

Spider mite allergy in apple-cultivating farmers: European red mite (*Panonychus ulmi*) and two-spotted spider mite (*Tetranychus urticae*) may be important allergens in the development of work-related asthma and rhinitis symptoms

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Background: Recent investigations have suggested that the citrus red mite (*Panonychus citri*) is the most important allergen affecting citrus-cultivating farmers with asthma, allergic rhinitis, or both.

Objective: We sought to evaluate type I hypersensitivity to spider mites, particularly the European red mite (*Panonychus ulmi*) and the two-spotted spider mite (*Tetranychus urticae*), and to determine the relationship between hypersensitivity to spider mites and respiratory dysfunction.

Methods: We performed a cross-sectional survey. Questionnaires were given, and skin prick tests for 11 inhalant allergens common in Korea and 2 species of spider mites (European red mite and two-spotted spider mite) were performed in 725 apple-cultivating farmers in Korea.

Results: Results of skin prick tests in the apple farmers indicated that European red mite (23.2%) was the most common sensitizing allergen, followed by *Tyrophagus putrescentiae* (21.2%), two-spotted spider mite (16.6%), *Dermatophagoides farinae* (16.3%), *D pteronyssinus* (14.4%), cockroach (13.1%), and Hop Japanese (*Humulus Japonicus*) pollen (12.0%). Positive skin responses (mean wheal size ≥ 3 mm) to one or more of 13 inhalant allergens were found in 48.2% of farmers tested, whereas 40 subjects (8.6%) had an isolated skin response to the spider mites. Among 119 farmers with work-related asthmatic symptoms, the positive skin response rates to European red mite and two-spotted spider mite were 40.4% and 27.0%,

respectively. These figures were significantly higher than those found among farmers without work-related symptoms (19.1% and 14.1%, respectively; $P < .01$). The prevalence of work-related asthma symptoms was higher in farmers with positive skin responses to spider mites than in those with negative skin responses to spider mites and those with positive skin responses to any allergen tested (31.4% vs 15.0% vs 21.0%, respectively; $P < .05$).

Conclusion: Spider mites, particularly European red mite and 2-spotted spider mite, are common sensitizing allergens in apple-cultivating farmers. These spider mites may be important causative allergens in the development of work-related respiratory symptoms in these workers. (*J Allergy Clin Immunol* 1999;1285-92.)

Key words: Spider mites, European red mite, 2-spotted spider mite, allergy, apple farmer, asthma, occupational asthma

Allergic diseases caused by indoor mites are a major health problem worldwide. House dust mites, particularly *Dermatophagoides farinae* and *D pteronyssinus*, are important sources of allergens inside homes in humid areas worldwide.¹ Several studies conducted during the past few years have demonstrated that storage mites are major sensitizing allergens among farmers.²⁻⁴ In addition, allergy to storage mites has not only been associated with occupational exposure but also with damp housing conditions.⁵

Spider mites (Tetranychidae) were negligible pests in fruit cultivation before World War II. However, these mites have increased in the fruit-cultivation industry since pesticides were introduced to eliminate fruit moths 40 years ago.⁶ A survey in Korea demonstrated that the European red mite (*Panonychus ulmi*) and the 2-spotted spider mite (*Tetranychus urticae*) were the most common pests in apple orchards.⁷

Our recent investigations have demonstrated that the citrus red mite (*Panonychus citri*) was the most important causative allergen in citrus-cultivating farmers with asthma, rhinitis, or both.^{8,9} Citrus red mite belongs to the

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TABLE I. Relationship of spider mites to domestic mites

Order	Suborder	Family	Genus	Species
Acari	Astigmata	Pyroglyphidae	<i>Dermatophagoides</i>	<i>D pteronyssinus</i>
				<i>D farinae</i>
		Glycyphagidae	<i>Euroglyphus</i>	<i>E maynei</i>
			<i>Glycyphagus</i>	<i>G domesticus</i>
			<i>Lepidoglyphus</i>	<i>L destructor</i>
		Acaridae	<i>Blomia</i>	<i>B tropicalis</i>
			<i>Acarus</i>	<i>A siro</i>
	Prostigmata	Tetranychidae (spider mites)	<i>Tyrophagus</i>	<i>T putrescentiae</i>
			<i>Tetranychus</i>	<i>T urticae</i>
			<i>Panonychus</i>	<i>P ulmi</i>
			<i>P citri</i>	

TABLE II. Allergic respiratory symptoms on a questionnaire

Symptoms	Percentage
Responses for asthmatic symptoms (n = 725)	
Ever had wheezing	29.4
Wheezing in last 12 months	27.0
Work-related symptoms	16.4
Exercise-induced wheezing	25.0
Nocturnal cough	32.7
Responses for rhinitis symptoms (n = 725)	
Ever had nasal symptoms	44.0
Nasal symptoms in last 12 months	38.2
Work-related symptoms	17.8

order of mites (Acari), the suborder of Prostigmata, the family of Tetranychidae, and the genus of *Panonychus*. It represents its own species. Taxonomically, citrus red mite is more similar to the European red mite and 2-spotted spider mite than to house dust mites or storage mites (Table I). There have been sporadic case reports of occupational allergy to the European red mite or 2-spotted spider mite.¹⁰⁻¹² However, a role of allergens derived from European red mites and 2-spotted spider mites in the development of allergic respiratory diseases has yet to be identified. The aim of this study was to evaluate type I hypersensitivity to European red mites and 2-spotted spider mites and to determine the relationship between such hypersensitivity and allergic respiratory symptoms in apple-cultivating farmers.

METHODS

Subjects

A total of 725 farmers involved in apple production and 21 non-farmer control subjects living around apple orchards in Korea were enrolled in this study, which was conducted in January 1999. The apple farmers had worked in apple orchards for a mean duration of 15.5 years (range, 1-60 years). Six hundred fourteen were men, and 111 were women. Ninety-three were younger than 40 years, 181 were 41 to 50 years of age, 217 were 51 to 60 years of age, and 234 were older than 61 years. The mean occupational duration ($\pm$ SEM) in the 4 groups was 11.5 ± 0.73 years, 14.1 ± 0.61 years, 15.9 ± 0.71 years, and 18.0 ± 0.77 years, respectively. All subjects responded to a questionnaire, and 465 farmers and 14 control subjects underwent skin prick tests to spider mites (European red mite and 2-spotted

spider mite) and 11 inhalant allergens common in Korea. The subjects gave their written informed consent as regulated by Seoul National University Hospital, Seoul, Korea.

Questionnaire survey

Medical students administered a questionnaire, which was developed by the International Study of Asthma and Allergies in Childhood¹³ and translated into Korean with some modification. The questionnaire included demographic data, occupational history, and medical history. The medical history included questions about asthma symptoms ("Have you ever had wheezing, wheezing in the last 12 months, exercise-induced wheezing, and nocturnal cough?") and rhinitis symptoms ("Have you ever had nasal symptoms and nasal symptoms in last 12 months?"). It also included questions on the temporal relationship between exposures at the workplace and the aggravation of respiratory symptoms.

Preparation of European red mites, 2-spotted spider mites, and Hop Japanese (*Humulus japonicus*) pollen extracts

European red mites and 2-spotted spider mites were provided by the Apple Research Institute in Korea. They were extracted with PBS (pH 7.5, 1:5 wt/vol) at 4°C for 24 hours, followed by centrifugation at 3000g. The supernatants were passed through a syringe filter (MSI). For skin prick tests, the 1:10 (wt/vol) extract was mixed with an equal amount of sterile glycerin. The supernatant was dialyzed (cut-off molecular weight, 6000 d) against 4 L of distilled water at 4°C for 48 hours. Hop Japanese pollen was collected during pollination season and prepared by following the above method, with a final concentration of 1:10 (wt/vol). For the skin prick tests, the extract (1:10 wt/vol) was mixed with an equal amount of sterile glycerin.

Skin prick tests

None of the subjects had received antihistamines orally for 3 days preceding the study. European red mite, 2-spotted spider mite, Hop Japanese pollen, and 10 commercially available inhalant allergens (*D pteronyssinus*, *D farinae*, *Tyrophagus putrescentiae*, 2 mixtures of indoor and outdoor fungi, a grass pollen mixture, mugwort and ragweed pollen, animal epithelium, and cockroach; Allergopharma Co) were used for the skin prick tests. A positive control of histamine (1 mg/mL; Allergopharma Co), along with a negative control of diluent (Allergopharma Co), was included in all tests. Skin prick tests were performed on the volar side of both forearms. Fifteen minutes after the prick, the mean diameter of a wheal formed by the allergen was measured. If the wheal size caused by the allergen was larger than 3 mm compared with that produced by the diluent, the reaction was defined as positive.

TABLE III. Skin responses to inhalant allergens

	≤40 y (n = 46)	41-50 y (n = 101)	51-60 y (n = 146)	≥61 y (n = 172)	Total (n = 465)
Indoor allergens (%)*					
<i>D pteronyssinus</i>	26.1	13.8	14.4	11.6	14.4
<i>D farinae</i>	28.3	17.8	13.7	14.5	16.3
<i>T putrescentiae</i>	28.3	21.8	21.2	18.6	21.1
Animal epithelium	2.2	3.0	0	2.3	1.7
Cockroach	23.9	16.8	13.0	8.1	13.1
FG1	8.7	3.0	4.1	5.8	4.9
Outdoor allergens (%)*					
<i>Panonychus ulmi</i>	39.1	24.8	26.0	15.7	23.2
<i>Tetranychus urticae</i>	26.1	16.8	17.8	12.8	16.6
Grass	0	5.9	2.7	1.2	2.6
Ragweed	2.2	1.0	2.1	3.5	2.4
Mugwort	10.9	6.9	4.8	2.3	4.9
Hop Japanese	19.6	13.9	12.3	8.7	12.0
FG2	0	1.0	1.4	1.2	1.1
SPT (%)*	65.2	52.5	50.0	39.5	48.2
SPT (-SM) (%)*	58.7	42.6	37.6	34.3	39.6
SM (%)*	41.3	26.7	29.5	16.9	25.4

Animal epithelium, Mixture of animal epithelium, including cat and dog; *FG1*, mixture of indoor fungi; *FG2*, mixture of outdoor fungi; *SPT*, positive skin reaction to one or more inhalant allergens, including spider mites; *SPT (-SM)*, positive skin reaction to one or more inhalant allergens except spider mites; *SM*, spider mites.

*Wheal formed by an allergen larger than 3 mm compared with that produced by diluent.

Statistical analysis

Results were expressed as means ± SEM unless otherwise indicated. The χ^2 test and ANOVA with the Student *t* test were applied to determine the statistical significance. A *P* value of .05 or less was regarded as significant.

RESULTS

Response to questionnaires on allergic respiratory symptoms

Responses to questionnaires on allergic respiratory symptoms are shown in Table II. Positive response rates to the question, "Have you ever experienced wheezing?" and "Have you ever had rhinitis symptoms?" were 29.4% and 44.0%, respectively, of the 725 citrus-cultivating farmers. The prevalence of wheezing and rhinitis symptoms of the farmers in the last 12 months was 27.0% and 38.2%, respectively, whereas the prevalence in 21 non-farmer control subjects was 14.2% and 19.1%, respectively, which was significantly lower than that found in the farmers (*P* < .05). Of the farmers, 16.4% and 17.8%, respectively, had work-related asthma and rhinitis symptoms. The work-related asthma and rhinitis symptoms showed no significant difference according to age.

Skin responses to inhalant allergens

Skin responses to inhalant allergens are shown in Table III. Of a total of 425 farmers who underwent skin prick tests, 224 (48.2%) had positive skin responses to one or more inhalant allergens. If European red mites and 2-spotted spider mites were excluded from the inhalant allergens, 184 (39.6%) demonstrated positive skin responses to one or more inhalant allergens, whereas 40 (8.6%) had an isolated skin response to spider mites. The

most common sensitizing allergen was European red mite (23.2%), followed by *T putrescentiae* (21.1%), 2-spotted spider mite (16.6%), *D farinae* (16.3%), *D pteronyssinus* (14.4%), cockroach (13.1%), and Hop Japanese pollen (12.0%). A positive skin response to one or more inhalant allergens was observed in 3 (21.4%) of 14 nonfarmer control subjects, which was significantly lower than that found in the farmers (*P* < .05). None of the control subjects had an isolated skin response to spider mites.

Positive skin responses to one or more of 13 inhalant allergens, including spider mites, showed decreasing trends as the subjects became older. When looking at spider mites alone, the figures showed a similar trend. Among the subjects younger than 40 years, 65.2% had positive skin responses to one or more inhalant allergens, whereas 6.5% had an isolated skin response to spider mites. Among the subjects from 41 to 50 years of age, 52.5% exhibited positive skin responses to one or more inhalant allergens, whereas 9.9% had isolated skin responses to spider mites. Among those from 51 to 60 years of age, 50% exhibited positive skin responses to one or more inhalant allergens, whereas 12.4% had an isolated skin response to spider mites. Among the oldest group, 39.5% had positive skin responses to one or more inhalant allergens, whereas 15.2% had an isolated skin response to spider mites. The prevalence of isolated skin responses to spider mites tended to increase as the subjects became older.

Among the youngest group, the most common sensitizing allergen was European red mite (39.1%), followed by *T putrescentiae* (28.3%), *D farinae* (28.3%), 2-spotted spider mite (26.1%), *D pteronyssinus* (26.1%), cockroach (23.9%), and Hop Japanese pollen (19.6%).

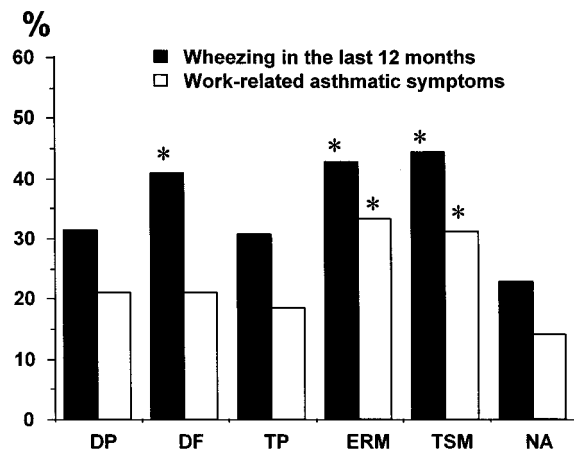


FIG 1. Asthmatic symptoms on a questionnaire in relation to sensitization to individual mites. DP, *Dermatophagoides pteronyssinus*; DF, *Dermatophagoides farinae*; TP, *Tyrophagus putrescentiae*; ERM, European red mite (*Panonychus ulmi*); TSM, 2-spotted spider mite (*Tetranychus urticae*); NA, negative skin response to all the allergens tested (nonatopic). *Significant difference compared with the positive response rate in nonatopic farmers ($P < .05$).

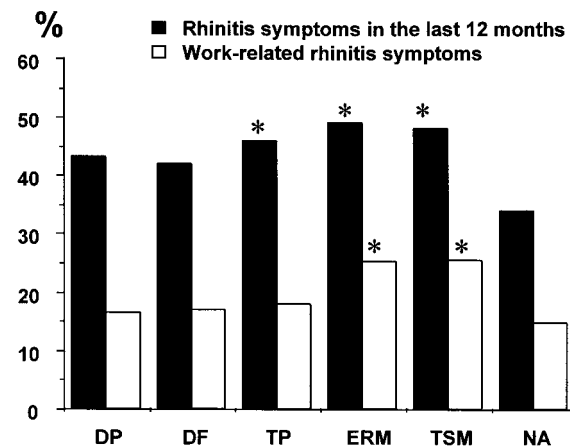


FIG 2. Rhinitis symptoms on a questionnaire in relation to sensitization to individual mites. DP, *Dermatophagoides pteronyssinus*; DF, *Dermatophagoides farinae*; TP, *Tyrophagus putrescentiae*; ERM, European red mite (*Panonychus ulmi*); TSM, 2-spotted spider mite (*Tetranychus urticae*); NA, negative skin response to all the allergens tested (nonatopic). *Significant difference compared with the positive response rate in nonatopic farmers ($P < .05$).

TABLE IV. Allergic respiratory symptoms in relation to sensitization to spider mites

	Skin test response		
	Positive spider mite (n = 118)	Negative spider mite (n = 347)	Positive SPT (n = 224)
Responses for asthmatic symptoms (%)			
Ever had wheezing	43.2*	31.4	39.3
Wheezing in last 12 months	41.5*	30.0	35.7*
WRS	31.4†	15.0	21.0
Responses for rhinitis symptoms (%)			
Ever had nasal symptoms	52.5*	42.1	47.8
Nasal symptoms in last 12 months	49.2*	37.2	44.2
WRS	24.8*	16.6	20.7

SPT, Skin prick test; WRS, work-related symptoms.

*The prevalence was higher than that found in those with negative skin responses to spider mite allergen ($P < .05$).

†The prevalence was higher than that found in those with negative skin responses to spider mite allergen and those with positive skin responses to any allergen ($P < .05$).

Among those subjects aged 41 to 50 years and those aged 51 to 60 years, the most common sensitizing allergen was also European red mite (24.8% and 26.0%), followed by *T putrescentiae* (21.8% and 21.2%), 2-spotted spider mite (16.8% and 17.8%), *D farinae* (17.8% and 13.7%), *D pteronyssinus* (13.8% and 14.4%), cockroach (16.8% and 13.0%), and Hop Japanese pollen (13.9% and 12.3%). This trend was also observed among the oldest groups.

Relationship between skin responses to spider mites and respiratory symptoms

Table IV shows the relationship between respiratory symptoms listed on the questionnaires and skin responses to spider mites. A positive response to "Have you ever experienced wheezing and wheezing in last 12 months?" was higher in subjects with positive skin responses to spider mites than in those with negative responses to spider mites (43.2% vs 31.4%, $P = .02$; 41.5% vs 15.0%, $P = .006$), whereas this figure in those with positive skin responses to spider mites was not different from those with positive skin responses to any allergen ($P > .05$). The work-related asthma symptoms in those with positive skin responses to spider mites were higher than in those with negative skin responses to spider mites and those with positive skin responses to any allergen (31.4% vs 15.0% vs 21.0%; $P = .0001$ and $P = .04$, respectively).

The positive responses to rhinitis symptoms in the last 12 months and work-related rhinitis symptoms were also higher in those with positive skin responses to spider mites than in those with negative responses to spider mites (49.2% vs 37.2%, $P = .02$; 24.8% vs 16.6%, $P = 0.058$), although the statistical significance was less marked. The positive responses to recent and work-related rhinitis symptoms were not different between those with positive skin responses to spider mites and those with positive skin responses to any allergen (49.2% vs 44.2% and 24.8% vs 20.7%; $P > .05$).

Fig 1 shows the relationships between asthmatic symptoms on the questionnaire and skin responses to individual mites. The prevalence of wheezing in the last 12 months was higher in farmers with positive skin response to *D farinae*, European red mite, or 2-spotted spider mite than in those with negative skin response to

TABLE V. Relationships between sensitization to spider mites and to other common sensitizing allergens

	<i>Panonychus ulmi</i>			<i>Tetranychus urticae</i>		
	Positive (n = 108)	Negative (n = 357)	P value	Positive (n = 122)	Negative (n = 565)	P value
Indoor allergens (%)*						
<i>D pteronyssinus</i>	39.8	6.7	.0001	41.6	9.0	.0001
<i>D farinae</i>	37.9	9.8	.0001	41.6	11.3	.0001
<i>T putrescentiae</i>	47.2	13.2	.0001	44.2	16.5	.0001
Cockroach	39.8	5.0	.0001	40.3	7.7	.0001
Outdoor allergens (%)*						
<i>Panonychus ulmi</i>	—	—	—	84.4	11.1	.0001
<i>Tetranychus urticae</i>	60.2	3.4	.0001	—	—	—
Hop Japanese	21.3	9.2	.0007	22.1	10.1	.003
SPT (-SM) (%)*	73.1	29.4	.0001	71.4	33.2	.0001

SPT (-SM), Positive rate of skin response to one or more inhalant allergens except spider mites.

*Wheal larger than 3 mm formed by an allergen compared with that formed by diluent.

TABLE VI. Characteristics of study subjects in relation to work-related symptoms

	Asthma			Rhinitis		
	Positive WRS (n = 119)	Negative WRS (n = 606)	P value	Positive WRS (n = 122)	Negative WRS (n = 565)	P value
Age (y)	55.3 ± 1.0	53.8 ± 0.4	>.05	54.5 ± 0.9	54.1 ± 0.4	>.05
Occupational duration (y)	16.5 ± 1.0	15.3 ± 0.4	>.05	15.7 ± 0.9	15.4 ± 0.4	>.05
Indoor allergens (%)*						
<i>D pteronyssinus</i>	15.7	14.1	>.05	12.2	14.9	>.05
<i>D farinae</i>	23.6	14.6	>.05	22.0	20.9	>.05
<i>T putrescentiae</i>	21.3	21.0	>.05	17.1	11.0	>.05
Cockroach	15.7	12.5	>.05	15.9	12.5	>.05
Outdoor allergens (%)*						
<i>Panonychus ulmi</i>	40.4	19.1	.0007	30.5	21.7	.09
<i>Tetranychus urticae</i>	27.0	14.1	.003	22.0	15.4	.15
Hop Japanese	13.5	14.7	>.05	30.5	21.7	>.05
SPT (%)*	57.3	46.0	>.05	52.4	47.3	>.05
SPT (-SM) (%)*	40.4	39.4	>.05	42.7	38.9	>.05
SM (%)*	41.6	21.5	.0001	32.9	23.8	.08

WRS, Work-related symptoms; SPT, positive skin reaction to one or more inhalant allergens, including spider mites; SPT (-SM), positive skin reaction to one or more inhalant allergens except spider mites; SM, spider mites.

*Wheal larger than 3 mm formed by an allergen compared with that formed by the diluent.

any allergen, including spider mites (40.8%, 42.6%, or 44.2% vs 22.8%, respectively; $P < .05$). However, the prevalence of recent wheezing in those with positive skin responses to *D pteronyssinus* or *T putrescentiae* was not different from that found in those without skin response to all the inhalant allergens (31.3% or 30.6% vs 22.8%, respectively; $P > .05$). In regard to work-related asthmatic symptoms, the prevalence in those with positive skin response to *D pteronyssinus*, *D farinae*, or *T putrescentiae* was not different from that found in those without skin responses to all the inhalant allergens (20.9%, 21.1%, or 18.4% vs 14.2%, respectively; $P > .05$), although the prevalence was higher in those with positive skin responses to European red mite or 2-spotted spider mite than in those without skin responses to all the inhalant allergens (33.3% or 31.2% vs 14.2%, respectively; $P < .05$).

Fig 2 shows relationships between rhinitis symptoms listed on the questionnaire and skin responses to individual mites. The prevalence of rhinitis in the last 12 months

was higher in farmers with positive skin responses to *T putrescentiae*, European red mite, or 2-spotted spider mite than in those with negative skin responses to all the inhalant allergens (45.9%, 49.1%, or 48.1% vs 34.0%, respectively; $P < .05$). However, the prevalence of recent rhinitis symptoms in those with positive skin responses to *D pteronyssinus* or *D farinae* was not different from that found in those without skin responses to all the inhalant allergens (43.3% or 42.1% vs 34.0%, respectively; $P > .05$). In regard to work-related rhinitis symptoms, the prevalence in those with positive skin responses to *D pteronyssinus*, *D farinae*, or *T putrescentiae* was not different from that found in those without skin responses to any allergen, including spider mites (16.4%, 16.9%, or 18.0% vs 14.1%, respectively; $P > .05$), although the prevalence was higher in those with positive skin responses to European red mite or 2-spotted spider mite than in those without skin responses to any allergen (25.3% or 25.4% vs 14.7%, respectively; $P < .05$).

Relationship between skin response to spider mites and positive skin reactions to the other allergens

The relationship between skin responses to spider mites and positive skin reactions to the other allergens is shown in Table V. The positive skin responses to *D pteronyssinus*, *D farinae*, 2-spotted spider mite, and *T putrescentiae* were higher among subjects sensitized to European red mite than among those who were not (*D pteronyssinus*: 39.8% vs 6.7%, $P < .001$; *D farinae*: 37.9% vs 9.8%, $P < .001$; 2-spotted spider mite: 47.2% vs 13.2%, $P < .001$; *T putrescentiae*: 60.2% vs 3.4%, $P < .001$). These differences were also observed for cockroach, Hop Japanese pollen, and for skin responses to one or more of 11 inhalant allergens, with the exception of spider mites (cockroach: 39.8% vs 5.0%, $P < .001$; Hop Japanese: 21.3% vs 9.2%, $P < .001$; spider mites: 73.1% vs 29.4%, $P < .001$). The positive skin responses to *D pteronyssinus*, *D farinae*, *T putrescentiae*, cockroach, Hop Japanese pollen, and European red mite were also higher among those sensitized to 2-spotted spider mite than among those who were not. The skin responses to one or more of the 11 inhalant allergens, with the exception of spider mites, showed a similar result in relation to 2-spotted spider mite sensitization.

Risk factors associated with work-related respiratory symptoms

Risk factors associated with work-related respiratory symptoms are shown in Table VI. Age and occupational duration were the same in subjects with work-related symptoms of asthma and rhinitis as in those without work-related symptoms. The distribution of positive skin responses to each allergen demonstrated that positive responses to European red mite or 2-spotted spider mite, but no other allergens, were higher in subjects with work-related symptoms of asthma than in those without such symptoms (European red mite alone: 40.4% vs 19.1%, $P < .001$; 2-spotted spider mite alone: 27.0% vs 14.1%, $P < .01$; European red mite or 2-spotted spider mite: 41.6% vs 21.5%, $P = .0001$). The skin responses to European red mite or 2-spotted spider mite were also greater among those with work-related symptoms of rhinitis than among those without such symptoms, although there was no statistical difference between the 2 groups (European red mite alone: 30.5% vs 21.7%; 2-spotted spider mite alone: 22.0% vs. 15.4%; European red mite or 2-spotted spider mite: 32.9% vs 23.8%, respectively). In farmers with work-related symptoms that developed after work in apple orchards who also had positive skin responses to spider mites, the mean duration of latency, defined as the period from initial exposure to onset of symptoms, was 11.7 ± 1.6 years for asthma and 9.25 ± 1.4 years for rhinitis.

DISCUSSION

This study revealed that European red mites and 2-spotted spider mites were common sources of sensitizing

allergens among apple-cultivating farmers. Approximately 9% of the farmers showed isolated positive skin responses to spider mites, and the figure was more marked among older farmers. As for the clinical manifestation of allergic respiratory symptoms, the prevalence of asthma and rhinitis symptoms was higher in those sensitized to European red mites or 2-spotted spider mites than in those who were not sensitized. The work-related asthma symptoms were also more prevalent in those sensitized to the spider mites than in those with negative skin responses to spider mites and those with positive skin responses to any allergen. The prevalence in those with sensitization to *D pteronyssinus*, *D farinae*, or *T putrescentiae* was not different from those with negative skin responses to any allergen, including spider mites. The skin responses to European red mite or 2-spotted spider mite allergens were also higher among those with work-related symptoms than among those without such symptoms, but the responses to other allergens were not.

Allergens are ubiquitous but are present in different concentrations in different environments. Our previous study demonstrated that citrus red mites were the most common sensitizing allergen among citrus-cultivating farmers.⁹ The present study revealed that European red mite allergen was the most common sensitizing allergen among apple-cultivating farmers, and that 2-spotted spider mite allergen was also a common sensitizing allergen. Sensitization to inhaled mite allergens and subsequent occurrence of respiratory symptoms may be dependent on the mite allergen levels and exposure duration, as well as the specific species of mite responsible.¹⁴ European red mites and 2-spotted spider mites were negligible pests in fruit cultivation before World War II. However, these mites have been the main pests on fruits since pesticides to eliminate other fruit pests began to be applied approximately 40 years ago.⁶ A survey in 1984 showed that European red mites and 2-spotted spider mites were the most predominant and widely distributed species in 15 commercial apple orchards in 6 major apple-growing areas in Korea.⁷ The spider mites are not carried indoors and hardly ever cause indoor exposure. However, when the housing environment is near apple orchards, the indoor exposure to these mites may contribute to the sensitization. From the results of this study, we can speculate that outdoor mites, particularly spider mites, have potent allergenicity and that many workers with high levels of environmental exposure of long duration may be sensitized to spider mites.

Studies that have correlated individual levels of specific IgE with asthmatic symptoms provide strong evidence of an IgE-associated mechanism for the clinical manifestations of asthma. In this study the prevalence of asthmatic symptoms was higher in subjects with positive skin responses to European red mites or 2-spotted spider mites than in those without positive skin responses. This study also showed that the sensitization to these mites was positively correlated with work-related asthmatic symptoms. These findings are consistent with the results of our previous study that skin responses and serum-spe-

cific IgE responses to citrus red mites were associated with work-related asthmatic symptoms.⁹ From these findings, we can assume that specific IgE responses to outdoor mites, particularly spider mites, may be important in the development of occupational asthma in fruit-cultivating farmers.

House dust mites are important allergens inside homes in humid areas worldwide.¹ Several studies conducted during the past few years have demonstrated that storage mites are major sensitizing allergens among farmers.²⁻⁴ In addition, allergy to storage mites has not only been associated with occupational exposure but also with damp housing conditions.⁵ In Korea predominant species among domestic mites were *D farinae*, *D pteronyssinus*, and *T putrescentiae*.¹⁵ According to geographic area in Korea, *D pteronyssinus* was predominant in relatively low-humidity area, and *D farinae* and *T putrescentiae* were predominant in relatively high-humidity area.¹⁵ The results of this study showed that mites other than spider mites, such as *D pteronyssinus*, *D farinae*, and *T putrescentiae*, were also common sensitizing allergens among apple-cultivating farmers. However, the prevalence of asthmatic symptoms in farmers sensitized to *D pteronyssinus* or *T putrescentiae* were not different from those without sensitization to all the 13 inhalant allergens tested, although the prevalence in those sensitized to *D farinae* was higher than in those without sensitization to all the allergens. In regard to work-related asthmatic symptoms, the prevalence in farmers sensitized to *D pteronyssinus*, *D farinae*, or *T putrescentiae* was not different from those not sensitized to all the allergens tested. These findings suggest that the sensitization to *T putrescentiae*, as well as to *D pteronyssinus* or *D farinae*, does not play an important role in the development of work-related asthmatic symptoms.

This study showed that approximately 17% of farmers with work-related asthmatic symptoms exhibited an isolated positive skin response to spider mites and that about 9% of farmers were sensitized only to spider mites. These findings suggest that many cases of asthma thought to be intrinsic in nature might in fact be occupational in origin because of allergens derived from outdoor phytophagous mites.

The latent period for the development of occupational asthma is highly variable, ranging from several weeks to several years.¹⁶ The duration of latency seems to depend on the nature of the causal agent and the duration and intensity of exposure to a causal allergen. In subjects continuously exposed to the causative agent, the latent period was shorter than in those who were intermittently exposed.¹⁷ Our previous study showed that the mean length of the latent period was more than 10 years in citrus red mite-induced occupational asthma.^{8,9} The present study also showed that the mean duration of latency was 11.7 years in spider mite-sensitive subjects with work-related asthmatic symptoms that developed after the exposure to spider mites. This long latency may be explained by the fact that apple-cultivating farmers were intermittently exposed to spider mite-derived allergens,

which have 2 peaks in late spring and mid-fall and are minimal during other periods, particularly in winter.

Sensitization to high-molecular-weight allergens is known to occur at a higher rate among atopic individuals.^{18,19} There is also an agreement that the closer the taxonomic relationship between mites, the greater the level of cross-allergenicity.²⁰⁻²² Spider mites belong to the order of mites (Acari), to the suborder of Prostigmata, and to the family of spider mites (Tetranychidae). European red mites and citrus red mites belong to the genus of *Panonychus*, and 2-spotted spider mites belong to the genus of *Tetranychus*. Our previous study revealed that citrus red mite-derived allergens contained species-specific allergens in addition to the allergens commonly shared with house dust mites.^{8,9} The present study showed that positive skin responses to cockroach and Hop Japanese pollen, which have no taxonomic relationship to mites, were higher among subjects sensitized to spider mites than among those who were not thus sensitized. This finding suggests that sensitization to spider mites is influenced by a genetic predisposition to a specific IgE response to common inhalant allergens.

In conclusion, outdoor mites, particularly spider mites, are not only common sensitizing allergens but also associated with the development of occupational asthma among fruit-cultivating farmers. These allergens should be included in the skin test battery for screening as possible causative allergens in individuals exposed to phytophagous mites.

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REFERENCES

1. Spiekma FTM. Domestic mites: their role in respiratory allergy. Clin Exp Allergy 1991;21:655-60.
2. Blainey AD, Topping MD, Ollier S, Davies RJ. Allergic respiratory disease in grain workers: the role of storage mites. J Allergy Clin Immunol 1989;84:296-303.
3. Luczynska CM, Griffin P, Davies RJ, Topping MD. Prevalence of specific IgE to storage mites (*A. siro*, *L. destructor* and *T. longior*) in an urban population and cross-reactivity with the house dust mite (*D. pteronyssinus*). Clin Exp Allergy 1990;20:403-6.
4. Van Hage-Hamsten M, Johansson E, Wiren A, Johansson SGO. Storage mites dominate the fauna in Swedish barn dust. Allergy 1991;46:142-6.
5. Iversen M, Dahl R. Allergy to storage mites in asthmatic patients and its relation to damp housing conditions. Allergy 1990;45:81-5.
6. Lee SW, Lee MH, Choi KM, Hyun JS, Yiem MS. The effect of pesticide applications on the major apple insects pests and their natural enemies [in Korean]. J Agri Sci 1994;36:383-94.
7. Lee SW, Lee MH, Choi KM, Hyun JS. Survey on occurrences of European red mite (*Panonychus ulmi* Koch) and two-spotted spider mite (*Tetranychus urticae* Koch), and their control status in apple orchards [in Korean]. J Agri Sci 1984;27:86-91.
8. Kim YK, Son JW, Kim HY, Park HS, Lee MH, Cho SH, et al. New occupational allergen in citrus farmers: citrus red mite (*Panonychus citri*). Ann Allergy Asthma Immunol 1999;82:223-8.
9. Kim YK, Son JW, Kim HY, Park HS, Lee MH, Cho SH, et al. Citrus red mite (*Panonychus citri*) is the most common sensitizing allergen in citrus farmers with asthma and rhinitis. Clin Exp Allergy 1999;29:1102-9.
10. Reunala T, Bjorksten F, Forstrom L, Kanerva L. IgE-mediated occupational allergy to a spider mite. Clin Exp Allergy 1983;13:383-8.
11. Kroidl R, Maasch HJ, Wahl R. Respiratory allergies (bronchial asthma and rhinitis) due to sensitization of type I allergy to red spider mite (*Panonychus ulmi* Koch). Clin Exp Allergy 1992;22:958-62.

12. Burches E, Pelaez A, Morales C, Braso JV, Rochina A, Lopez S, et al. Occupational allergy due to spider mites: *Tetranychus urticae* (Koch) and *Panonychus citri* (Koch). Clin Exp Allergy 1996;26:1262-7.
13. Pearce N, William S, Keil U, Langridge P, Anderson HR, Struchan D, 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;6:1455-61.
14. Platts-Mills TAE, Thomas WR, Aalberse RC, Vervloet D, Chapman MD. Dust mite allergens and asthma: report of a second international workshop. J Allergy Clin Immunol 1992;89:1046-60.
15. Ree HI. Fauna and geographical distribution of house dust mites in Korea [in Korean]. Korean J Parasitol 1997;35:9-17.
16. Malo JL, Ghezzi H, D'Aquino C, L'Archeveque J, Cartier A, Chan-Yeung M. Natural history of occupational asthma: relevance of type of agent and other factors on the rate of development of symptoms in subjects with disease. J Allergy Clin Immunol 1992;90:937-44.
17. Cockcroft A, McCarthy P, Dewards J, Andersson N. Allergy in laboratory animal workers. Lancet 1981;1:827-30.
18. Platts-Mills TA, Longbottom J, Edwards J, Cockcroft A, Wilkins S. Occupational asthma and rhinitis related to laboratory rats: serum IgG and IgE antibodies to the rat urinary allergen. J Allergy Clin Immunol 1987;79:505-15.
19. Slovak AJ, Hill RN. Laboratory animal allergy: a clinical survey of an exposed population. Br J Ind Med 1981;38:38-41.
20. Platts-Mills TAE, Heymann PW, Charpman MD, Hayden ML, Wilkins SR. 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.
21. Arlian LG, Geis DP, Vyszynski-Moher DL, Bernstein IL, Gallagher JS. Cross antigens and allergenic properties of the house-dust mite *Dermatophagoides farinae* and the storage mite *Tyrophagus putrescentiae*. J Allergy Clin Immunol 1984;74:172-9.
22. Griffin P, Ford AW, Alterman L, Thompson J, Parkinson C, Blainey AD et al. Allergenic and antigenic relationships between three species of storage mite and the house dust mite, *Dermatophagoides pteronyssinus*. J Allergy Clin Immunol 1989;84:108-17.