

Differences in sensitization rates to outdoor aeroallergens, especially citrus red mite (*Panonychus citri*), between urban and rural children

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

Objective: A cross-sectional survey was performed to evaluate the prevalence of asthma and chronic rhinitis symptoms and sensitization to common indoor and outdoor aeroallergens, including CRM and Japanese cedar pollen, in rural and urban Korean children.

Methods: A total of 2,055 children (1,055 subjects living in rural areas with citrus farms and 1,000 controls in urban areas without citrus farms) were enrolled. They were evaluated by a questionnaire, and by skin prick tests with 13 common indoor and outdoor aeroallergens, including CRM and Japanese cedar pollen.

Results: The prevalence of wheezing and chronic rhinitis symptoms during the last 12 months was 8.3% and 35.7% in the rural children and 10.5% and 22.4% in the control group. The most common sensitizing allergens in order of decreasing frequency were *Dermatophagoides pteronyssinus* (26.6%), *Dermatophagoides farinae* (22.7%), CRM (14.2%), cockroach (11.3%), and Japanese cedar pollen (9.7%) among the rural children, but the sensitization rates to CRM and Japanese cedar pollen were 1.3% and 0.2% among the control children, respectively. The prevalence of wheeze during the last 12 months was not different between rural children with sensitization to CRM or Japanese cedar pollen and those without sensitization (5.4% vs 6.1%; 6.9% vs 5.9%). However, the prevalence of chronic rhinitis during the last 12 months was higher among those with sensitization to CRM or to Japanese cedar pollen than among those without sensitization (40.8% vs 34.4%; 51.5% vs 33.5%).

Conclusions: CRM is a common sensitizing allergen in rural children, and the sensitization rates to outdoor aeroallergens, especially CRM and Japanese cedar pollen, are very different between children from rural and urban areas in Korea.

Ann Allergy Asthma Immunol 2001;86:691–695.

INTRODUCTION

Allergic diseases attributable to indoor allergens derived from house dust

mites and pets are a major health problem worldwide. House dust mites are

the most important sources of allergens inside homes in humid areas.¹ Positive skin test responses to individual inhalant allergens have a wide range of regional differences, and our previous study² demonstrated that the most common allergens were *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* among Korean children. Although the allergen-specific IgE response requires exposure to only a small quantity, exposure to high levels of allergen may be associated with a higher risk of sensitization.

Spider mites (family Tetranychidae) form the family of phytophagous mites and have the severest economic effect on agriculture. Several of these mites are injurious to many crops all over the world.³ The citrus red mite (*Panonychus citri*, CRM) is a spider mite that damages citrus leaves throughout the world, especially subtropical areas.⁴ This mite rapidly proliferates into injurious numbers in late spring and mid-fall, damaging leaves and sometimes causing defoliation. A recent survey revealed that CRM was the most common sensitizing allergen in citrus-cultivating farmers with asthma and/or allergic rhinitis in Korea.⁵

We used a cross-sectional survey to evaluate the prevalence of asthma and chronic rhinitis symptoms and the sensitization rates to indoor and outdoor aeroallergens, including CRM and Japanese cedar pollen, among children living near the citrus-cultivating areas and in urban areas without citrus farms in Korea.

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This study was supported by a research grant (HMP-98-M-1-0001) from the Ministry of Health and Welfare, Korea.

Received for publication January 31, 1999.

Accepted for publication in revised form September 20, 2000.

SUBJECTS AND METHODS

Study Subjects

A total of 2,055 children 7 to 16 years old (1,055 children living in rural areas with citrus farms and 1,000 children living in urban areas without citrus farms) were enrolled in this study. All participants responded to a questionnaire, and skin prick tests to 13 aeroallergens including CRM and Japanese cedar pollen were performed on 2,037 children. 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 Childhood (ISAAC)⁶ was used. It included demographic data and medical history such as symptoms for asthma and chronic rhinitis. The asthma symptom questions concentrated on wheezing episodes (ever experiencing wheezing and wheeze during the last 12 months), exercise-induced wheeze, and recurrent nocturnal cough. The chronic rhinitis symptoms concentrated on recurrent sneezing or nasal obstruction without upper respiratory infections (ever experiencing chronic rhinitis symptoms and chronic rhinitis symptoms during the last 12 months).

CRM was obtained from the Entomology Unit of Cheju Citrus Research Institute. The CRM extract was prepared by mixing the whole body of

CRM with modified Coca's solution in a 1:20 wt/vol ratio as previously described.⁵ After incubation at room temperature for 24 hours, the extract was centrifuged at 3,000 *g* for 30 minutes. The supernatant was dialyzed in phosphate-buffered saline (PBS) at 4° C for 48 hours, passed through a 0.45- μ m pore for sterilization, and then lyophilized. An equal volume of glycerin and PBS was added with a final concentration of 1:40 wt/vol compared with mass of lyophilized powder, and it was used for the skin prick test. Japanese cedar pollen was collected during the pollination season, and an extract was prepared following the above method with a final concentration of 1:40 wt/vol.

Skin tests by the prick method were performed using a panel of 11 aeroallergens (Allergopharma Co., Reinbek, Germany), Japanese cedar pollen, and CRM. None of the children had received antihistamines orally for 3 days preceding the study. The indoor aeroallergen panel included house dust mites (*D. pteronyssinus*, *D. farinae*), cat fur, indoor mold (*Aspergillus fumigatus*), and cockroach (*Blattella germanica*). The outdoor allergen panel included outdoor mold (*Alternaria alternata*), tree pollen mixture 1 (alder, hazel, poplar, elm, and willow tree), tree pollen mixture 2 (birch, beech, oak, and plane tree), grass pollen mixture (velvet, orchard, rye, timothy, Kentucky blue, and meadow grasses), mugwort pollen, and ragweed pollen. A positive control of histamine (1 mg/mL) and a negative diluent control were included in all tests.

Fifteen minutes after the prick test, the mean diameter of the wheal formed by an allergen was compared with that formed by histamine. If the former was the same as or larger than the latter (allergen/histamine ratio >1.0), the reaction was defined as positive.

Statistical Analysis

The StatView program (Abacus, Berkeley, CA) was used for statistical analysis. The statistical significance was evaluated by calculating the 95% confidence interval (CI) using normal approximation.

RESULTS

Prevalence of Asthma and Chronic Rhinitis Symptoms

Table 1 shows the prevalence of asthma and chronic rhinitis symptoms on the questionnaire in the study subjects. The positive responses to ever experiencing wheezing, wheeze during the last 12 months, wheeze during or after exercise, and recurrent nocturnal cough without respiratory tract infections among those in rural areas with citrus farms were significantly lower than the response from children living in urban areas without citrus farms. In contrast, the positive responses to ever experiencing chronic rhinitis symptoms and the rhinitis symptoms during the last 12 months among the rural children were significantly higher than the number of positive responses from the urban controls.

Skin Test Response to Aeroallergens Including CRM and Japanese Cedar Pollen

Table 2 summarizes the prick test responses to indoor and outdoor aeroallergens, including CRM and Japanese cedar pollen. The prevalence of positive skin test responses to all aeroallergens including CRM was not different between the rural children and the urban controls. Likewise, the prevalence of positive responses to all aeroallergens except CRM was not different between the two groups. The most common sensitizing allergens among the rural children in decreasing order were *D. pteronyssinus* (26.6%), *D.*

Table 1. Prevalence of Asthma and Chronic Rhinitis Symptoms

	Rural children (n = 1,055)	Urban children	
		(n = 1,000)	95% CI*
Asthma symptoms			
Ever experiencing wheezing	88 (8.3)	139 (13.9)	11.9–16.2
Wheeze in last 12 months	63 (6.0)	105 (10.5)	8.8–12.6
Wheeze at exercise	56 (5.3)	152 (15.2)	13.1–17.6
Nocturnal cough	80 (7.6)	135 (13.5)	11.5–15.6
Chronic rhinitis symptoms†			
Ever experiencing rhinitis	429 (40.7)	346 (34.6)	31.7–37.6
Rhinitis in last 12 months	377 (35.7)	244 (22.4)	21.6–27.1

Data are expressed as numbers of positive responses to questionnaire (%).

* Calculated using normal approximation.

† Recurrent sneezing or nasal obstruction without upper respiratory tract infections.

Table 2. Skin Test Responses to Indoor and Outdoor Allergens

	Rural children (n = 1,037)	Urban children	
		(n = 1,000)	95% CI*
SPT (+CRM)†	391 (37.7)	362 (36.2)	33.9–39.2
SPT (–CRM)‡	368 (35.5)	362 (36.2)	33.9–39.2
Indoor allergens			
<i>D. pteronyssinus</i>	276 (26.6)	268 (26.8)	24.1–29.6
<i>D. farinae</i>	235 (22.7)	251 (25.1)	22.5–27.9
Cockroach	117 (11.3)	95 (9.5)	7.8–11.5
Cat fur	25 (2.4)	16 (1.6)	1.0–2.6
<i>Aspergillus</i>	4 (0.4)	8 (0.8)	0.4–1.6
Outdoor allergens			
Citrus red mite	147 (14.2)	13 (1.3)	0.8–2.2
Japanese cedar pollen	101 (9.7)	2 (0.2)	0.05–0.7
Tree pollen 1	4 (0.4)	38 (3.8)	2.8–5.2
Tree pollen 2	6 (0.6)	46 (4.6)	3.5–6.1
Grass pollen	11 (1.1)	10 (1.0)	0.5–1.8
Mugwort pollen	18 (1.7)	46 (4.6)	3.5–6.1
Ragweed pollen	9 (0.9)	40 (4.0)	3.0–5.4
<i>Alternaria</i>	18 (1.7)	17 (1.7)	1.1–2.7

Data are expressed as numbers of positive responses (%).

* Calculated using normal approximation.

† Positive skin-test response (allergen/histamine ratio >1.0) to one or more inhalant allergens including CRM.

‡ Positive skin-test response (allergen/histamine ratio >1.0) to one or more inhalant allergens excluding CRM.

farinae (22.7%), CRM (14.2%), cockroach (11.3%), and Japanese cedar pollen (9.7%). Among the urban children, the most common sensitizing allergens in decreasing order were *D. pteronyssinus* (26.8%), *D. farinae* (25.1%), cockroach (9.5%), mugwort (4.6%), tree pollen mixture 2 (4.6%), ragweed pollen (4.0%), and tree pollen mixture 1 (3.8%). The urban children showed significantly lower skin test-positive responses to CRM (1.3%) and Japanese cedar pollen (0.2%) than did the rural children, whose responses were 14.2% for CRM and 9.7% for Japanese cedar pollen.

Table 3 shows positive skin test responses to common sensitizing allergens in the rural children according to age. The positive skin responses to one or more allergens including CRM were significantly higher among those aged 13 to 16 years than those aged 7 to 12 years. For individual allergens, the positive responses to indoor allergens such as *D. pteronyssinus*, *D. farinae*, and cat fur were not different between

the younger and the older children. For individual outdoor allergens, the positive skin responses to Japanese cedar pollen were not different between the younger and the older children. However, the positive responses to CRM were significantly higher among the older children compared with younger ones.

Table 3. Skin Test Responses to Common Sensitizing Allergens in Rural Children According to Age

	7–12 years (n = 378)	13–16 years	
		(n = 659)	95% CI*
SPT (+CRM)†	133 (35.2)	258 (39.2)	35.5–42.9
SPT (–CRM)‡	128 (33.9)	117 (36.0)	32.8–40.2
<i>D. pteronyssinus</i>	98 (25.9)	178 (27.0)	23.7–30.5
<i>D. farinae</i>	81 (21.4)	154 (23.4)	20.3–26.7
CRM	43 (11.4)	104 (15.8)	13.2–18.8
Cockroach	36 (9.5)	81 (12.3)	10.0–15.0
Japanese cedar pollen	33 (8.7)	68 (10.3)	8.2–12.9
Cat fur	8 (2.1)	17 (2.6)	1.6–4.1

Data are expressed as numbers of positive responses (%).

* Calculated using normal approximation.

† Positive skin-test response (allergen/histamine ratio >1.0) to one or more inhalant allergens including CRM.

‡ Positive skin-test response (allergen/histamine ratio >1.0) to one or more inhalant allergens excluding CRM.

Relationship between Sensitization to CRM and Prevalence of Asthma and Rhinitis Symptoms and Sensitization to Other Common Aeroallergens

Table 4 shows the prevalence of asthma and chronic rhinitis symptoms and the sensitization rates to common aeroallergens in the rural children according to sensitization to CRM. The positive responses to wheeze during the last 12 months on the questionnaire were not different between those with and without sensitization to CRM. However, the positive responses to chronic rhinitis symptoms during the last 12 months were significantly higher among those with sensitization to CRM than among those without sensitization. The positive skin responses to *D. pteronyssinus*, *D. farinae*, Japanese cedar pollen, and cockroach were significantly higher among those children also sensitized to CRM than for those who were not sensitized.

Table 5 shows the prevalence of asthma and chronic rhinitis symptoms in the rural children according to their sensitization to Japanese cedar pollen. The positive responses to wheeze during the last 12 months on the questionnaire were not different between those children with and without sensitization to Japanese cedar pollen. However, the positive responses to chronic rhinitis symptoms during the last 12 months were significantly higher among those

with sensitization to Japanese cedar pollen than among those without sensitization.

DISCUSSION

Our results showed that CRM and Japanese cedar pollen are common sensitizing allergens among children living in rural areas with citrus farms, but the sensitization rates to these allergens were very rare among children living in urban areas without citrus farms. Among the rural children, sensitization to CRM or Japanese cedar pollen was significantly correlated with the prevalence of chronic rhinitis symptoms, but not with asthma symptoms.

There are conflicting reports about the differences between the prevalence of asthma in urban and rural areas. Gergen et al⁷ reported a higher prevalence rate of asthma in urban areas compared with rural areas, but Burrows et al⁸ reported no regional differences. Our study showed that the prevalence of asthma symptoms was lower among the rural children than among the urban ones, but positive skin responses to one or more allergens including CRM and Japanese cedar pollen were not different between the urban and rural children. Thus, other risk factors such as exposure to indoor and outdoor air pollutants as well as atopy may be important in the development of asthma symptoms.

Two main environmental characteristics of Cheju Island, where the rural children had been living, are the clean outdoor air quality and the citrus farms. On this island, Japanese cedar trees protect citrus trees from strong wind, and Japanese cedar pollinosis was one of the main allergic diseases in early spring among the residents.⁵ Citrus trees were introduced almost 50 years ago and citrus products have become the main crops of this island. CRM is one of the main pests of citrus trees. This mite rapidly develops to injurious levels of population density with two peaks, one in late spring (from May to June) and the other in midfall (from October to November), and damages leaves and citrus fruits.⁴

Table 4. Prevalence of Asthma and Rhinitis Symptoms and Skin Test Responses to Common Aeroallergens According to Sensitization to Citrus Red Mite in Rural Children

	Skin reactivity to CRM		
	Positive (n = 147)	Negative (n = 890)	95% CI*
Ever experiencing wheezing	10 (6.8)	77 (8.7)	7.0–10.7
Wheeze in last 12 months	8 (5.4)	54 (6.1)	4.7–7.8
Ever experiencing rhinitis	70 (47.6)	348 (39.1)	35.9–42.3
Rhinitis in last 12 months	60 (40.8)	306 (34.4)	31.3–37.6
SPT (–CRM)†	120 (81.6)	216 (24.3)	21.6–27.2
<i>D. pteronyssinus</i>	106 (72.1)	170 (19.1)	16.8–21.7
<i>D. farinae</i>	99 (67.3)	136 (15.3)	13.1–17.8
Cockroach	54 (36.7)	63 (7.1)	5.6–9.0
Japanese cedar pollen	39 (26.5)	62 (6.7)	5.5–8.8

Data are expressed as numbers of responses (%).

* Calculated using normal approximation.

† Positive skin-test response (allergen/histamine ratio >1.0) to one or more aeroallergens except CRM.

Table 5. Prevalence of Asthma and Rhinitis Symptoms According to Sensitization to Japanese Cedar Pollen in Rural Children

	Skin reactivity to Japanese cedar pollen		
	Positive (n = 101)	Negative (n = 936)	95% CI*
Ever experiencing wheezing	14 (13.9)	78 (7.8)	6.7–10.3
Wheeze in last 12 months	7 (6.9)	55 (5.9)	4.5–7.6
Ever experiencing rhinitis	58 (57.4)	360 (38.5)	35.4–41.6
Rhinitis in last 12 months	52 (51.5)	314 (33.5)	30.6–36.6

Data are expressed as numbers of responses (%).

* Calculated using normal approximation.

Allergens are ubiquitous but are present in different concentrations in different environments. Features of modern-day housing, such as the trend toward 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.^{9,10} In this study, the most common sensitizing allergens among the children living in the rural areas with citrus farms were *D. pteronyssinus* (26.6%), *D. farinae* (22.6%), CRM (14.1%), cockroach (13.3%), and Japanese cedar pollen (10.3%), but sensitization rates to outdoor pollens (except Japanese cedar pollen) were very low. In contrast, the sensitization rates to tree pollens (except Japanese cedar pollen and weed pollens) were higher among the urban children compared with the rural ones. Further, the

sensitization rate to CRM was very low among the urban children. These findings suggest that environmental conditions determine the expression of allergen-specific IgE responses to aeroallergens.

Although sensitization to aeroallergens requires exposure to only a small quantity, it is possible that exposure to high levels may be associated with the greatest risk of sensitization. Sporik et al¹¹ showed that exposure to high levels of house dust mites increased the risk of sensitization. In this study, house dust mites were the most common sensitizing allergen among the rural children, but there was no difference in the sensitization rate between younger and older children. CRM was also a common sensitizing allergen, and the sensitization rate to CRM was higher among the older children. These findings imply that sensitization to

house dust mites begins early and reaches the plateau level at a younger age compared with sensitization to CRM. This difference may be explained by the fact that house dust mites are a perennial indoor allergen to which children are exposed all day and year-round. In contrast, CRM has two peaks of population growth in late spring and midfall, and 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.

Several studies within countries have investigated urban-rural differences in the prevalence of allergic rhinitis. These are potentially confounded by demographic differences, diagnostic practices, and the possibility that allergic individuals may selectively migrate between urban and rural areas for reasons that may or may not be connected with their allergy. Among 7,000 Swedish twin pairs, the lifetime prevalence of reported hay fever was 16% in cities, 14% in rural areas, and 20% in intermediate areas.¹² In Denmark, 19% of Copenhagen residents consulted physicians for their hay fever compared with 6% and 11% in the rural areas of Fyn and Jylland, respectively.¹³ In Michigan, a community study of all ages found a prevalence of probable allergic rhinitis three times higher in city residents (73% to 79%) compared with the surrounding rural areas (24% to 27%).¹⁴ However, this study showed that the prevalence of self-reported chronic rhinitis was significantly higher among the rural children compared with the urban ones. This may in part be explained by our finding that sensitization rates to outdoor allergens, such as CRM and Japanese cedar pollen, were significantly higher among the rural children compared with the urban ones, although the sensitization rates to indoor allergens, such as house dust mites, were not different between the two groups.

In addition, the rural children who were sensitized to CRM or Japanese cedar pollen reported chronic rhinitis symptoms during the last 12 months more often than did those without sensitization.

CONCLUSION

CRM is a common sensitizing allergen among children exposed to this mite. The sensitization rates to outdoor aeroallergens, especially CRM and Japanese cedar pollen, depend on the location, whether rural or urban, in Korea.

ACKNOWLEDGMENTS

We would like to thank Hyuk-Mo Kwon, PhD and Dong-Hwan Kim, PhD in Cheju Citrus Research Institute for their help in collecting CRM, and Jong-Myon Bae, MD in the Department of Preventive Medicine, Cheju University College of Medicine, for his advice about statistical analysis.

REFERENCES

1. Spiekma FTM. Domestic mites: their role in respiratory allergy. *Clin Exp Allergy* 1991;21:655-660.
2. Kim YY, Cho SH, Min KU, et al. Prevalence of childhood asthma based on questionnaires and methacholine bronchial provocation test in Korea. *Clin Exp Allergy* 1997;27:761-768.
3. Bolland HR, Gutierrez J, Flechtman CHW. Key to the genera of the world. In: Bolland HR, Gutierrez J, Flechtman CHW, eds. *World Catalogue of the Spider Mite Family (Acari: Tetranychidae)*. Leiden, The Netherlands: Brill Academic Publishers, 1998:5-11.
4. Davies FS, Albrigo LG. Mites. In: Davies FS, Albrigo LG., eds. *Citrus*. Oxon, UK: CAB International, 1994: 172-178.
5. Kim YK, Son JW, Kim HY, et al. Citrus red mite (*Panonychus citri*) is the most common sensitizing allergen of asthma and rhinitis in citrus farmers. *Clin Exp Allergy* 1999;29:1102-1109.
6. 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.

7. Gergen PJ, Mullally DI, Evans RE. National survey of prevalence of asthma among children in United States, 1976 to 1980. *Pediatrics* 1988; 81:1-7.
8. Burrows B, Lebowitz MD, Barbee RA. Respiratory disorders and allergy skin-test reactions. *Ann Intern Med* 1976; 84:134-139.
9. Harving H, Korsgaard J, Dahl R. House-dust mites and associated environmental conditions in Danish homes. *Allergy* 1993;48:106-109.
10. Luczynska CM, Li Y, Chapman MD, et al. Airborne concentrations and particle size distribution of allergen derived from domestic cats (*Felis domesticus*). Measurements using cascade impactor, liquid impinger, and a two-site monoclonal antibody assay for Fel d I. *Am Rev Respir Dis* 1990;141: 361-367.
11. Sporik R, Holgate S, Platts-Mills T, et al. Exposure to house-dust mite allergen (Der p I) and the development of asthma in childhood. A prospective study. *N Engl J Med* 1990;323: 502-507.
12. Edfors-Lubs ML. Allergy in 7000 twin pairs. *Acta Allergol* 1971;26:249-285.
13. Pedersen PA, Weeke ER. Allergic rhinitis in Danish general practice. Prevalence and consultation rates. *Allergy* 1981;36:375-379.
14. Broder I, Higgins MW, Mathews KP, Keller JB. Epidemiology of asthma, and allergic rhinitis in a total community, Tecumseh, Michigan. 3. Second survey of the community. *J Allergy Clin Immunol* 1974;53:127-138.

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