

Seasonal variation of skin reactivity and specific IgE antibody to house dust mite

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Background: House dust mite is an important cause of bronchial asthma worldwide. While the allergen is present all year-round, a seasonal variation of house dust mite allergen levels has been found. There have been few reports, however, on seasonal variation of specific immune response to house dust mite.

Objective: We studied the changes in skin reactivity and specific IgE antibody to house dust mite associated with seasonal variation of house dust mite allergen levels in houses of mite-sensitive asthmatic patients.

Methods: In 14 mite-sensitive asthmatic patients, house dust mite allergen (Der f 1) contents in bedding were measured monthly. Skin reactivity on prick test and specific IgE antibody to house dust mite, *Dermatophagoides farinae* (*D. farinae*), were determined every 3 months from July to December.

Results: The concentration of Der f 1 in dust from bedding reached maximum levels in August and September, and significantly decreased in November and December compared with August and September ($P < .05$). Skin reactivity (a ratio of mean wheal diameter of allergen to histamine) to *D. farinae* decreased significantly in December compared with September ($P < .05$). Serum levels of total IgE and specific IgE antibody to *D. farinae* decreased significantly in December compared with September ($P < .05$).

Conclusion: These findings suggest that seasonal changes in natural exposure to house dust mite allergen might lead to concurrent changes in skin reactivity and specific IgE antibody to house dust mite in mite-sensitive asthmatic patients.

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INTRODUCTION

House dust mite is an important cause of bronchial asthma worldwide.¹ IgE antibody responses to house dust mite allergen have been considered to play an important role in the development of bronchial asthma.² Although, traditionally, house dust mite has been considered a perennial allergen, aggravation of clinical symptoms related to house dust mite sensitivity in association with seasonal increase in mite numbers has been frequently observed

by practitioners.³ Recently, changes in airway hyperreactivity of asthmatic patients in association with seasonal changes in house dust mite allergen were reported.⁴ In pollen-sensitive patients, seasonal rise in pollen-specific IgE was associated with a rise in pollen count.⁵ Several cross-sectional studies have suggested that environmental house dust mite allergen concentration correlates with specific IgE response and skin reactivity to house dust mite.^{6,7} To the best of our knowledge, however, changes in specific immune response to house dust mite in association with seasonal changes in environmental house dust mite allergen level have not been demonstrated.⁴

To further evaluate the influence of natural exposure to house dust mite allergen on specific immune response to house dust mite, we measured changes in skin reactivity and specific IgE antibody to house dust mite in 14

mite-sensitive asthmatic patients, and changes in house dust mite allergen levels in their houses for 6 months.

MATERIALS AND METHODS

Patients

Fourteen asthmatic patients who were sensitized to house dust mite, *Dermatophagoides farinae* (*D. farinae*), participated in this study. All patients, nine males and five females, had a clinical history of asthma and nonspecific bronchial hyperreactivity. Mean age was 25 years (range: 16 to 42). Their sensitivity to house dust mite was determined by skin prick test with 50 common allergens (Bencard Allergy Service, Bredford, Middlesex, UK) and serum-specific IgE antibody detected by a fluoroallergosorbent test (FAST; 3M, Santa Clara, CA).⁸ The allergens used included grass, tree, and weed pollens, mold spores, cat and dog epidermal antigens, and *D. farinae*. All patients had an isolated allergy to *D. farinae* and showed negative skin reactions to any other allergens. None had ever received desensitization treatment or ingested antihistaminic and antiallergic drugs during the study period, and they were treated with inhalation of cromoglycate, budesonide, and salbutamol, and oral theophylline if needed without changes in dosage during the study period. All patients lived in Seoul, Korea. Written informed consent was obtained from each, and the study was approved by the Medical Ethical Committee of Severance Hospital. The study was conducted from July to December of 1993.

Collection and Extraction of House Dust

The patients' houses were visited monthly from June to December. Dust samples from the surface of beddings were collected (2 min/m²) using a vac-

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uum cleaner (092V, Daewoo, Korea), fitted with a filter holder (pore size, 10 μm in diameter) according to the recommendations of the second international workshop on dust mite allergens and asthma.⁹ Samples were prepared by extracting 100 mg of sieved dust in 2 mL of phosphate-buffered saline with overnight shaking at 4 °C.

The samples were centrifuged and the supernatants were stored at -20 °C. Mean data of outdoor temperature and relative humidity each month were obtained from the Korea Meteorological Administration in Seoul. These values represent the monthly means of four measurements per day.

Measurement of House Dust Mite Allergen in House Dust Extracts

Level of group I allergen of *D. farinae* (Der f 1) in house dust extracts was measured simultaneously by ELISA according to a previously described method,¹⁰ using monoclonal antibodies (kindly provided by M D Chapman).

Skin Testing and Serum Sampling

Every 3 months during the study period, all patients underwent skin prick testing with *D. farinae* extract (Bencard Allergy Service, Bredford, Middlesex, UK) by the same person, who was unaware of the purpose of this study. The same batch of allergen extract was used throughout the study.

Normal saline and histamine (1 mg/mL) were used as negative and positive controls, respectively. Skin test response was read at 15 minutes. The longest and orthogonal diameters of the wheal and erythema were measured with a millimeter rule. Both diameters were recorded, summed, and divided by 2. A wheal diameter 3 mm greater than the negative control was considered a positive reaction. The results of skin reactivity to *D. farinae* were expressed as a ratio of mean wheal diameter of allergen to histamine (A/H ratio). At same intervals, venous blood was sampled and the sera were stored at -20 °C.

Serum Total IgE and *D. farinae*-Specific IgE

Total IgE and specific IgE antibodies to *D. farinae* in patient's sera were measured simultaneously by fluoroallergosorbent test (FAST; 3M, Santa Clara, CA)⁸ and expressed as IU/mL.

Spirometry and Measurement of Airway Hyperreactivity

In all subjects, pulmonary function and airway hyperreactivity to methacholine were tested at the start of the study. Forced expiratory volume in one second (FEV₁) and vital capacity were measured. Airway hyperreactivity to methacholine was determined by a method described previously.¹¹ An

aerosol of 0.9% NaCl followed by serially doubled concentrations of methacholine (0.075 to 25 mg/mL) was inhaled until a decrease in FEV₁ of 20% or more was observed. From the decline in FEV₁, the methacholine provocation concentration causing a 20% fall in FEV₁ (PC₂₀) was calculated. All medication was stopped 72 hours before the challenge.

Statistics

Data were expressed as the mean $\pm$ standard error of the mean except for house dust mite allergen levels which were expressed as a geometric mean $\pm$ geometric standard error of mean. The changes in house dust mite allergen, total IgE, specific IgE antibody, and skin reactivity to house dust mite were compared by a Wilcoxon signed-rank test.

RESULTS

Seasonal Changes in House Dust Mite Allergens in Bedding

Der f 1 levels in dust from bedding tend to increase gradually from June and reach a peak in August and September and gradually decrease until December. Der f 1 levels significantly decreased in November and December compared with August and September ($P < .05$) (Fig 1, Table 1). Changes in temperature and humidity coincided with decreases in Der f 1 (Fig 1).

Seasonal Changes in Skin Reactivity to *D. farinae*

Skin reactivity to *D. farinae*, expressed as A/H ratio, significantly decreased ($P < .05$) in December compared with June and September with no difference in skin reactivity to histamine (Fig 2, Table 1).

Seasonal Changes in Total IgE and *D. farinae*-Specific IgE Antibodies

Serum total IgE levels significantly increased in September compared with June ($P < .05$), and the levels significantly decreased in December compared with September ($P < .05$) (Fig 3, Table 1). There were no significant changes ($P > .05$) in levels of serum *D. farinae*-specific IgE antibodies between June and September, but the lev-

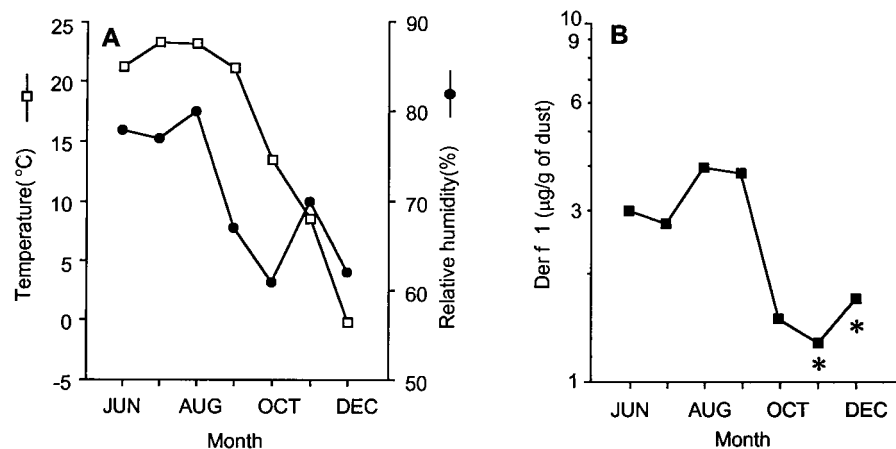


Figure 1. Seasonal changes in mean values of outdoor temperature and relative humidity (A) and geometric mean values of house dust mite allergen (Der f 1) levels in bedding (B). * House dust mite allergen significantly decreased in November and December compared with August and October ($P < .05$).

Table 1. Seasonal Changes in House Dust Mite Allergen (Der f 1) Levels in Bedding, Total IgE, Skin Reactivity (A/H ratio), and Specific IgE Antibody to *D. farinae* in 14 Mite-Sensitive Asthmatic Patients

	June	September	December
Der f 1, $\mu\text{g/g}$ of dust	3.01 ± 1.44	3.81 ± 1.36	$1.71 \pm 0.69^*$
Total IgE, IU/mL	697.9 ± 267.1	$948.6 \pm 318.7^\dagger$	$765.9 \pm 253.2^*$
Specific IgE, IU/mL	32.8 ± 16.6	39.3 ± 19.7	$32.5 \pm 16.7^*$
Skin reactivity ‡	3.1 ± 0.5	2.7 ± 0.3	$1.7 \pm 0.2^*\S$
Histamine reactivity ‡	3.3 ± 0.2	3.3 ± 0.2	3.1 ± 0.3

Data were expressed as the mean $\pm$ standard error of the mean except for house dust mite allergen levels which were expressed as a geometric mean $\pm$ geometric standard error of mean.

* Significant decrease in December compared with September ($P < .05$).

† Significant increase in September compared with June ($P < .05$).

‡ The results of skin reactivity to *D. farinae* were expressed as a ratio of mean wheal diameter of allergen to histamine (A/H ratio), and histamine reactivity was expressed as a mean wheal diameter (mm).

$\S$ Significant decrease in December compared with June ($P < .05$).

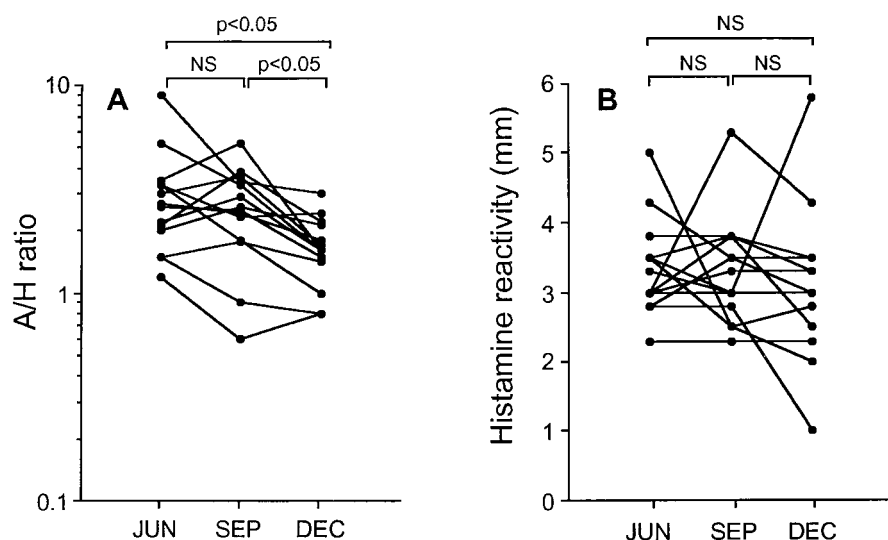


Figure 2. Seasonal changes in skin reactivity (A/H ratio) to *D. farinae* (A) and histamine (B). The results of skin reactivity to *D. farinae* were expressed as a ratio of mean wheal diameter (mm) of allergen to histamine (A/H ratio), and histamine reactivity was expressed as a mean wheal diameter (mm).

els significantly decreased in December compared with September ($P < .05$) (Fig 3, Table 1).

DISCUSSION

There have been notable variations in previous reports about the kinetics of seasonal changes in house dust mite allergen levels, which may be due to differences in geographic location, climate, and life style.^{12,13} In this study, house dust mite allergen levels reached a peak level in August and September, and then significantly decreased in No-

vember and December to less than 2 $\mu\text{g/g}$ of dust which is a threshold for sensitization to house dust mite suggested by Platts-Mills.¹⁴ These changes paralleled changes in relative humidity as previously described.^{3,12} Our findings of significant decrease in house dust mite allergen levels in winter were comparable to results of a study in Japan.¹⁵ In comparison with previous studies from North America,^{3,12} a more prominent decrease of house dust mite allergen levels was noted in winter.¹²

We could propose several reasons for the more dramatic fall in house dust mite allergen levels in this study. No subject participating in this study used a mattress, and instead they used a "yo" (Korean bedding filled with cotton wadding) for bedding. None had a carpeted floor, and no one used an air conditioning system during summer. These things might have influenced the kinetics of seasonal changes in house dust mite allergen levels. Our results also support a close relationship between changes in humidity and house dust mite allergen contents in house dust.

The association between allergen-specific IgE response and allergen exposure was suggested by previous studies which showed an increase of serum total IgE and pollen-specific IgE antibody levels in patients with hay fever during pollination season.^{5,16} Seasonal changes in house dust mite allergen levels were reported to be associated with seasonal variation in airway hyperresponsiveness in nine mite-sensitive asthmatic patients without significant changes in total IgE and house dust mite-specific IgE antibodies in sera.⁴ In this study, specific IgE antibody levels varied significantly according to the changes in house dust mite allergen levels. The reason for this discrepancy is not yet known. One possibility is that patients in this study were younger than those in the previous study⁴; another is that our patients had higher baseline skin reactivities to house dust mite than those of the previous report.⁴ We believe that more rapid and obvious changes in house dust mite allergen levels are also responsible for the discordance of our study with previous data.⁴

We have no experimental data to explain how serum total IgE levels change according to changes in house dust mite allergen levels. It was suggested that seasonal enhancement of interleukin-4 induced IgE synthesis by peripheral blood mononuclear cells was associated with a seasonal rise of IgE antibodies in patients with pollen allergy.¹⁷ We can speculate that activation of house dust mite-specific T lym-

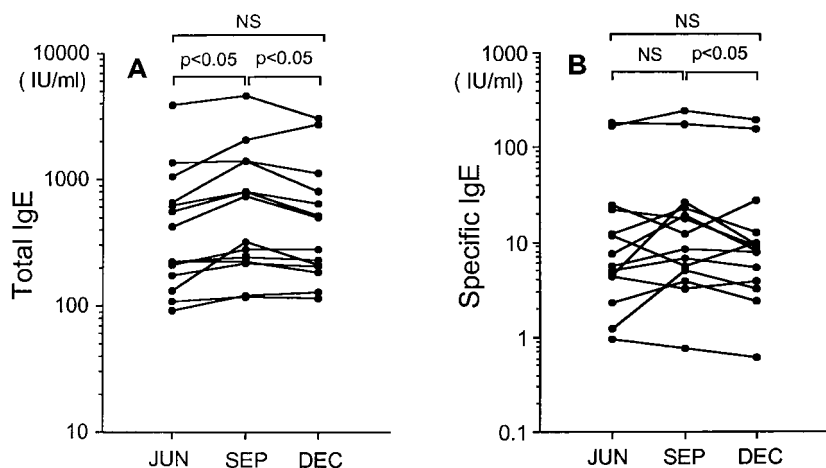


Figure 3. Seasonal changes in total IgE (A) and *D. farinae*-specific IgE (B) antibodies.

phocyte clones with increased allergen exposure may result in overproduction of interleukin-4 and polyclonal expansion of IgE-producing B lymphocytes as well as specific IgE-producing B lymphocytes.

Seasonal variation of skin reactivity to seasonal and perennial allergens, and even reactivity to histamine were reported.¹⁸ In this study, changes in skin reactivity to house dust mite coincided with environmental changes in house dust mite allergen levels without significant changes in skin reactivity to histamine. A significant decay in activity of house dust mite extract during storage has been reported.¹⁹ Although, in this study, we showed that significant decrease in skin reactivity to *D. farinae* in December coincided with the decrease in *D. farinae*-specific IgE antibodies, we could not completely exclude the possibility that decrease in potency of *D. farinae* extract during storage might influence the decrease in skin reactivity to *D. farinae* in December.

Environmental control of house dust mite is the first line management for mite-sensitive asthmatic patients. For the evaluation of allergen exposure in asthmatic patients, collection and processing of house dust is widely used,⁹ which cannot be done easily in clinical practice. Several cross-sectional studies have suggested that environmental house dust mite concentration corre-

lates with specific IgE response and skin reactivity to house dust mite allergen,^{6,7} and it has been suggested that levels of specific IgE antibodies can be used to evaluate exposure to house dust mite allergen because there is a significant correlation between specific IgE and environmental house dust mite allergen levels in mite-sensitive patients.⁷ Avoidance of exposure to house dust mite allergen at high altitude, where no house dust mite was recovered, resulted in decreases of serum house dust mite-specific IgE antibody levels.²⁰

Due to more rapid changes in nasal-specific IgE than serum-specific IgE, measurement of nasal-specific IgE has been proposed as a sensitive marker for monitoring allergen exposure in patients with allergic rhinitis.²⁰ Measurement of specific IgE in the target organ of asthmatic patients may be more difficult and complicated.

Together with previous cross-sectional studies on the significant correlation between house dust mite-specific IgE and environmental house dust mite allergen concentration,^{6,7} our results suggest that sufficient long-term decrease in natural exposure to house dust mite allergen can result in a decrease in skin reactivity and specific IgE antibody to house dust mite. Further studies might be needed on the use of skin reactivity and specific IgE antibody to house dust mite as an index

of environmental exposure to house dust mite allergen in mite-sensitive asthmatic patients.

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