

Citrus red mite (*Panonychus citri*) is a common sensitizing allergen among children living around citrus orchards

Myung-Hyun Lee, MD*, Sang-Heon Cho, MD†‡, Hae-Sim Park, MD§, Joon-Woo Bahn, MD†, Byung-Jae Lee, MD†, Jee-Woong Son, MD‡, Yoon-Keun Kim, MD†‡, Young-Yull Koh, MD‡, Kyung-Up Min, MD†‡, and You-Young Kim, MD†‡

Background: A recent investigation has suggested that *Panonychus citri* (citrus red mite) is the most common causative allergen in citrus-cultivating farmers with asthma or allergic rhinitis.

Objective: A cross-sectional survey was performed to evaluate the prevalence of asthma and sensitization to *P. citri* among children living around citrus orchards.

Methods: A total of 1,055 children living around citrus orchards were enrolled. There were 544 boys and 511 girls with a mean age of 12.3 (range 7 to 16) years. They were evaluated by the ISAAC questionnaire, and a skin prick test with 13 common aeroallergens including *P. citri* and Japanese cedar pollen. Children who recorded ever having experienced wheezing on the questionnaire were evaluated by methacholine bronchial provocation test and determined to have asthma if they showed bronchial hyperresponsiveness to methacholine simultaneously.

Results: The positive skin test response to one or more inhalant allergens except *P. citri* was 35.5%, but when including *P. citri*, the positive response increased to 37.7%. The most common sensitizing allergens in the order of decreasing frequency were *Dermatophagoides pteronyssinus* (26.6%), *D. farinae* (22.7%), *P. citri* (14.2%), cockroach (11.3%), and Japanese cedar pollen (9.7%). Among the children without sensitization to house dust mites, the sensitization rate to *P. citri* was significantly higher in those 13 and over than in those under 12 (5.8% versus 2.5%, $P < .05$). The prevalence of asthma was not different between the children with sensitization to *P. citri* and those without it (5.4% versus 4.0%, $P > .05$), although the prevalence was higher in those with sensitization to *D. pteronyssinus* or *D. farinae* than in those without sensitization to these allergens (7.9% versus 2.9%, $P < .05$; 9.7% versus 2.6%, $P < .05$).

Conclusion: Citrus red mite is a common sensitizing allergen among children living around citrus orchards. The features of sensitization and development of asthma are different between citrus red mite and house dust mites.

Ann Allergy Asthma Immunol 2000;85:200–204.

INTRODUCTION

The mite is a pest of citrus trees throughout the world, especially in

subtropical areas.¹ In particular, the spider mites (Family *Tetranychidae*) are broadly distributed, with the citrus red mite (*Panonychus citri*, CRM) being the most common species infesting citrus leaves.¹ This mite rapidly proliferates into injurious populations in late spring and mid-fall, damaging leaves and sometimes causing defoliation. House dust mites are known to be a major cause of respiratory allergy in subtropical areas and in Korea.² A recent survey revealed that CRM was the most common sensitizing allergen in

citrus-cultivating farmers with asthma and/or allergic rhinitis in Korea.³

In this study, a cross-sectional survey was performed to evaluate the sensitization to aeroallergens including CRM and Japanese cedar pollen among children living around the citrus-cultivating areas.

SUBJECTS AND METHODS

Subjects

A total of 1,055 children living around citrus orchards were enrolled in this study. According to age and sex, they consisted of 387 children under 12 years old (younger children) with a mean age of 9.5 (range 7 to 12) years and 668 children 13 years old and over (older children) with a mean age of 13.9 (range 13 to 16) years, and 544 boys and 511 girls. All the subjects responded to a questionnaire, and skin prick test to 13 aeroallergens including CRM and Japanese cedar pollen was performed on 1,037 subjects. Methacholine bronchial provocation test was performed on subjects who recorded ever having a wheeze on the questionnaire. Prevalence of asthmatic symptoms and asthma according to age and sex is shown in Table 1. The prevalence of asthmatic symptoms such as wheeze, wheeze during the last 12 months, wheeze during or after exercise, and nocturnal cough on the questionnaire was 8.3%, 6.0%, 5.3%, and 7.6%, respectively. The prevalence of asthma based on the questionnaire and methacholine bronchial provocation test was 4.2%. According to age, the prevalence of asthma was 4.7% among the younger children, and 3.9% among the older children. According to sex,

* Department of Pediatrics, Cheju University College of Medicine, Cheju; † Department of Internal Medicine, Seoul National University College of Medicine; ‡ Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul; § Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea.

Received for publication August 5, 1999.

Accepted for publication in revised form December 4, 1999.

Table 1. Prevalence of Asthma and Positive Skin Responses to Common Sensitizing Allergens in Study Subjects

	7–12 years	13–16 years	Total
Prevalence of asthma	(n = 387)	(n = 668)	(n = 1,055)
Asthma†	18 (4.7)	26 (3.9)	44 (4.2)
Wheeze ever	42 (10.9)*	46 (6.9)	88 (8.3)
Recent wheeze	27 (7.0)	36 (5.4)	63 (6.0)
Wheeze at exercise	27 (7.0)	29 (4.3)	56 (5.3)
Nocturnal cough	59 (15.2)*	21 (3.1)	80 (7.6)
Skin responses	(n = 378)	(n = 659)	(n = 1,037)
<i>D. pteronyssinus</i>	98 (25.9)	178 (27.0)	276 (26.6)
<i>D. farinae</i>	81 (21.4)	154 (23.4)	235 (22.7)
Citrus red mite	43 (11.4)	104 (15.8)	147 (14.2)
Cockroach	36 (9.5)	81 (12.3)	117 (11.3)
Japanese cedar pollen	33 (8.7)	68 (10.3)	101 (9.7)
Cat fur	8 (2.1)	17 (2.6)	25 (2.4)
SPT (+CRM)‡	133 (35.2)	258 (39.2)	391 (37.7)
SPT (–CRM)§	128 (33.9)	240 (36.4)	368 (35.5)

Data are expressed as number of candidates (%).

* $P < .05$ compared with that of the older children (over 13 years old).

† Wheeze ever on a questionnaire and bronchial hyperresponsiveness to methacholine.

‡ Positive skin-test responses (allergen/histamine ratio ≥ 1.0) to one or more inhalant allergens including citrus red mite.

§ Positive skin-test responses (allergen/histamine ratio ≥ 1.0) to one or more inhalant allergens excluding citrus red mite.

the prevalence was 4.8% in boys, and 3.5% in girls. The parents gave written informed consent for the study, and the children agreed to participate with parental consent. The study protocol was approved by the Ethics Committee of Seoul National University Hospital.

Methods

A questionnaire developed by the International Study of Asthma and Allergic diseases in Children (ISAAC)⁴ was translated into Korean and included demographic data, and medical history such as asthma symptoms (wheeze ever, wheeze during the last 12 months, wheeze during or after exercise, and repeated cough). If the subject had ever experienced wheezing on the questionnaire, methacholine bronchial challenge was performed to diagnose asthma.

Citrus red mite was obtained from the Entomology unit of Cheju Citrus Research Institute. Citrus red mites were extracted as previously described.³ In brief, the mites were mixed with modified Cocos solution with a 1:5 wt/vol ratio. After incubation at room temperature for 24 hours, it was centrifuged at 3,000 g for 30 minutes.

The supernatant was dialyzed in phosphate buffered saline at 4°C for 48 hours, and then passed through a 0.45- μ m pore for sterilization and then lyophilized. Same amount of glycerin was added with final concentration of 1:40 wt/vol, and it was used for skin prick tests. Japanese cedar pollen was collected during pollination season and prepared following the above method with a concentration of 1:40 wt/vol.

A total of 1,037 subjects underwent skin testing by the prick method using a panel of 11 common available aeroallergens (Allergopharma Co., Germany), Japanese cedar pollen and CRM. None of the subjects had received antihistamines orally for 3 days preceding the study. The panel included house dust mites (*Dermatophagoides pteronyssinus*, *D. farinae*), cat fur, molds (*Aspergillus fumigatus*, *Alternaria alternata*), pollens (tree pollen mixture 1 [alder, hazel, poplar, elm, and willow tree] and 2 [birch, beech, oak, and plane tree], grass pollen mixture [velvet grass, orchard grass, rye grass, timothy grass, Kentucky blue grass, and meadow grass], mugwort, and ragweed), and

cockroach (*Blattella germanica*). A positive control of histamine (1 mg/mL) along with a negative diluent control was included in all tests. After 15 minutes of the prick, mean diameter of a wheal formed by the allergen was compared with that formed by histamine. If the former was the same or larger than the latter (allergen/histamine ratio ≥ 1.0), the reaction was defined as positive.

Forced expiratory volume in 1 second (FEV₁) was measured with a portable spirometer (Micro Spirometer, Micro Medical, Rochester, Kent, UK), and the largest value of triplicate FEV₁ was adopted. Methacholine challenge was carried out using the modified method described by Chai et al.⁵ Subjects with recent viral upper respiratory infections were excluded in the methacholine challenge. None of the subjects had received bronchodilators or antihistamines for 3 days preceding the challenge. Concentrations of 1.25, 2.5, 6.25, 12.5, and 25 mg/mL of methacholine were prepared by dilution with buffered saline. A Rosenthal-French dosimeter (Laboratory for Applied Immunology, Baltimore, MD, USA) was used to deliver the aerosol generated by a nebulizer (DeVilbiss, USA). Subjects with “wheeze ever” on the questionnaire inhaled five inspiratory capacity breaths of increasing concentrations of methacholine until FEV₁ fell by more than 20% of its baseline value or the highest concentration was reached. All of the subjects had baseline FEV₁ of higher than 70% of the value predicted for the reference group. The largest value of triplicate FEV₁ at 90 or 180 seconds after each inhalation was adopted for analysis. If the concentration of methacholine which caused a 20% fall in FEV₁ (PC₂₀) was less than 12 mg/mL, a subject was considered to have bronchial hyperresponsiveness to methacholine. Asthma was diagnosed if a subject had a wheeze ever on the questionnaire and bronchial hyperresponsiveness to methacholine.

Statistical Analysis

Positive rates between the two groups were analyzed using the chi-squared

test. A *P* value of .05 or less was regarded as significant.

RESULTS

Skin-Test Response to Aeroallergens Including Citrus Red Mite and Japanese Cedar Pollen

Skin-test response to aeroallergens including CRM and Japanese cedar pollen is shown in Table 1. The positive skin-test response to aeroallergens including CRM was 37.7%. The positive rate was not different between younger and older children (35.2% versus 39.2%, *P* > .05), and between boys and girls (40.0% versus 35.2%, *P* > .05). When the data for younger and older children were analyzed separately, the positive rate was not different between boys and girls (36.4% versus 33.9%, *P* > .05; 42.2% versus 36.0%, *P* > .05), although the positive rate showed a higher tendency among the males in the older group. The positive skin-test response to aeroallergens except CRM was 35.5%. The positive rate was not different between younger and older children (33.9% versus 36.4%, *P* > .05), and between males and the females (38.5% versus 32.3%, *P* > .05). When the data for younger and older children were analyzed separately, the positive skin response showed a similar trend compared with that to aeroallergens including CRM.

According to the results of the skin-prick test, the most common sensitizing allergens in decreasing order were

D. pteronyssinus (DP, 26.6%), *D. farinae* (DF, 22.7%), CRM (14.2%), cockroach (11.3%), and Japanese Cedar pollen (9.7%). As for *D. pteronyssinus*, *D. farinae*, and CRM, the positive skin-test response was not different between younger and older children (25.9% versus 27.0%, *P* > .05; 21.4% versus 23.4%, *P* > .05; 11.4% versus 15.8%, *P* > .05) or between boys and girls (27.4% versus 25.7%, *P* > .05; 25.8% versus 19.4%, *P* > .05; 15.2% versus 13.1%, *P* > .05). As for skin responses to cockroach, and Japanese cedar pollen there were also no differences according to age and sex (*P* > .05, respectively). In children without sensitization to house dust mites, however, the positive skin-test response to CRM was higher among the older children than among the younger ones (5.8% versus 2.5%, *P* < .05), although, in children without sensitization to CRM, the positive skin response to HDM was not different between the two groups (17.6% versus 17.0%, *P* > .05).

Relationship Between Sensitization to Citrus Red Mite, and Prevalence of Asthma and Sensitization to Other Common Inhalant Allergens

In forty-four children diagnosed with bronchial asthma, positive skin-test response to aeroallergens was 68.2% (30/44), while it was 59.1% (26/44) when CRM was excluded. The most common sensitizing allergens in decreasing order were *D. farinae*

(52.2%), *D. pteronyssinus* (50.0%), CRM (20.4%), Japanese cedar pollen (20.4%), and cockroach (11.3%).

Table 2 shows the prevalence of asthma and wheeze ever, and the sensitization rate to common inhalant allergens according to sensitization to CRM. The prevalence of asthma and wheeze ever on the questionnaire was not different between children with and without sensitization to CRM (5.4% versus 3.9%, *P* > .05; 6.8% versus 8.7%, *P* > .05), although the prevalence of asthma was higher among those sensitized to *D. pteronyssinus* or *D. farinae* than among those without sensitization to these allergens (7.9% versus 2.8%, *P* < .05; 9.7% versus 2.6%, *P* < .05). When the data for younger and older children were analyzed separately, a similar trend was observed in both younger and older children. The positive skin-test responses to *D. pteronyssinus*, *D. farinae*, Japanese cedar pollen, and cockroach were higher among those sensitized to CRM than among those without sensitization (72.1% versus 19.1%, *P* < .001; 67.3% versus 15.3%, *P* < .001; 36.7% versus 7.1%, *P* < .001; 26.5% versus 6.7%, *P* < .001, respectively). The positive skin response to one or more of the 12 inhalant allergens also showed a similar trend according to sensitization to CRM (81.6% versus 24.3%, *P* < .001).

DISCUSSION

Many epidemiologic surveys of asthma have gathered and reported only subjective data.⁶⁻⁹ Even though this method can be performed in a large population at low cost, limitations such as lack of specificity in diagnosing asthma cannot be avoided.^{6,10} In our previous study,^{2,3} only 20.6% of children and 40% of adults who complained of asthmatic symptoms on the questionnaire were shown to have bronchial hyperresponsiveness to methacholine. In this study, diagnosis of asthma was based on a wheeze ever on the questionnaire and bronchial hyperresponsiveness to methacholine. Among the younger children, the prevalence of

Table 2. Prevalence of Asthma and Skin-Test Response to Common Inhalant Allergens According to Sensitization to Citrus Red Mite

	Skin Reactivity to CRM*		<i>P</i>
	Positive (n = 147)	Negative (n = 990)	
Wheeze ever	10 (6.8)	77 (8.7)	>.05
Asthma	8 (5.4)	77 (4.0)	>.05
SPT (–CRM)†	120 (81.6)	216 (24.3)	.0001
<i>D. pteronyssinus</i>	106 (72.1)	170 (19.1)	.0001
<i>D. farinae</i>	99 (67.3)	136 (15.3)	.0001
Cockroach	54 (36.7)	63 (7.1)	.0001
Japanese cedar pollen	39 (26.5)	62 (6.7)	.0001

* Data are expressed as number of candidates (%).

† CRM: citrus red mite. Positive skin-test responses (allergen/histamine ratio ≥ 1.0) to one or more inhalant allergens except citrus red mite.

asthma was lower in Cheju island than in Seoul, the capital city of Korea, (4.7% versus 8.3%), although among the older children, there was no statistical difference between the two areas (3.9% versus 5.8%). This difference may be explained by the differences in environmental conditions, not in genetic susceptibility.

One of the main features of Cheju island is a volcano named Halla, which is over 6,400 feet in height and located in the southern part of the Korean peninsula. It is famous for its scenic wonder including warm climate and clean outdoor conditions. Furthermore the indoor environment is not so modernized as that of most cities in inland Korea. Citrus trees were introduced in the 1950s and have become the main crops of this island. Over half a million people dwell on the island, and about 50,000 adults have been cultivating citrus for about 40 years, rarely migrating to other places. Citrus red mite is one of the main pests of citrus trees. This mite rapidly develops to injurious levels of population density with two peaks in late spring (from May to June) and mid-fall (from October to November), and finally damages leaves and citrus fruits.¹

In our previous study,² the most common sensitizing allergens among children of inland Korea were *D. farinae* (30.9%), *D. pteronyssinus* (27.5%), cat fur (20.4%), and cockroach (11.8%). In this study, however, the most common sensitizing allergens among children were *D. pteronyssinus* (26.6%), *D. farinae* (22.6%), CRM (14.1%), cockroach (13.3%), and Japanese cedar pollen (10.3%). This finding suggests that environmental conditions determine the expression of allergen-specific IgE formation to aeroallergens. Features of modern-day housing such as the trend towards houses that are sealed against cold winters and as a result are poorly ventilated, have led to increased exposure to house dust mites and allergens shed by animals. Low indoor air-exchange rates have been associated with increased levels of cat allergen and house dust mites.^{11,12} Indoor and out-

door environments of Cheju island are very different from inland Korea since the housing patterns are not modernized, the outdoor air is not polluted, and there are many citrus farms with Japanese cedar trees protecting citrus trees from wind. These differences could explain the lower sensitization rate to indoor allergens such as house dust mites and cat fur, and higher sensitization rate to outdoor allergens, such as CRM and Japanese cedar pollen among children in Cheju island compared with those of Korean mainland.

Although sensitization to inhalant allergens requires exposure to only a small dose, it is possible that exposure to high levels may be associated with the greatest risk of sensitization. Sporik et al¹³ showed that exposure to house dust mites with high levels increased the risk of sensitization. In this study, house dust mites were the most common sensitizing allergens among children of Cheju island, and there was no difference in sensitization rate between younger and older groups. Meanwhile, CRM was also a common sensitizing allergen, and among children without sensitization to house dust mites, the sensitization rate to CRM was higher among the older ones. This finding implies that sensitization to house dust mites begins early and reaches the plateau level before the age of 7, while sensitization to CRM begins relatively later compared with house dust mites. This difference may be explained by the fact that house dust mites are a "perennial" indoor allergens to which children are exposed all day long and all year long, but CRM is an outdoor allergen to which children are exposed only when they go to the citrus farm area after the age of 4 or 5 years and CRM has two peaks of population growth in late spring and mid-fall, which makes it a "seasonal" allergen.

Exposure level to allergens may also determine the development of asthmatic symptoms. In subjects with continuous exposure to the causative allergen, the latent period is shorter than in those who are intermittently exposed.

Several investigators reported that exposure to house dust mites and animal-derived allergens with high levels was associated with early onset of asthmatic symptoms.¹⁴⁻¹⁶ In fact, in urban areas of inland Korea, the most common sensitizing allergens were house dust mites and cat fur in asthmatic children, and the prevalence of asthma was higher among younger children sensitized to these allergens than among those without sensitization.² This study also showed that the prevalence of asthma was higher among younger children sensitized to house dust mites than among those without sensitization. This study, however, revealed that there was no difference in the prevalence of asthma whether or not subjects were sensitized to CRM. This finding suggested that among children aged 7 to 16 years, the sensitization to house dust mites implied more possibilities of developing asthmatic symptoms compared with CRM. The long duration of the latent period in CRM-sensitive asthma was consistent with our previous results in which the latent period in CRM-induced occupational asthma in citrus farmers was 13.5 years.³ From these findings, we can speculate that children sensitized to house dust mites will show asthma at an early age, but those sensitized to CRM will not show asthma at an early age and they will become overt asthmatics beyond childhood.

Sensitization to high-molecular-weight allergens is known to occur at a higher rate among atopic individuals.^{17,18} There is also an agreement in the suggestion that the closer the taxonomic relationship between mites is, the greater the level of cross-allergenicity.¹⁹⁻²¹ Citrus red mite belongs to the order of mites (Acari), to the sub-order of Prostigmatia, to the family of spider mites (*Tetranychidae*) and represents its own species. Our previous study revealed that CRM-derived allergens contained species-specific allergens in addition to common sharing allergens with HDM.³ In this study, skin-test response to common aeroallergens, such as Japanese cedar pollen having no taxonomic relationship with

CRM, as well as house dust mites, was higher among the children sensitized to CRM than among those without sensitization. This finding suggests that genetic predisposition to specific IgE response to common inhalant allergens also determines the sensitization to CRM.

In conclusion, citrus red mite is a common sensitizing allergen in children living around citrus orchards. The features of sensitization and development of asthma are different between citrus red mite and house dust mites.

ACKNOWLEDGEMENT

We would like to thank Hyuk-Mo Kwon PhD and Dong-Hwan Kim PhD of Cheju Citrus Research Institute for their entomological advice and help in collecting CRM. This study was supported by a research grant (HMP-98-M-1-0001) from the Ministry of Health and Welfare, Korea.

REFERENCES

1. Davies FS, Albrigo LG. Mites. In: Davies FS, Albrigo LG, eds. Citrus. UK: CAB International, 1994:172-178.
2. Kim YY, Cho SH, Kim WK, et al. Prevalence of childhood asthma based on questionnaire and methacholine bronchial provocation test. Clin Exp Allergy 1997;27:761-768.
3. Kim YK, Son JW, Kim HY, et al. Citrus red mite is the most common sensitizing allergen in citrus farmers with asthma and rhinitis. Clin Exp Allergy 1999;29(8), in press.
4. Ferris BG. Epidemiology standardization project II. Recommended respiratory disease questionnaires for use with adults and children in epidemiological research. Am Rev Respir Dis 1978;118:10-35.
5. Chai H, Farr RS, Froehlich LA, et al. Standardization of bronchial inhalation challenge procedures. J Allergy Clin Immunol 1975;56:534-539.
6. Battemore PK, Asher MI, Harrison AC, et al. The interrelationship among bronchial hyperresponsiveness, the diagnosis of asthma and asthma symptoms. Am Rev Respir Dis 1990;142:549-554.
7. American Thoracic Society. Chronic bronchitis, asthma, and pulmonary emphysema. Am Rev Respir Dis 1987;136:224-225.
8. Dodge RR, Burrows B. The prevalence and incidence of asthma and asthma-like symptoms in a general population sample. Am Rev Respir Dis 1980;122:567-575.
9. Pearce N, Weiland S, Keil U, et al. Self-reported prevalence of asthma symptoms in children in Australia, England, Germany and New Zealand: an international comparison using the ISAAC protocol. Eur Respir J 1993;6:1455-1461.
10. Adelroth E, Hargreave FE, Ramsdale EH. Do physicians need objective measurement to diagnose asthma? Am Rev Respir Dis 1986;134:704-707.
11. Luczynska CM, Li Y, Chapman MD, et al. Airborne concentrations and particle size distribution of allergen derived from domestic cats (*Felis domesticus*): measurements using a cascade impactor, liquid impinger and a two-site monoclonal antibody for Fel d1. Am Rev Respir Dis 1990;141:361-367.
12. Harving H, Korsgaard J, Dahl R. House dust mite and associated environmental conditions in Danish homes. Allergy 1993;48:106-109.
13. Sporik R, Holgate ST, Platts-Mills TA, et al. Exposure to house dust mite allergen (Der p 1) and the development of asthma in childhood. A prospective study. New Engl J Med 1990;323:502-507.
14. Gergen PJ, Mullally DI, Evans III R. National survey of prevalence of asthma among children in the United States, 1976 to 1980. Pediatrics 1988;75:859-868.
15. Aberg N, Engstrom I. Natural history of allergic disease in children. Acta Paediatr Scand 1990;79:206-211.
16. Horwood LJ, Fergusson DM, Shannon FT. Social and familial factors in the development of early childhood asthma. Pediatrics 1985;75:859-868.
17. Platts-Mills TA, Longbottom J, Edwards J, et al. Occupational asthma and rhinitis related to laboratory rats: serum IgG and IgE antibodies to the rat urinary allergen. J Allergy Clin Immunol. 1987;79:505-515.
18. Slovak AJM, Hill RN. Laboratory animal allergy: a clinical survey of an exposed population. Brit J Industr Med 1981;38:38-41.
19. Platts-Mills TA, Heymann PW, Chapman MD, et al. Cross-reacting and species-specific determinants on a major allergen from *Dermatophagoides pteronyssinus* and *D. farinae*: development of a radioimmunoassay for antigen P1 equivalent in house dust mite extracts. J Allergy Clin Immunol 1986;78:398-407.
20. Arlian LG, Geis DP, Vyszynski-Moher DL, et al. Cross antigens and allergenic properties of the house-dust mite *Dermatophagoides farinae* and the storage mite *Tyrophagus putrescentiae*. J Allergy Clin Immunol 1984;74:172-179.
21. Griffin P, Ford AW, Alterman L, et al. Allergenic and antigenic relationships between three species of storage mite and the house dust mite, *Dermatophagoides pteronyssinus*. J Allergy Clin Immunol 1989;84:108-117.

Requests for reprints should be addressed to:
Yoon-Keun Kim, MD
Department of Internal Medicine
Seoul National University College of Medicine
28 Yongon-dong Chongno-gu
Seoul 110-744
Korea