

number of responders to cow's milk-based preparations because they were increasingly hydrolyzed. Although there have been recent studies of allergic reactions to Nutramigen, it is still to be regarded as a hypoallergenic formula with low potential for sensitization.

Seven of the tested subjects had positive skin reactions to *intermediately* hydrolyzed whey and casein products, including a commercially available formula. This finding indicates that "hypoallergenic" formulas may retain epitopes capable of eliciting skin test reactions; unfortunately, related clinical symptoms from ingestion of these products are not possible to predict from these data without provocation tests, and such tests are in progress. Before use in cow's milk-allergic children, an SPT with the recommended formula should be performed, and if the results are negative, only a small amount of the formula should be given as a test dose because the SPT can only predict

IgE-mediated hypersensitivity reactions. Before *intermediately* hydrolyzed products are routinely recommended for use in infants at risk for allergy, they should be further investigated and probably modified. This recommendation is especially important since animal experiments indicate that low doses of antigen are particularly sensitizing compared with that of high doses of antigen.³ SPT studies appear promising as a screening procedure for rest allergenicity in formula products.

REFERENCES

1. Businco L, Cantani A, Longhi MA. Anaphylactic reactions to a cow's milk whey protein hydrolysate (Alfaré, Nestlé) in infants with cow's milk allergy. *Ann Allergy* 1989;62:333-5.
2. Dreborg S. The skin prick test, methodological studies, and clinical applications [medical dissertation No. 239]. Linköping, Sweden: University of Linköping, 1987.
3. Jarrett EEE. Activation of IgE regulatory mechanisms by trans-mucosal absorption of antigen. *Lancet* 1977;2:223-5.

Reducing domestic exposure to dust mite allergen reduces bronchial hyperreactivity in sensitive children with asthma

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IgE-mediated hypersensitivity to the house dust mites, *Dermatophagoides pteronyssinus* (Dpt) and *D. farinae* (Df) is frequently found in children with asthma and is considered to be a relevant environmental trigger for acute asthmatic attacks as well as for BHR.¹ An association between the degree of sensitization to *Dermatophagoides* and domestic expo-

Abbreviations used

BHR: Bronchial hyperreactivity
BB: Benzyl benzoate
PC₂₀: Provocative concentration that caused a 20% fall in FEV₁

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Supported by Deutsche Forschungsgemeinschaft (DFG Wa 409 5-2).

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sure to the major dust mite allergens, *Der p 1* and *Der f 1*, has been demonstrated.²

To examine whether a biologically significant mite-allergen reduction (i.e., one resulting in a loss of nonspecific BHR in patients with asthma) can be achieved in the domestic environment, we studied two elimination procedures: the covering of mattresses, comforts, and pillows with polyurethane-coated en-

casings in combination with treatment of carpets with tannic acid, and, second, the treatment of mattresses and carpets with the acaricide, BB.

MATERIAL AND METHODS

Patients

Twenty-four children, aged 7 to 15 years (median, 10 years), with mild or moderate bronchial asthma (definition according to American Thoracic Society) and hypersensitivity to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (positive skin prick test and elevated specific serum IgE [Pharmacia CAP class ≥ 3 , Uppsala, Sweden]) were included in our study. All patients were exposed to high concentrations of mite allergen on their mattresses (sum of the major allergens *Der p* 1 plus *Der f* 1 ≥ 2 $\mu\text{g/gm}$ of dust). Patients were allocated randomly to three treatment groups. Each patient was studied for 12 months. Patients' homes were visited by the same investigator who performed the treatments and collected dust samples from mattress and carpet.

BB and placebo-treated group

Mattresses were treated with either BB or placebo foam (60 gm/m^2) and carpets were treated with powder (60 gm/m^2) in a double-blind fashion on day 0, and at months 4 and 8. Residues were removed by vacuuming 4 hours after treatment. Foam and powder were kindly provided by Dr. E. Bischoff and Werner & Mertz, Mainz, Germany (Acarosan). BB foam (2.6% concentration of solidified BB) also contained methacrylate-copolymerisate, tensides (sodium lauryl sulfate and olefine sulphonate), fatty acids, sodium hydroxide, antimicrobial preserving agent (1,2-benzisothiazoline-3), propane/butane, and water. BB powder (5% concentration of solidified BB) also contained cellulose, isoparaffin, sodium aluminium silicate, silicium dioxide, sodium chloride, antimicrobial preserving agent (1,2-benzisothiazoline-3), and water. Placebo foam and powder were delivered in the same devices containing the same mixture without BB. The code was broken at the end of the study.

Encasing-regimen group

Mattresses, pillows, and comforts were covered with cotton encasings coated on one side with polyurethane (Allergy Control Covers, Allergy Control Products, Inc., Ridgefield, Conn.). Carpets (4/8 households) were sprayed with 3% tannic acid (Allergy Control Solution, Allergy Control Products) on day 0 and at months 4 and 8.

Dust collection

Dust samples were collected on days 0 and 14 and at months 4, 8, and 12 before treatment with the same vacuum cleaner (Hoover 800 W) and a new disposable dust bag.

Vacuum time for mattresses (2 m^2) and carpets (4 m^2) was five minutes. Dust bags were sent immediately to our laboratory and stored at -20°C .

Dust extraction and house dust mite ELISA were performed as described previously.²

Evaluation of BHR

Before evaluation of BHR theophylline, topical steroids and sodium cromoglycate were withheld for 48 hours, and β_2 -stimulants for at least 8 hours. No patient was receiving antihistamines.

Subjects first performed spirometry correctly three times on a body plethysmograph (E. Jäger, Würzburg, Germany). An aerosol of phosphate-buffered saline was then inhaled, and this was followed at 5-minute intervals by aerosols of histamine acid phosphate (HAP) starting at 0.125 mg/ml and doubled at each step, up to a maximum of 8 mg/ml . Solutions were nebulized in a plastic bag of 10 l volume (Provokationstest Paul Ritzau Pariwerk GmbH, Starnberg, Germany), and patients inhaled the whole contents through a mouthpiece during tidal mouth breathing wearing a nose clip.

Spirometry was repeated once at 30 and at 180 seconds after each inhalation. The challenge procedure was stopped after a fall in FEV_1 of $\geq 20\%$, and spirometry was then repeated at 3 minutes. The PC_{20} FEV_1 was calculated from the highest postsaline FEV_1 and the highest FEV_1 after histamine acid phosphate from the dose-response curve in non-cumulative units.

Statistical significance was tested with Wilcoxon's matched-pairs signed-rank test, Friedman's rank test, Kruskal-Wallis test and Mann-Whitney-Wilcoxon's test.

RESULTS

Mite-allergen concentrations on mattresses

Although BB and placebo treatment did not result in a significant reduction of mite allergen, there was a significant decrease in concentrations of mite allergen on mattresses covered by polyurethane encasings ($p < 0.005$; Fig. 1). Relative to day 0, there was already a significant decrease in allergens by day 14 of 91% ($p < 0.05$), rising to 98% by month 12. In the encasing-regimen group, 4/10 mattress-dust samples still revealed allergen concentrations between 2 and 7.5 $\mu\text{g/gm}$ of dust on day 14. This finding is probably due to contamination because mattress dust samples under the encasing were also collected at this time.

Mite-allergen concentrations on bedroom carpet

In the encasing-regimen group in which carpets were treated with tannic acid, and in the BB-treated group, there was a tendency to mite-allergen reduction (data not presented).

BHR

The degree of BHR (PC_{20}) in each of the three treatment groups varied widely (Fig. 2). Median values for PC_{20} on day 0 were comparable in the different groups.

In the placebo-treated group, the median value for

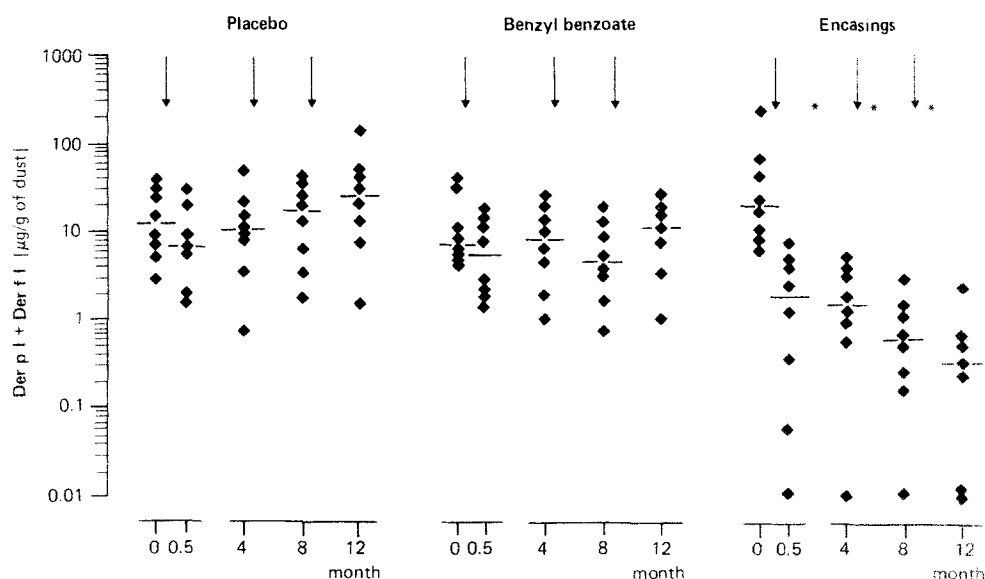


FIG. 1. Mite-allergen levels in three groups before and after treatment (arrows); * $p < 0.05$; bars, median values.

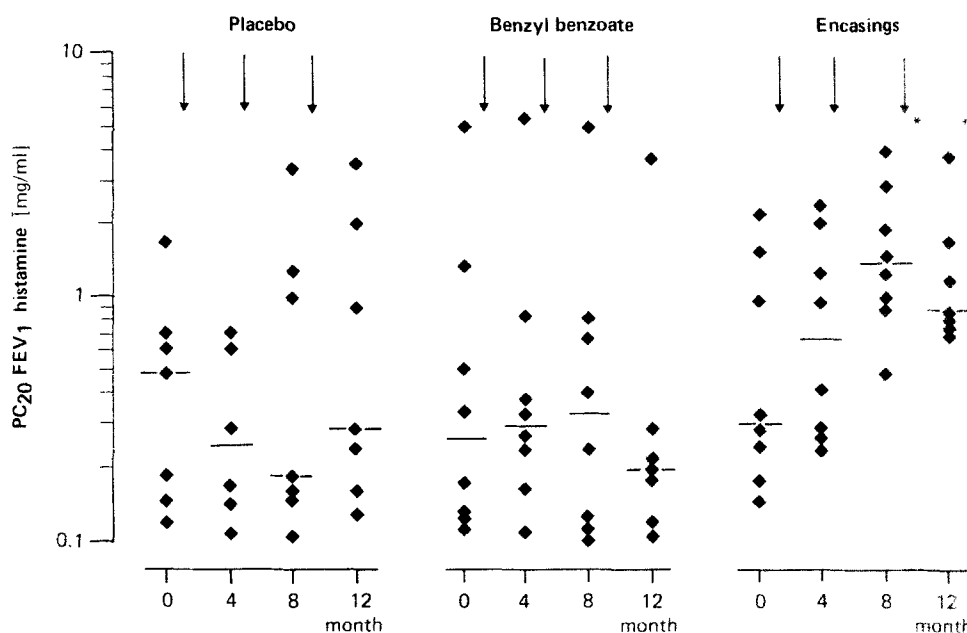


FIG. 2. BHR (PC_{20} of histamine) in three groups before and after treatment (arrows); * $p < 0.05$; bars, median values.

PC_{20} decreased from 0.5 mg/ml on day 0 to 0.27 mg/ml in month 12 (not significant). BHR in the BB-treated group stayed virtually constant. There was a statistically significant increase of PC_{20} only in the encasing-regimen group (comparison between groups Kruskal-Wallis test, $p < 0.05$; comparison within groups, Friedman's test, $p < 0.01$).

PC_{20} increased steadily up to month 8 and demonstrated a slight decrease in month 12. Comparing different times within the encasing group, in months 8 and 12, the increase in PC_{20} was statistically significant compared with that of day 0 ($p < 0.05$). The increase was 2.2-fold in month 4, 4.5-fold in month 8, and 2.7-fold in month 12.

DISCUSSION

Our data indicate that a reduction of the domestic mite-allergen exposure below a previously proposed threshold level of 2 $\mu\text{g/gm}$ of mattress dust² may be achieved by the encasing procedure already after 14 days, whereas BB treatment, as applied during our study, appears to be ineffective, which is in accordance with a study on the short-term effect of BB.³ More importantly, we have been able to demonstrate that an effective allergen reduction in homes with high mite-allergen concentrations is accompanied by a significant reduction of BHR in children with asthma after 8 months of treatment.

Avoidance measures should achieve a reduction of at least 90% to reduce mite-allergen exposure to below the threshold concentrations of 2 μg and 10 $\mu\text{g/gm}$ of dust, respectively, which have been associated with an increased risk of sensitization and acute asthmatic symptoms.¹ Only the encasing regimen achieved a significant reduction on mattresses up to 98%.

PC₂₀ significantly increased up to 4.5-fold in the encasing-regimen group after 8 months. Similar improvement of lung function was reported when patients were in the mite-free environment of a hospital in which PC₃₀ for histamine increased eightfold or more after 4 months in five adult patients.⁴ Walshaw and Evans⁵ observed only a twofold increase of PC₂₀ for histamine 1 year after introduction of cleaning measures and plastic-coated covers for pillows and mattresses in 22 adult patients with asthma.

The use of polyurethane-covered encasings for bedding and mattresses, which are permeable for moisture but not for allergens, appears to be a safe, nontoxic, and a convenient method for reducing mite allergen that can easily be used in any household. All patients in our study tolerated the encasings well. The biologic effect, that is, the improvement of unspecific BHR, was demonstrated to last for several months. It is likely that the effect would last for an even longer period. There should be large epidemiologic studies to investigate whether the use of encasings can avoid or postpone sensitization and development of atopic diseases, such as asthma, rhinitis, and eczema.

REFERENCES

1. Platts-Mills TAE, Thomas WR, Aalberse RC, Vervloet D, Chapman MD. Dust mite allergen and asthma: report of a second international workshop. *The UCB Institute of Allergy*, 1991;11-29.
2. Lau S, Falkenhurst G, Weber A, et al. High mite-allergen exposure increases the risk of sensitization in atopic children and young adults. *J ALLERGY CLIN IMMUNOL* 1989;84:718-25.
3. Lau-Schadendorf S, Rusche AF, Weber AK, Buettner-Goetz P, Wahn U. Short-term effect of solified benzyl benzoate on mite-allergen concentration in house dust. *J ALLERGY CLIN IMMUNOL* 1991;87:41-7.
4. Platts-Mills TAE, Tovey ER, Mitchell ER, Moszoro H, Nock P, Wilkins SR. Reduction of bronchial hyperreactivity during prolonged allergen avoidance. *Lancet* 1982;2:675-8.
5. Walshaw MJ, Evans CC. Allergen avoidance in house dust mite-sensitive adult asthma. *Q J Med* 1986;226:199-215.

Correction

In the JACI, 1991;88:409-13, Rostrum article by Graft, in Dr. Valentine's paragraph, page 410, first column, fifth line should read 100 μg .