Allergic sensitisation to common environmental allergens in adult asthmatics in Hong Kong

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The relationship between immediate skin reactivity to common allergens and adult asthma is not well defined. We retrospectively evaluated the profile of allergen sensitisation to common environmental allergens in 666 adult asthma patients at an asthma clinic in a teaching hospital in Hong Kong. Four hundred and seventy-one asthmatics (70.7%) were atopic; there were more males than females, although the difference did not reach statistical significance. The skin test positivity rate decreased significantly with age so that asthmatics aged 35 years and older were four to six times less likely to be atopic and eight to 12 times less likely to be allergic to *Dermatophagoides pteronyssinus*, compared with young asthmatics aged 15 to 24 years (P<0.001). Inhalant allergy was more common than food allergy and of the inhalants, indoor allergens, including house dust mite and cockroach were more important than outdoor allergens. The allergens most frequently associated with positive skin tests were *D. pteronyssinus* (62.2%), *D. farinae* (60.0%), cockroach (40.7%), cat dander (24.0%), and royal jelly (16.8%). In conclusion, allergen sensitisation is common in adult asthmatics in Hong Kong, and allergen avoidance should be included as part of the preventive strategies for controlling the disease in the community.

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Key words: Asthma; Hypersensitivity; Hong Kong

Introduction

The tendency to form specific IgE antibodies against environmental allergens is genetically determined and up to 40% of the population have this genetic predisposition and are said to be atopic. The prevalence of skin test reactivity in any population depends on the age and sex of subjects, and geographical variations in allergen load and sensitivity. Allergic sensitisation to common environmental allergens is closely linked to asthma and has been associated with asthma prevalence[1] and bronchial hyperresponsiveness.[2] Recent epidemiological studies suggest that sensitisation to allergens from indoor rather than outdoor sources is important in asthma pathogenesis and correlates with the degree of bronchial hyperresponsiveness.[3] In particular, allergies to house dust mite and cats have been associated with the development,[4,5] exacerbation,[6] and the severity of asthma symptoms in children.[7]

In a recent longitudinal study of 981 subjects from infancy to four years, sensitisation to both *Alternaria* and *Cladosporium* species was significantly associated with the development of asthma, rhinitis, and eczema.[8] On the other hand, allergy to grass pollen is not a significant factor in asthma exacerbations in children.[9,10] Most of the available data on the relationship between allergen sensitisation and asthma is derived from populations of Caucasian children, but there is only scanty information on immediate skin reactivity in Asian adult asthmatics. This paper aims to retrospectively review the atopic profile of adult asthmatics presenting to an asthma clinic in a teaching hospital in Hong Kong.

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Methods and materials

From January 1995 to June 1996, a total of 666 consecutive skin prick tests were performed on adult asthmatics (aged ≥15 years) at the asthma clinic of the Department of Medicine, Prince of Wales Hospital, Hong Kong. These subjects had been either newly diagnosed with asthma by the clinic or had been recently admitted to the hospital for acute exacerbation of asthma that had not previously been treated at our hospital.

Skin prick tests were performed according to Pepys' methods[11] using normal saline and histamine (10 mg/mL) as negative and positive controls, respectively. If a reaction occurred within 15 minutes, the transverse and vertical diameter of the wheal were measured and mean values recorded. Wheals of 3 mm or greater were regarded as positive in the absence of a reaction to normal saline and subjects with one or more positive reactions were considered atopic. Allergens and lancets (1 mm) used to perform the skin tests were obtained from Hollister-Stiers (Spokane, Wa, US). Cockroach extract was a mixture of American, German, and Oriental spp. Grass pollen extract was a mixture of prevalent grasses in areas of temperate climate (Kentucky Blue, Orchard, Redtop, Timothy, Sweet Vernal, Meadow Fescue, Perennial Rye). Royal jelly extract was directly obtained from a manufacturer of royal jelly supplements (Beijing Dietetic Preparation Manufactory, Beijing, China). The extraction of elutable latex proteins from latex gloves was performed according to the protocol devised by Turjanmaa et al,[12] which involves cutting 1 gm of glove into small pieces

Table 1. Skin test reactivity to common environmental allergens in adult asthmatics in Hong Kong

	Prevalence (95% CI) (n=666)	**Mean size of reaction in mm (SD)**
Men	45	
Women	55	
Age (y)	39.2 ± 18.0	
Inhalant allergens	(% with response)	
D. pteronyssinus	62.2 (58.5, 65.9)	7.2 (3.3)
D. farinae	60.0 (56.3, 63.7)	6.4 (2.9)
Cockroach	40.7 (36.3, 45.1)	4.0 (1.4)
Cat dander	24.0 (20.7, 27.3)	4.5 (2.1)
Dog hair	15.4 (12.6, 18.2)	3.5 (0.8)
Penicillium	13.2 (10.0, 16.4)	3.4 (0.6)
Cladosporium	10.7 (7.8, 13.6	3.2 (0.6)
Aspergillus	7.6 (3.6, 11.6)	3.3 (0.9)
Alternaria	7.5 (4.9, 10.1)	3.3 (0.6)
Bermuda grass	9.0 (6.2, 11.8)	3.4 (0.7)
Grass pollen	6.5 (2.8, 10.2)	3.6 (0.9)
Food allergens		
Egg yolk	12.5 (9.2, 15.8)	3.2 (0.5)
Egg white	7.7 (5.1, 10.3)	3.1 (0.3)
Shellfish	12.1 (8.9, 15.3)	3.2 (0.5)
Fish	6.9 (4.4, 9.4)	3.5 (1.0)
Peanut	6.4 (4.0, 8.8)	3.1 (0.4)
Cow's milk	4.1 (2.1, 6.1)	3.4 (0.5)
Other allergens		
Royal jelly	16.8 (13.5, 20.1)	4.4 (1.8)
Latex	2.0 (-1.0, 3.0)	3.2 (0.8)
Atopy (≥1 positive skin test)	70.7 (67.3, 74.2)	

Table 2. Skin test reactivity to common environmental allergens by age and sex. Values are percentages.

	Sex		Age (y)				
	M	F	15-24	25-34	35-44	45-54	≥55
Inhalant allergens							
D. pteronyssinus	68.5	57.1	86.7	75.6	57.7	46.8	33.3
D. farinae	65.9	55.2	86.0	72.3	54.0	42.1	33.3
Cockroach	43.8	38.2	50.4	55.2	35.1	31.5	25.9
Cat dander	23.2	24.7	30.2	36.6	18.5	20.8	12.0
Dog hair	18.2	13.1	21.2	22.9	14.1	11.8	4.9
Penicillium	14.3	12.2	14.5	21.2	7.9	6.1	13.0
Cladosporium	10.8	10.5	10.3	12.9	12.4	6.1	10.0
Aspergillus	6.8	8.3	9.8	11.8	7.7	0	5.9
Alternaria	8.0	7.0	4.8	11.5	9.6	7.3	5.5
Bermuda grass	11.2	7.0	7.5	14.1	9.6	4.9	7.8
Grass pollen	6.8	6.3	9.8	11.8	0	9.1	2.9
Food allergens							
Egg yolk	12.2	12.9	15.4	22.8	13.5	9.3	1.1
Egg white	5.9	9.4	12.5	10.1	8.1	0	3.3
Shellfish	13.8	10.5	20.2	15.2	12.3	2.4	4.4
Fish	9.6	4.4	9.5	8.9	12.2	0	1.1
Peanut	8.6	4.5	5.8	9.0	10.8	2.4	3.3
Cow's milk	4.8	3.5	2.9	7.7	4.1	4.8	2.2
Other allergens							
Royal jelly	18.0	15.7	31.3	22.1	13.5	5.6	3.6
Latex	2.0	1.7	–	–	–	–	–
Atopy							
(≥1 positive skin test)	74.3	67.8	89.0	82.7	65.7	55.8	50.7

and soaking these at room temperature in 5 mL of normal saline for 15 minutes. The latex allergen content of the gloves used to prepare the latex extract was unknown. The number of allergens tested in each subject varied as reflected by the width of the 95% confidence interval for each allergen.

The data were entered into a computer and analysed with SPSS for Windows. The effect of age on atopic tendency was assessed by the test for trend in proportion, using the statistical package EGRET (Serc, Seattle, Wa, US). Logistic regression was used to determine risk factors for atopy; female sex and age (categorised into 10-year age groups) were baseline variables.

Results

Table 1 shows the results of the skin test responses to a panel of common environmental allergens. Atopy, defined as the presence of one or more positive skin test, was present in 70.7% of adult asthmatics in Hong Kong. The two species of house dust mite were the most common allergens and gave rise to positive skin tests in about two-thirds of adult asthmatics in Hong Kong. Ninety-eight subjects (20.8% of atopic asthmatics) were monoreactors to *D. pteroynissinus* or *D. farinae* and did not react to other allergens. Cockroach and cat dander were also important allergens, with 40% and 24% of subjects mounting positive skin tests to these allergens, respectively. Of the four species of indoor mould tested, *Penicillium* was the most frequent cause of positive skin test. Grass pollen allergy was uncommon and fewer than 10% reacted to Bermuda grass or mixed grass pollen. Allergic sensitisation to foods was much less common than was sensitisation to inhalants. Interestingly, one in six asthmatics (16.8%) had positive skin tests to royal jelly, a protein-rich food supplement commonly consumed by

Chinese communities. Latex allergy, although common in high risk groups such as health care workers, was found in only 2% of adult asthmatics. In general, the mean size of the positive skin test followed the same trend as the prevalence of immediate skin reactivity.

Table 3. Age and sex as risk factors for atopy in asthmatics

	Univariate odds ratio (95% CI)*
Male	1.2 (0.98, 1.6)
Age (y)	
25-34	0.59 (0.29, 1.19)
35-44	0.24 (0.12, 0.44)
45-54	0.16 (0.08, 0.32)
>55	0.13 (0.07, 0.23)

* baseline for comparison - female, aged 15-24 years.

Table 2 shows the prevalence of immediate skin reactivity by age and sex and Table 3 shows sex and age as risk factors for atopic sensitisation in adult asthmatics in Hong Kong. Male asthmatics more frequently had positive skin tests than did females with respect to most allergens tested and the overall atopy rate was 1.2 times higher in men. When the subjects were separated into 10-year age groups, a decreasing trend in immediate skin reactivity with increasing age was evident and this change was statistically significant (test for trend in proportion, $P<0.001$). Compared with young asthmatics aged 15 to 24 years, asthmatics aged 35 years or older were four to six times less likely to be atopic and eight to 12 times less likely to have dust mite allergy.

Discussion

We found that 70.7% of adult asthmatics in Hong Kong are atopic and have immediate skin test reactivity to at least one common environmental allergen. Men were more allergic than women and positive skin test responses decreased significantly with age. This variation of skin test reactivity with age has been described previously. Barbee and co-workers studied 3101 subjects of all ages in a general population and found an overall prevalence of skin reactivity of 34%, with a peak prevalence of 52% occurring in the third decade, decreasing steadily with age thereafter and reaching a low of 16% in subjects older than 75 years.[13] This pattern was later confirmed in other population studies.[14,15] In studying 428 adult asthmatics in Vancouver, Lin et al found increased atopy in those younger than 35 years (53.4%) and reduced reactivity in older subjects aged 55 years or more (36.8%).[16] In the same study, men were also found to have a higher rate of positive skin test than women (55% vs 42%). The correlation between skin test reactivity and sex remains controversial, however, as a slight male predominance has previously been demonstrated by some[14,17] but not by others.[13]

There have been few surveys of immediate skin test reactivity in asthmatics in the Asian Pacific region (Table 4). Two studies were on children only, one involved asthmatics of all ages and one study was on adults only. The overall prevalence rates of atopy were high for children, affecting more than 90% of asthmatics.[18,19] For adults, about two-thirds of asthmatics were atopic as shown by Tan and Teoh[20] and the current study shows a drop-off in immediate skin reactivity with age. The prevalence rates of skin test positivity in adult asthmatics in Caucasian populations are generally lower compared with Asians and range from 43% to 56%.[16,21,22] Atopy rates have also been found to be higher in Orientals than in Caucasians living in the same environment in both the asthmatic population[16] and the general community.[23] A number of chromosome markers that are linked to asthma and atopy have recently been discovered,[24,25] but none have been tested in Asian populations. Whether there is a racial predisposition to allergic sensitisation in Asians is unknown, but certainly deserves further investigation.

We found inhalant allergens to be more commonly associated with adult asthma than food allergens, which is consistent with results from other Asian Pacific cities. Allergic sensitisation to inhalant allergens has been found to be an important risk factor for acute asthma exacerbations in adults.[21] In Hong Kong, house dust mite and cockroach were the two allergens that were responsible for 90% of immediate skin reactivity in our subjects. In other words, atopic status can be identified by using a minimum of these two allergens, and increasing the number of allergens is unlikely to increase the yield much further. This contrasts with a mere 75% identification rate for atopy when the two allergens that most frequently gave rise to positive skin tests in Vancouver, namely house dust mite and mixed Pacific grass pollen, were used in skin testing.[16] Hence, the number of allergens required to determine immediate skin sensitivity in a population varies between geographic locations. An increase in atopy rate from

Table 4. Studies of atopic profiles in asthmatics in the Asian Pacific region

Study authors	City	Age (y)	No. surveyed	Atopy (%)	Inhalant allergens						Food allergens			
					House dust mite	Mould	Cockroach	Cat	Dog	Grass	Cow's milk	Egg	Wheat	Shellfish
Tan, 1979	Singapore	10-73	92	≥65.2	65.2	6.5*	–	5.4	3.3	1.1	2.2	0	2.2	–
Hsieh, 1984	Taipei	1-16	1000	≥90.2	90.2	22.1†	17.9	7.4	8.2	–	8.1	10.3	0	9.1
Tuchinda, 1987	Bangkok	0-12	350	93.7	61.4	54.6	46.0	–	–	39.7		10.3‡		
Leung, 1996	Hong Kong	>15	666	70.7	62.2	9.8	40.7	24.0	15.4	7.8	4.1	10.1	–	12.1

* *Aspergillus fumigatus*
† average of *Aspergillus fumigatus* (26.7%), *Cladosporium* (22.8%), *Penicillium* (22.3%), *Alternaria* (16.7%)
‡ descending order of frequency: shrimp, egg white, cow's milk, beef, chicken, fish

31% to 49% was achieved when the number of allergens tested was increased from eight to 12 in a study of Finnish adolescents.[17]

Among the inhalants, the indoor allergens as a group more frequently gave rise to positive skin tests than did outdoor allergens. House dust mite is the most important indoor allergen and its repeated exposure has been associated with sensitisation and subsequent development of asthma symptoms in children[4] and its avoidance has led to improved asthma control.[26] Although similar longitudinal data in adult asthma is lacking, dust mite exposure has been found to be an independent risk factor for both asthma symptoms[27,28] and bronchial hyper-responsiveness[27] in adults. A significant association between dust mite exposure and adult asthma has been established in areas of high mite infestation such as Sydney, Australia,[27] as well as in central Sweden,[28] where dust mite is infrequently found due to the cool, dry climate. The hot and humid climate in Hong Kong no doubt facilitates their growth. A survey of 45 homes unselected for asthma in Hong Kong showed that 49% contained at least 10 μg/g of *Der p* I in dust samples recovered from mattresses, while only 24% of these samples had low levels (less than 2 μg/g, unpublished data). In contrast, floors in the bedroom, lounge room, and kitchen contained fewer mite allergens.

However, besides *Dermatophagoides* spp., other species of dust mites such as the storage mites including *Bromia tropicalis* are prevalent in parts of Southeast Asia, in particular Malaysia and Singapore, and are important indoor allergens associated with high exposure and bronchial asthma.[29] The association between mite allergy and childhood asthma in Hong Kong has previously been reported.[30] The same climate provides an ideal habitat for house mould growth in Hong Kong and other Southeast Asian countries such as Thailand and Taiwan and is reflected by the high prevalence of mould allergy in asthmatics. We have previously reported that 25% of unselected children in Hong Kong are allergic to house mould[30] and the predominant species collected by settle plates include *Cladosporium* spp. (97%), *Penicillium* spp. (37%) and *Aspergillus* spp. (20%).[31]

We found cockroach sensitivity in 40% of our subjects, similar to findings in Bangkok.[19] In Taiwan, nearly 50% of the urban atopic population with asthma and allergic rhinitis had positive skin tests to cockroach extracts.[32] Allergic sensitisation to cockroach is a strong risk factor for asthma in children of lower socioeconomic class living in multi-family dwellings.[33,34]

Domestic animal allergy is more common in Hong Kong compared with neighbouring Southeast Asian countries and may be related to its more Western lifestyle. In Sweden, more than 50% of homes have pets and the association between domestic animal allergy and childhood asthma has been firmly established there, as with other Western populations.[35] The importance of sensitisation to domestic animals in adult asthma has not been well studied, although a history of ongoing exposure and the presence of specific IgE to dog and cat were found to be substantially more common in adult emergency room asthmatic patients than in controls in a recent study.[36]

Outdoor allergens such as pollens of grasses, weeds, and trees are frequent causes of seasonal allergies including hayfever and asthma. At a population level, however, the relationship between pollen sensitivity and asthma remains controversial as some studies show a positive correlation,[27] but others fail to demonstrate an association when acute asthma exacerbation is considered.[9,10] Hong Kong is densely built, there is little grassland and grass pollen exposure is likely to be low, despite the lack of objective pollen data. This is reflected by the low prevalence of pollen sensitivity (less than 10%, in both the asthmatic population and the general community).[30]

Our study shows that food allergy is uncommon in adult asthmatics in Hong Kong and neighbouring countries. Asian subjects frequently relate asthma symptoms to certain foods, which may be a cultural phenomenon and cannot be explained by the severity of asthma.[37] However, in a study of 40 asthmatics with suspected food triggers for recurrent attacks in China, all had specific IgE to at least one suspected foodstuff and four subjects had positive bronchial challenges when aerosolised food extracts were tested.[38]

Besides IgE-related food reactions, food additives and preservatives have also been associated with asthma exacerbations, presumably via non-IgE–mediated mechanisms. In Hong Kong, fewer than 10% of adult asthmatics demonstrated allergic sensitisation to foods such as cow's milk, eggs, and shellfish. On the other hand, it is surprising to find that one sixth of adult asthmatics have IgE antibodies to royal jelly, a food supplement commonly consumed in Oriental communities. The major allergenic proteins of royal jelly are thought to have molecular weights of 47 to 55 kD.[39] In a recent survey of 1472 hospital employees, we found that 31.2% admitted taking royal jelly at some time in the past and 7.4% had a positive skin test to royal jelly.[40] The high prevalence of specific IgE to royal jelly indicates the possibility of cross-reactivity between royal jelly and other commonly occurring environmental allergens. As royal jelly ingestion has been linked with acute asthma and anaphylactic deaths, asthmatic subjects sensitised to royal jelly proteins should be discouraged from taking supplements containing it.

Natural rubber latex has recently been recognised as an important source of allergens and latex allergy is estimated to affect 5% to 10% of health care workers through contact with rubber gloves.41 We have shown that 3.3% of hospital employees in Hong Kong have symptoms suggestive of latex allergy.[42] Besides dermatomucosal contact, airborne exposure to latex allergens adsorbed onto glove powder has been reported to cause acute asthma.[43] There is also intriguing evidence to indicate that latex allergens on rubber tyre fragments of respirable sizes are present in abundance in urban air.[44] Of the 100 adult asthmatics who underwent latex skin test in our study, only two had a positive reaction. It is difficult to interpret the result with the small number of subjects but further evaluation of the role of airborne latex allergens in adult asthma at a population level is needed.

Two thirds of adults with asthma in Hong Kong are atopic and are frequently allergic to indoor inhalants including dust mite, cockroach, house mould, and animal dander. As allergen avoidance has resulted in improved asthma control in children, preventive strategies to control adult asthma should also include similar approaches.

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