

Occupational allergy due to spider mites: *Tetranychus urticae* (Koch) and *Panonychus citri* (Koch)

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Summary

Background Allergy to both house dust and storage mites is well established, but information about other species of mites is scant.

Objective One hundred and fifty patients directly exposed to an occupational environment were studied to assess whether spider mites (*Tetranychidae*) caused their allergic symptoms. We also studied a group of 50 patients from an urban environment, who were not occupationally exposed to spider mites, with a strong sensitization to *Dermatophagoides pteronyssinus* (RAST class 4).

Methods Case history (including questions about work-related symptoms), skin tests, RAST and conjunctival provocation tests were performed in both groups using *Tetranychus urticae* and *Panonychus citri* extracts as allergens. Cross-reactivity between spider mites and *D. pteronyssinus* was determined by RAST inhibition.

Results Fifty-four of 150 rural workers were positive to *Tetranychidae* and in all cases there was an associated sensitization to *D. pteronyssinus*. All individuals belonging to the urban group were positive to spider mites. RAST inhibition demonstrated a significant cross-reactivity between *Tetranychidae* and *D. pteronyssinus*. Five of fifty-four rural workers sensitized to spider mites developed symptoms only when they handled plants or fruits infested with spider mites and they became asymptomatic when exposure ceased.

Conclusion In the rural population studied, 36% of workers were found to be sensitized to spider mites and 10% had symptoms associated with occupational exposure. Since specific IgE antibodies to spider mites could not be detected in the absence of the specific IgE antibodies to *D. pteronyssinus*, and as all the affected workers were RAST positive to *D. pteronyssinus*, prior sensitization to house dust mites may be a risk factor for occupational allergy to spider mites.

Keywords: spider mites, *Tetranychidae*, *Tetranychus urticae*, *Panonychus citri*, *Dermatophagoides pteronyssinus*, occupational allergy

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Introduction

Mites are one of the main etiologic agents in allergic diseases. It has been well established that genus *Dermatophagoides* is the most important source of house dust allergens [1] and that storage mites can cause allergic

diseases in exposed individuals [2,3,4]. Information about the impact of other species of mites as etiologic factors in allergic diseases is scant. *Tetranychidae* (denominated spider mites) are herbivorous mites that belong to suborder *Prostigmata* and many of them constitute a common pest in several kinds of trees and cultivated plants. They are distributed world-wide; however, reports about allergy to spider mites are rare.

Panonychus ulmi (Koch) is a well-known pest for fruit and vegetable plants. Several authors have described

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allergic symptoms (respiratory, ocular and dermatological) amongst fruit-growers and suggested that *Panonychus ulmi* might be the cause [5,6].

Tetranychus urticae (Koch) attacks cultivated vegetables (greenhouse as well as outdoor). Respiratory and skin symptoms have been reported in exposed agricultural workers [7,8,9]. *Tetranychus telarius* parasiting cut flowers also induced IgE-mediated rhinitis in a greenhouse worker [10].

In Spain, we conducted a preliminary study in which sensitization to *Tetranychus urticae* and *Panonychus citri* (a rather common orange tree pest) in agricultural workers was demonstrated [11]. Subsequently, other authors have described two cases with rhinoconjunctivitis and asthma related to these mites [12,13].

The purpose of this work was to evaluate the prevalence of sensitization to *Tetranychus urticae* and *Panonychus citri* and their role in the development of allergic symptoms in a selected group of individuals with occupational exposure.

Materials and methods

In our study, we selected a group of 150 workers in horticultural and citric culture environments (open fields), referred to an allergy unit for evaluation of respiratory (rhinitis and asthma), conjunctival and skin symptoms. There were 102 males and 48 females with a mean age of 37.17 ± 13.24 (range 21 to 68 yr); 53 had rhinoconjunctivitis, 39 had rhinitis and asthma and 58 had skin symptoms. We also selected another group of 50 patients (with a mean age of 31.36 ± 10.65 , range 18 to 55 yr) from an urban environment who were not occupationally exposed to spider mites. This group presented a strong sensitization to *D. pteronyssinus* (RAST class 4). An additional control group included 15 non-atopic individuals unexposed to spider mites and not sensitized to *D. pteronyssinus*.

Allergological evaluation was made by means of a clinical history including case history (which also contained questions about work-related symptoms), physical examination, skin tests (with common allergens and spider mites) and blood sampling for specific-IgE determination by RAST method.

Mites *T. urticae* and *P. citri* were obtained from the Entomology Unit of ETSIA-Polytechnical University of Valencia. Mites were grown under controlled conditions of temperature and humidity. The extracts were prepared by mixing the source material (whole-body mites) with phosphate buffered saline (PBS, pH 7.3) in a 10% (W/V) ratio. After centrifugation at 3000 g for 30 min, the supernatant was dialysed (dialysis membrane: Medicell International

Ltd, London, UK) in PBS for 24 h and then passed through a 0.45 μm pore (Millex-HA: Millipore, Molsheim, France) for sterilization and then lyophilized. Protein concentration of the reconstituted solution was measured by the Lowry method (protein assay kit: Sigma Diagnostics, St Louis, USA) and was 1 g/ml.

Skin prick tests were done with the antigenic preparations described above and a battery of commercially available allergens were also tested (Alergia e Inmunología Abelló, Madrid, Spain), including mites (*D. pteronyssinus* storage mites), moulds, pollens (grass, trees and weeds) and animal danders. Prick tests were performed with a prick test lancet (Dome/Hollister-Stier, UK) and recorded according to a grading system proposed by Aas and based on the relationship between the reactions induced by the allergen and the histamine reference [14]. As for mites (*D. pteronyssinus*, *T. urticae* and *P. citri*), we also performed intracutaneous tests (*T. urticae* and *P. citri* extracts diluted 1/1000) and the reactions were graded by the method proposed by Norman [15].

RAST was performed according to the manufacturer's instructions (Pharmacia Diagnostics, Uppsala, Sweden) using the commercially available Phadezym RAST. The results are expressed in PRU (Phadebas RAST Units) per ml. As for *T. urticae* and *P. citri*, the allergen discs were prepared by coupling the allergen extract undiluted to CNBr-activated paper discs, according to the method proposed by Ceska [16]. Allergen discs with *D. pteronyssinus* were obtained from Pharmacia. To investigate the possible interference of high total IgE in the assay, serum from two non-atopic subjects with IgE levels greater than 4000 KU/L was also included. The results were compared with those of the Phadezym RAST Reference System and expressed in terms of RAST classes according to Pharmacia indications: class 0, <0.35 PRU/ml; class 1, 0.35–0.70 PRU/ml; class 2, 0.70–3.50 PRU/ml; class 3, 3.50–17.50 PRU/ml; class 4, >17.50 PRU/ml. A positive result was defined as a value ≥ 0.35 PRU/ml.

RAST inhibition experiments were performed essentially as previously described by Iman *et al.* [17], using 30 μl of allergen extract. Sera were collected from five patients sensitized to both *Tetranychidae* and *D. pteronyssinus*. Extracts and sera were diluted in PBS; 30 μl of serial dilutions of the mite extracts (1/1, 1/10, 1/100, 1/1000) was added with 20 μl aliquots of serum and was incubated for 3 h at room temperature. Then, paper discs were added and the rest of the procedure was identical to the RAST method previously described.

Cross-reactivity between *D. pteronyssinus* and spider mites was determined by comparing the capability of each mite (*T. urticae* and *P. citri*) extract, at different concentrations, to inhibit the binding of human anti-mite IgE to the allergens of the mite species adsorbed to the disc as the solid

phase (*D. pteronyssinus*). Furthermore, RAST inhibition of the homologous system (where *D. pteronyssinus* extract calibrated to the same protein content inhibited the positive RAST to *D. pteronyssinus* allergen discs) was tested.

The reverse RAST inhibition assay was performed using *T. urticae* and *P. citri* in the solid phase and *D. pteronyssinus* in the fluid phase.

In patients from a rural environment with a positive result (skin tests and RAST) to *Tetranychidae*, conjunctival provocation tests were performed with *Tetranychidae* extracts (1/10000 dilution) and *D. pteronyssinus* (Alergia e Inmunología Abelló, Madrid, Spain). Itching and congestion of the conjunctival mucosa defined positivity. Moreover, in the group of patients from an urban environment, conjunctival provocation tests were performed with the same extracts. In both cases, one drop of control solution was instilled in one eye.

Results

Patient population skin tests and clinical evaluation

One hundred and fifty individuals, submitted for study of allergic diseases and working in a rural environment, were skin tested. Ninety-six were negative to *T. urticae* and *P. citri* (prick tests as well as intracutaneous tests). Fifty-four of the 150 (36%) were positive to *T. urticae* and *P. citri*. These subjects were also positive to *D. pteronyssinus*.

The clinical evaluation showed that 5 of 54 positive patients (3.33% of 150 patients skin tested) developed symptoms (rhinoconjunctivitis in three cases, contact urticaria in two cases) only when they handled plants or fruits infested with spider mites and they became asymptomatic after avoidance exposure (Table 1). In the other 49 subjects, hypersensitivity to spider mites should be considered in the context of clinical history. Sixteen of the 49 patients also showed a positive response to pollens and the predominating symptoms were due to outdoor exposure in springtime but did not occur exclusively in fields infested with spider mites. Twenty-six of the 49 patients were positive only to mites (*D. pteronyssinus*, spider mites and, in some cases, storage mites) but allergic symptoms also occurred due to indoor home exposure. Seven patients presented with chronic urticaria; however, their complaints could not be explained by sensitization to mites.

The clinical characteristics of these 54 patients were as follows: 18 patients had clinical diagnosis of rhinitis and asthma, 27 patients had clinical diagnosis of rhinoconjunctivitis and nine patients had clinical diagnosis of urticaria. The most prevalent allergens were mites. Positive skin tests to storage mites were found in 21 patients. A positive skin

Table 1. Clinical characteristics of patients with positive skin tests to spider mites

Diagnoses	Patients (n)
Rhinitis and asthma	18
Rhinoconjunctivitis	27
Urticaria	9
Total	54
Predominating symptoms caused by spider mites	5
Predominating symptoms caused by other allergens or other diseases	49
House dust mites	26
Pollens	16
Chronic urticaria	7

test to moulds (two cases) and animal danders (three cases) was rare.

In the group referred from an urban environment and strongly sensitized to *D. pteronyssinus*, all patients had positive skin tests to both *Tetranychidae*.

The control group of 15 non-atopic individuals not sensitized to *D. pteronyssinus* and unexposed to spider mites did not display sensitization to spider mites.

Conjunctival provocation tests

In 48 subjects out of 54, the results were positive to *Tetranychidae* and *D. pteronyssinus*, while six patients had a negative result. In the urban group, the test was positive in all patients with both types of mites.

RAST and RAST inhibition

Prevalence of specific IgE to *T. urticae* and *P. citri* was detected in all subjects of the rural group with positive skin tests to these mites. A positive result was defined by a value ≥ 0.35 PRU/ml. The relationship between skin tests and RAST is shown in Tables 2 and 3. All agricultural workers who showed positive RAST against *Tetranychidae* also had positive scores to *D. pteronyssinus* (with the same class in RAST results). To estimate the strength of the relationship between the various mite species, Spearman rank correlation coefficients between RAST scores (*T. urticae* and *D. pteronyssinus*, *P. citri* and *D. pteronyssinus*) were calculated with a significant result (correlation coefficient 0.67, $P = 0.0001$, correlation coefficient 0.75, $P = 0.0001$).

Table 2. Relationship between SPT and RAST with Tu in 54 rural patients

	0	1	RAST class 2	3	4
SPT					
4+		5	2	2	
3+		23	7		
2+		11	4		
1+					

In the group of 50 individuals from an urban environment (with a RAST class 4 to *D. pteronyssinus*) the prevalence of specific *T. urticae* and *P. citri* IgE was 100% (no significant result in Spearman rank correlation coefficients between RAST scores to *D. pteronyssinus* and spider mites).

RAST inhibition assays demonstrated important cross-reactivity between spider mites (*T. urticae*, *P. citri*) and *D. pteronyssinus*. Spider mite (*T. urticae*, *P. citri*) allergens in the fluid phase inhibited the binding of specific IgE to *D. pteronyssinus* solid phase by up to 80%. The results are depicted in Table 4 and Fig. 1. RAST inhibition of the homologous system (where *D. pteronyssinus* inhibited the positive RAST to *D. pteronyssinus* allergen discs) was 100%. The reverse RAST inhibition assays showed a final inhibition in a range similar to that described using *D. pteronyssinus* as a solid phase and spider mites as a fluid phase, although the levels obtained were slightly lower (final inhibition in a range of 55% to 68%).

Discussion

Storage mites and other non-pyroglyphid mites have

Table 3. Relationship between SPT and RAST with Pc in 54 rural patients

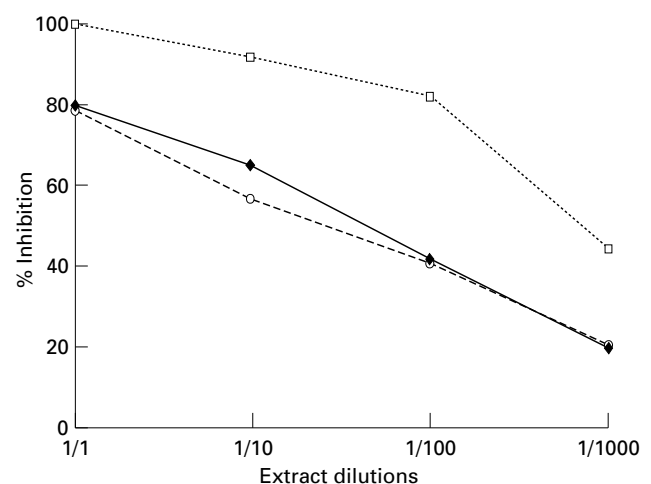
	0	1	RAST class 2	3	4
SPT					
4+		1	2	2	
3+		22	8		
2+		10	8		
1+		1			

Table 4. RAST inhibition of sera from five patients using Dp as solid phase and Tu, Pc as fluid phase

Patient No	Inhibition of Dp RAST with Tu and Pc (%) Tetranychus	Panonychus
1	80	79
2	76	80
3	73	78
4	75	65
5	80	73

gained increasing interest in recent years because of their role as allergens in farmers and other agricultural workers. Although *Tetranychidae* are herbivorous mites widely spread in nature, allergy to these mites is poorly documented.

In our study, the prevalence of sensitization to *Tetranychidae* in patients occupationally exposed was 36% as detected by skin tests, RAST and conjunctival provocation test. Sensitization did not always lead to development of clinical symptoms and, in fact, only in five subjects (3.33%) could a causal relationship be established. Besides, these patients had an associated sensitization to house dust mites. However, sensitization to spider mites was also present in subjects from an urban environment. These findings suggested a strong

**Fig. 1.** RAST-inhibition using sera of one patient sensitized to both spider and house dust mites. Dp is the solid phase, with Tu (◆), Pc (○) and Dp (□) as fluid phase. (Dp = *D. pteronyssinus*, Tu = *T. urticae*, Pc = *P. citri*).

cross-reactivity between *D. pteronyssinus* and spider mites and this assumption was confirmed by data obtained by RAST inhibition assays, in which *T. urticae* and *P. citri* allergens in the fluid phase inhibited the binding of specific IgE to *D. pteronyssinus* solid phase by up to 80%. In contrast to our findings, Reunala did not observe (in two subjects that developed an IgE-mediated allergy working in a greenhouse infested with spider mites) sensitization to *D. pteronyssinus* and found no cross-reactivity between *D. pteronyssinus* and *T. urticae* [7]. Conversely, Kroidl described six patients with hypersensitivity to *Panonychus ulmi* who related their complaints to working on fruit trees. Five of these patients also showed sensitization to *D. pteronyssinus*, and in a RAST inhibition assay using *D. pteronyssinus* as a solid phase, a *P. ulmi* extract reached 67% inhibition of IgE binding. By IEF and immunoprint the most common allergen bands to *D. pteronyssinus* and *P. ulmi* were observed in a pH-range between 4.1 and 4.45 [6]. Previously (in 1970), Bernecker reported a high percentage of positive reactions to spider mites (*T. urticae* and *P. ulmi*) in patients with positive skin tests to *D. pteronyssinus* [18].

Recently, it has been proposed that from the inhibitory capacities exhibited by different allergens in the RAST inhibition assay it could be determined which is the primary sensitizer. A well-known model is allergy to common inhalants (pollen, house dust mites) associated with IgE-mediated reactions to food (vegetable or animal source) which are due to epitopes with a lower affinity to the allergen-specific IgE of the patients [19]. The inhibition potency of primary immunogen would be considerably higher than that of secondary allergens. Following these conclusions, the slight differences obtained in our RAST inhibition results (whether the solid phase was *D. pteronyssinus* or spider mites) do not allow us to achieve definite results regarding which is the primary sensitizer.

Our results suggest that sensitization to spider mites may occur by direct exposure, as well as by an allergenic cross-reactivity with *D. pteronyssinus* (in both groups of patients). Moreover, in some patients (3.33% in our study), spider mites that infest vegetable products may be the major cause of allergic diseases and work-related symptoms. In workers that only developed symptoms after exposure to spider mites, the possibility in the future of clinical allergy to *D. pteronyssinus* should be considered. We think that the low prevalence of clinical diseases linked to spider mites in our rural patients is related to the fact that they work in open-cultivated fields and not in greenhouses.

Future work involving the identification and purification of major *T. urticae* and *P. citri* allergens is needed to establish a better knowledge of these mites.

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