

Short communication

Prevalence of sensitization to the storage mites *Acarus siro*, *Tyrophagus putrescentiae*, and *Lepidoglyphus destructor* in allergic patients with different degrees of sensitization to the house-dust mite *Dermatophagoides pteronyssinus*

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The prevalence of sensitization to the storage mites *Acarus siro* (AS), *Tyrophagus putrescentiae* (TP), and *Lepidoglyphus destructor* (LD) was studied in 250 sera of patients with different degrees of sensitization to the house-dust mite *Dermatophagoides pteronyssinus* (DP) by measuring IgE binding to extracts of the storage mites. Additionally, allergenic cross-reactivity between DP and the storage mite species was studied by RAST inhibition with five individual sera (and a pool of these sera) with moderate IgE levels to all three storage mites and to DP. Increased serum IgE to storage mites was found in 46% of the 200 patients sensitized to DP.

Increased prevalence rates of IgE titers to storage mites were associated with higher IgE levels to DP. In 50 sera without sensitization to DP, only five sera showed increased IgE to one of the storage mites. Extracts of TP almost completely inhibited the IgE binding to AS, and vice versa. DP inhibited IgE binding to all storage mites up to 60%, whereas IgE binding to DP was only minimally inhibited by extracts of storage mites. In conclusion, cosensitization to storage mites is a frequent finding in patients sensitized to DP. Although this is largely the result of cross-reactivity between different mite species, it may nevertheless be of clinical significance in patients exposed to storage mites.

Key words: allergens; cross-reactivity; house-dust mite; IgE; sensitization; storage mite.

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In Europe, allergens of the house-dust mite *Dermatophagoides pteronyssinus* (DP) are the most important inducers of allergic reactions. Allergens from other mite genera, such as storage mites, are known sensitizers in occupational allergic diseases, as shown for farmers (1–3), bakers (4), and grain handlers (5, 6). Spijksma & Spijksma-Boezeman showed that storage mites were found in dust from houses in urban areas as well (8).

In recent years, evidence has accumulated that sensitization to storage mites frequently also occurs in urban populations (3, 7, 9), especially in regions with damp housing conditions (5, 10, 11). Some studies indicate that prevalence of sensitization to storage mites occurs predominantly in patients sensitized to allergens from house-dust mites (3, 5, 9). The question arises whether these findings are caused by cross-reactivity between common allergens of

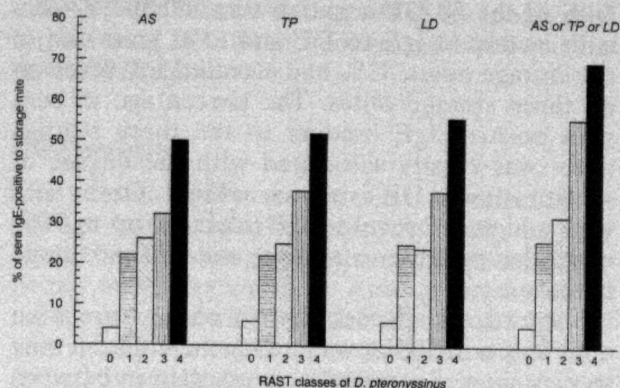


Fig. 1. Percentage of sera with increased IgE binding (>0.35 PRU/ml) to extracts of storage mites in relation to corresponding sensitization to *D. pteronyssinus* (RAST classes 0–4). AS: *A. siro*, TP: *T. putrescentiae*, LD: *L. destructor*.

both mite species or by simultaneous sensitization to the different mites (3, 9, 12, 13). We therefore studied the prevalence of IgE binding to allergenic extracts of the three storage mites *Acarus siro* (AS), *Tyrophagus putrescentiae* (TP), and *Lepidoglyphus destructor* (LD) in 250 sera of atopic patients with different concentrations of IgE antibodies to the house-dust mite DP, including sera without IgE to DP (RAST class 0). Additionally, we studied allergenic cross-reactivity by RAST inhibition.

Material and methods

Serum samples

Serum samples were collected from adult atopic patients visiting the outpatient department of allergology, who were routinely screened for IgE antibodies to the house-dust mite DP. For each of the five classes (0–4) defined according to the Phadezym RAST (Pharmacia Diagnostics AB, Uppsala, Sweden), 50 sera were selected.

Allergenic extracts of the house-dust mite and of storage mites

Biologically standardized, freeze-dried allergenic extracts of DP and the storage mites AS, TP, and LD were obtained from ALK-Benelux Groningen, The Netherlands. Extracts of the media used for culturing DP and the storage mites, respectively, were used as controls in RAST inhibition.

Measurement of mite-specific IgE antibodies

IgE binding to the different mite extracts was measured by Phadezym RAST. Paper disks were activated by cyanogen bromide (CNBr), as described by Ceska & Lundkvist (14). The mite

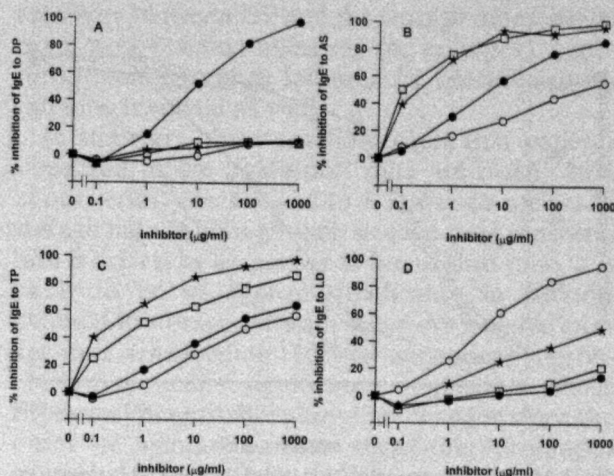


Fig. 2. Assessment by RAST inhibition of allergenic cross-reactivity by preincubating pool serum with increasing concentrations of allergenic extracts of *D. pteronyssinus* (●), *A. siro* (□), *T. putrescentiae* (★), and *L. destructor* (○). Inhibitions were performed in duplicate, and mean values are shown. CV of duplicate values was less than 6%. A) Inhibition of IgE binding to DP, B) inhibition of IgE binding to AS, C) inhibition of IgE binding to TP, D) inhibition of IgE binding to LD.

Table 1. Spearman rank correlation coefficients of IgE levels against four mite species. In each analysis, sera were included which had positive IgE level (>0.35 PRU) to at least one of two corresponding mites. DP = *D. pteronyssinus*; AS = *A. siro*; TP = *T. putrescentiae*; LD = *L. destructor*

	DP	AS	TP	LD
DP	—	0.187*	0.166*	0.248*
AS		—	0.742**	0.001
TP			—	0.081
LD				—

* $P < 0.05$; ** $P < 0.001$.

extracts were coupled to the CNBr-activated disks in optimal concentrations, as described by Karr et al. (15). For AS and TP, optimal binding to CNBr-activated disks was obtained with 0.01 mg dry weight extract/ml coupling solution, with 10 disks per 2.5 ml solution. For DP and LD, the optimal concentration was 1 mg/ml.

RAST-inhibition analyses of cross-reacting allergens

The degree of allergenic cross-reactivity between the different mite extracts was studied by RAST inhibition, as described by Karr et al., with sera with moderate levels of IgE antibodies to all four mite extracts (15). Briefly, five sera with moderate levels of IgE antibodies to all four mite extracts were incubated for 2 h at room temperature with increasing concentrations of the different mite

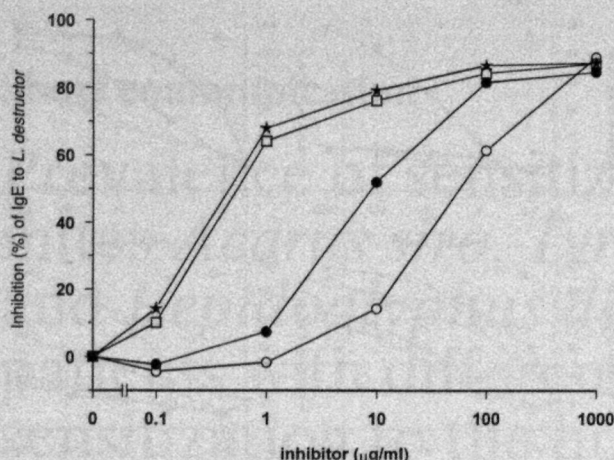


Fig. 3. Measurement of inhibition of IgE binding to *L. destructor* by preincubating serum of patient H, with increasing concentrations of allergenic extracts of *D. pteronyssinus* (●), *A. siro* (□), *T. putrescentiae* (★), and *L. destructor* (○). Serum of patient H. contained moderate concentration of IgE to LD (8 PRU/ml) and high levels of IgE to DP (648 PRU/ml), AS (161 PRU/ml), and TP (125 PRU/ml).

extracts. Incubations were performed in duplicate. In addition to the five sera, a pool serum, prepared by mixing equal volumes of the five individual sera, was also used in the inhibition experiments. Sera were always diluted such that the optical density at A_{420} nm was approximately 1.0 when preincubated with buffer instead of mite allergen (0% inhibition). After the preincubation step, the remaining concentration of free IgE antibodies to the relevant mite was determined by the standard Phadezym RAST.

Statistical analysis

Statistical analysis was performed with the SPSS package for PCs (SPSS, Inc., Chicago, USA). Antigenic relationships between the four different mite species (three storage mites and DP) were studied by Spearman rank order analyses of RAST results. Correlation analysis was performed with those sera which had a positive RAST to at least one of the mites investigated. Differences with $P < 0.05$ were considered to be significant.

Results

Influence of sensitization to DP on sensitization to storage mites

It appeared that 46% of the sera positive to DP ($n=200$) were also positive to at least one of the storage mites. Increased IgE to one of the storage mites without sensitization to DP occurred in

10% of the 50 DP-negative sera. Of the 92 sera with increased IgE to DP and to at least one of the storage mites, 43% had elevated IgE levels to all three storage mites. The percentage of sera with positive IgE binding to the three storage mites was clearly associated with the degree of sensitization to DP, as shown in Fig. 1. Of the sera with a high IgE level to DP (class 4), up to 70% were also positive to at least one of the storage mites.

Spearman rank order analysis of the correlation of mite-specific IgE levels among the different mite species showed a remarkable association between AS and TP, as shown in Table 1. The combination of AS with LD or TP with LD did not show any relationship. The IgE titer to DP correlated in a limited but statistically significant way with IgE titers to AS, TP, and LD.

Allergenic cross-reactivity among the four mite species

The observed relationship of IgE binding between AS and TP was additionally investigated by RAST inhibition using a pool serum of five sera with moderate IgE titers against AS, TP, and LD and with high levels of IgE against DP (AS: 28, TP: 30, LD: 79, and DP: 336 PRU/ml). The RAST to DP was minimally inhibited by preincubation of the pool serum with increasing amounts of extracts of the three storage mites, whereas inhibition with the homologous allergen (DP) completely inhibited the RAST to DP, as shown in Fig. 2A. The RAST to AS was inhibited by TP as well as by AS itself (Fig. 2B), and inhibition of TP by AS approached the inhibition by TP itself (Fig. 2C). Although the storage mites did not inhibit the IgE RAST to DP (Fig. 2A), DP, in high concentrations, inhibited the RAST to AS and TP by up to 80%. However, the concentration of DP necessary to inhibit 50% of the RAST to AS or TP was 200–300 times greater than the inhibition by the homologous extract. The inhibitions with five individual sera showed a similar pattern to that found with the pool serum, except for one serum demonstrating a remarkable inhibition of the RAST to LD: preincubation of this serum with increasing concentrations of the different mite extracts showed a stronger inhibition with the heterologous allergens (AS, TP, and DP) than with the homologous allergen LD (Fig. 3). The relatively low level of LD-specific IgE in this serum (possibly associated with IgE production to relatively few epitopes on LD allergens with low-affinity characteristics) may be responsible for the unusual RAST-inhibition pattern observed.

RAST inhibition with extracts of the media used for culturing DP and the storage mites showed less than 10% inhibition.

Discussion

The present study showed that sensitization to storage mites in the northern part of The Netherlands occurs predominantly in patients sensitized to *D. pteronyssinus*. Among patients sensitized to storage mites, sensitization to AS and TP was clearly associated. This association was confirmed by a high degree of allergenic cross-reactivity between AS and TP, as was shown by RAST inhibition. Although IgE binding to DP was not inhibited by allergenic extracts of the storage mites, DP could inhibit IgE binding to AS, TP, and LD by up to 80% (Fig. 2). In The Netherlands, sensitization to the house-dust mite DP is the most important cause of allergic reactions due to airborne allergens (16). Until a few years ago, information about allergic reactions to other mite species (such as storage mites) was limited to occupational allergic reactions, as in farmers (1, 2, 14, 17) and bakers (4), who are known to be frequently exposed to high levels of allergens from storage mites (17–20). In recent years, evidence has accumulated that sensitization to storage mites may also commonly occur in urban areas (3, 7, 9), in accordance with the early report of Spieksma & Spieksma-Boezeman that storage mites are regularly observed in house dust (8). In general, there are fewer storage mites than DP in house-dust samples. In damp homes, however, the number of storage mites may exceed that of house-dust mites (3, 7–9, 11, 12).

In our study, using sera (and the corresponding pool serum) with moderate levels of IgE antibodies to all four mites investigated, we found the highest allergenic cross-reactivity between the two storage mites AS and TP (Fig. 2A and B), in agreement with the close biologic relationship between these two species (21). Less cross-reactivity was found between LD and the other mites, although LD could still inhibit IgE binding to AS and TP by up to 50%. The study of allergenic cross-reactivity among extracts of different mite species is complex because the results are strongly dependent on the characteristics of the allergenic extracts and, more importantly, on the sera used for RAST-inhibition experiments (patient sera, monoclonal antibodies). This may explain why some studies did not show allergenic cross-reactivity between DP and storage mites (12, 13) whereas others revealed a remarkable allergenic identity among these mites (3, 9, 22, 23). Our results suggest that sensitization to storage mites may partly be explained by allergenic cross-

reactivity between DP and the storage mites. Aside from cross-reacting allergens (or epitopes), exposure to storage mites followed by specific sensitization is involved as well.

In summary, these results suggest that patients sensitized to the house-dust mite are often (46% in our series) cosensitized to at least one species of storage mite. Although such storage-mite sensitization is driven by responses to house-dust mite, it is likely to be of clinical significance in patients exposed to storage-mite allergens. An isolated storage-mite sensitization (10% in our series) is probably of particular significance in patients whose exposure circumstances have not changed since the onset of symptoms, thus suggesting prolonged exposure to storage-mite allergens. For the interpretation of the clinical relevance of the observed allergenic cross-reactivity and mite-specific responses, more information is needed about natural exposure to allergens of storage mites in different populations and corresponding IgE-sensitization patterns.

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