# **Original Article**

## Aetiology of allergic rhinitis in Hong Kong

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### ABSTRACT

In a 1993 survey, allergic rhinitis was identified as the most common allergic disease in Hong Kong, affecting 29.1% of schoolchildren. Recently (1995), the International Study of Asthma and Allergies in Childhood (ISAAC) also reported 44.5% current rhinitis among Hong Kong teenagers. Our objective was to study the aetiology of allergic rhinitis in Hong Kong using serological tests of allergen sensitization. In 57 allergic rhinitis patients and in the same number of age- and sex-matched controls the following were measured: serum total IgE, mixed aeroallergen IgE (Phadiatop<sup>™</sup>) and specific IgE versus house dust mite (HDM), cockroach, cat and dog dander, mould mixture (Penicillium, Cladosporium, Aspergillus and Alternaria species) and four local pollens (Bermuda grass, Timothy, ragweed and mugwort). Compared with controls, allergic rhinitis patients (26 males, 31 females; mean ( $\pm$  SD) age 25  $\pm$  11 years) had a significantly elevated serum total IgE concentration (mean  $\pm$  SEM: 496  $\pm$  88 vs 179  $\pm$  38 kU/L) and an increased proportion of positive Phadiatop (95 vs 33%) and specific IgE tests versus HDM (90 vs 44%) and cockroach (42 vs 9%; Mann–Whitney U-test and  $\chi^2$ tests all P < 0.005). There was no significant difference in sensitization to other allergens tested. House dust mite and cockroach are ubiquitous in Hong Kong with a warm, humid climate and crowded living conditions. Their identification as aetiological agents of allergic rhinitis should help in the development of environmental strategies for reducing the inhalant allergen load to prevent and control this prevalent and costly health problem in our community.

**Key words:** allergic rhinitis, cockroach, inhalant allergens, *in vitro* allergy tests, Hong Kong, house dust mite.

#### INTRODUCTION

Allergic diseases, such as allergic rhinitis and asthma, are prevalent and have been increasing worldwide.<sup>1-4</sup> Statistics in 1990 estimated that > 20 million Americans had seasonal allergic rhinitis, while nearly 10 million suffered from asthma.<sup>5</sup> The consequent economic burden has been tremendous in terms of medical expenditure and loss of productivity or schooldays.<sup>6</sup>

Allergic diseases have been generally less common in Asia than in Western countries, but prevalence is rapidly catching up.<sup>7</sup> Taking asthma as example, rates have increased over the past 10 years from 2.4 to 5.1% in China, 5.5 to 8.7% in Malaysia and 7.9 to 13.2% in Japan.<sup>8–10</sup> These differences may have been caused by changes in environmental factors and in life style that enhanced allergen exposure, sensitization and airway inflammation.<sup>11</sup>

Until recently, the prevalence of allergy and atopy in Hong Kong has been poorly documented.<sup>12</sup> In 1993, Leung and Tseng studied 1062 schoolchildren aged 10–20 years, initially with a questionnaire.<sup>13</sup> Allergic rhinitis was the most common allergic symptom, affecting 29.1% of children. The prevalence of wheezing and asthma were 8.6 and 7.2%, respectively. Half (471) the children underwent skin prick tests and 57.7% had more than one positive reaction. The most common sensitizing

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aeroallergens were house dust mite (HDM; 96.3%), cockroach (44.6%) and house moulds (40.6%). In 1995, the International Study of Asthma and Allergies in Childhood (ISAAC), using a videotaped questionnaire developed for > 50 countries, documented 44.5% current rhinitis among Hong Kong teenagers.<sup>14</sup>

Therefore, allergic rhinitis is a serious health problem in our urbanized community with a warm, humid climate and a very high population density (6.5 million per 1091 km<sup>2</sup>). We set out to study the aetiology of allergic rhinitis using an extensive panel of serological tests for allergen sensitization.

## **M**ETHODS

Fifty-seven patients (26 males and 31 females; mean  $(\pm$  SD) age = 25  $\pm$  11 years, range 10–62 years) were recruited at the ENT Outpatient Clinic of the Prince of Wales Hospital from October 1994 to May 1995, with allergic rhinitis diagnosed by a specialist otorhinolaryngologist (HKF) using established criteria based on history and rhinoscopic examination.<sup>15</sup> The same number of sex- and age-matched (to  $\pm$  5 years in same decade) controls (26 males and 31 females; age 24  $\pm$ 10 years, range 11-65 years) were identified over the same period among our laboratory colleagues, their friends and relatives, with allergic rhinitis and other forms of allergy excluded by rhinoscopy (same ENT surgeon) and a negative history in a guestionnaire survey that enquired about current and previous symptoms of rhinitis and a past and family history of other allergic diseases.

A 10 mL venous blood sample was collected from each patient and control subject after obtaining their informed consent and our University's ethical approval for this study. The resultant sera were preserved at −70°C until they were assayed for total IgE, mixed aeroallergen-specific IgE (Phadiatop<sup>TM</sup>; Pharmacia Diagnostics AB, Uppsala, Sweden) and a panel of allergen-specific IgE (Table 1).

Serum total IgE was assayed using the IMx analyser (Abbott Laboratories, Chicago, IL, USA) with a measuring range of 4–4000 kU/L. Phadiatop and specific IgE tests were performed with a CAP FEIA analyser (Pharmacia Diagnostics AB). The former was a qualitative test yielding either a positive or negative result for sensitization to common inhalant allergens. The latter had a linearity interval from 0.35 to 100 kU/L with concentration values automatically evaluated for simultaneous printing of 'RAST classes' from negative to positive tests of increasing severity. During the study period, interassay precision (coefficient of variation) of our total IgE assay was 3.0% at 80 kU/L and that of specific IgE assay was 5.5% at 8.1 kU/L, with a low bias of < 0.9 standard deviation index (SDI) in Pharmacia's international quality assessment programme.

We used the  $\chi^2$  test for the comparison, between patients and controls, of the proportion of positive/ negative Phadiatop and specific IgE tests. The nonparametric Mann–Whitney U-test was used for assessment of difference between two groups of numerical results; namely, patient versus control serum total IgE and specific IgE concentrations. A probability (*P*) value < 0.05 was considered as significant.

## RESULTS

Results of the above measurements, in total 11 assays on each of the 114 patient and control sera, are summarized in Tables 2 and 3, which report and compare the prevalence and severity of allergen sensitization.

As shown in Table 2, 54 of the 57 allergic rhinitis patients (94.7%) gave a positive Phadiatop screening test for inhalant allergy, compared with a significantly lower proportion among control subjects (19/57 = 33.3%; P < 0.0005,  $\chi^2$  test).

In the former group, HDM sensitization was most prevalent, affecting 51 of 57 patients (89.5%), while 42.1% had positive specific IgE tests versus cockroach. This was followed by sensitization to cat and Bermuda grass (14.0 and 15.8%, respectively) and down to dog,

Table 1.Panel of specific IgE tests using the Pharmacia™CAP system allergens

C/( system unergens	
Households Dust mite (Dermat Cockroach (Blatell Cat dander Dog dander	ophagoides pteronyssinus) a germanica)
Mould mixture Pencillium notatum Cladosporium herl Aspergillus fumiga Alternaria alternate	parum tus
Bermuda grass (C) Timothy (Phleum p	ratense) I (Ambrosia elatior)

Group	Phadiatop	Dust mite	Cockroach	Cat	Dog	Mould	Bermuda	Timothy	Ragweed	Mugwort
(n = 57)						mixture	grass			
No. patients (%)	54 (94.7)	51 (89.5)	24 (42.1)	8 (14.0)	2 (3.5)	6 (10.5)	9 (15.8)	5 (8.8)	4 (7.0)	3 (5.3)
No. controls (%)	19 (33.3)	25 (43.9)	5 (8.8)	0 (0)	O (O)	2 (3.5)	3 (5.3)	2 (3.5)	2 (3.5)	2 (3.5)
P value ( $\chi^2$ test)	< 0.0005	< 0.0005	< 0.0005	< 0.005	< 0.2 (NS)	< 0.2 (NS)	< 0.1 (NS)	< 0.3 (NS)	< 0.4 (NS)	< 0.7 (NS)

 Table 2.
 Number and proportion of patients and controls with positive Phadiatop and specific IgE tests and their statistical analysis

NS, not significant.

Table 3. Serum total IgE and allergen-specific IgE and their statistical analysis

	Total IgE	Allergen-specific IgE (kU/L)								
Group	(kU/L)	Dust mite	Cockroach	Cat	Dog	Mould	Bermuda	Timothy	Ragweed	Mugwort
(n = 57)						mixture	grass			
Patients	$496 \pm 88$	43 ± 4.8	1.75 ± 0.17	0.27 ± 0.09	$0.03 \pm 0.02$	$0.09 \pm 0.04$	$0.14 \pm 0.05$	$0.10 \pm 0.04$	$0.09 \pm 0.05$	0.07 ± 0.04
Controls	$179\pm38$	$6.96~\pm~2.5$	$0.30\pm0.13$	$0.0\pm0.0$	$0.0\pm0.0$	$0.04\pm0.01$	$0.15 \pm 0.11$	$0.07 \pm 0.06$	$0.03 \pm 0.02$	$0.01 \pm 0.01$
P value	< 0.0005	< 0.0005	< 0.05	0.07 (NS)	0.32 (NS)	0.32 (NS)	0.14 (NS)	0.21 (NS)	0.32 (NS)	0.38 (NS)
(Mann Wh	itney U-test)									

Data are the mean  $\pm$  SEM. NS, not significant.

mould mixture and other grass and weed pollens tested (all < 10%).

Dust mite sensitization was also demonstrated in 25 of 57 control subjects (43.9%). Positive specific IgE test for cockroach was 8.8%. Less than 6% controls had been sensitized to other allergens tested and none (0%) was positive for cat and dog allergens.

Statistical evaluation of these results showed that patients had an increased proportion of sensitization to HDM, cockroach, and cat dander compared with controls (all P < 0.005).

Table 3 shows that allergic rhinitis patients had significantly elevated serum total IgE concentrations compared with controls (mean  $\pm$  SEM of 496  $\pm$  88 vs 179  $\pm$  38 kU/L; *P* < 0.0005, Mann–Whitney *U*-test). However, the distribution of these two groups of results showed considerable overlap from approximately 22 to 1000 kU/L, with modes at 200 and 80 kU/L for patient and control values, respectively.

Comparing the severity of sensitization to individual allergens, patients had significantly elevated specific IgE concentrations versus HDM and cockroach compared with controls (both P < 0.005). Between the two groups, there was no significant difference in specific IgE concentrations versus other allergens measured, including IgE versus cat dander (P = 0.07), which was shown above to have an increased proportion of positive tests in patients.

Of the 54 patients (94.7% of the patient group) with a positive Phadiatop test, 47 (87.0%) had multiple inhalant allergy with positive specific IgE tests versus at least two aeroallergens. This suggests that they were atopic and most (46 patients) were sensitized to HDM. Four (7.4%) of the seven remaining Phadiatop-positive patients presented with single allergy (exclusively vs dust mite and no other allergens). The three patients left who were Phadiatop positive showed no detectable specific IgE versus all allergens tested.

#### DISCUSSION

#### Patients and controls

Patients in the present study have been recruited from the ENT Specialist Clinic of our 1400-bed university teaching hospital. All had unresolving symptoms of rhinitis and had been referred by their primary care physicians. Diagnosis of allergic rhinitis was made by an ENT surgeon (HKF) using established criteria from a detailed medical and family history, plus general physical and otorhino-laryngological examination.<sup>15</sup> Patients with allergic rhinitis (all perennial rhinitis) but no other allergic diseases were included consecutively into our study. Their ages ranged from 11 to 62 years with a mean of 25 years and a mode of 20 years, results that are in full agreement with corresponding findings in surveys of several other

populations that allergic rhinitis is most prevalent among young adolescents.<sup>2,18</sup>

The control subjects, who had been sex- and agematched (to  $\pm$  5 years in the same decade) with patients were our laboratory colleagues, their friends and relatives. We had direct knowledge from a previous study of their socioeconomic and residential conditions for matching with allergic rhinitis patients and they should all have had good enough educational and intellectual levels to understand and complete the questionnaire that was explained to them. Those with no past and present history of allergic rhinitis and other allergic diseases were questioned and examined by the same ENT surgeon before they were finally admitted to the present study. The above procedure was to facilitate our specific study of allergenic sensitization in allergic rhinitis after controlling for other factors (age, sex, other allergy and environment) that would influence our observations using serum assays.

#### Major allergens in allergic rhinitis

A primary objective of our study has been to survey the aetiology of allergic rhinitis in Hong Kong. This was attempted by performing serum-specific IgE tests on both patients and controls using the Pharmacia CAP analyser, capable of reporting both qualitative (> 0.35 kU/L = positive) and quantitative (specific IgE concentration in kU/L) results. We have selected an extensive panel of common indoor and outdoor aeroallergens comprising HDM, cockroach, cat and dog dander, mould mixture (*Penicillium, Cladosporium, Aspergillus* and *Alternaria* species) and four locally prevalent pollens: Bermuda grass, Timothy, ragweed and mugwort.<sup>16,17</sup>

As reported in Results, allergic rhinitis patients had a significantly increased proportion of sensitization to HDM, cockroach and cat compared with controls. Dust mite sensitization was most prevalent, affecting 89.5% of patients, and also most severe (mean  $\pm$  SEM specific IgE of  $43.0 \pm 4.80$  compared with  $6.96 \pm 2.50$  kU/L in controls). Cockroach was the second most important allergen, with 42% patients positively sensitized to less severely elevated specific IgE concentrations of  $1.75 \pm$ 0.17 kU/L compared with corresponding figures of 8.8% and  $0.30 \pm 0.13$  kU/L in controls (P < 0.005 and 0.05, respectively). Sensitization of patients to cat dander, although more prevalent than controls (14 vs 0%; P <0.005), was not severe enough to result in a significant difference in specific IgE concentration between the two groups. Some aspects of these and other allergens are discussed below with respect to Hong Kong's climatic and other environmental conditions.

#### House dust mite

House dust mite is probably the most prevalent and potent indoor allergen that has been linked to asthma, bronchial hypersensitivity and allergic rhinitis in many tropical and subtropical countries from Europe, US, Central and South America, Australia, Papua New Guinea, island of Mauritius to the Far East, including Japan, Taiwan and Hong Kong.<sup>19–24</sup> In Hong Kong, information on mite sensitization associated with allergic rhinitis has been limited. Recently, Leung and Tseng observed that 96.3% atopic school children were skintest positive for *Dermatophagoides pteronyssinus* sensitization and this allergy was strongly associated with perennial rhinitis with an odds ratio of 3.9.<sup>13</sup>

Hong Kong has a tropical climate, with a mean monthly temperature ranging from approximately 15°C in January to approximately 28°C in July and a mean monthly relative humidity ranging from 52% in November to > 80% from April to September. It is also a densely populated city with a very high inhabitant density (e.g. 5 persons/room), which ensures ample supplies of desquamated human skin scales on which mites feed and propagate. Gabriel et al. confirmed that quilts used by Chinese patients were an important source of allergen by studying the seasonal variation of mite counts therein.<sup>24</sup> With the limited dwelling area in Hong Kong, quilts are usually removed and stored in cabinets during the hot, humid summer months, at a time when temperature, relative humidity and rainfall rate are at their highest, thereby providing optimal conditions for mite multiplication and enabling infestation to spread from one quilt to another. It is interesting that our patients and controls were recruited from October and November 1994, which was the beginning of a Hong Kong winter, when guilts were put back on the beds. This should also be a period when symptoms of allergic rhinitis began or worsened to warrant ENT specialist referral and blood samples were taken for serum total and specific IgE assays. Presence of mite allergens at high concentrations, the length of exposure (quilts during sleeping) and instantaneous aqueous solubility of the major allergen Der p 1 on the nasal mucosa must have a substantial enhancing effect on sensitization in predisposed individuals when all these concentration, exposure and potency factors are compared with other allergens. This explains the greatly increased proportion and severity (in terms of markedly elevated specific IgE concentrations) of mite sensitization in our patients and some controls resulting from continuous exposure to large amounts of such a potent allergen.

#### Cockroach

The cockroach has been shown to be an important source of allergen, particularly in inner city dwellings.<sup>25</sup> The prevalence of 42.1% sensitization in our allergic rhinitis patients is in keeping with the 40.6% positive skin tests among Leung and Tseng's atopic schoolchildren.<sup>13</sup> Again, due to the crowded residential conditions in Hong Kong, some patients may live in a public housing estate where they may use the same room for eating and sleeping, and some also for cooking. This is a factor that probably accounts for the high prevalence of cockroach sensitization in the Hong Kong population.

## Cat and dog

Sensitization to animal allergens can be an important cause of allergic rhinitis.<sup>26</sup> This is both because many of these allergens are highly immunogenic and because patients insist on having close contact with animals. Cat and dog allergens have been found in most household dust in many Western countries.<sup>27</sup> Besides being of a small particle size (< 5  $\mu$ m) and being readily airborne, cat allergens are also 'sticky', adhering to walls, clothing (e.g. that of schoolchildren) and other surfaces.<sup>28</sup> Consequently, exposure to cat allergens is a prevalent phenomenon, even in homes where such animals have not been kept.<sup>29</sup>

We have chosen to test only for specific IgE versus cat and dog because there is little farming (involving horses and cows) in Hong Kong and other animal pets are rarely kept. Considering the above properties of cat allergens, it is not surprising that some (14%) of our allergic rhinitis patients, who belong to a genetically predisposed population to allergy, have acquired a mild degree of sensitization to cat allergens from limited exposure. Our finding that only two patients and no controls were sensitized to dog dander concurs with the fact that dogs are seldom kept in small high-rise residential apartments in Hong Kong.

#### Pollens

In Hong Kong, documentation of pollinosis is lacking, except for a single report of 11.1% positive skin tests in atopic children.<sup>13</sup> It is generally taken that under crowded living conditions with few grasslands and trees in residential areas, pollen allergy is uncommon. This explains that only a small number of our patients (15.8%) showed detectable specific IgE antibodies versus Bermuda grass pollen and the proportion of affected patients and their corresponding specified IgE concentrations were not statistically different from the control group. There was also no significant difference in the small proportion of positive tests and very low specific IgE concentrations versus other common local pollens studied (Timothy, ragweed and mugwort).

#### Moulds

The inhalation of airborne moulds is known to cause both asthma and allergic rhinitis.<sup>30</sup> A recent study in Hong Kong reported that 40.6% atopic children had skin sensitivity to a mixed extract of Aspergillus, Penicillium, Alternaria and Cladosporium. Using Pharmacia's specific IgE reagent containing the same mould mixture, we found a much lower proportion of sensitization in our allergic rhinitis patients (10.5%). The disagreement between these two findings could be caused by species differences in the mould mixture and skin test extract in which major allergens have not been clearly standardized. This interpretation will have to be confirmed by more exhaustive studies of individual mould allergenicity and cross reactivity. For example, we plan to isolate common house moulds in Hong Kong for Pharmacia to tailor-make specific IgE reagents for our use. However, another possibly important reason for a higher rate of skin sensitivity than positive serum IgE test may be related to the poorly characterized mould allergen extract that may contain irritants inducing false-positive reactions that can be further exacerbated by the inclusion of preservatives in the extract that also cause irritability.<sup>31</sup>

#### Conclusions

In genetically predisposed individuals there is a clear relationship between allergen exposure, sensitization and the development of allergic rhinitis, the most common allergic disease worldwide.

House dust mite and cockroach are ubiquitous in Hong Kong with a warm, humid climate and crowded living conditions. Their identification as aetiological agents of allergic rhinitis should help the development of environmental strategies for reducing the inhalant allergen load to prevent and control this prevalent and costly health problem in our community. 28 CWK LAM ET AL.

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