

Clinical and immunologic aspects of storage mite allergy

van Hage-Hamsten M, Johansson E. Clinical and immunologic aspects of storage mite allergy.
Allergy 1998; 53 (Suppl 48): 49–53. © Munksgaard 1998.

M. van Hage-Hamsten, E. Johansson

Department of Clinical Immunology, Karolinska
Hospital, Stockholm, Sweden

Exposure to storage (nonpyroglyphid) mites has been increasingly recognized as a cause of asthma and rhinitis. Several species have been identified in Europe: e.g., *Lepidoglyphus destructor*, *Acarus farris/siro*, *Tyrophagus* spp., *Glycyphagus domesticus*, and *Blomia tjobodas*. *Blomia tropicalis*, on the other hand, predominates in subtropical and tropical areas. Studies from several countries have shown that IgE-mediated allergy in rural populations is of considerable importance and that storage mites are major allergens. Since these mites are found in homes, especially in regions with damp housing conditions, urban populations are at risk of becoming sensitized. Therefore, sensitization is not restricted only to those with occupational exposure. Several major allergens from storage mites have been identified and characterized. There seems to be a limited allergenic cross-reactivity between storage- and house dust mites. Molecular cloning has demonstrated that the Group 2 allergens from storage mites (Lep d 2 and Tyr p 2) show more than 40% sequence identity with the Group 2 allergens from *Dermatophagoides* spp. The availability of a large number of recombinant dust mite allergens will make it possible to investigate their homology and the number of allergens required for the diagnosis and treatment of storage mite allergy.

Key words: allergens; allergy; storage mites

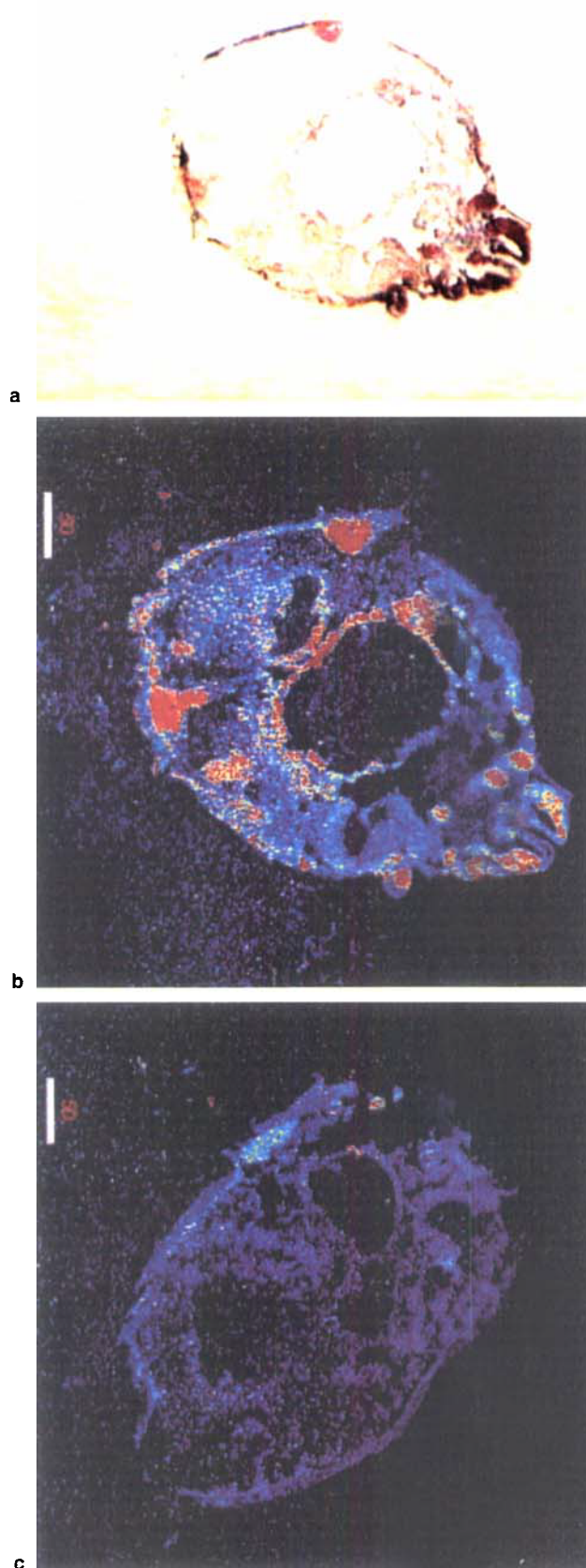
Marianne van Hage-Hamsten
Department of Clinical Immunology
Karolinska Hospital
S-171 76 Stockholm
Sweden
Tel: +46 8 51 77 59 42
Fax: +46 8 335 724
E-mail: marianne.van.hage-hamsten@mb.ks.se

Asthma and other respiratory diseases caused by sensitization to mites are a problem throughout the world (1). These mites belong predominantly to the Pyroglyphidae family, but the nonpyroglyphid mites, or storage mites, are also of clinical importance. Since the nonpyroglyphid mite species are found in both temperate and subtropical climates, a large number of individuals are exposed. Several species have been identified in the rural environment in Europe: e.g., *Lepidoglyphus destructor*, *Acarus farris/siro*, *Tyrophagus* spp., *Glycyphagus domesticus*, and *Blomia tjobodas* (2–4). We have characterized the mite fauna in barn dust from 30 farms on the Swedish island of Gotland. All samples contained mites; however, densities varied from 660 to 200 500 specimens/g dust. *L. destructor* was found on all farms and was the predominant species in nearly all samples. *Tyrophagus* spp., *Acarus siro*-complex, and *Glycyphagus* were also present in high numbers (3). In a case control study of Wisconsin (USA) farmers to assess the role of antibodies to a panel of antigens, Marx et al. found that IgE antibodies to house dust-

and storage mites, especially *L. destructor*, were the most prevalent (5). *Blomia tropicalis* has a different geographic distribution and has been found mainly in the southern hemisphere (6, 7). Since storage mites have been found in house dust (2, 6–8), the term “domestic mites” has been proposed (9). However, an even better term would be “dust mites”, since they exist in dust related to both indoor and agricultural environments.

IgE-mediated sensitization

Earlier studies from Europe have shown that allergy to storage mites is of major importance as a cause of bronchial asthma and/or allergic rhinitis in rural settings (10–13). Interestingly, these allergens are more significant among the rural population than allergens from pollens and animal danders (14). In an epidemiologic 12-year follow-up study in 1996 among farmers on the island of Gotland in the Baltic Sea, we have shown that they developed significantly more respiratory symptoms that were severe, and that storage mites remain



predominant allergens with a prevalence of positive RAST to storage mites of 8.1% (15).

Storage mites have for many years been found in European homes. In recent years, there has been an increasing interest in studying an IgE-mediated response to storage mites, and there is now evidence of sensitization to storage mites in urban populations (13, 16, 17), especially in regions with damp housing conditions (18). Systemic anaphylaxis following consumption of storage-mite-infested food has recently been reported (19). Taken together, these data suggest a wider clinical importance of storage mites as a cause of allergies than previously recognized.

Characterization of storage mite allergens

Allergen characterization is required for understanding the mechanisms of allergic disease. Molecular cloning has led to identification and sequencing of dust mite allergens, as well as production of recombinant allergens. An important clinical issue is whether the dual immune response to pyroglyphid and nonpyroglyphid mites depends on multiple sensitization to unique species-specific allergens or to cross-reacting allergens. Results from recent studies of allergenic cross-reactivity between different mite species indicate that closely related species cross-react to a higher degree than unrelated species. One of the most common storage mites, *L. destructor*, has been studied in greater detail. By an immunoblot-inhibition technique, we have demonstrated that *L. destructor* shares at least one allergenic determinant with *Dermatophagoides pteronyssinus*. The IgE antibodies to the 25-kDa allergen component in *D. pteronyssinus* were inhibited to the same degree by extracts of *D. pteronyssinus* and *L. destructor*. Der p 2 was also inhibited, but to a lesser degree (20). We obtained a limited amount of allergenic cross-reactivity between Lep d 1 (now designated Lep d 2), the major allergen of *L. destructor*, and *D. pteronyssinus*, a fact which

Fig. 1. *L. destructor* mite bodies express 15-kDa allergen. Cryosections, 10 μ m thick, were probed with (a and b) mAb against Lep d 2 of *L. destructor* and stained by alkaline-antialkaline phosphatase (APAAP) complex method with chromogenic substrate Fast Red. Sections were counterstained with Mayer's hematoxylin. Specificity test comprised replacement with subclass-matched irrelevant mAb which showed negative staining (c). a) Section seen in ordinary light microscope ($\times 150$); b) same section analyzed in CLSM. b and c) Extended focus projections. Intensity of staining in b and c is color-banded (range: red-yellow-green-blue-black, where red is strongest). Staining is widespread with localized parts in regions of mouth and gut. Size bar = 50 μ m. Photograph is published with permission of Blackwell Scientific Ltd. It originally appeared in *Clinical and Experimental Allergy* 1995;25:536-42.

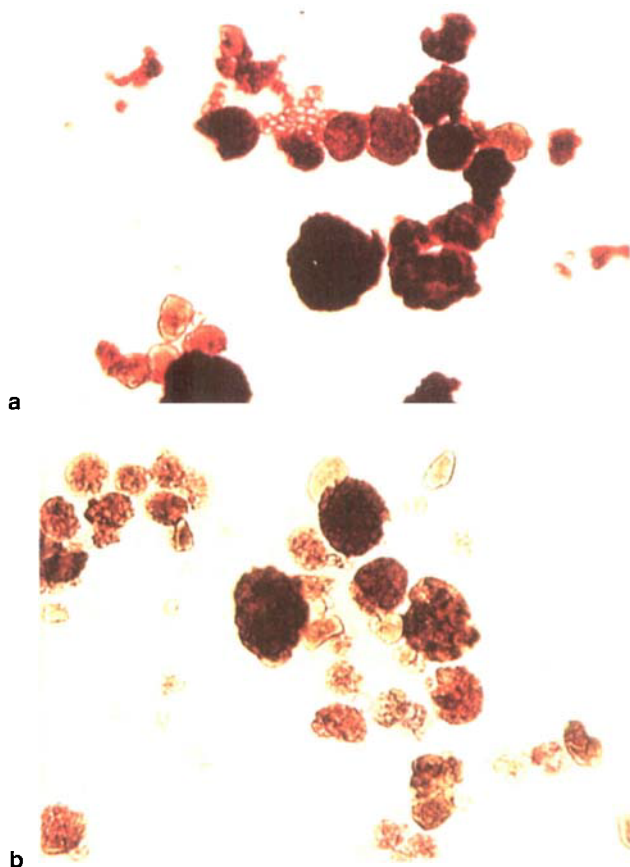


Fig. 2. Fecal pellets of *L. destructor* probed with (a) mAb against Lep d 2 of *L. destructor*; b shows replacement with subclass-matched irrelevant mAb. Pellets were stained by APAAP method with chromogenic substrate Fast Red. Note red positive staining (a), and that unstained fecal pellets (b) are brownish. Magnification $\times 370$ in ordinary light microscope. Photograph is published with permission of Blackwell Scientific Ltd. It originally appeared in *Clinical and Experimental Allergy* 1995;25:536–42.

indicates that the majority of *L. destructor*-allergenic determinants are unique.

The major allergen Lep d 2 has been well characterized (21–23). We have recently reported the complete cDNA of Lep d 2 encoding two isoallergens (24). The B-cell epitopes of Lep d 2 have been investigated (25) and recombinant mutants have been produced (26). These allergens show more than 50% sequence identity with the Group 2 allergens of *Dermatophagoides* spp. Lep d 2 has been expressed (27), and the recombinant allergen has been evaluated in a skin prick test trial with promising results (data to be published). We have localized Lep d 2 of *L. destructor* with the use of an anti-Lep d 2 monoclonal antibody (mAb) and confocal laser scanning microscopy (CLSM) (28). Cryostat-cut sections of mite bodies and fecal pellets were probed with the mAb. The Lep d 2 allergen disclosed a widespread labeling of the mite

body, with the most intense area in the region of the mouth (Figs. 1a and b). The exoskeleton was left unlabeled. Some staining was also observed around the gastrointestinal tract, but whether its content is labeled cannot be determined, since the gut content was generally lost during staining. The mAb labeled most of the fecal pellets (Fig. 2). The study indicates that the allergen could be associated with the digestive tract, a fact which makes it reasonable to assume that it is an enzyme.

A number of studies have been performed on *Tyrophagus putrescentiae* allergens. Arlian et al. have demonstrated 20 antigens and five allergens from this mite species by means of CIE and CRIE (29). By SDS-PAGE and immunoblotting, we have previously identified four allergens from *T. putrescentiae* (16–33 kDa) (30). A major allergen, the 16-kDa component, was recognized by about 80% of sera RAST positive to this mite species. As regards the allergenicity of *T. putrescentiae*, we have found that this mite species seems to be more closely related to *L. destructor* than to *A. siro* (30). This suggests that besides *L. destructor*, *A. siro* should be included in the storage mite panel of *in vivo*, as well as *in vitro*, tests. One has to keep in mind that results regarding allergenic cross-reactivity are dependent on several variables, such as the properties of the allergen extracts and the sera used; i.e., the principal mite species in the environment giving rise to sensitization. Future studies using molecular biology techniques will elucidate the question regarding similarity between different dust mite allergens and the number of allergens required for the diagnosis and treatment of storage mite allergy.

We have recently described the complete cDNA sequence encoding Tyr p 2, a major allergen of *T. putrescentiae*, which shows more than 50% identity with Lep d 2 but less with the Group 2 allergens from *Dermatophagoides* spp. (about 40%) (31). Molecular cloning has also identified allergens from *B. tropicalis*. A major *B. tropicalis* allergen, Blo t 5, shows 40% amino acid sequence homology with Der p 5 (32). The prevalence of IgE antibodies to this allergen is 60–70% in patients from tropical countries. Cross-reactivity between *L. destructor* and *B. tropicalis* was recently demonstrated by immunoblotting techniques using mite extracts and recombinant Lep d 2 (33). The results suggest that a *B. tropicalis* allergen of approximately 15 kDa is antigenically cross-reactive with the recombinant *L. destructor* allergen, Lep d 2.

Method for detection of storage mite allergens

We have developed an inhibition ELISA for detection of storage mite allergens in farming

environments. In addition to *L. destructor*, other dust mites such as *G. domesticus*, *A. siro*, and *T. putrescentiae* are detected by the mAb used in the assay (34).

Conclusion

Nowadays, there should be an increased awareness of the possibility of sensitization and allergic reactions to storage mites in both urban populations and those with occupational histories of exposure to these mite species. However, more studies are needed to establish their clinical importance. Several major allergens from storage mites have been identified, cloned, and sequenced. Knowledge of the immune response to dust mite allergens presents an opportunity to develop more rational strategies for the immunotherapy of allergic diseases. Several new approaches are soon to be investigated.

Acknowledgments

Financial support for this study was received from the Swedish Council for Work Life Research, the Swedish Foundation for Health Care Sciences and Allergy Research, the Swedish Asthma and Allergy Association, the Swedish Society of Medicine, the Hesselman Foundation, the Konsul Th. C. Bergh Foundation, and the Karolinska Institute.

References

- Platts-Mills TAE, de Weck AL. Dust mite allergens and asthma. A world wide problem. *J Allergy Clin Immunol* 1989;**43**:416–27.
- Iversen M, Korsgaard J, Hallas T, Dahl R. Mite allergy and exposure to storage mites and house dust mites in farmers. *Clin Exp Allergy* 1990;**20**:211–19.
- Boström S, Johansson E, Härfast B, et al. Characterization of the mite fauna (Acari) in Swedish barn dust. *Int J Acarol* 1997;**23**:127–32.
- Franz J-TH, Masuch G, Müsken H, Bergmann K-CH. Untersuchungen zur Vorratsmilbenfauna von Bauernhöfen in Nordrhein-Westfalen: Ostwestfalen. *Allergologie* 1995;**18**:25–30.
- Marx JJ, Twigg JT, Ault BJ, Merchant JA, Fernández-Caldas E. Inhaled aeroallergen and storage mite reactivity in a Wisconsin farmer nested case-control study. *Am Rev Respir Dis* 1993;**147**:354–8.
- Hurtado I, Parini M. House dust mites in Caracas, Venezuela. *Ann Allergy* 1987;**59**:128–30.
- Fernández-Caldas E, Fox RW, Bucholtz GA, et al. House dust mite allergy in Florida. Mite survey in households of mite-sensitive individuals in Tampa, FL. *Allergy Proc* 1990;**11**:263–7.
- Spieksma FTHM, Spieksma-Boezeman MIA. The mite fauna of house dust with particular reference to the house-dust mite *Dermatophagoides pteronyssinus*. *Acarologia* 1967;**9**:226–41.
- Platts-Mills TAE, Thomas WR, Aalberse RC, et al. Dust mite allergens and asthma: report of a second international workshop. *J Allergy Clin Immunol* 1992;**89**:1046–60.
- van Hage-Hamsten M, Johansson SGO, Höglund S, Tüll P, Wirén A, Zetterström O. Storage mite allergy is common in a farming population. *Clin Allergy* 1985;**15**:555–64.
- Cuthbert OD, Brostoff J, Wraith D, Brighton W. "Barn allergy", asthma and rhinitis due to storage mites. *Clin Allergy* 1979;**9**:229–36.
- Alvarez MJ, Tabar AI, Quirce S, et al. Diversity of allergens causing occupational asthma among cereal workers as demonstrated by exposure procedures. *Clin Exp Allergy* 1996;**26**:147–53.
- Ebner C, Feldner H, Ebner H, Kraft D. Sensitization to storage mites in house dust mite (*Dermatophagoides pteronyssinus*) allergic patients. Comparison of a rural and an urban population. *Clin Exp Allergy* 1994;**24**:347–52.
- van Hage-Hamsten M, Johansson SGO, Zetterström O. Predominance of mite allergy over allergy to pollens and animal danders in a farming population. *Clin Allergy* 1987;**17**:417–23.
- Kronqvist M, Johansson E, Pershagen P, Johansson SGO, van Hage-Hamsten M. Increasing prevalence of asthma over 12 years among farmers on Gotland: storage mites remain dominant allergens. *Clin Exp Allergy* 1999;**29**:35–44.
- Luczynska C, Griffin R, 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;**2**:403–6.
- van Hage-Hamsten M, Machado L, Barros MT, Johansson SGO. Comparison of clinical significance and allergenic cross-reactivity of the storage mites *Blomia kulagini* and *Lepidoglyphus destructor* in Sweden and Brazil. *Allergy* 1990;**45**:409–17.
- Iversen M, Dahl R. Allergy to storage mites in asthmatic patients and its relation to damp housing conditions. *Allergy* 1990;**45**:81–5.
- Matsumoto T, Hisano T, Hamaguchi M, Miike T. Systemic anaphylaxis after eating storage-mite-contaminated food. *Int Arch Allergy Immunol* 1996;**109**:197–200.
- Johansson E, Borgå Å, Johansson SGO, van Hage-Hamsten M. Immunoblot multi-allergen inhibition studies of allergenic cross-reactivity of the dust mites *Lepidoglyphus destructor* and *Dermatophagoides pteronyssinus*. *Clin Exp Allergy* 1991;**21**:511–18.
- van Hage-Hamsten M, Bergman T, Johansson E, et al. N-terminal amino acid sequence of principal allergen of storage mite *Lepidoglyphus destructor*. *Lancet* 1992;**340**:614.
- Ventas P, Carreira J, Polo F. Purification and characterization of *Lep d 1*, a major allergen from the mite *Lepidoglyphus destructor*. *Clin Exp Allergy* 1992;**22**:454–60.
- Varela J, Ventas P, Carreira J, Barbas JA, Gimenez-Gallego G, Polo F. Primary structure of *Lep d 1*, the main *Lepidoglyphus destructor* allergen. *Eur J Biochem* 1994;**225**:93–8.
- Schmidt M, Olsson S, van der Ploeg I, van Hage-Hamsten M. cDNA analysis of the mite allergen *Lep d 1* identifies two different isoallergens and variants. *FEBS Lett* 1995;**370**:11–14.
- Elfman LHM, Whitley P, Schmidt M, van Hage-Hamsten M. IgE binding capacity of synthetic and recombinant peptides of the major storage mite (*Lepidoglyphus destructor*) allergen, *Lep d 2*. *Int Arch Allergy Immunol* 1998;**117**:167–73.
- Olsson S, van Hage-Hamsten M, Whitley P. Contribution of disulphide bonds to antigenicity of *Lep d 2*, the major

- allergen of the dust mite (*Lepidoglyphus destructor*). Mol Immunol 1998;in press.
27. Olsson S, van Hage-Hamsten M, Whitley P, Hoffman DR, Johansson E, Schmidt M. Expression of two isoforms of Lep d 2, the major allergen of *Lepidoglyphus destructor*, in both prokaryotic and eukaryotic systems. Clin Exp Allergy 1998;**28**:984–91.
28. van Hage-Hamsten M, Olsson S, Emilson A, Härfast B, Svensson A, Scheynius A. Localization of major allergens in the dust mite *Lepidoglyphus destructor* with confocal laser scanning microscopy. Clin Exp Allergy 1995;**25**:536–42.
29. Arlian LG, Geis DP, Vyszynski-Moher DL, Bernstein IL, Gallagher JS. Antigenic and allergenic properties of the storage mite *Tyrophagus putrescentiae*. J Allergy Clin Immunol 1984;**74**:166–71.
30. Johansson E, Johansson SGO, van Hage-Hamsten M. Allergenic characterization of *Acarus siro* and *Tyrophagus putrescentiae* and their cross-reactivity with *Lepidoglyphus destructor* and *Dermatophagoides pteronyssinus*. Clin Exp Allergy 1994;**24**:743–51.
31. Eriksson T, Johansson E, Whitley P, Schmidt M, Elsayed S, van Hage-Hamsten M. Cloning and characterization of a Group II allergen from the dust mite *Tyrophagus putrescentiae*. Eur J Biochem 1998;**251**:443–7.
32. Arruda LK, Vailes LD, Platts-Mills TAE, et al. Sensitization to *Blomia tropicalis* in patients with asthma and identification of allergen Blo t 5. Am J Respir Crit Care Med 1997;**155**:343–50.
33. Johansson E, Schmidt M, Johansson SGO, Machado L, Olsson S, van Hage-Hamsten M. Allergenic cross-reactivity between *Lepidoglyphus destructor* and *Blomia tropicalis*. Clin Exp Allergy 1997;**27**:691–9.
34. Härfast B, Johansson E, Johansson SGO, van Hage-Hamsten M. ELISA method for detection of mite allergens in barn dust. Allergy 1996;**51**:257–61.