

Allergen-avoidance measures in homes of house-dust-mite-allergic asthmatic patients: effects of acaricides and mattress encasings

van der Heide S, Kauffman HF, Dubois AEJ, de Monchy JGR. Allergen-avoidance measures in homes of house-dust-mite-allergic asthmatic patients: effects of acaricides and mattress encasings. Allergy 1997; 52: 921–927. © Munksgaard 1997.

This double-blind, placebo-controlled study investigated whether the application of an acaricide (Acarosan®) on mattresses and on textile floor coverings in living rooms and bedrooms can contribute to improvement in lung function and airway hyperresponsiveness in 40 adult asthmatic patients sensitized to house-dust mite. In a second group of 19 patients who refused chemical intervention, the clinical effects of application of allergen-impermeable mattress encasings were studied. In all three treatment groups, Der p 1 levels in mattress dust were statistically significantly decreased after 12 months. However, this decrease was much greater in the group who received mattress encasings (final mean level 430 ng/g) than in groups with acaricide- or placebo-treated mattresses (final mean levels 1730 and 2100 ng/g, respectively). Treatment of textile floors with either Acarosan or placebo chemical caused a statistically significant decrease in the level of the house-dust-mite allergen Der p 1 in floor dust. In the group with mattress encasings, no significant changes of floor dust Der p 1 were found. Airway hyperresponsiveness (as measured by the PC₂₀ histamine) improved significantly in the mattress cover group after 6 months. The Acarosan group also showed a small but statistically significant improvement after 12 months.

**S. van der Heide, H. F. Kauffman,
A. E. J. Dubois, J. G. R. de Monchy**

Department of Allergology, Division of Internal
Medicine, University Hospital, Groningen,
The Netherlands

Key words: acaricides; airway
hyperresponsiveness; allergen avoidance;
asthma; house-dust mites; mattress encasings.

Sicco van der Heide
Department of Allergology
Division of Internal Medicine
University Hospital Groningen
Hanzeplein 1
9713 GZ Groningen
The Netherlands

Accepted for publication 29 April 1997

Exposure to indoor allergens is an important cause of allergic reactions in sensitized asthmatic patients (1, 2). A significant reduction of indoor allergen exposure may lead to improvement in the clinical symptoms of these patients (3–5). As a means to reduce exposure to indoor allergens, several allergen-avoidance measures have been developed in recent years, including allergen-impermeable mattress encasings, smooth (nontextile-covered) floors, application of acaricides (agents capable of killing house-dust mites [HDM]), increased air ventilation, and reduction of indoor humidity (5–7). However, the clinical relevance of the different interventions is not always clear (1). Clinical improvements after application of acaricides in the homes of HDM-allergic patients have been modest or absent (8–12). Although the application of allergen-impermeable mattress encasings seems more effective in reducing the exposure to HDM allergens than the use of acaricides (12–15), the observed improvements

in clinical parameters are still moderate (9, 11, 12) and short-lived (11).

This study investigated the effects of application of an acaricide (Acarosan®) on mattresses and textile floor coverings in the homes of asthmatic patients sensitized to HDM. Allergen levels in floor dust and mattress dust were measured, and pulmonary and immunologic parameters were studied in these patients. In a second group of patients who refused chemical intervention in their homes, the clinical efficacy of the application of allergen-impermeable mattress encasings was studied.

Material and methods

Patients

Fifty-nine patients with a history of asthma and nonspecific airway hyperreactivity were selected

from the outpatient clinics of allergology and pulmonology. All patients were sensitized to HDM (*Dermatophagoides pteronyssinus*). Sensitization to other airborne allergens (tree pollen, grass pollen, and cat and dog dander) was also recorded. All patients showed nonspecific airway hyperresponsiveness, as measured by a histamine threshold of ≤ 32 mg/ml, by the 30-s inhalation procedure (16). All patients gave their written informed consent, and the study was approved by the medical ethical committee of University Hospital Groningen.

Study protocol

The effects of applying Acarosan (benzyl benzoate plus detergent) on mattresses and textile floor coverings were studied in a double-blinded, placebo-controlled manner (the Acaricide⁺ group indicating those receiving Acarosan and the Acaricide⁻ group indicating those receiving the placebo chemical). Patients who refused to participate in this study were offered allergen-impermeable mattress and pillow encasings (Mattress-encasing group). The patients visited the outpatient clinic for spirometry and determination of airway hyperresponsiveness (PC₂₀ histamine) before and 6 and 12 months after the intervention. Venous blood was also collected for measurement of total serum IgE and eosinophil count. Before the interventions and after 3, 6, and 12 months, dust samples from floors (living room and bedroom) and from mattresses were collected by vacuum-cleaning.

Interventions

Textile floors were treated with Acarosan powder (Werner & Mertz, Mainz, Germany) or with the detergent Sapur[®] (Henkel BV, Nieuwegein, The Netherlands) according to the instructions of the manufacturers. Mattresses were treated with Acarosan foam or with the detergent Groupriem[®] (AFA BV, Meppel, The Netherlands). Both placebo treatments (Sapur and Groupriem) were chosen because of their resemblance to Acarosan. All chemical intervention materials were packaged and coded by an independent laboratory worker to prevent unblinding of the study. The chemical interventions were carried out at the start of the study and repeated after 6 months. Nontextile floors were not treated.

In the group of patients who refused chemical intervention, mattresses and pillows were encased with Intervent encasings (WL Gore & Associates, Surrey, UK) at the start of the study (Mattress encasing group).

No special cleaning instructions for floors or mattresses were given to the patients.

Collection and extraction of house dust

Before the interventions and after 3, 6, and 12 months, dust samples from floors of bedrooms and living rooms and mattresses were collected with a vacuum cleaner (Philips, The Netherlands; type T560, 1100 W, with a double-filtering system). The vacuum-cleaning of the floors after 6 months in the groups with chemical intervention was carried out at least 2 weeks after the second chemical intervention. The entire floor area was sampled and the dust from each room was collected in separate bags. After sieving (pore size 0.35 mm), the amount of fine dust was weighed, and a 10% (w/v) extract in 0.01 M NH₄HCO₃ buffer (pH=7.4) was obtained by overnight rotation at 4°C. Mattress dust was collected by vacuum-cleaning the whole mattress with a special filter device (ALK, Horsholm, Denmark). The encased mattresses were vacuum-cleaned with the mattress encasings *in situ*. Dust from mattresses was extracted without sieving. All extracts were centrifuged and the supernatants stored at -20°C until measurement of HDM allergen.

Detection of HDM allergens

HDM allergen Der p 1 was measured as described previously (17). Briefly, monoclonal antibodies to Der p 1 were bound to CNBr-activated paper disks. The dust extracts were incubated in an appropriate dilution with the antibody-coated disks for 2 h at room temperature. Afterward, the disks were incubated for 3 h with a pool serum which consisted of the sera of 25 HDM-allergic patients (RAST class ≥ 4). The amount of human IgE bound to the disk complex was then measured according to the instructions for the Phadezym RAST kit (Pharmacia Diagnostics, Uppsala, Sweden). A reference HDM extract, which was calibrated for content of Der p 1 with the WHO/IUIS *D. pteronyssinus* NIBSC 82/518 standard, was used in serial dilutions for calculation of the allergen content of the house-dust samples.

Spirometry and measurement of airway hyperresponsiveness

Lung function (FEV₁ and VC) was determined with a water-sealed spirometer. Nonspecific airway hyperresponsiveness was measured by stepwise inhalation of increasing concentrations of histamine solution for 30 s until a decrease in FEV₁ of 20% or more was observed (16). From the fall in FEV₁, the histamine concentration causing a 20% decrease in FEV₁ was calculated by linear interpolation (PC₂₀ histamine). All medication (except

inhaled steroids) was stopped before the tests: β -agonists and ipratropium bromide for 12 h, cromoglycate and antihistamines for 72 h. No patients received astemizole, oral steroids, or long-acting bronchodilators.

Skin testing and IgE measurements

Before inclusion in the study, patients underwent intracutaneous skin testing with a panel of common inhalant allergens (ALK-Benelux, Groningen, The Netherlands), as described previously (18). Aside from *D. pteronyssinus*, patients were tested with allergenic extracts from cat, dog, grass pollen, and tree pollen. The results of the skin tests were expressed in histamine equivalent wheal size (HEWS), which was calculated by dividing the wheal size obtained with the allergen extract by the wheal size of a standard histamine solution (19). A skin test with a HEWS of ≥ 0.7 was regarded as positive. At the start of the study, after 6 months, and after 12 months, serum total IgE was measured by Pharmacia IgE-EIA (Pharmacia Diagnostics, Sweden).

Statistics

Statistical analyses were performed with the SPSS software package for PC (SPSS Inc., Chicago, IL, USA). Before analysis, data of PC₂₀ histamine and allergen levels were log transformed to normalize distributions. Results of PC₂₀ histamine were expressed as ²log units because these reflect doubling doses. Differences were detected by Student's *t*-test. *P* values (two-tailed) less than 5% were considered statistically significant.

Results

Patient characteristics

Patient characteristics at the start of the study are summarized in Table 1.

Textile floor covering was less often present in the bedrooms of the Mattress encasing group. The other characteristics were similar for the three groups. The degree of allergic sensitization (percentage of patients with a positive skin test) to the main inhalant allergens (HDM, grass pollen, tree pollen, and domestic animals), was also comparable for the three patient groups.

Five patients were sensitized to HDM allergens only. The other patients were multiply sensitized. Most patients (75%) used inhaled steroids for maintenance therapy (Table 1), and this medication did not change during the study.

Of the 59 patients, 36 were not exposed to tobacco smoke in their homes, 13 were exposed to tobacco smoke only from coresidents, and 10 themselves smoked.

Effects of allergen-avoidance measures on Der p 1 levels in mattress dust

At the start of the study, the concentrations of Der p 1 in mattress dust were comparable in the groups in which the mattresses were treated with Acarosan (Acaricide⁺) or placebo detergent (Acaricide⁻), as shown in Fig. 1. In the Mattress encasing group, the Der p 1 concentration in mattress dust before the intervention was significantly lower than in the other two groups. Despite this lower initial Der p 1 concentration, the greatest decrease of Der p 1 in mattress dust was found after application of mattress encasings. Treatment of mattresses with chemicals (Acaricide⁺ and Acaricide⁻) also showed a statistically significant reduction of Der p 1. For the placebo treatment, this reduction became significant only after the second application of the detergent (Acaricide⁻, after 6 months). Although the Der p 1 concentration in mattress dust showed a statistically significant decrease in both groups with chemical intervention (Acaricide⁺ and Acaricide⁻), the Der p 1 concentration after 1 year was still about 2000 ng/g, while encasing the mattresses with

Table 1. Characteristics of three patient groups. Results are presented as means and SD (age, FEV₁, %pred) or as geometric means and 95% CI (PC₂₀ histamine, total IgE)

	Acaricide ⁺ (n=21)	Acaricide ⁻ (n=19)	Mattress encasing (n=19)
*Age (years)	31.5 (8.8)	30.1 (7.2)	32.3 (5.8)
*FEV ₁ %pred	88.7 (13.6)	89.4 (13.3)	92.4 (12.8)
*PC ₂₀ histamine (mg/ml)	1.97 (1.22–3.16)	2.23 (1.19–4.15)	3.87 (2.24–6.62)
*Serum total IgE (U/ml)	288 (187–454)	499 (251–998)	186 (100–351)
*Female (%)	66	47	68
*Patients (%) using inhalation steroids	81	79	74
*Smoke exposure (%)#	48	37	32
*Domestic animals (%)	43	58	58
Textile floor covering in bedrooms (%)	77	89	52

In parentheses: SD or 95% CI; #smoking by patients and/or their coresidents. **P*<0.05 compared with Acaricide⁺ and Acaricide⁻.

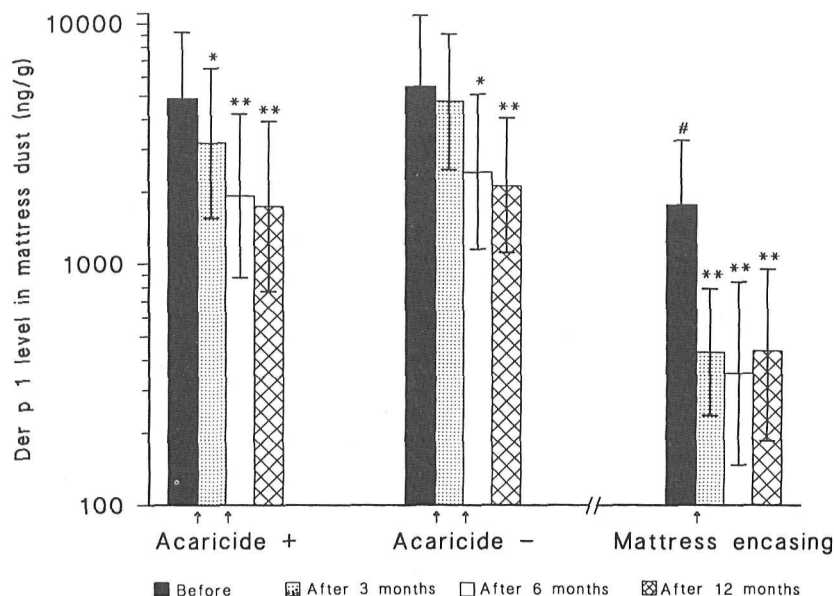


Fig. 1. Changes of Der p 1 levels in mattress dust after allergen-avoidance measures. Chemical intervention on mattresses with acaricide (Acaricide⁺) or placebo detergent (Acaricide⁻) was carried out at $t=0$ and $t=6$ months (see arrows). Mattress encasings were applied at $t=0$ months. * and **: $P<0.05$ and <0.01 , respectively, compared to before. # $P<0.05$ compared to both other groups.

special covers resulted in a reduction of Der p 1 to 200 ng/g.

Effects of allergen-avoidance measures on Der p 1 levels in floor dust

Der p 1 levels in floor dust decreased in the two groups in which the textile floor covering was treated with either Acaroson (Acaricide⁺) or with placebo detergent (Acaricide⁻), as shown in Fig. 2 (living rooms and bedrooms, respectively). In the Mattress encasing group (in which only mattress encasings were used), no significant changes of Der p 1 in floor dust were observed in living rooms and bedrooms. Before the interventions, the Mattress encasing group showed a trend to lower Der p 1 levels in floor dust in both living room and bedroom than in the chemically treated floors ($P<0.05$ with Acaricide⁻ in both rooms, $P=0.090$ with Acaricide⁺ in bedrooms). This was probably due to the lower percentage of textile floor covering in the mattress encasing group (Table 1). The non-significant trend to lower Der p 1 concentrations in floor dust in living rooms may have been due to a placebo effect: a change in cleaning pattern due to participation in a study.

Patients who used inhaled corticosteroids had significantly higher concentrations of Der p 1 in floor dust at the start of the study than patients not treated with inhaled steroids (living rooms: 1604 vs 482 ng/g, $P=0.012$; bedrooms: 1598 vs 687 ng/g, $P=0.037$).

Effects of allergen-avoidance measures on lung function and PC₂₀ histamine

Before and after the interventions, no significant changes in lung function (FEV₁ and VC) were found within or between the groups. Airway hyperresponsiveness, however, decreased significantly (higher PC₂₀ histamine) in the Acaricide⁺ group and in the Mattress encasing group (Fig. 3). A trend to improvement in airway hyperresponsiveness was found in the placebo chemical group Acaricide⁻ ($P=0.09$ at $t=12$ months). Although the Mattress encasing group started with less severe airway hyperresponsiveness (higher initial PC₂₀ histamine [before: $P=0.066$, compared with before value of the other groups]), a significant improvement was still found in this group after 6 and 12 months. However, the observed changes in PC₂₀ histamine were small (less than one doubling dose).

Changes in serum total IgE and skin reaction to HDM allergens

In all three groups, no statistically significant changes in serum total IgE were found. At the start of the study, however, the mattress encasing group had a significantly lower serum total IgE than the group with placebo chemical intervention (182 kU/l in the Mattress encasing group vs 501 kU/l in the Acaricide⁻ group, $P=0.046$). The lower IgE level in the Mattress encasing group fits with

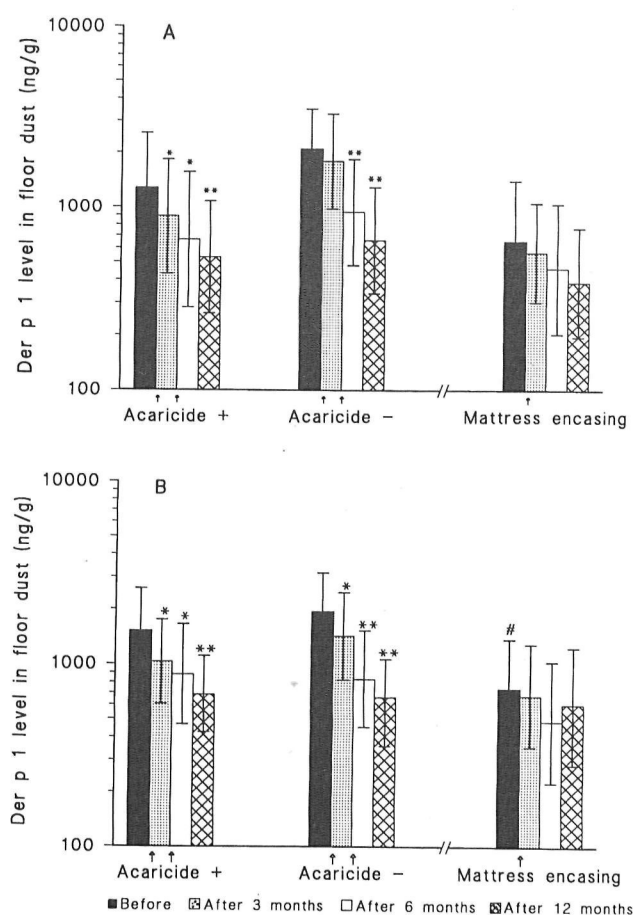


Fig. 2. Changes of Der p 1 levels in floor dust of living rooms (A) and bedrooms (B) after allergen-avoidance measures. Chemical intervention on textile floors with acaricide (Acaricide⁺) or placebo detergent (Acaricide⁻) was carried out at $t=0$ and $t=6$ months (see arrows). In mattress encasing group, floors were not treated (mattress encasings were applied at $t=0$ months). * and **: $P<0.05$ and <0.01 , respectively, compared to before. # $P<0.05$ with Acaricide⁻ (before).

the lower level of airway hyperresponsiveness in this group and lower exposure to HDM allergens.

In patients who used inhaled steroids, the serum total IgE concentration before the study was significantly higher than for patients without inhaled steroids (359 vs 162 kU/l, $P=0.049$).

During the study, the skin reaction to HDM allergens (as expressed in HEWS) did not change within or between the patient groups. However, as was also found for serum total IgE, the initial skin reaction to HDM allergens was significantly higher in patients using inhaled steroids than in patients without steroids (1.32 vs 1.19, $P=0.044$).

Discussion

Allergen-avoidance measures are often recommended for allergic asthmatic patients. In this study, which was partly double-blind and placebo-

controlled, it was shown that application of allergen-impermeable mattress encasings in bedrooms of HDM-allergic asthmatic patients did contribute to a statistically significant (small) improvement of airway hyperresponsiveness. In the group of patients for whom mattresses and textile floor coverings were treated with an acaricide, airway hyperresponsiveness also improved but to a lesser extent and only after two applications of the HDM killing agent (Fig. 3).

The use of acaricides in the struggle against exposure to HDM allergens is still controversial (20–22). In general, the observed clinical efficacy is low or absent. The application of the chemical is time-consuming and should be repeated 2–4 times a year. Furthermore, as was also found in the present study, the residual HDM-allergen levels in mattress dust after two applications of the acaricide were still substantial (about 2000 ng/g in the present study) (10, 22). Moreover, many patients refused chemical intervention in their homes. Therefore, the use of acaricides seems to be restricted to particular locations other than mattresses in which better exposure-reduction measures cannot be applied.

In most studies, the application of mattress encasings clearly showed a substantial decrease in exposure to HDM allergens from mattresses (9, 14, 15). However, in Sydney, Australia, where levels of HDM allergens in mattress dust are exceptionally high, the effects of application of mattress encasings on Der p 1 levels in mattress dust were limited and short-lived (11). Moreover, mattress encasings reduce exposure only to HDM allergens from mattresses, whereas exposure to HDM allergens in other locations is not influenced.

In the present study, the observed changes in airway hyperresponsiveness after intervention with mattress encasings were small (about one doubling dose or less) when compared with the 4.5-fold improvement found in a German study of similar allergen-avoidance measures (9). The latter studied asthmatic children sensitized to HDM who had high levels of Der p 1 allergen in their mattress dust. Information about their medication and allergen sensitization pattern was absent. In the present study, 78% of the adult patients used inhaled corticosteroids as maintenance therapy, and most patients (92%) were sensitized to several inhalant allergens other than HDM.

Patients with inhaled steroids were exposed to higher levels of HDM allergen Der p 1 in floor dust from living rooms and bedrooms and had a higher serum total IgE level and skin reaction to HDM allergens. These results suggest that patients with inhaled steroids were the more severe asthmatic patients with a higher level of allergenic

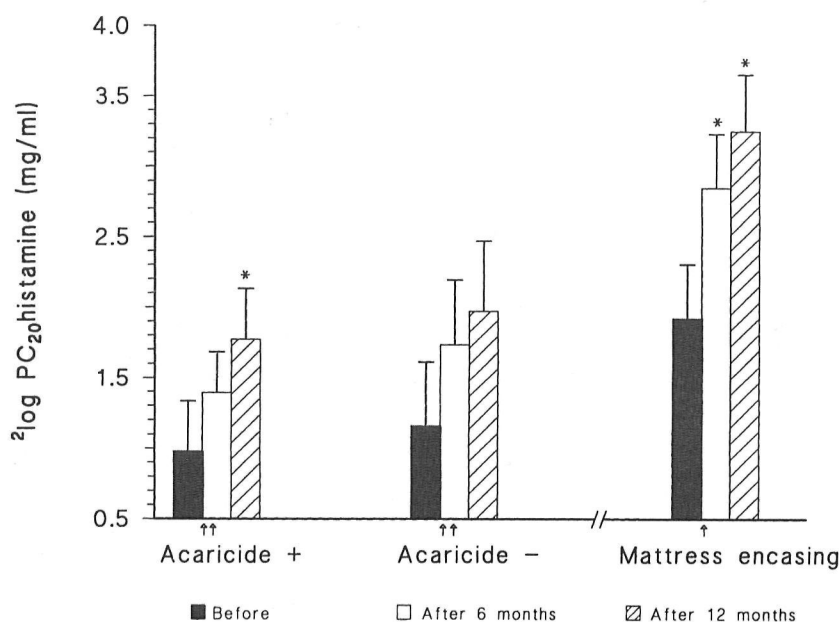


Fig. 3. Changes of airway hyperresponsiveness (PC_{20} histamine) after allergen-avoidance measures. Chemical intervention on textile floors and mattresses with acaricide (Acaricide⁺) or placebo detergent (Acaricide⁻) was carried out at $t=0$ and $t=6$ months (see arrows). Measurement of PC_{20} histamine after 6 months was performed after second intervention. In mattress encasing group, mattress encasings were applied at $t=0$ months. * and **: $P<0.05$ and <0.01 , respectively, compared to before.

sensitization. However, because of their steroid medication, their lung function and airway hyperresponsiveness were not different from those of patients without steroids. Furthermore, because of the improvement of airway hyperresponsiveness by the inhaled steroids, the scope for additional improvement by allergen-avoidance measures is limited.

The small improvement of airway hyperresponsiveness in the present study corresponds with the results of a recent study by Carswell et al. in which a large reduction of exposure to HDM allergens from mattresses by application of mattress encasings (and an acaricide) was accompanied by a moderate improvement of airway hyperresponsiveness in asthmatic children sensitized to HDM among other allergens (12). The relationship between reduction in HDM-allergen exposure and reduction in airway hyperresponsiveness was assessed by Marks et al., who found that a fivefold reduction of Der p 1 concentrations simultaneously in the bed, the bedroom floor, and the living-room floor, was needed for a 1.9-fold increase in PD_{20} histamine (24). A similar but weaker relationship was found by Custovic et al. (25). In the present study, the observed change in PC_{20} histamine in the group with mattress encasings was smaller, probably because only the mattresses were treated without affecting textile floors in living rooms and bedrooms. Sensitization to additional airborne allergens (other than HDM) and exposure to these allergens may be an important factor that interferes

with clinical improvements due to allergen-avoidance measures directed only against HDM.

Allergen-avoidance measures may play an important role in the treatment of allergic asthmatic patients (4, 26). Because allergic patients are often sensitized to HDM, many allergen-avoidance measures concentrate on reduction of exposure to these allergens (mattress encasings, acaricides). However, a considerable number of allergic patients are sensitized to multiple allergens. Therefore, a combination of allergen-avoidance measures which take into account the severity of the disease, the degree of sensitization of the patient to the different airborne allergens, and the local exposure to these allergens should be tailor-made to the individual allergic patient.

Acknowledgments

We thank Mrs Liesbeth Koese, Mrs Jose Duipmans, and Mrs Ellen Klammer for their skillful assistance in the collection of the dust samples and the performance of spirometry and measurement of PC_{20} histamine. The cell line for the monoclonal antibody to Der p 1 was kindly provided by Prof. Dr Rob Aalberse of the Allergy Division of the Dutch Central Laboratory of the Blood Transfusion Service (Amsterdam, The Netherlands). The calibration of a reference extract for the content of Der p 1 was also performed by this laboratory. We thank the Department of Pulmonology of our hospital for their cooperation with the selection of the patients. The collection of the data was carried out with the practical support of the Provinciale Groene Kruis (Groningen, The Netherlands). The study was financially supported by a grant from the Dutch Ministry of Welfare, Public Health, and Cultural Affairs.

References

1. Gelber LE, Seltzer LH, Bouzoukis JK, Pollart SM, Chapman MD, Platts-Mills TAE. Sensitization and exposure to indoor allergens as risk factors for asthma among patients presenting to hospital. *Am Rev Respir Dis* 1993;147:573-8.
2. Peat JK, Tovey E, Toelle BG, et al. House dust mite allergens. A major risk factor for childhood asthma in Australia. *Am J Respir Crit Care Med* 1996;153:141-6.
3. Kerrebijn KF. Endogenous factors in childhood CNSLD: methodological aspects in population studies. In: Orie NGM, van der Lende R, editors. *Bronchitis III. Proceedings of the Third International Symposium on Bronchitis, The Netherlands, 1969*. Assen: Royal Van Gorcum, 1970: 38-48.
4. 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.
5. Colloff MJ, Ayres J, Carswell F, et al. The control of allergens of dust mites and domestic pets: a position paper. *Clin Exp Allergy* 1992;22 Suppl 2:1-28.
6. Bessot JC, De Blay F, Pauli G. From allergen sources to reduction of allergen exposure. *Eur Respir J* 1994;7:392-7.
7. Chapman MD, Heymann PW, Sporik RB, Platts-Mills TAE. Monitoring allergen exposure in asthma: new treatment strategies. *Allergy* 1995;50 Suppl 25:29-33.
8. Kniest FM, Young E, van Praag MC, et al. Clinical evaluation of a double-blind dust-mite avoidance trial with mite-allergic rhinitic patients. *Clin Exp Allergy* 1991;21: 39-47.
9. Ehnert B, Lau-Schadendorf S, Weber A, Buettner P, Schou C, Wahn U. Reducing domestic exposure to dust mite allergen reduces bronchial hyperreactivity in sensitive children with asthma. *J Allergy Clin Immunol* 1992;90: 135-8.
10. Dietemann A, Bessot JC, Hoyet C, Ott M, Verot A, Pauli G. A double-blind, placebo controlled trial of solidified benzyl benzoate applied in dwellings of asthmatic patients sensitive to mites: clinical efficacy and effect on mite allergens. *J Allergy Clin Immunol* 1993;91:738-46.
11. Marks GB, Tovey ER, Green W, Shearer M, Salome CM, Woolcock AJ. House dust mite allergen avoidance: a randomized controlled trial of surface chemical treatment and encasement of bedding. *Clin Exp Allergy* 1994;24: 1078-83.
12. Carswell F, Birmingham K, Oliver J, Crewes A, Weeks J. The respiratory effects of reduction of mite allergen in the bedrooms of asthmatic children - a double-blind controlled trial. *Clin Exp Allergy* 1996;26:386-96.
13. Owen SJ, Morganstern M, Hepworth J, Woodcock AA. Control of house dust mite antigen in bedding. *Lancet* 1990;335:396-7.
14. Wickman M, Nordvall SL, Pershagen G, Korsgaard J, Johansen N, Sundell J. Mite allergens during 18 months of intervention. *Allergy* 1994;49:114-19.
15. Weeks J, Oliver J, Birmingham K, Crewes A, Carswell F. A combined approach to reduce mite allergen in the bedroom. *Clin Exp Allergy* 1995;25:1179-83.
16. de Vries K, Goei JT, Booij-Noord H, Orie NGM. Changes during 24 hours in lung function and histamine hyper-reactivity of the bronchial tree in asthmatic and chronic bronchitis patients. *Int Arch Allergy Appl Immunol* 1962; 20:93-101.
17. van der Heide S, De Monchy JGR, De Vries K, Bruggink TM, Kauffman HF. Seasonal variation in airway hyperresponsiveness and natural exposure to house dust mite allergens in patients with asthma. *J Allergy Clin Immunol* 1994;93:470-5.
18. Niemeijer NR, Goedewaagen B, Kauffman HF, De Monchy JGR. Optimization of skin testing. I. Choosing allergen concentrations and cutoff values by factorial design. *Allergy* 1993;48:491-7.
19. Brand PL, Kerstjens HA, Jansen HM, Kauffman HF, De Monchy JGR. Interpretation of skin tests to house dust mite and relationship to other allergy parameters in patients with asthma and chronic obstructive pulmonary disease [Dutch CNSLD Study Group]. *J Allergy Clin Immunol* 1993;91:560-70.
20. Ridout S, Twiselton R, Matthews S, et al. Acarosan and the Acarex test in the control of house dust mite allergens in the home. *Br J Clin Pract* 1993;47:141-4.
21. Kalra S, Crank P, Hepworth J, Pickering CA, Woodcock AA. Concentrations of the domestic house dust mite allergen Der p 1 after treatment with solidified benzyl benzoate (Acarosan) or liquid nitrogen. *Thorax* 1993;48:10-13.
22. Huss RW, Huss K, Squire EN Jr, et al. Mite allergen control with acaricide fails. *J Allergy Clin Immunol* 1994;94:27-32.
23. Manjra A, Berman D, Toerinn A, Weinberg EG, Potter PC. The effects of a single treatment of an acaricide, Acarosan, and a detergent, Metsan, on Der p 1 allergen levels in the carpets and mattresses of asthmatic children. *S Afr Med J* 1994;84:278-80.
24. Marks GB, Tovey ER, Green W, Shearer M. The effect of changes in house dust mite allergen exposure on the severity of asthma. *Clin Exp Allergy* 1995;25:114-18.
25. Custovic A, Taggart SC, Francis HC, Chapman MD, Woodcock A. Exposure to house dust mite allergens and the clinical activity of asthma. *J Allergy Clin Immunol* 1996;98:64-72.
26. Bousquet J, Dhivert H, Michel FB. Current trends in the management of allergic diseases. *Allergy* 1994;49 Suppl 18:31-6.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.