

ing lawn mowing was likely to be the result of increased airborne grass-allergen concentrations associated with lawn mowing.

It is unlikely that the assay detected other, nongrass allergens. When various tree, weed, dog, and mold extracts were assayed, trace or undetectable grass allergen was measured. The grass allergen detected in red maple, oak mix, and common cocklebur extracts may represent cross-reactivity between grass and nongrass allergens or contamination of the extracts with grass allergen.

The peak grass-pollinating period in the area studied was the last week of May through the first week of June. Consistently increased grass-allergen concentrations were noted in the during-mowing samplings from early May through June. Possible explanations include grass-pollen grains settling onto lawns and then being propelled back into the air by lawn mowers

or that nonpollen parts of the grass plant contain allergenic proteins.

REFERENCES

1. Rowe MS, Bailey J, Ownby DR. Evaluation of the cause of nasal and ocular symptoms associated with lawn mowing. *J ALLERGY CLIN IMMUNOL* 1986;77:714-9.
2. Enberg RN, Leickly FE, McCullough J, Bailey J, Ownby DR. Watermelon and ragweed share allergens. *J ALLERGY CLIN IMMUNOL* 1987;79:867-75.
3. Gjesing B, Jager L, Marsh DG, Lowenstein H. The international collaborative study establishing the first international standard for timothy (*Phleum pratense*) grass pollen allergenic extract. *J ALLERGY CLIN IMMUNOL* 1985;75:258-67.
4. Connell JT. Quantitative intranasal pollen challenge. II. Effect of daily pollen challenge, environmental pollen exposure, and placebo challenge on the nasal membrane. *J ALLERGY* 1968;41:123-39.
5. Naclerio RM, Meier HL, Kagey-Sobotka A, et al. Mediator release after nasal airway challenge with allergen. *Am Rev Respir Dis* 1983;128:597-602.

Allergenicity screening of "hypoallergenic" milk-based formulas

G. Oldæus, MD, C. K. Bradley, MBA, RD,* B. Björkstén, MD, PhD, and
N.-I. M. Kjellman, MD, PhD Linköping, Sweden, and Evansville, Ind.

Presently available, extensively hydrolyzed, milk-based formulas, like Nutramigen (Mead Johnson, Evansville, Ind.), have a poor taste, sometimes limiting their use. Recently, formulas containing less extensively hydrolyzed milk proteins have been produced. Various amounts of remaining antigenic determinants are left in these products, and there are reports of serious adverse reactions from the use of commercially available hydrolyzed whey protein-based formula in cow's milk-allergic children.¹

From the Department of Pediatrics, Faculty of Health Sciences, University of Linköping, Linköping, Sweden, and *Mead Johnson Research Center, Evansville, Ind.

Supported by grants from the Swedish Medical Research Council (Grant No. 7510) and Stiftelsen Frimurare Barnhuset, Stockholm, Sweden.

Reprint requests: N.-I. Max Kjellman, MD, Associate Professor of Pediatrics, Department of Pediatrics, Faculty of Health Sciences, S-581 85 Linköping, Sweden.

1/1/38561

Abbreviations used

SPT: Skin prick test

DH: Degree of hydrolysis

We used the SPT with blinded extracts of various hydrolyzed formulas (new or already on the market) in children with a history of cow's-milk allergy as the first step in the clinical evaluation of rest allergenicity of formula products aimed for use in milk-allergic children or as a part of an allergy-prevention program.

MATERIAL AND METHODS

Four girls and 12 boys, aged 3 to 13 years (median, 8 years), with a history of immediate-type cow's-milk allergy, participated. Fourteen age-matched milk-tolerant subjects served as control subjects in the SPT part of the study. All parents gave informed consent,

TABLE I. Number of children with cow's-milk allergy who demonstrated positive SPTs (i.e., wheal diameters >3 mm) to milk-based preparations

Preparation	Responders	<i>p</i>
Nutramigen	0/15	<0.001
Alfaré	1/15	<0.001
Formula B	5/15	<0.01
Beba HA	7/15	<0.05
Formula A	7/15	<0.05
Similac	13/15	NS
Enfamil	15/15	NS

NS, Not significant.

A comparison is made with the number of responders (*N* = 15) to cow's milk (chi square test).

and the study was approved by the Human Research Ethics Committee of the Faculty of Health Sciences, Linköping, Sweden.

Inclusion criteria consisted of a verified history of symptomatic IgE-mediated cow's-milk allergy (skin symptoms in 12 and gastrointestinal symptoms of immediate type in 10 children) and a current SPT wheal with cow's milk of at least 3 by 3 mm. No provocation test was performed for the purpose of the present study, but a previous provocation test was positive in 10 of the subjects, whereas in the rest of the group, provocation had not been done because of large SPT reactions confirming a convincing history. Concomitant food allergies with no relevance to the present study were reported in 14 of the 16 children. All children were receiving an elimination diet completely avoiding cow's milk and other known allergens. No medication interfering with SPT results was allowed.

All tests were done in duplicate, as recommended by Dreborg.² One millimeter tip lancets (Dome-Hollister-Stier, Miles, Spokane, Wash.) were pressed into the skin at a 90 degree angle for 3 seconds through a drop of test material. After 15 minutes, the wheal area was transferred by transparent tape to a protocol. All mean wheal diameters of 3 mm or more were regarded as positive.

All the test materials were coded, and the code was broken only after calculating the test results:

1. Formula based on 100% whey proteins enzymatically treated (Beba HA, batch WJ PAS 1; sold as Good Start HA, Carnation, Los Angeles, Calif.) from Nestlé, Vevey, Switzerland
2. Partially hydrolyzed milk protein formula A (60% whey and 40% casein enzymatically treated by bacterial proteases), from Mead Johnson, Evansville, Ind.; DH (DH, percent of peptide bonds broken), 8.2

3. Partially hydrolyzed milk protein formula B (60% whey and 40% casein enzymatically treated by pancreatin), from Mead Johnson; DH, 18.1
4. Formula based on 100% whey proteins enzymatically treated (Alfaré, batch D 523 MD5), from Nestlé
5. Formula based on extensively hydrolyzed casein (Nutramigen, batch from the shelf in Sweden), from Mead Johnson; DH, >50
6. Routine cow's milk-based infant formula (Enfamil, batch MFJ 003), from Mead Johnson
7. Routine cow's milk-based infant formula (Similac, batch EMF H003), from Ross Laboratories, Columbus, Ohio)
8. Undiluted pasteurized cow's milk (fat content, 5 mg/ml, and protein content, 34 mg/ml)
9. Histamine chloride (10 mg/ml) served as positive control

Formula products were used at standard feeding dilution (20 kcal per fluid ounce; protein concentration was approximately 20 mg/ml).

Since the tested subjects were not randomly selected, comparisons of mean values and standard deviations of wheal sizes obtained with each tested preparation were not performed. The chi-squared McNemar's test of frequencies in matched samples was performed.

RESULTS AND DISCUSSION

None of the control children reacted in the SPT to cow's milk or any of the hydrolysates. Among the children with a history of milk allergy, the number of responders to the coded preparations varied (Table I) between none (for Nutramigen, based on extensively hydrolyzed casein) and 13 to 15 for cow's milk and ordinary cow's milk-based formula. This difference was statistically significant ($p < 0.001$). Intermediate numbers of responders were found with the other hydrolysates. Additionally, there were fewer cases with a positive reaction to the extensively hydrolyzed casein included in Nutramigen (0/15) than to the formula containing partially hydrolyzed whey proteins (Beba HA, 7/15; $p < 0.05$).

No side effects were noted during the tests or later reported by the families.

In this study, SPT was used as a model for testing "rest allergenicity" in various cow's milk-based products in comparison to cow's milk. All the subjects chosen for the study had a convincing history of IgE mediated-type cow's-milk allergy. A few of the subjects had already started to tolerate minute amounts of dietary cow's milk, but none had reached clinical tolerance to normal intake of cow's milk.

The SPTs demonstrated a generally decreasing

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

Brigitte Ehnert, MD, Susanne Lau-Schadendorf, MD, Anne Weber, BSc,
Petra Buettner, PhD,* Carsten Schou,** and Ulrich Wahn, MD
Berlin, Germany

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

From the University Children's Hospital, Berlin, and *Institute of Medical Statistics and Informatics FU Steglitz, Berlin, Germany, and **ALK Research Department, Horsholm, Denmark.

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

Reprint requests: U. Wahn, MD, Universitätsklinikum Rudolf Virchow, Kinder- und Poliklinik KAVH, Heubnerweg 6, 1000 Berlin 19, Germany.

1/1/38548

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-