.org) has been shown to be useful in monitoring the frequencies of sensitization to allergens of the European baseline series (4). On the basis of such results, the composition of the European baseline series is constantly revised, and its relevance to allergen exposure can be maintained (5).

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Environmental exposure to allergens can vary from region to region, owing to local differences in lifestyle, therapeutic practices, and industry (5). Up to now, time trends in the sensitivity rates for allergens in the European baseline series have not been reported for our region.

The aim of the present study was to determine the prevalence of and trends in contact allergy to the European baseline series in patients with suspected allergic contact dermatitis in Beijing, China.

Patients and Methods

A retrospective analysis of all patch test data from our database was performed. A total of 1354 patients with suspected allergic contact dermatitis in the Department of Dermatology of Beijing Chaoyang Hospital were studied between 2001 and 2006, including 363 men (26.8%) and 991 women (73.2%). The average age was 38.0 ± 14.1 years (range, 5–81 years).

The patch tests were performed with a modified European baseline series of allergens (Chemotechnique Diagnostics, Malmö, Sweden) and an IQ Chamber[®] (Chemotechnique Diagnostics). Twenty allergens or mixtures of allergens were tested (Table 1). Allergens were applied to the upper back, and the results were recorded at D2 and D3 according to the International Contact Dermatitis Research Group criteria (6). A positive outcome was defined as a morphologically + to +++ reaction on D3. An irritant response, a doubtful (+?) reading or a negative reading was interpreted as a negative outcome. All of the tests were performed and the results were read by the same two specially trained technicians.

Data analysis was performed with SPSS 11.0 (Systat version 11.0; SPSS, Chicago, IL, USA). Evaluation of sensitivity rates between males and females was performed with a χ^2 -square test. Evaluation of differences in sensitivity rates for allergens between years was performed with a χ^2 -square trend test. Linear regression analysis was additionally used to test for, and quantify, average time trends. Linear regression of allergens was calculated from a regression equation, with intercept a and slope coefficient b : $Y = a + bX$. The independent factor X represents year, and the dependent outcome Y represents sensitivity rate. A p -value < 0.05 was regarded as significant.

The study was approved by the Chaoyang Hospital Ethics Committee.

Results

Positive reactions to all 20 allergens or mixes of allergens in the series were noted (Table 1). Sensitivity to potassium dichromate was most frequent (50.1%), followed by nickel

Table 1. Sensitivity rates for 20 allergens in a modified European baseline series

Allergens	Concentration % (wt/wt)	Patch test-positive rates (%)		
		Males	Females	Total
Benzocaine	5.0	12.9	12.6	12.7
Mercapto mix	2.0	7.1*	3.5	4.6
Imidazolidinyl urea	2.0	2.3	3.3	3.0
<i>N</i> -(Cyclohexylthio) phthalimide	1.0	11.6*	6.0	7.7
<i>p</i> -Phenylenediamine base	1.0	18.2*	11.8	13.5
Potassium dichromate	0.5	53.4	49.5	50.1
Ethylenediamine dihydrochloride	1.0	14.8	11.2	12.2
Colophonium	20	9.1	7.4	7.8
Formaldehyde	1.0	20.9*	13.9	15.8
Epoxy resin	1.0	9.6	8.1	8.5
2-Bromo-2- nitropropane-1,3-diol	0.25	8.0*	3.3	4.5
Thiuram mix	1.0	6.3*	3.0	3.9
Paraben mix	16.0	26.8*	13.0	20.0
Nickel sulfate	5.0	32.2*	46.8	42.9
Sesquiterpene lactone mix	0.1	9.9	6.5	7.5
Fragrance mix I	8.0	18.5*	23.7	22.2
Tixocortol-21-pivalate	1.0	9.2	9.2	9.2
Black rubber mix	0.6	13.2*	8.4	9.8
Carba mix	3.0	33.3*	22.2	24.9
Thimerosal	0.1	26.8*	18.9	21.0

IQ Chambers[®] were used.

* $p < 0.01$.

sulfate (42.9%), and sensitivities to imidazolidinyl urea (3.0%) and the thiuram mix (3.9%) were least frequent. At least one positive patch reaction was observed in 1159 (85.6%) patients, and a significant trend towards increasing sensitivity with time was observed (Fig. 1). Descriptive characteristics of the test population according to the MOAHLFA index are presented in Table 2.

Clear sex differences were observed for 12 allergens. Sensitivity rates for 10 allergens in males were higher than those in females. Sensitivity rates for two allergens in females were higher than those in males (Table 1).

A significant increase in sensitivity rates for 10 allergens with time was observed, with $p_{\text{trend}} < 0.05$ (Figs 2–4). Sensitivity rates for the other 10 allergens remained stable or showed only a trend (fragrance mix) towards an increase ($p_{\text{trend}} > 0.05$).

Discussion

The European baseline series is composed of 23 allergens. Variations in sensitivity rates exist within Europe (7)

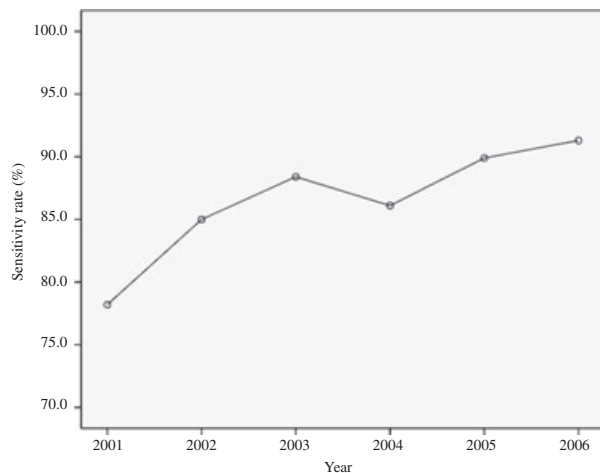


Fig. 1. Increasing trends in sensitivity rate of patients with at least one positive reaction. $Y = 2.3X - 4440.3$, $R^2 = 0.802$, $p = 0.017$ ($\chi^2 = 22.260$, $p < 0.001$).

and even between different patch testing centres in the same country (8). In China, the modified European baseline series, which consists of 20 allergens, is used in most hospitals (9, 10). Variations in sensitivity rates have been observed between different hospitals (9, 10). In the present study, the sensitivity rates exceeded the rates reported in Europe, Asia, and other parts of China (9–12). In our laboratory, the patch tests have been performed by two specially trained technicians during the last decade. Preparation and application of the tests were standardized, and the reading times were defined and unchanged. Thus, the risk of inconsistencies in methodology was minimized. After standardization, the adjusted data indicated no significant influence of sex and age on sensitivity rates. The following factors may contribute to the high sensitivity rates.

First, all of the patients who were patch tested were suspected of having clinical allergic contact dermatitis.

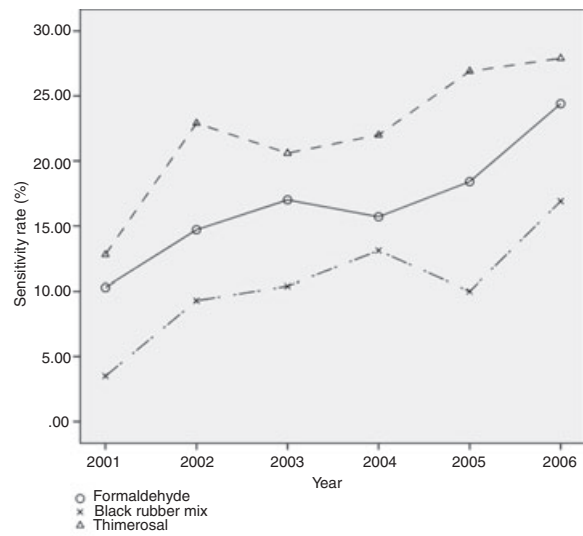


Fig. 2. Increasing trends in sensitivity rates for formaldehyde, black rubber mix, and thimerosal. Formaldehyde: $Y = 2.3X - 4579.9$, $R^2 = 0.85$, $p = 0.009$ ($\chi^2 = 17.507$, $p = 0.004$). Black rubber mix: $Y = 2.1X - 4099.5$, $R^2 = 0.748$, $p = 0.026$ ($\chi^2 = 25.855$, $p < 0.001$). Thimerosal: $Y = 2.5X - 5066.7$, $R^2 = 0.773$, $p = 0.021$ ($\chi^2 = 20.837$, $p < 0.001$).

In the present study, 85.6% of patients had at least one positive reaction, and 21.3% of patients had suspected occupational dermatitis. In contrast, a small proportion (4.7%) of patients had atopic dermatitis, and a large proportion (42.2%) of patients had the face as the primary site. This suggests that patients who were patch tested were highly selected (patients with suspected allergic contact dermatitis caused by occupation or cosmetics). Of course, the predominance of positive test results does not reflect the prevalence of contact allergy in the general population.

Second, the high sensitization rates could be explained by chronic occupational exposure to allergens widely used by our local industries. Chaoyang District, where 95% of

Table 2. Descriptive characteristics of the test population ($n = 1354$) according to the MOAHLFA index

	Male (%)	Occupational dermatitis (%)	Atopic dermatitis (%)	Primary site: hand (%)	Primary site: leg* (%)	Primary site: face* (%)	Age 40 years and above (%)
2001	29.50	16.80	4.70	8	20.80	44.36	46.20
2002	30.80	30.60	13.88	28	21.25	45.31	44.80
2003	25.90	23.10	4.00	16.30	10.74	55.63	39.50
2004	20.70	12.00	0.00	23.90	12.17	57.76	39.90
2005	21.90	2.90	0.00	15.50	8.24	58.82	37.10
2006	29.90	21.40	0.66	17.65	2.82	75.36	42.70
Total	26.80	21.30	4.65	17.80	15.73	51.52	42.24

* $p < 0.001$ between 2001 and 2006.

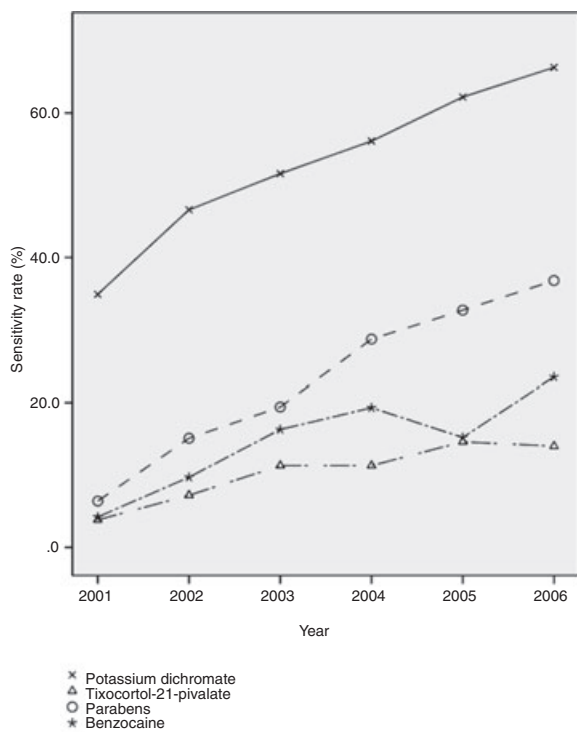


Fig. 3. Increasing trends in sensitivity rates for potassium dichromate, tixocortol-21-pivalate, parabens, and benzocaine. Potassium dichromate: $Y = 5.0X - 11871.0$, $R^2 = 0.966$, $p < 0.001$ ($\chi^2 = 61.670$, $p < 0.001$). Tixocortol-21-pivalate: $Y = 2.1X - 4179.8$, $R^2 = 0.890$, $p = 0.005$ ($\chi^2 = 23.450$, $p < 0.001$). Parabens: $Y = 6.1X - 12232.5$, $R^2 = 0.981$, $p < 0.001$ ($\chi^2 = 88.509$, $p < 0.001$). Benzocaine: $Y = 3.3X - 6625.5$, $R^2 = 0.797$, $p = 0.017$ ($\chi^2 = 46.021$, $p < 0.001$).

the study population lived, had been a large industrial region since the 1960s. Industries in Chaoyang District include textiles, chemicals, automobiles, and electronics. Although many of the factories relocated after 1995, there may have been persistence of allergens causing continued exposure of the local population.

Information on changes in the prevalence of contact allergies can lead to preventive interventions. In Europe, such interventions have been made, and have had an impact on the burden of allergic diseases. In a study that involved 16 centres in Europe, an increased rate of patch test reactivity to the preservative methylidibromo glutaronitrile was reported (13). The rate of positive reactions increased from 0.7% in 1991 to 3.5% in 2000. Methylidibromo glutaronitrile was banned from use in cosmetic products in the EU countries, and a significant decrease in sensitivity rate occurred following regulatory intervention. Wesley and Maibach (14) examined the effects of legislation aimed at reducing the population's

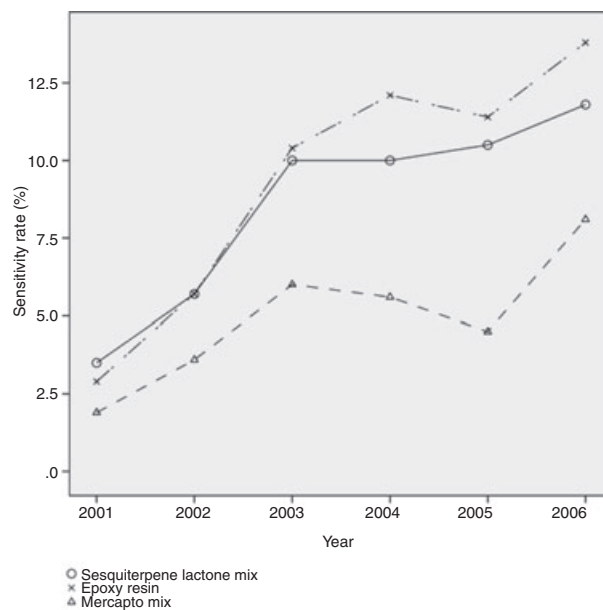


Fig. 4. Increasing trends in sensitivity rates for sesquiterpene lactone mix, epoxy resin, and mercapto mix. Sesquiterpene lactone mix: $Y = 1.6X - 3191.3$, $R^2 = 0.855$, $p = 0.008$ ($\chi^2 = 19.247$, $p = 0.002$). Epoxy resin: $Y = 2.1X - 4186.5$, $R^2 = 0.88$, $p = 0.006$ ($\chi^2 = 27.568$, $p < 0.001$). Mercapto mix: $Y = 1.0X - 1901.2$, $R^2 = 0.696$, $p = 0.039$ ($\chi^2 = 11.770$, $p = 0.038$).

exposure to allergens. They found decreasing trends of sensitivity rates for nickel, glyceryl monothioglycolate, fragrances, chromate, and thiuram rubber accelerators.

In the present study, an increasing frequency of positive patch test reactions to 10 allergens was demonstrated between 2001 and 2006. These are mainly relevant to construction materials, drugs, and cosmetics. We suggest that the increasing frequency of sensitization may be related to the increasing exposure to these allergens from these product types.

In the last two decades in Beijing, there has been much new construction. Materials of poor quality have frequently been used. Guan et al. (15) reported that, within 1 month after decoration, formaldehyde exceeded the acceptable levels in 72.6% of new houses in Weifang, a city in northern China. In one house, the concentration of formaldehyde was 31.6 times higher than normal. Another study demonstrated that the concentrations of formaldehyde and benzene were higher than the allowed levels in 56.1% and 16.8%, respectively, of new houses 6 months after decoration. Three years after decoration, 7.6% of houses had high levels of formaldehyde (16). We believe that the increasing prevalence of sensitization correlates with the situation across China. There is a need

for local governments to routinely check the quality of construction and decoration materials.

In Germany and the United States, an increasing prevalence of allergic reactions to neomycin have been observed, and may be attributed to the fact that neomycin is frequently prescribed as a topical antibiotic by physicians. After prescription of neomycin had been limited, a decline in prevalence was reported (1, 17). In China, the use of topical steroid creams has increased significantly in the past decade. In 2000, the sales of steroid creams were \$20 million. Sales of steroid creams reached \$31 million in 2006, and peaked in 2009 at \$56 million. The increasing sensitivity rate for tixocortol-21-pivalate was consistent with the increasing use of steroid creams in China. In addition, a traditional Chinese medicine ointment containing sesquiterpene lactones as a basic component is commonly used to treat sprains and bruises. Most of these topical drugs are sold over the counter. Therefore, the use of some topical medicines may need to be restricted.

Many substances may cause facial dermatitis, in particular cosmetic ingredients. In Denmark, increasing trends in the frequency of contact allergy to *Myroxylon pereirae* and fragrance mix were observed for several years prior to 1999 (18, 19). Following an opinion on labelling of certain fragrance ingredients present in cosmetic products, the frequency of contact allergy to *M. pereirae* and fragrance mix decreased significantly among adult Danish women between 1999 and 2007 (20). In the present study, allergies to fragrance mix increased, although with a $p_{\text{trend}} > 0.05$ according to the χ^2 -test. A large proportion (42.2%) of patients had the face as the primary site, and females had a greater rate of sensitivity to fragrance mix than did males, suggesting increasing use of cosmetics containing fragrances among women in China. The results of our study suggested that the concentration of fragrance chemicals in cosmetics should be lowered.

Parabens comprise a group of *p*-hydroxybenzoic acid esters that are commonly used in cosmetics as preservatives. More than two-fifths of patch-tested patients had the face as the primary allergy site. Although parabens are very weak allergens, the increasing use of cosmetics could be a cause of the increase in sensitivity to parabens in China.

The number of patients whose primary site for contact dermatitis is the face is increasing. However, we concluded that the increasing patient number is not the reason for this, but the result; that is, increasing rates of sensitivity to fragrance mix and parabens are causing the increasing number of patients with facial dermatitis.

Our results, however, should be interpreted with caution, because the population in the present study was composed of patients suspected of having a contact allergy at a central hospital in the district. The results do not represent the prevalence of contact allergy in the general population. In the absence of population data, however, our clinical data give us a basis for further epidemiological surveillance. We hope that the current study provides epidemiological data for local clinics to monitor changes in contact allergy and force local governments to implement disease control policies when increasing sensitivity rates are observed.

Our study is the first to monitor trends in sensitization rates for allergens in China. In spite of the differences from other studies, we conclude that the time trend in sensitization rates is important for monitoring allergic contact dermatitis in China. The trends should be followed closely.

In conclusion, high sensitization rates were noted in the study. Clear sex differences in sensitization rates for 12 allergens were found. Significant increasing trends in sensitization rates for 10 allergens, probably reflecting changes in exposure, were found.

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