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Pattern of Sensitization to Common Environmental Allergens amongst Atopic Singapore Children in the First 3 Years of Life

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SUMMMARY **This study was aimed to investigate the sensitization pattern to a range of common allergens in young Singaporean children. A cross-sectional study involving 75 children aged below 3 years was carried out. They presented between December 1995 and April 2000 with symptoms of asthma, rhinitis, eczema, or food allergy. Their levels of allergen-specific serum IgE to a panel of foods (egg white, milk, soy protein, shrimp, wheat and peanut), pet dander, dust mites and cockroaches were measured with Pharmacia CAP™ System radioallergosorbent test kits. Serum IgE levels greater than 0.35 kU/l represented a positive result. Four children could not be tested with the complete panel because of insufficient serum. The prevalence of sensitization was highest for cow's milk (45.9%) followed by egg white (38.7%), dust mites *Dermatophagoides pteronyssinus* (31.4%) and *Blomia tropicalis* (25.5%). Sensitization to ingested allergens was significantly more prevalent in children aged 1 year or younger than in the older children (70.4% of those below 1 year, and 50% of those aged 1-3 years; $p < 0.02$). Sensitization to inhaled allergens, such as dust mites, was more likely to manifest as respiratory symptoms (allergic rhinitis and asthma), while ingested allergens were associated with gastrointestinal symptoms and eczema ($p < 0.001$). It was concluded that infants and young children are at high risk of sensitization to common environmental substances. Allergen avoidance is therefore important even in the very young. The prevalence of sensitization to food allergens is higher compared to inhalant allergens in young children.**

In the last 30 years, the prevalence of atopic diseases such as asthma, allergic rhinitis and eczema has increased among children worldwide.[1-3] The social, personal and economic impact of allergic diseases weigh heavily on patients, their families and the health care system.[1-3] Children are exposed to a wide variety of potential allergens from infancy onward, including common foods such as cow's milk and eggs, as well as pets and dust mites. In susceptible infants, the development of hypersensitivity reactions in early childhood may form the basis for atopic disease in later years.[4-6]

IgE sensitization is a major predictive marker of children at high risk of developing allergic disease.[4-12] Specific IgE and IgG antibodies to food and inhaled allergens have been found in children who subsequently developed eczema and asthma.[4-13] Few studies of IgE and IgG sensitization have been conducted in very young children in Asia. Our study was designed to investigate the pattern of sensitization to food and inhaled allergens in atopic children below 3 years of age in Singapore. This is important in the diagnosis and management of atopic patients, as avoidance of allergens may prevent the development of chronic allergic disease in sensitized children.[14,15]

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MATERIALS AND METHODS

Subjects

Our study population consisted of 75 children below the age of 3 years, who presented with symptoms suggestive of atopic disease at the paediatric clinic of the National University Hospital of Singapore between December 1995 and April 2000. The spectrum of presentation of atopic disease included asthma, allergic rhinitis, eczema, food allergies, and urticarial reactions to specific substances. The diagnosis of atopic disease was made from the history and clinical examination by a pediatrician. Some of the children had positive skin prick tests for allergens such as cow's milk and dust mites.

Informed consent was obtained from the parents of participants after the purpose and nature of this study was explained to them. The study was approved by the hospital's ethics committee.

IgE sensitization

The levels of total and specific IgE for a panel of allergens were measured in samples of blood drawn from the subjects. Certain food (cow's milk, egg white, soy, peanut, wheat, shrimp) and inhalant allergens (cat and dog dander, dust mites *Dermatophagoides pteronyssinus* [Der p] and *Blomia tropicalis* [Blo t], cockroach) were chosen be-cause these are common substances found to be allergenic in numerous studies.[5-8,11-14]

The Pharmacia CAP System radioallergosorbent (RAST) fluoroenzymeimmunoassay (FEIA) was used to measure serum IgE levels; levels more than 0.35 kU/l represented a positive result. This was the lower limit for detection of sensitization.[16]

Statistical analysis

Sensitization to food and inhalant allergens was compared between infants and children above 1 year of age, using the Chi square test. All p values were two-sided.

RESULTS

The mean age of our 75 subjects was 18.8 months (range 1 month to 3 years). There were 45 (60%) males and 30 (40%) females. Forty-five were Chinese (60%), with 18 (24%) Malays, 6 (8%) Indians and 6 (8%) Eurasian children. There were 27 children (36%) below the age of 1 year, and 48 (64%) children aged 1 to 3 years.

Total levels of IgE ranged from 3.6 to 14,600 kU/l in children aged 1 year and below (geometric mean 3.9 kU/l); older children had IgE levels between 4.5 and 13,690 kU/l (geometric mean 4.7 kU/l). The overall geometric mean of IgE level for the whole cohort was 4.5 kU/l.

Allergen sensitization

The prevalence of sensitization was highest for cow's milk (45.9%) and egg white (38.7%), followed by dust mites (31.4% for Der p and 25.5% for Blo t, respectively) (Table 1).

Overall, 22 children (29.3%) were sensitized only to ingested allergens, 34 (45.3%) to inhalants, and 13 (17.3%) to both types of allergens. There was a significantly higher prevalence of sensitization to food allergens in children aged 1 year and below (66.7%) compared to the older children (50%) ($p < 0.02$). However, with regard to specific allergens, the prevalence of sensitization to egg white, wheat and shrimp was higher in the older age group (children 1-3 years of age).

The highest specific IgE levels were found for the dust mites *Dermatophagoides pteronyssinus* (geometric mean 15.5 kU/l) and *Blomia tropicalis* (14.8 kU/l) (Table 2). In a large proportion of children, the levels of allergen-specific IgE to all the allergens measured were low. Six children had class IV IgE (> 100 kU/l) to *Dermatophagoides pteronyssinus*. For all the other allergens, only 1 child had class IV IgE each to cow's milk, egg white, soy protein and *Blomia tropicalis*.

Relationship to symptoms

There were 36 (48%) children with respiratory symptoms (allergic rhinitis, recurrent wheezing and asthma), 32 children (42.7%) with only skin manifestations and gastrointestinal symptoms such as diarrhea and vomiting; the rest of the children (9.3%) had both types of symptoms. Among the 39 children with skin and GI symptoms, sensitization to food allergens (58.9%) was significantly ($p < 0.001$) more prevalent than to inhaled allergens (12.8%). Conversely, sensitization to inhalants (48.8%) was significantly higher ($p < 0.001$) among children with rhinitis, wheezing and asthma than sensitization to purely ingested allergens (23.2%).

DISCUSSION

This was a cross sectional study to evaluate the pattern of allergen-specific sensitization in very young atopic children in our population. We found that sensitization to food allergens was significantly

Table 1 Prevalence of specific allergen sensitization in Singaporean children (n = 75)

Allergens	Overall sensitization	% Sensitized in children aged 1 year old and below (n = 27)	% Sensitization in children aged > 1 year (n = 48)	*p* value
Ingested				
Cow's milk	45.9	55.3	28.6	0.025
Egg white	38.7	17.9	51.1	< 0.001
Soy protein	4.2	10.7	0.0	< 0.001
Wheat	12.2	7.2	14.9	0.022
Shrimp	11.5	3.6	10.6	0.015
Peanut	12.0	7.4	14.5	0.022
Inhaled				
Cat dander	1.5	3.6	0.0	< 0.001
Dog dander	6.5	7.2	4.3	0.041
Der p#	31.4	10.6	40.4	< 0.001
Blo t#	25.5	7.2	54.2	< 0.001
Cockroach	8.5	3.6	10.0	0.022

#Der p = *Dermatophagoides pteronyssinus*; Blo t = *Blomia tropicalis*

Table 2 Levels of allergen-specific IgE (n = 75)

Allergens	Geometric mean of specific IgE (kU/l)	Range of specific IgE (kU/l)
Ingested allergens		
Cow's milk	1.41	0.36 – 100
Egg white	1.45	0.36 – 100
Soy protein	1.07	0.88 – 100
Wheat	1.12	0.37 – 18.9
Shrimp	2.00	0.43 – 8.9
Peanut	1.89	0.41 – 19.6
Inhaled allergens		
Cat dander	1.0	1.04
Dog dander	1.5	0.78 – 2.9
Der p#	15.5	0.41 –100
Blo t#	14.8	0.68 – 100
Cockroach	1.4	0.45 – 4.5

#Der p = *Dermatophagoides pteronyssinus* ; Blo t = *Blomia tropicalis*

more prevalent in infants compared to children above 1 year of age ($p < 0.02$). These findings are consistent with studies in other populations in Europe, Australia and Japan.[4-10] It has been postulated that increased gut mucosal permeability in infancy allows better antigen penetration and sensitization.[17,18] The subsequent early transient rise of specific IgE to ingested allergens may induce the hypersensitivity reactions that manifest as food allergy and atopic dermatitis.

In terms of inhaled allergens, however, this study also found a higher prevalence of sensi-

tization to dust mites (*Dermatophagoides pteronyssinus* and *Blomia tropicalis*) than in other populations.[8,9,13] A very high prevalence (up to 96.8%) of sensitization to dust mites in asthma and allergic rhinitis patients in Singapore has been observed in a recent study;[19] clearly, sensitization to dust mites starts very early in Singapore.

Children in Singapore, like those in other countries, also demonstrate allergy to common foods such as milk and egg white, but the prevalence of sensitization to shrimp (11.5%) is higher in the local population, as compared to children in Australia and Sweden.[5,8] Factors contributing to this phenomenon may be the introduction of shrimp to Singaporean diets at an earlier age than in those countries, or cross sensitivity of shrimp with tropomyosin (dust mite protein) – dust mites have been shown to be prevalent in Singaporean homes.[20] However, sensitization to other common inhalant allergens (cat and dog dander) was less common in children here than in Europe and Japan;[5,8,13] this might be attributable to the lower pet ownership among Singaporeans, the majority of whom live in apartments.

A site-specific pattern of atopic manifestation was also demonstrated, where specific pattern of allergen sensitization was associated with disease manifestation. Sensitization to ingested allergens was associated with symptoms of diarrhoea and eczema, while inhalant sensitization with wheezing and rhinitis. This has also been observed in other studies.[6,8-10] Local IgE production triggered by allergen exposure at the skin, gastrointestinal tract or respiratory tract may cause organ-specific symptoms at that site – the "shock organ" theory.[21] However, specific sensitization of target tissues has not yet been extensively studied, and an allergic reaction is possible even when challenged in "non-involved" sites. For instance, a positive skin test to pollen may be obtained in a subject with hay fever.[21]

Our study showed that IgE sensitization is common even in very young children, which has also been observed in several studies.[4-7,10-11,13] Although sensitization does not necessarily equate to the presence of chronic atopic disease, it has been shown that even in very young children with no atopic symptoms (who may be at risk of atopic disease due to family history or other factors), IgE sensitization to common allergens heralds the onset of allergic disease in later childhood.[4-11] Therefore, identification of sensitized children by elevated allergen-specific IgE levels or positive skin-prick tests is useful, because avoidance of trigger foods or inhaled substances in very young children before onset of symptoms may prevent the development of chronic asthma or eczema.[14,15] In this study, we have documented the pattern of allergen sensitization in very young atopic children.

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