

Original article

A multicentre study assessing the prevalence of sensitizations in patients with asthma and/or rhinitis in China

Background: The prevalence of sensitization in patients with asthma and rhinitis in mainland China remains unclear.

Objective: Our aim was to estimate the prevalence of allergy in patients with respiratory allergic diseases such as asthma and/or rhinitis attending respiratory clinics within mainland China. The study also investigated regional and annual differences in the prevalence and pattern of sensitization among the patients in China.

Method: A cross-sectional survey was performed in 6304 patients suffering from asthma and/or rhinitis in 17 cities from 4 regions of China. Patients completed a standardized questionnaire asking for the presence of respiratory and allergic symptoms. They also underwent skin prick tests with 13 common aeroallergens.

Results: Among the 6304 patients, 4545 (72.1%) had at least one positive skin prick reaction. The overall prevalence of positive skin prick responses was 59.0% for *Dermatophagoides farinae*, 57.6% for *Dermatophagoides pteronyssinus*, 40.7% for *Blomia tropicalis*, 16.1% for American cockroach, 14.0% for dog, 11.5% for *Blatella germanica*, 11.3% for *Artemisia vulgaris*, 10.3% for cat, 6.5% for *Ambrosia artemisifolia*, 6.3% for mixed mould I, 4.4% for mixed mould IV, 3.5% for mixed grass pollen and 2.2% for mixed tree pollen. Sensitizations to common allergens varied widely between geographical areas and demonstrated unique pattern in patients by stratification with age groups, with asthma and/or rhinitis. Severity of rhinitis and asthma was significantly correlated with skin index of reactivity to *Artemisia vulgaris*, *Ambrosia artemisifolia* and to *D. pteronyssinus*, *D. farinae* and *Blomia tropicalis* respectively ($P < 0.001$). Positive reactivity to the tested allergens and concomitant reactivity to multiple allergens including to house dust mites and *Blomia tropicalis* was markedly increased in patients with both asthma and rhinitis.

Conclusion: House dust mites were the most prevalent allergens in patients with asthma and/or rhinitis in China. There were significant differences in patterns of sensitizations in patients from different geographical areas, age groups as well as asthma and/or rhinitis.

J. Li¹, B. Sun¹, Y. Huang², X. Lin³, D. Zhao⁴, G. Tan⁵, J. Wu⁶, H. Zhao⁷, L. Cao⁸, N. Zhong¹, China Alliance of Research on Respiratory Allergic Disease (CARRAD)*

¹State Key Laboratory of Respiratory Disease, The First Affiliated Hospital, Guangzhou Medical College, Guangzhou, Guangdong, China; ²The Children's Hospital, Chongqing University of Medical Sciences, Chongqing, China; ³The General Hospital of Shenyang Military Command, Shenyang, Liaoning, China; ⁴Nanjing Children's Hospital, Nanjing, Jiangsu, China; ⁵The Third Hospital of Xiangya Medical University, Changsha, Hunan, China; ⁶The First Hospital of Xiamen, Xiamen, Fujian, China; ⁷The Second Hospital of Shanxi Medical University, Taiyuan, Shanxi, China; ⁸Capital Institute of Pediatrics, Beijing, China

Key words: aeroallergens; asthma; epidemiology; rhinitis; sensitization; skin prick test.

Nanshan Zhong, MD
State Key Laboratory of Respiratory Disease
The First Affiliated Hospital
Guangzhou Medical College
Guangzhou
Guangdong, 510120
China

*China Alliance of Research on Respiratory Allergic Disease (CARRAD):

Jing Li, Baoqing Sun, Chunqing Zhang, Hongyu Wang, Dehui Chen, Ying Huang, Xiaoping Lin, Deyu Zhao, Guolin Tan, Jinzhun Wu, Hailiang Zhao, Jing Zhao, Ling Cao, Guangfa Wang, Changchun Sun, Dongdong Zhu, Xiaoqin Zhou, Nan Su, Jiangtao Lin, Xuefen Wang, Jianying Zhou, Wen Li, Huahao Shen, Yijiang Huang, Shi Chen, Xiaofan Liu, Chuangli Hao, Hong Han, Shaohua Chen, Huanying Wan, Xiaoyan Dong, Yixiao Bao, Luo Zhang, Dehou Xue, Michael D. Spangfort, Nanshan Zhong

Accepted for publication 2 November 2008

The prevalence of respiratory allergic disease has increased in developed countries over recent decades. The causes of such increase are not known. However, the increase appears to link to factors associated with westernization, improvement of socioeconomic standards and urbanization (1). In fact, countries undergoing rapid

changes towards 'western' lifestyle would concomitantly experience an increasing prevalence of allergic respiratory disease (2, 3). International multicentre population-based studies in adults (4) and children (5) have documented significant variations in prevalence of allergic respiratory disease and sensitization against environmental allergens

between and within countries. Furthermore, the pattern of sensitization against allergens varies according to differences in environmental factors.

China is the most populous country in the world and is having a rapidly growing economy. In parallel with the rapidly changing lifestyle and socioeconomic improvement in China, an increasing prevalence of allergic respiratory disease is very likely. The prevalence of sensitization as reflected by skin prick test (SPT) reactivity in school-children has been investigated in two Chinese studies (6–8). Substantial differences in the prevalence of sensitization between regions were demonstrated. A high prevalence of sensitization was seen in the more westernized city of Hong Kong. However, due to the large geographical area of China, further studies are needed to evaluate the possible regional variations in the prevalence and the type of allergens in different locations.

The objective of this study was to estimate the prevalence of allergen sensitivity in patients with respiratory diseases such as asthma and/or rhinitis attending respiratory clinics within mainland China. The study also investigated regional differences and seasonal variations in the prevalence and pattern of sensitization among the patients in China.

Methods

Study population and definitions

This cross-sectional study was conducted from February 2006 to March 2007 in 17 cities with 24 participating centres from northern, eastern, south western and southern coastal regions. The study covered mid-temperate, warm-temperate, subtropical and tropical zones of China. A total of 6304 patients aged 5–65 years attending outpatient clinics of these 24 centres participated consecutively in this survey. The patients were diagnosed with asthma alone, rhinitis alone or asthma accompanied with rhinitis by evaluation of history, questionnaire and the relevant tests. Rhinitis was defined as having symptoms of sneezing, or a running, itchy or blocked nose when the patient did not have a cold or flu. Asthma was defined by a history of recurrent dyspnoea, wheezing or cough episodes, positive airway reversibility testing (FEV_1 increasing $\geq 12\%$ and 200 ml after inhalation of 400 mg of salbutamol) or positive airway responsiveness testing (FEV_1 decreasing $\geq 20\%$ when ≤ 7.8 μmol of cumulative dose of histamine is administered). The study was approved by the Ethics Review Board of each study centre and all patients gave written consent to participate in the study.

Questionnaire

The standardized questionnaire was administered by the physicians or research nurses face-to-face with questions on demographic characteristics, family history of allergic diseases, symptoms of rhinitis, wheezing or cough, eczema and burning or itching of the eyes, smoking habits, environment exposure factors, pets ownership and dietary habits.

Questions about allergic symptoms included atopic rhinitis; eczema; respiratory distress with bronchial wheezing, cough and tightness of breath; itching; burning and redness of the eyes; and allergic symptoms associated with exposure to a dusty environment,

or close to furry dolls, or near pillows or duvets, allergic symptoms secondary to contact with trees, grass or flowers, limitation of daily activities, work and school absence because of the allergic symptoms, impairment of sleep because of the allergic symptoms and use of medications and/or rescue inhaler or nebulizer for controlling allergic symptoms.

Assessment of severity of rhinitis and asthma

Patients with rhinitis and/or asthma visit out-patient clinics in hospitals at the first place and with equal chances in China, regardless of their severity. Severity of rhinitis and asthma was evaluated by a standardized quality of life questionnaire in association enquiring about impairments in patients' daily activities, work or school, sleep disorders, daily or nocturnal symptoms and uses of rescue and other asthma medication (9, 10).

Skin prick test (SPT)

The sensitivity to six groups (thirteen kinds) of common aeroallergens was tested and they included mites (*Dermatophagoides pteronyssinus*, *D. farinae* and *Blomia tropicalis*), dog (*Canis familiaris*), cat (*Felis domesticus*), cockroach (American cockroach and *Blattella germanica*), pollen (*Artemisia vulgaris*, *Ambrosia artemisiifolia*, mixed grasses and mixed trees) and moulds (mould mix I and IV) was performed. Allergen extracts and control solutions were obtained from ALK (Horsholm, Denmark). Histamine (10 mg/ml) and diluent were used as positive and negative controls. SPT was performed on the volar side of the forearm. The wheal reaction after 15 min was measured as the mean of the longest diameter and the length of the perpendicular line through its middle. A positive skin reaction was defined as a wheal size ≥ 3 mm, after subtraction of the negative control. The result was also expressed as skin index (SI = mean size of allergen wheal/mean size of histamine wheal). Atopy was defined as the presence of at least one positive skin reaction to any allergen tested.

Quality control

Uniform protocol, questionnaire, allergen testing set, and operating procedures were used among all the centres. All questionnaire interviewers and performers of skin prick test were trained before the study. Results of questionnaire and skin prick tests were sent every month to Guangzhou, where the data were entered and analysed. Quality control reports were then prepared for each centre. Each completed questionnaire and skin test report was verified by the centre supervisor and the results were double-checked by the principal investigator and fed back to each centre. All questionnaire and skin test data were coded and input into a programmed database by two persons independently. The entered data were checked for out-of-range values and logic mistakes.

Statistical analysis

The prevalence of positive skin tests to allergens was calculated as uncorrected rates and 95% confidence intervals (CIs). Geographical area, sex, age groups and rhinitis and/or asthma groups were treated as categorical variables. The differences in the sensitization rate between the variables were determined by chi-square tests. Spearman correlation analysis was used to measure the association between skin index of sensitization and severity of rhinitis and asthma. All data were categorized and analysed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) for

Windows Release 13.0. A P -value of ≤ 0.05 was considered significant.

Results

Allergen sensitizations in patients from four regions of China

Of the 6304 patients, 4545 (72.1%) had at least one positive skin reaction. The overall prevalence of positive skin responses was 59.0% for *D. farinae*, 57.6% for *D. pteronyssinus*, 40.7% for *Blomia tropicalis*, 16.1% for American cockroach, 14.0% for dog, 11.5% for *Blatella germanica*, 11.3% for *Artemisia vulgaris*, 10.3% for cat, 6.5% for *Ambrosia artemisifolia*, 6.3% for mixed mould I, 4.4% for mixed mould IV, 3.5% for mixed grass pollen and 2.2% for mixed tree pollen. The sensitizations against various allergens in four regions of China are listed in Table 1. The prevalence of sensitizations to house dust mites was the highest in the south-western and the lowest in the northern regions. Sensitivity against dog and cat was significantly higher in the northern and southern coastal areas than in the eastern and south-western regions. Sensitizations to American cockroach and *Blatella germanica* were the highest in the coastal region in the south and the lowest in the north. Patients in the north had significantly higher positive rates to pollens (*Artemisia vulgaris*, *Ambrosia artemisifolia*, mixed grass and mixed tree pollen) and moulds (mixed mould I and IV) than in the other three regions.

Comparison of allergen sensitizations among different age groups

As can be seen in Table 1, children had significantly higher positive rates to mites (*D. farinae*, *D. pteronyssinus* and *Blomia tropicalis*, $P < 0.001$), cat ($P < 0.001$), mixed mould I ($P < 0.001$) and IV ($P < 0.05$) than adults. However, sensitivity against dog ($P < 0.05$), cockroaches (American cockroach and *Blatella germanica*, $P < 0.005$), *Artemisia vulgaris* ($P < 0.001$) and *Ambrosia artemisifolia* ($P < 0.001$) was significantly increased in adults than in children. A sub-analysis was performed to compare the positivity to allergens in patients by stratification with different age groups. The result showed the highest prevalence of mite sensitivity was seen in the youngest age group and the positive rate decreased with increasing age (Fig. 2). In contrast, the positive skin tests to dog, cat and cockroaches were found to be the highest among those in age group of 15–24 years, while the reactivity to pollens also increased with ages and peaked in age group of 25–34 years followed by a gradual decline. For moulds, the sensitivity was higher in age groups of 5–14 and 15–24 years (Fig. 2).

Allergen sensitization and severity of rhinitis and asthma

By using Spearman's correlation analysis (Table 2), skin index of sensitization to *Artemisia vulgaris* and *Ambrosia*

Table 1. Comparison of allergen sensitizations between children and adults in four regions of China

	North [n (%)]			East [n (%)]			Western south [n (%)]			Southern coast [n (%)]		
	Total (n = 2333)	Children (n = 547)	Adults (n = 1786)	Total (n = 1251)	Children (n = 732)	Adults (n = 519)	Total (n = 1561)	Children (n = 997)	Adults (n = 519)	Total (n = 1204)	Children (n = 736)	Adults (n = 468)
<i>Dermatophagoides pteronyssinus</i>	893 (38.3)	277 (50.6)	616 (34.5) [†]	743 (59.4)	499 (68.2) [†]	244 (47.0) ^{†,‡}	1170 (77.2)	812 (81.4) ^{†, b}	358 (69.0) ^{†, B}	828 (68.8)	559 (76.0) ^{†, b, c}	269 (57.5) ^{†, B, C, ‡}
<i>Dermatophagoides farinae</i>	963 (41.3)	274 (50.1)	689 (38.6) [†]	756 (60.4)	501 (68.4) [†]	255 (49.1) ^{†,‡}	1186 (78.2) ^{ab}	818 (82.0) ^{†, b}	368 (70.9) ^{†, B}	817 (67.9)	538 (73.1) ^{†, b, c}	279 (59.6) ^{†, B, ‡}
<i>Blomia tropicalis</i>	665 (28.5)	175 (32.0)	490 (27.4) [†]	441 (35.3)	247 (33.7)	194 (37.4) [†]	832 (54.9) ^{ab}	557 (55.9) ^{†, b}	275 (53.0) ^{†, B}	628 (52.2)	400 (54.3) ^{†, b}	228 (48.7) ^{†, B, C}
Dog	35 (15.0)	82 (15.0)	269 (15.1)	147 (11.8)	70 (9.6) [†]	77 (14.8) [†]	178 (11.7) ^a	117 (11.7)	61 (11.8)	207 (17.2)	124 (16.8) ^{†, c}	83 (17.7) ^c
Cat	272 (11.7)	104 (19.0)	168 (9.4) [†]	108 (8.6)	68 (9.3) [†]	40 (7.7)	128 (8.4) ^a	100 (10.0) ^a	28 (5.4) ^{†,‡}	141 (11.7)	96 (13.0) ^{†, b, c}	45 (9.6) ^c
American cockroach	265 (11.4)	48 (8.8)	217 (12.2) [†]	216 (17.3)	91 (12.4) ^a	125 (24.1) ^{†,‡}	264 (17.4) ^a	146 (14.6) ^a	118 (22.7) ^{†,‡}	271 (22.5)	157 (21.3) ^{†, b, c}	114 (24.4) [†]
<i>Blatella germanica</i>	229 (9.8)	38 (6.9)	191 (10.7) [†]	124 (9.9)	30 (4.1) ^a	94 (18.1) ^{†,‡}	197 (13.0) ^{ab}	109 (10.9) ^{†, b}	88 (17.0) ^{†,‡}	175 (14.5)	80 (10.9) ^{†, b}	95 (20.3) ^{†,‡}
<i>Artemisia vulgaris</i>	563 (24.1)	108 (19.7)	455 (25.5) [†]	56 (4.5)	23 (3.1) ^a	33 (6.4) ^{†,‡}	61 (4.0) ^a	37 (3.7) ^a	24 (4.6) [†]	30 (2.5)	12 (1.6) ^{a, c}	18 (3.8) ^{†,‡}
<i>Ambrosia artemisifolia</i>	306 (13.1)	53 (9.7)	253 (14.2) [†]	39 (3.1)	19 (2.6) ^a	20 (3.9) [†]	45 (3.0) ^a	33 (3.3) ^a	12 (2.3) [†]	19 (1.6)	13 (1.8) ^{a, c}	6 (1.3) ^{†, B}
Mixed grass pollen	124 (5.3)	38 (6.9)	86 (4.8)	34 (2.7)	22 (3.0) ^a	12 (2.3) [†]	39 (2.6) ^a	26 (2.6) ^a	13 (2.5) [†]	24 (2.0)	13 (1.8) ^a	11 (2.4) [†]
Mixed tree pollen	93 (4.0)	33 (6.0)	60 (3.4) [†]	16 (1.3)	8 (1.1) ^a	8 (1.5) [†]	17 (1.1) ^a	14 (1.4) ^a	3 (0.6) [†]	15 (1.2)	13 (1.8) ^a	2 (0.4) [†]
Mixed mould I	216 (9.3)	121 (22.1)	95 (5.3) [†]	65 (5.2)	44 (6.0) [†]	21 (4.0)	77 (5.1) ^a	63 (6.3) [†]	14 (2.7) ^{†,‡}	37 (3.1)	21 (2.9) ^{†, b, c}	16 (3.4)
Mixed mould IV	140 (6.0)	63 (11.5)	77 (4.3) [†]	53 (4.2)	26 (3.6) [†]	27 (5.2)	50 (3.3) ^a	36 (3.6) ^a	14 (2.7) [†]	36 (3.0)	25 (3.4) ^a	11 (2.4) [†]

Children: ^a $P < 0.05$, ^b $P < 0.01$ compared with North; ^c $P < 0.05$, ^d $P < 0.01$ compared with East; ^e $P < 0.05$, ^f $P < 0.01$ compared with Western south; Adult: ^A $P < 0.05$, ^B $P < 0.01$ compared with North; ^B $P < 0.05$, ^B $P < 0.01$ compared with East; ^C $P < 0.05$, ^C $P < 0.01$ compared with Western south; [†] $P < 0.05$, [‡] $P < 0.01$ compared with children.

Table 2. Correlations between skin index of allergen sensitizations and severity of rhinitis and asthma with Spearman's analysis

	Severity of rhinitis		Severity of asthma	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Skin index of				
<i>Dermatophagoides pteronyssinus</i>	−0.013	0.369	0.143	0.000
<i>Dermatophagoides farinae</i>	−0.008	0.575	0.141	0.000
<i>Blomia tropicalis</i>	−0.002	0.875	0.136	0.000
Dog	0.026	0.075	−0.022	0.184
Cat	0.004	0.764	−0.002	0.683
American cockroach	0.024	0.093	0.013	0.371
<i>Blatella germanica</i>	0.007	0.631	0.008	0.542
<i>Artemisia vulgaris</i>	0.115	0.000	0.007	0.665
<i>Ambrosia artemisifolia</i>	0.094	0.000	−0.011	0.337
Mixed grass pollen	0.015	0.297	0.003	0.810
Mixed tree pollen	0.012	0.409	0.016	0.208
Mixed mould I	−0.026	0.072	0.004	0.731
Mixed mould IV	−0.013	0.345	0.006	0.515

artemisifolia was found to be significantly correlated with severity of rhinitis ($P < 0.001$), whereas severity of asthma was significantly correlated with skin index of reactivity to *D. pteronyssinus*, *D. farinae* and *Blomia tropicalis* ($P < 0.001$).

Seasonal variations in allergen sensitizations

Figure 1 shows variations in sensitizations of mites (*D. farinae*, *D. pteronyssinus* and *Blomia tropicalis*) and pollens (*Artemisia vulgaris* and *Ambrosia artemisifolia*) in the 12 consecutive months of survey in four regions. Percentages of sensitizations to mites fluctuated without robust changes in four regions in 12 months with the western south ranking on the top place, the southern coast on the second, the east on the third and the north on the lowest for most of the months. Positive rates to *Artemisia vulgaris* and *Ambrosia artemisifolia* in the north stayed on top which peaked in August simultaneously. In other three regions, they were low without obvious fluctuations.

Differences in allergen sensitizations in patients with asthma alone, rhinitis alone and asthma accompanied with rhinitis

Distribution of the sensitizations to allergens in patients with asthma alone, rhinitis alone and asthma accompanied with rhinitis by stratification with different age groups is shown in Fig. 2. The results clearly demonstrate that patients with both asthma and rhinitis had increased positive rates to mites, dog and cat than those with asthma or rhinitis alone in all age groups. Sensitization to pollens was increased in patients with both asthma and rhinitis in the two younger groups with a significance in the group of 5–14 years ($P < 0.01$). In other age groups, patients with rhinitis alone and with

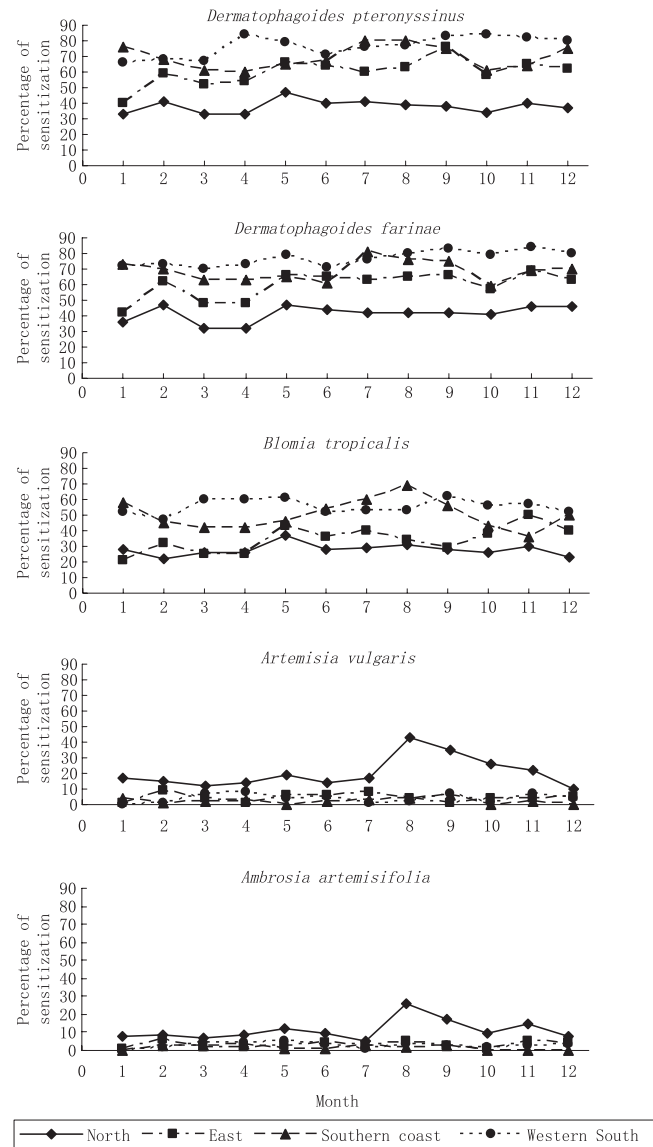


Figure 1. One-year variation on sensitizations for five main allergens in four different regions in China.

both asthma and rhinitis, when compared with asthma alone, also had significantly increased positive rates against pollens ($P < 0.01$). In contrast, in most of the age groups, an increase in prevalence of sensitization to cockroaches and moulds was found in patients with asthma alone, and those with both asthma and rhinitis, with significant increase in the younger age groups ($P < 0.01$).

As shown in Fig. 3, the percentages of single and double allergen-sensitizations in patients with asthma (6.2% and 16.2% respectively), rhinitis (8.1% and 17.8% respectively) and both (5.6% and 16.1% respectively) were not significantly different. However, significantly greater number of patients with both asthma and rhinitis (26.3%, 13.9% and 20.0% respectively) were sensitized to

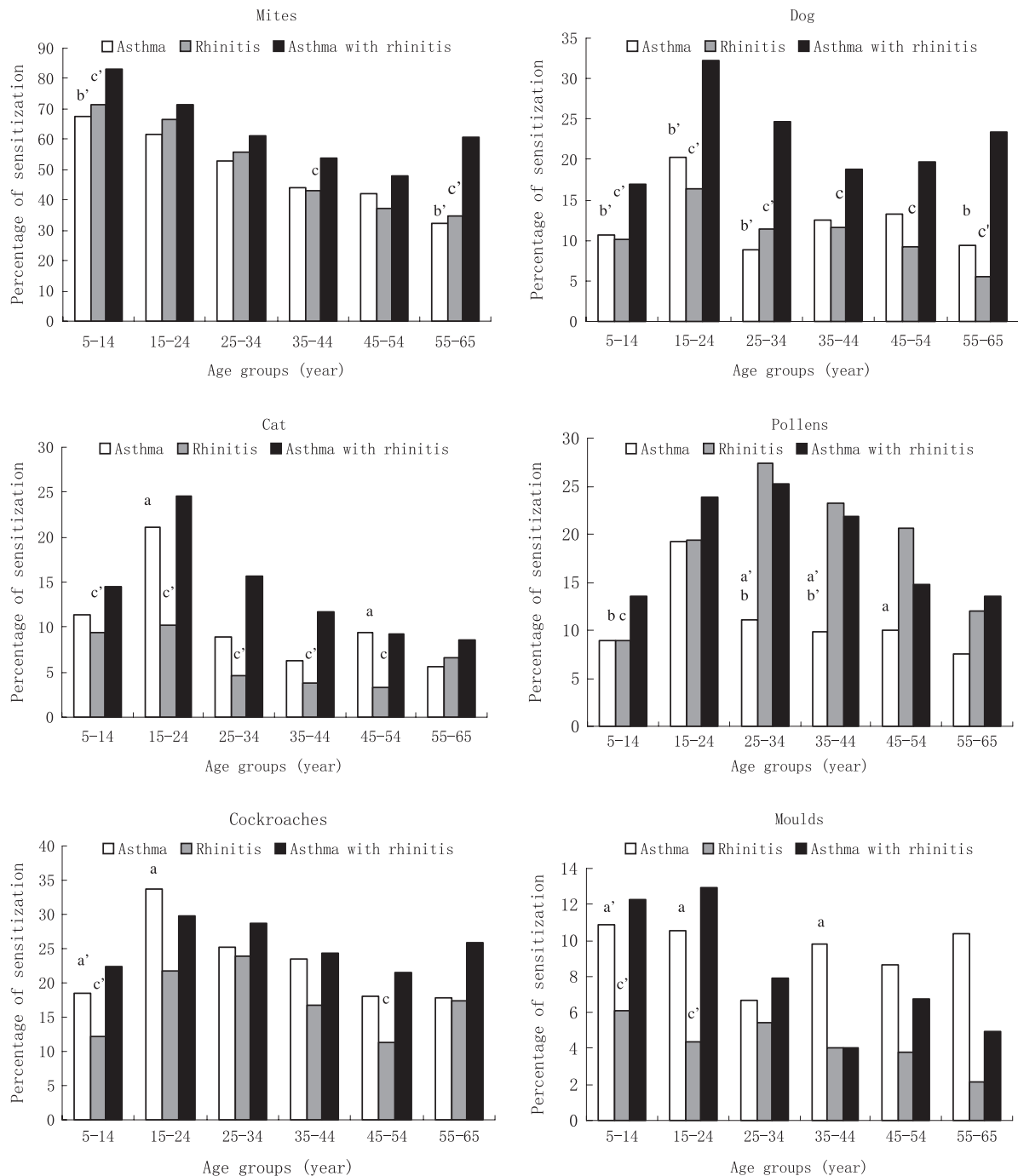


Figure 2. Distribution of sensitization among different groups of allergens in patients with asthma, rhinitis and asthma with rhinitis by stratification in age groups. ^a $P < 0.01$, ^{a'} $P < 0.001$ Asthma vs Rhinitis; ^b $P < 0.01$, ^{b'} $P < 0.001$ Asthma vs Asthma with rhinitis; ^c $P < 0.01$, ^{c'} $P < 0.001$ Rhinitis vs Asthma with rhinitis.

3, 4 and more than 5 allergens simultaneously than patients with asthma (16.9%, 12.2% and 13.8% respectively) and rhinitis (18.8%, 11.2% and 13.1% respectively) ($P < 0.001$).

With regard to mite sensitizations, very few of patients with asthma (2.4%, 3.0% and 0.7% respectively), rhinitis (1.3%, 2.8% and 0.9% respectively) and both (1.7%,

2.7% and 0.8% respectively) were mono-allergic to *D. pteronyssinus* or *D. farinae* or *Blomia tropicalis*. This is in contrast to sensitization against both *D. pteronyssinus* and *D. farinae* simultaneously, which was increased significantly in patients with all three diagnosis groups (asthma 17.1%, rhinitis 17.3% and both 18.1%). The concomitant sensitization rates to all the three mites were

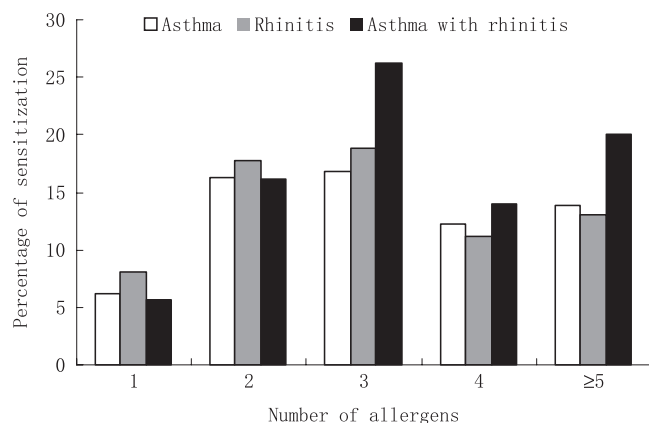


Figure 3. Multiple sensitizations in patients with asthma, rhinitis and asthma with rhinitis. 1: sensitized to one allergen; 2: sensitized to two allergens; 3: sensitized to three allergens; 4: sensitized four allergens; ≥5: sensitized to more than 5 allergens.

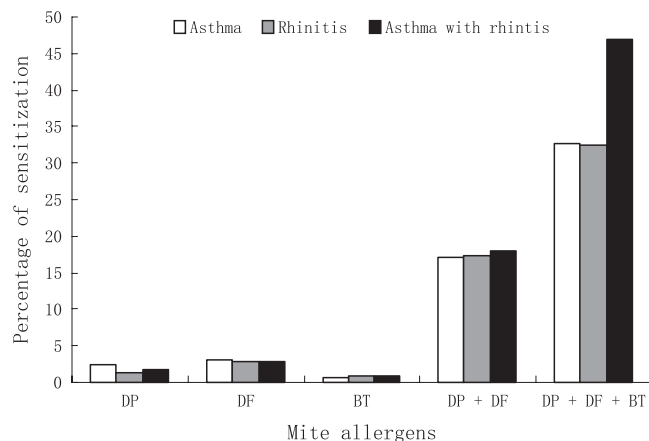


Figure 4. Mono- and poly-sensitizations to *Dermatophagoides pteronyssinus* (DP), *Dermatophagoides farinae* (DF), and *Blomia tropicalis* (BT) in patients with asthma, rhinitis and asthma with rhinitis.

even higher in all three diagnosis groups (asthma 32.7%, rhinitis 32.5% and both 46.9%) (Fig. 4).

Discussion

The study shows that the main allergens in patients with asthma and/or rhinitis in China are house dust mites and the prevalence rates of sensitization to common inhaled allergens varied widely between regions. Secondly, prevalence rates of sensitization against house dust mites, dog, cat, cockroaches and *Artemisia vulgaris* were significantly different among children and adults, while sensitization to each group of allergens demonstrated unique pattern in these patients by stratification with age groups. Thirdly, we found that the prevalence of sensitizations to the

tested allergens and concomitant reactivity to multiple allergens including to house dust mites and *Blomia tropicalis* was markedly increased in patients with both asthma and rhinitis. These results are unique in the following important aspects: (1) this was the first cross-sectional multicentre epidemiological study of allergen sensitizations in patients with asthma and/or rhinitis in mainland China by using a standardized research protocol in many centres representative of different regions of China; (2) the data are from a large, geographically and climatically representative population of patients; (3) the data have been obtained at a time to provide the baseline data when the prevalence of asthma and allergic rhinitis is likely to increase because of rapid economic development and urbanization.

The most common aeroallergen in China is house dust mites. Of all of the atopic patients, 87.2% were sensitive to one or more species of house dust mites (*D. farinae*, *D. pteronyssinus* or *Blomia tropicalis*). The prevalence of sensitization to mites was higher in the south-western and southern coast regions including seven cities located in subtropical and tropical areas with higher temperatures and relative humidity throughout the year when compared with other two regions. House dust mites are abundant in environment with higher humidity and ambient temperature (11). The indoor environment in the south-western and coastal regions of China is suitable for growth of dust mite. One recent study (12) in China analysed dust samples taken from air-conditioners in the bedrooms and found a significantly higher percentage of dust samples from the air-conditioners in city of Shenzhen (in southern coastal region) expressing Der p1 and Der f1 gene fragments than those from Beijing (in northern region). This suggests the indoor concentration of house dust mite is higher in the southern China and hence it may explain the greater prevalence of sensitization to house dust mite in patients in the southern area. Another study from Taichung, Taiwan (13), a city located in subtropical area of China, reported more than 90% of children with asthma had positive skin test responses to house dust mite and *D. pteronyssinus* was found to be the dominant species. Among the sampled locations, child's mattress has the highest concentration of mites with *D. pteronyssinus* (77%) and *D. farinae* (13%) as the predominant species. However, in Nordic countries where the winter is long and cold, low incidence of house dust mite allergy has been observed in previous studies (14–16). It is believed that due to the cold and dry weather, the houses are well insulated and provided with central heating and the heaters are on for 8–9 months a year, resulting in very low indoor humidity, and, therefore, unfavourable for house dust mite proliferation.

In our study, we found a large percentage of asthmatic and/or rhinitis patients in mainland China sensitized to house dust mite. Moreover, the positive rates increased from the north to south consistent with increasing temperature and humidity.

Multiple sensitization is common in patients with asthma and/or rhinitis in this study with more than 90% of the subjects being sensitized to two or more allergens. Among them, 83.7% were concomitantly sensitized to *D. pteronyssinus* and *D. farinae* indicating that house dust mites are the important sources of aeroallergens and sensitization to them is associated with increased risk of airway allergic diseases. This is consistent with many other studies (17–20) that the majority of house dust mite allergic patients are co-sensitized to *D. pteronyssinus* and *D. farinae*. The co-sensitization might be due to parallel sensitization, or be a consequence of the existence of several very closely related allergens (21). IgE antibodies to Der p 1 and Der f 1, Der p 2 and Der f 2 as well as Der p 10 and Der f 10 are known to cross react to a great extent (19, 22–25). The identification of Der 10, or house dust mite tropomyosin, has drawn special attention to the cross reactivity between house dust mites and other invertebrates (25).

In our study, only 0.8% of our patients were sensitized to *Blomia tropicalis* alone, whereas 37.2% were concomitantly allergic to *D. pteronyssinus*, *D. farinae* and *Blomia tropicalis*. This finding is different from other studies in the tropical countries. In south Asia and south America where sensitization to *Blomia tropicalis* alone occurs in 12% of Singaporean and 11.5% of Venezuelan patients (26, 27). In Sweden, although house dust mite allergic patients are possibly not exposed to the tropical mites, 86% of them still had a positive skin reaction to *Blomia tropicalis* (28). However, in another group unexposed to *Blomia tropicalis*, only a few house dust mite allergic patients had IgE to Blo t 5 (29). It has been found that *Blomia tropicalis* extract was able, to a low to moderate degree, to inhibit house dust mite specific IgE binding and vice versa in atopic patients in Colombia and Singapore (30, 31). Crossed immunoelectrophoresis or crossed radioactive immunoelectrophoresis results suggested that house dust mite and *Blomia tropicalis* had two to four similar allergens (30, 32). Our results and those of other studies suggested that *Blomia tropicalis* should always be included as a routine skin test allergen in the subtropical and tropical regions in China.

Cockroach, cat, and dog allergens affected significant percentages of Chinese patients, with a majority of them also having dust mite allergy. According to the data of skin prick tests and questionnaire of raising dog and cat, sensitizations to dog and cat were twice as high in patients who had dog or cat at home as those who did not. Moreover, significantly higher percentage of patients in adolescent and young adult groups (15 to 44 years) were sensitized to dog and cat. This may be attributed to the fact that pet ownership is more common among them in China. Nevertheless, we also found relatively large numbers of patients who did not raise any pet but still having positive skin reactions to dog and/or cat. This finding may be because animal danders are brought into homes from other places and can remain for a prolonged

period. Many of our patients might also have developed the cat or dog allergy in the past, although the current symptoms were due to other concomitant allergens, particularly house dust mite.

The patterns of sensitization to outdoor allergens in the environment differ widely in different regions. A clear seasonal variation was seen as well, especially in the north. Among the tested pollens, *Artemisia vulgaris* and *Ambrosia artemisifolia* were found to have the highest prevalence in patients in the northern China. Their reactivity increased sharply in August, followed by a gradual reduction in 2–3 months. This phenomenon matched perfectly with the seasonal pollen count of *Artemisia vulgaris* which reaches the peak level in autumn (33, 34). Moreover, the pollen sensitization was predominantly found in young and middle age patients with rhinitis alone and those with combined asthma and rhinitis. This result agrees with other published findings from Europe (35, 36). In Poland, it was found that the patients who were sensitized to *Artemisia vulgaris*, the dominant pollen in the region, were mainly those suffering from rhinitis and conjunctivitis (15%), chronic urticaria (15%) and conjunctivitis (14.3%), whereas asthmatics only account for 2.4% (36). Pollen is a larger allergen compared with house dust mites and is mainly deposited in upper airway where it induces local inflammatory or pathological changes, whereas enzymatic activity of pyroglyphid mites and *Blomia tropicalis* as well as mold allergens seems to be important in the pathogenicity of lower airway and systemic inflammations (37–39).

In this study, significantly higher percentage of patients with both asthma and rhinitis were sensitized to the tested common aeroallergens than those with asthma or rhinitis alone. From the questionnaire data, these patients were more likely to have earlier age of onset of the allergic airway diseases that they were also more likely to be associated with asthma and severe running nose and watery eyes. It is well-documented that allergic rhinitis is closely related to asthma; both conditions together are often considered to be a single disease affecting the whole respiratory tract (40) with larger area in responding to allergen attack accounting for more severe airway inflammation and systemic reactions (41).

Our finding of an association between positive skin reactivity to allergens and severity of rhinitis and asthma supports the facts that outdoor allergens affect rhinitis and indoor allergens affect asthma significantly (42, 43). Many studies found when an atopic person is sensitized to any aeroallergen, the allergen can induce an allergic inflammatory reaction in the airway mucosa (44, 45). Airway inflammation may be associated with changes in airway hyperresponsiveness, airflow limitation, nasal and respiratory symptoms and disease chronicity (46). In agreement with our finding, Platts-Mills et al. (47) reported that the number of house dust mites is

associated with the onset of a respiratory allergy, especially bronchial asthma, and that there exists a threshold of house dust mite exposure to induce symptoms of asthma. Witteman et al. (48) demonstrated that the exposure to allergens such as Der p. can reduce FEV₁. However, pulmonary function shown to be associated with asthma severity and risk of symptom attacks (49) was not included in the analysis in this study.

Our study has several limitations. We did not include healthy controls with no asthma and rhinitis. Therefore, we cannot compare the rates of sensitization in patients and healthy controls. As indoor especially bedroom dust collection and analysis as well as seasonal pollen count were not performed along with the present study, we do not have the environmental levels of the tested allergen exposure in our patients. Although we do have serological data of specific IgE levels of the tested allergens (data not shown), we have not performed inhibition studies to determine the incidence of cross-reactivity as opposed to multiple sensitizations. This issue is particularly relevant in the group of patients in northern and eastern regions of China where *Blomia tropicalis* is not the likely source of allergen and skin prick test showed positive reactivity against *Blomia tropicalis* and Dermatophagoides extracts, implying that in this group of patients, sensitization to the pyroglyphid mites may be the primary response with some of the responses induced by *Blomia tropicalis* due to cross-reactivity.

In conclusion, over 50% of patients with asthma and/or rhinitis in China had identifiable sensitizations to aeroallergens detected by skin prick tests. The most common allergen was house dust mite (including *D. pteronyssinus*, *D. farinae* and *Blomia tropicalis*) and the prevalence increased with the regions locating further towards south. Sensitization to different group of allergens demonstrated unique pattern in patients by stratification with age groups. Multiple sensitizations

were found in more than 65% of the patients. The prevalence of positive skin reactivity and multiple sensitizations was markedly increased in patients with both asthma and rhinitis.

Acknowledgments

All authors contributed equally to this study. The authors thank Professor Gary Wing-kin Wong, Department of Paediatrics, The Chinese University of Hong Kong for help in editing the manuscript; Ms. Mei Jiang, Guangzhou Institute of Respiratory Disease, Guangzhou Medical College, China, for assistance in statistical considerations.

This study was supported by ALK-Abello A/S (FC409(10441)-ALK).

Conflicts of interest

All authors have no conflict to disclose of this manuscript.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Demographic characteristics of the study subjects.

Table S2. Allergen sensitizations between male and female in children in four regions of China.

Table S3. Allergen sensitizations between male and female in adults in four regions of China.

Please note: Wiley-Blackwell are not responsible for the content or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.

References

1. Douwes J, Pearce N. Asthma and the westernization 'package'. *Int J Epidemiol* 2002;**31**:1098–1102.
2. Krause T, Koch A, Friborg J, Poulsen LK, Kristensen B, Melbye M. Frequency of atopy in the Arctic in 1987 and 1998. *Lancet* 2002;**360**:691–692.
3. von Mutius E, Weiland SK, Fritzsche C, Duhme H, Keil U. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. *Lancet* 1998;**351**:862–866.
4. Burney PG, Luczynska C, Chinn S, Jarvis D. The European Community Respiratory Health Survey. *Eur Respir J* 1994;**7**:954–960.
5. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;**8**:483–491.
6. Leung R, Ho P, Lam CW, Lai CK. Sensitization to inhaled allergens as a risk factor for asthma and allergic diseases in Chinese population. *J Allergy Clin Immunol* 1997;**99**:594–599.
7. Wong GW, Li ST, Hui DS, Fok TF, Zhong NS, Chen YZ et al. Individual allergens as risk factors for asthma and bronchial hyperresponsiveness in Chinese children. *Eur Respir J* 2002;**19**:288–293.
8. Wong GW, Ko FW, Hui DS, Fok TF, Carr D, von Mutius E et al. Factors associated with difference in prevalence of asthma in children from three cities in China: multicentre epidemiological survey. *Bmj* 2004;**329**:486.
9. Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;**108**:S147–S334.
10. Rabe KF, Adachi M, Lai CK, Soriano JB, Vermeire PA, Weiss KB et al. Worldwide severity and control of asthma in children and adults: the global asthma insights and reality surveys. *J Allergy Clin Immunol* 2004;**114**:40–47.

11. Arlian LG, Platts-Mills TA. The biology of dust mites and the remediation of mite allergens in allergic disease. *J Allergy Clin Immunol* 2001; **107**:S406–S413.
12. Bai YLZG, Zhang HY, Ji KM, Lei C. Detection of the genes encoding house mite allergens Der f1 and Der p1 from the air-filters of air-conditioners. *Chinese Journal of Zoonoses* 2007; **23**:227–230.
13. Sun HL, Lue KH. Household distribution of house dust mite in central Taiwan. *J Microbiol Immunol Infect* 2000; **33**:233–236.
14. Munir AK, Kjellman NI, Björkstén B. Exposure to indoor allergens in early infancy and sensitization. *J Allergy Clin Immunol* 1997; **100**:177–181.
15. Ronmark E, Perzanowski M, Platts-Mills T, Lundback B. Different sensitization profile for asthma, rhinitis, and eczema among 7–8-year-old children: report from the Obstructive Lung Disease in Northern Sweden studies. *Pediatr Allergy Immunol* 2003; **14**: 91–99.
16. Munir AK. Mite sensitization in the Scandinavian countries and factors influencing exposure levels. *Allergy* 1998; **53**:64–70.
17. Squillace SP, Sporik RB, Rakes G, Couture N, Lawrence A, Merriam S et al. Sensitization to dust mites as a dominant risk factor for asthma among adolescents living in central Virginia. Multiple regression analysis of a population-based study. *Am J Respir Crit Care Med* 1997; **156**:1760–1764.
18. Leung R, Jenkins M. Asthma, allergy and atopy in southern Chinese school students. *Clin Exp Allergy* 1994; **24**: 353–358.
19. Yasueda H, Mita H, Yui Y, Shida T. Comparative analysis of physicochemical and immunochemical properties of the two major allergens from *Dermatophagoides pteronyssinus* and the corresponding allergens from *Dermatophagoides farinae*. *Int Arch Allergy Appl Immunol* 1989; **88**:402–407.
20. Biliotti G, Passaleva A, Romagnani S, Ricci M. Mites and house dust allergy. I. Comparison between house dust and mite (*Dermatophagoides pteronyssinus* and *D. farinae*) skin reactivity. *Clin Allergy* 1972; **2**:109–113.
21. Arlian LG, Bernstein IL, Vyszenski-Moher DL, Gallagher JS. Investigations of culture medium-free house dust mites. IV. Cross antigenicity and allergenicity between the house dust mites, *Dermatophagoides farinae* and *D. pteronyssinus*. *J Allergy Clin Immunol* 1987; **79**:467–476.
22. Lind P, Hansen OC, Horn N. The binding of mouse hybridoma and human IgE antibodies to the major fecal allergen, Der p 1, of *Dermatophagoides pteronyssinus*. Relative binding site location and species specificity studied by solid-phase inhibition assays with radiolabeled antigen. *J Immunol* 1988; **140**:4256–4262.
23. van der Zee JS, van Swieten P, Jansen HM, Aalberse RC. Skin tests and histamine release with P1-depleted *Dermatophagoides pteronyssinus* body extracts and purified P1. *J Allergy Clin Immunol* 1988; **81**:884–896.
24. Yasueda H, Saito A, Yanagihara Y, Akiyama K, Takaoka M. Species-specific measurement of the second group of *Dermatophagoides* mite allergens, Der p 2 and Der f 2, using a monoclonal antibody-based ELISA. *Clin Exp Allergy* 1996; **26**: 171–177.
25. Asturias JA, Arilla MC, Gomez-Bayon N, Martinez A, Martinez J, Palacios R. Sequencing and high level expression in *Escherichia coli* of the tropomyosin allergen (Der p 10) from *Dermatophagoides pteronyssinus*. *Biochim Biophys Acta* 1998; **1397**:27–30.
26. Kidon MI, Chiang WC, Liew WK, Lim SH, See Y, Goh A et al. Sensitization to dust mites in children with allergic rhinitis in Singapore: does it matter if you scratch while you sneeze? *Clin Exp Allergy* 2005; **35**:434–440.
27. Puccio FA, Lynch NR, Noya O, Noda A, Hagel I, Lopez E et al. Importance of including *Blomia tropicalis* in the routine diagnosis of Venezuelan patients with persistent allergic symptoms. *Allergy* 2004; **59**:753–757.
28. Casas R, Ferrandiz R, Wihl JA, Fernandez B, Dreborg S. Biologic activity of *Dermatophagoides siboney* and *Blomia tropicalis* allergens in exposed and unexposed mite-allergic individuals. Effect of patient selection on the biologic standardization of mite extracts. *Allergy* 1999; **54**:392–396.
29. Arruda LK, Vailes LD, Platts-Mills TA, Fernandez-Caldas E, Montealegre F, Lin KL et al. Sensitization to *Blomia tropicalis* in patients with asthma and identification of allergen Blo t 5. *Am J Respir Crit Care Med* 1997; **155**: 343–350.
30. Chew FT, Yi FC, Chua KY, Fernandez-Caldas E, Arruda LK, Chapman MD et al. Allergenic differences between the domestic mites *Blomia tropicalis* and *Dermatophagoides pteronyssinus*. *Clin Exp Allergy* 1999; **29**:982–988.
31. Puerta Llerena L, Fernandez-Caldas E, Caraballo Gracia LR, Lockey RF. Sensitization to *Blomia tropicalis* and *Lepidoglyphus destructor* in *Dermatophagoides* spp-allergic individuals. *J Allergy Clin Immunol* 1991; **88**: 943–950.
32. Arlian LG, Vyszenski-Moher DL, Fernandez-Caldas E. Allergenicity of the mite, *Blomia tropicalis*. *J Allergy Clin Immunol* 1993; **91**:1042–1050.
33. Sun HZ, Song YQ. Study on Allergy of Artemisia Plant in China. *J Environ Health (Chin)* 2006; **23**:283–285.
34. Deng Y, Zheng Z, Cour P, Huang CX, Duzer D, Calleja M et al. Relation between pollen ratios and climate in east China and an attempt of pelecoclimate reconstruction. *Acta Micropalaentologica Sinica (Chin)* 2002; **41**:508–516.
35. Gioulekas D, Papakosta D, Damialis A, Spiekma F, Giouleka P, Patakas D. Allergenic pollen records (15 years) and sensitization in patients with respiratory allergy in Thessaloniki, Greece. *Allergy* 2004; **59**:174–184.
36. Stach A, Garcia-Mozo H, Prieto-Baena JC, Czarnecka-Operacz M, Jenerowicz D, Silny W et al. Prevalence of *Artemisia* species pollinosis in western Poland: impact of climate change on aerobiological trends, 1995–2004. *J Investig Allergol Clin Immunol* 2007; **17**:39–47.
37. Baker SF, Yin Y, Runswick SK, Stewart GA, Thompson PJ, Garrod DR et al. Peptidase allergen Der p 1 initiates apoptosis of epithelial cells independently of tight junction proteolysis. *Mol Membr Biol* 2003; **20**:71–81.
38. Wan H, Winton HL, Soeller C, Gruenert DC, Thompson PJ, Cannell MB et al. Quantitative structural and biochemical analyses of tight junction dynamics following exposure of epithelial cells to house dust mite allergen Der p 1. *Clin Exp Allergy* 2000; **30**: 685–698.
39. Wan H, Winton HL, Soeller C, Taylor GW, Gruenert DC, Thompson PJ et al. The transmembrane protein occludin of epithelial tight junctions is a functional target for serine peptidases from faecal pellets of *Dermatophagoides pteronyssinus*. *Clin Exp Allergy* 2001; **31**: 279–294.
40. Bousquet J, Van Cauwenberge P, Bachert C, Canonica GW, Demoly P, Durham SR et al. Requirements for medications commonly used in the treatment of allergic rhinitis. European Academy of Allergy and Clinical Immunology (EAACI), Allergic Rhinitis and its Impact on Asthma (ARIA). *Allergy* 2003; **58**:192–197.

41. Li J, Saito H, Crawford L, Inman MD, Cyr MM, Denburg JA. Haemopoietic mechanisms in murine allergic upper and lower airway inflammation. *Immunology* 2005;**114**:386–396.
42. Bauchau V, Durham SR. Epidemiological characterization of the intermittent and persistent types of allergic rhinitis. *Allergy* 2005;**60**:350–353.
43. Sarpong SB, Karrison T. Skin test reactivity to indoor allergens as a marker of asthma severity in children with asthma. *Ann Allergy Asthma Immunol* 1998;**80**:303–308.
44. Weiss ST, O'Connor GT, DeMolles D, Platts-Mills T, Sparrow D. Indoor allergens and longitudinal FEV₁ decline in older adults: the Normative Aging Study. *J Allergy Clin Immunol* 1998;**101**:720–725.
45. Perzanowski MS, Sporik R, Squillace SP, Gelber LE, Call R, Carter M et al. Association of sensitization to Alternaria allergens with asthma among school-age children. *J Allergy Clin Immunol* 1998;**101**:626–632.
46. Lemanske RF Jr, Busse WW. 6. Asthma. *J Allergy Clin Immunol* 2003;**111**:S502–S519.
47. Platts-Mills TA, Thomas WR, Aalberse RC, Vervloet D, Champman MD. Dust mite allergens and asthma: report of a second international workshop. *J Allergy Clin Immunol* 1992;**89**:1046–1060.
48. Witteman AM, Mulder M, Aalberse RC, Jansen HM, van der Zee JS. Bronchial allergen challenge in subjects with low levels of allergic sensitization to indoor allergens. *Allergy* 1999;**54**:366–374.
49. Wijnhoven HA, Kriegsman DM, Hesselink AE, Penninx BW, de Haan M. Determinants of different dimensions of disease severity in asthma and COPD: pulmonary function and health-related quality of life. *Chest* 2001;**119**:1034–1042.

General description of the study

It was a multi-center study which covered four main climate zones in China for 12 consecutive months. During the period from February 2006 to March 2007, a total of 6411 subjects were recruited and 6393 subjects completed the skin prick tests. Among the 6411 questionnaires, 107 were invalid for inappropriate diagnosis, failure to complete the questionnaire, or absence of skin prick testing. Of the 6393 subjects who completed the skin prick tests, 89 were not eligible because of missing questionnaire data, wrong codings, or missing results from the positive and negative controls. The analyses were limited to 6304 subjects with complete questionnaire and skin prick data. Among them, 1778 had asthma alone, 2523 had rhinitis alone and 2002 with both asthma and rhinitis. Based on location of the centers, they are categorized into four regions, with children (age $\leq$ 14 years) and adult (age $>$ 14 years) as shown in Table S1.

Comparison of allergen sensitizations between male and female

Table S2 and S3 show the comparison of allergen sensitization between male and female in children and adults in four regions of China. In children, prevalence of sensitization to *D. farinae*, *D. pteronyssinus* and *Blomia tropicalis* was significantly higher in male than in female in all four regions ($p<0.05$). Male also had significant greater positive rate to dog and *Blatella germanica* in the southern coast, to cat, American cockroach and *Blatella germanica* in the western south, to American cockroach in the east and to *Blatella germanica* in the north ($p<0.05$). In adults, male again had significantly higher percentage of sensitization to *D. pteronyssinus* and *Blomia tropicalis* in the north and southern coast, to American cockroach and *Blatella germanica* in the north, east and western south, as well as to *Artemisia vulgaris* in the north ($p<0.05$).

Table S1. Demographic characteristics of the study subjects

Region	City	Total n	Age group				Sex group				Diagnosis					
			Children		Adults		Male		Female		Asthma		Rhinitis		Asthma with rhinitis	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
North	Beijing Shenyang Shijiazhuang Taiyuan Jilin	2333 (37.0)	547	18.2	1786	54.2	1153	33.4	1180	41.4	475	26.7	1190	47.1	668	33.4
East	Shanghai Nanjing Hangzhou Suzhou	1251 (19.8)	732	24.3	519	15.7	675	19.5	576	20.2	708	39.8	220	8.7	323	16.1
Western south	Changsha Wuhan Chongqing Chengdu	1516 (24.0)	997	33.1	519	15.7	880	25.5	636	22.3	334	18.8	700	27.7	482	24.1
Southern coast	Guangzhou Xiamen Haikou	1204 (19.1)	736	24.4	468	14.2	738	21.3	456	16.0	261	14.6	414	16.4	529	26.4
All regions		6304	3012	47.8	3292	52.2	3456	54.8	2848	45.2	1778	28.2	2524	40.0	2002	31.8

Table S2. Allergen sensitizations between male and female in children in four regions of China

	North n (%)			East n (%)			Western south n (%)			Southern coast n (%)		
	Male n=375	Female n=172	<i>p</i>	Male n=458	Female n=274	<i>p</i>	Male n=644	Female n=353	<i>p</i>	Male n=528	Female n=208	<i>p</i>
<i>D. pteronyssinus</i>	206(54.9)	71(41.3)	0.003	333(72.7)	166(60.6)	0.001	544(84.5)	268(75.9)	0.001	410(77.7)	149(71.6)	0.085
<i>D. farinae</i>	200(53.3)	74(37.8)	0.025	337(73.6)	164(59.9)	0.000	545(84.6)	273(77.3)	0.004	393(74.4)	145(69.7)	0.094
<i>Blomia tropicalis</i>	131(34.9)	44(25.6)	0.029	170(37.1)	77(28.1)	0.013	388(60.2)	169(47.9)	0.000	304(57.6)	96(46.2)	0.005
Dog	62(16.5)	20(11.6)	0.136	48(10.5)	22(8.0)	0.275	84(13.0)	33(9.3)	0.083	102(19.3)	22(10.6)	0.004
Cat	80(21.3)	25(9.1)	0.041	43(9.4)	25(9.1)	0.905	75(11.6)	25(7.1)	0.022	73(13.8)	23(11.1)	0.315
American cockroach	36(9.6)	12(7.0)	0.314	66(14.4)	25(9.1)	0.036	111(17.2)	35(9.9)	0.002	120(22.7)	37(17.8)	0.141
<i>Blatella germanica</i>	31(8.3)	7(4.1)	0.073	22(4.8)	8(2.9)	0.213	93(14.4)	16(4.5)	0.000	67(12.7)	13(6.3)	0.011
<i>Artemisia vulgaris</i>	80(21.3)	28(16.3)	0.168	18(3.9)	5(1.8)	0.114	26(4.0)	11(3.1)	0.462	10(1.9)	2(1.0)	0.368
<i>Ambrosia artemisifolia</i>	37(9.9)	16(9.3)	0.836	13(2.8)	6(2.2)	0.593	21(3.3)	12(3.4)	0.907	10(1.9)	3(1.4)	0.675
Mixed grass pollen	29(7.7)	9(5.2)	0.285	15(3.3)	7(2.6)	0.581	15(2.3)	11(3.1)	0.456	10(1.9)	3(1.4)	0.675
Mixed tree pollen	21(5.6)	12(7.0)	0.530	5(1.1)	3(1.1)	0.997	10(1.6)	4(1.1)	0.590	11(2.1)	2(1.0)	0.298
Mixed mould I	84(22.4)	37(21.5)	0.816	30(6.6)	14(5.1)	0.427	42(6.5)	21(5.9)	0.722	16(3.0)	5(2.4)	0.646
Mixed mould IV	46(12.3)	17(9.9)	0.418	17(3.7)	9(3.3)	0.763	23(3.6)	13(3.7)	0.928	19(3.6)	6(2.9)	0.630

Table S3. Allergen sensitizations between male and female in adults in four regions of China

	North n (%)			East n (%)			Western south n (%)			Southern coast n (%)		
	Male n=778	Female n=1008	<i>p</i>	Male n=217	Female n=302	<i>p</i>	Male n=236	Female n=283	<i>p</i>	Male n=220	Female n=283	<i>p</i>
<i>D. pteronyssinus</i>	296(38.0)	320(31.7)	0.005	108(49.8)	136(45.0)	0.286	156(66.1)	202(71.4)	0.196	141(64.1)	128(51.6)	0.006
<i>D. farinae</i>	317(40.7)	372(36.9)	0.098	108(49.8)	147(48.7)	0.806	163(69.1)	205(72.4)	0.400	141(64.1)	138(55.6)	0.063
<i>Blomia tropicalis</i>	245(31.5)	245(24.3)	0.001	90(41.5)	104(34.4)	0.102	129(54.7)	146(51.6)	0.485	119(54.1)	109(44.0)	0.029
Dog	124(15.9)	145(14.4)	0.363	39(18.0)	38(12.6)	0.088	27(11.4)	34(12.0)	0.840	50(22.7)	33(13.3)	0.008
Cat	71(9.1)	97(9.6)	0.721	23(10.6)	17(5.6)	0.036	11(4.7)	17(6.0)	0.499	26(11.8)	19(7.7)	0.128
American cockroach	117(15.0)	100(9.9)	0.001	68(31.3)	57(18.9)	0.001	59(25.0)	59(20.8)	0.261	62(28.2)	52(21.0)	0.070
<i>Blatella germanica</i>	104(13.4)	87(8.6)	0.001	48(22.1)	46(15.2)	0.044	52(22.0)	36(12.7)	0.005	53(24.1)	42(16.9)	0.055
<i>Artemisia vulgaris</i>	239(30.7)	216(21.4)	0.000	19(8.8)	14(4.6)	0.058	10(4.2)	14(4.9)	0.701	13(5.9)	5(2.0)	0.029
<i>Ambrosia artemisifolia</i>	124(15.9)	129(12.8)	0.059	11(5.1)	9(3.0)	0.223	3(1.4)	3(1.2)	0.393	3(1.4)	3(1.2)	0.883
Mixed grass pollen	39(5.0)	47(4.7)	0.732	7(3.2)	5(1.7)	0.240	7(3.0)	6(2.1)	0.539	7(3.2)	4(1.6)	0.263
Mixed tree pollen	31(4.0)	29(2.9)	0.198	4(1.8)	4(1.3)	0.636	0(0.0)	3(1.1)	0.113	1(0.5)	1(0.4)	0.932
Mixed mould I	49(6.3)	46(4.6)	0.105	15(6.9)	6(2.0)	0.005	6(2.5)	8(2.8)	0.842	12(5.5)	4(1.6)	0.022
Mixed mould IV	38(4.9)	39(3.9)	0.295	16(7.4)	11(3.6)	0.059	6(2.5)	8(2.8)	0.842	6(2.7)	5(2.0)	0.612