

TABLE I. Response of latex chemical dispersions in the ASTM D5712-95 test method for proteins

Aqueous dispersion	Concentration (%)	Apparent protein content of aqueous phase (ppm)
Sulfur	33	7
Zinc oxide	33	22
Titanium dioxide	33	13
Diphenylthiourea	33	9
Zinc dibutylthiocarbamate	33	17
Wingstay L (antioxidant)	25	12
Diphenylguanidine	20	4730
Dispersing agent alone	5	4

ppm, Parts per million.

interference in the test method. Specifically, DPG is evidently not removed by the protein precipitation method.

The rubber component of the synthetic rubber latex, polychloroprene latex, provided an *apparent* protein content of 20 µg/gm when tested according to ASTM D5712-95. When the latex was converted into rubber gloves by using an accelerator dispersion not containing DPG, the value found was 25 µg/gm. When DPG was included, the resulting gloves provided a value of 135 µg/gm, even though no protein had been introduced. This was confirmed by subjecting the same gloves to an ELISA (the latex ELISA for antigenic proteins)⁴ and a

RAST-inhibition assay⁵ for antigenic protein when results below the detection limit were obtained.

These results imply that rubber articles made with DPG (and possibly other chemicals) will fail to gain acceptance by the FDA as articles of low extractable protein content. It is not at present possible to demonstrate a low extractable protein content for such articles by a test acceptable to the FDA. We believe that this state of affairs is quite unsatisfactory given the usefulness of guanidine accelerators in the vulcanization of rubber. Clearly there is a need for alternative protein assays that are more specific, and regulatory bodies should not rely solely on ASTM D5712-95 as the only method. Other suitable assays include the latex ELISA for antigenic proteins and the RAST-inhibition assays.

REFERENCES

1. International latex conference: sensitivity to latex in medical devices, Baltimore, 1992.
2. American Society for Testing and Materials. ASTM D5712-95. Standard test method for analysis of protein in natural rubber and its products. Philadelphia: American Society for Testing and Materials; 1995.
3. Interim guidance on protein content labeling claim for latex medical gloves. Washington (DC): Food and Drug Administration, CDRH, Office of Device Evaluation; 1995.
4. Beezhold D. LEAP: latex ELISA for antigenic proteins. *Guthrie Journal* 1992;61:77-81.
5. Van Hage-Hamsten M, Johansson SGO, Johansson E, Wiren A. Lack of allergenic cross-reactivity between storage mites and *Dermatophagoides pteronyssinus*. *Clin Allergy* 1987;17:23-31.

Diagnosis of cow's milk allergy: Open or blinded?

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The common initial manifestation of atopic disease is food allergy. Despite advances in the understanding of its mechanisms, the methods for early detection of clinically significant food allergy are of poor diagnostic accuracy.¹ The aim of this study was to compare the accuracy of the open and double-blind placebo-controlled cow's milk challenge (DBPCCMC) for clinical practice.

Abbreviation used

DBPCCMC: Double-blind, placebo-controlled cow's milk challenge

METHODS

Altogether, 265 patients were enrolled in the study. The mean age at onset of symptoms was 3 months (range, 0.5 to 24 months). The duration of breastfeeding, exclusively and totally, was 3 months (range, 0 to 12 months) and 7 months (range, 0 to 24 months), respectively. To confirm or refute a diagnosis of allergy to cow's milk, the patients were randomly assigned an open challenge or a DBPCCMC. Skin prick (175 of 265 subjects) and patch (151 of 265 subjects) testing were done as previously described.² Cow's milk-specific skin prick test results

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were positive in 54 of 175 subjects (31%), and patch test results were positive in 78 of 151 (52%).

The clinician determined the substitute formula (elimination period, 2 to 4 weeks): an extensively hydrolyzed, a soy, or an amino acid formula or calcium supplementation. The challenge was begun in patients without symptoms at the mean age of 20 months (range, 3 months to 6 years). The challenges proceeded as described,² beginning with a small dose and increasing stepwise, with discontinuation on a positive reaction. Parents recorded symptoms on a diary card. A follow-up visit was scheduled a week after commencement. In the DBPCCMC, milk A was used during the first week, and milk B was used during the second week (computer generated randomization of sequence). An amino acid formula was used as the placebo (Neocate; SHS Int. Ltd.). One hundred milliliters of the formula was mixed with 10 gm of skim milk for the actual challenge. After both periods, one of the challenges, if any, was determined to be positive. The code was opened, and the diagnosis was confirmed.

The current clinical practice described above was evaluated by interviewing parents 13 months (mean) after the challenge. Specific questions were asked concerning the parents' perception of the challenge procedure, the time it had taken, and the reliability of the procedure and diagnosis.

Data are presented as mean or median with range as appropriate. The chi-square test was used for statistical comparisons.

RESULTS

The diagnosis of allergy to cow's milk was made in 44% of the 110 patients subjected to the DBPCCMC and in 56% of the 155 subjected to the open challenge ($\chi^2 = 4.02, p = 0.04$). Of the 135 positive challenges, 113 (84%) involved skin symptoms, and a total of 42% of patients had gastrointestinal symptoms.

The response rate was 105 of 155 in the open-challenge group (68%) and 75 of 110 in the DBPCCMC group (68%). The parents of those patients who had a diagnosis of allergy to cow's milk responded more often than the parents whose child had a negative reaction to challenge (101 of 135 [75%] vs 79 of 130 [60%], respectively; $\chi^2 = 5.99, p = 0.01$).

The diagnosis was unambiguous for a greater proportion of parents of patients in the DBPCCMC group than in the open-challenge group, not depending on the result of the challenge (Table I).

DISCUSSION

The proportion of patients receiving a diagnosis of allergy to cow's milk was significantly decreased with the

TABLE I. Number of parents of patients agreeing or disagreeing with result of diagnostic cow's milk challenge

	CMA +		CMA -	
	Open	DBPCCMC	Open	DBPCCMC
No. who agree	53	37	32	34
No. who disagree	10	1	10	3

$\chi^2 = 7.12, p = 0.007$.

CMA+, Child with allergy to cow's milk; CMA-, Child without allergy to cow's milk.

DBPCCMC. This method may therefore give improved diagnostic accuracy in clinical practice. However, previous results show that in experienced hands the open challenge would be sufficient.² When considering the nutritional hazards associated with elimination diets,³ it is important to be able to make the diagnosis as accurately as possible. Atopic patients do not benefit from empirical elimination diets begun without a diagnosis of food allergy.⁴ This is the first study to assess parental acceptance of the diagnosis of allergy to cow's milk. The length of time from challenge to assessment was equal in the groups and did not affect the results.

The clinical implications of these results are twofold. First, with a correct diagnosis, the elimination diets are begun in the patients who are most likely to benefit. Second, it may be speculated that adherence to the assigned elimination diet is better when the diagnosis is considered unequivocal. In this study, the parents considered double-blind diagnosis significantly more often definite.

REFERENCES

1. Zeiger RS. Atopy in infancy and early childhood: natural history and role of skin testing. *J Allergy Clin Immunol* 1985;75:633-9.
2. Isolauri E, Turjanmaa K. Combined skin prick and patch testing enhances identification of food allergy in infants with atopic dermatitis. *J Allergy Clin Immunol* 1996;97:9-15.
3. Isolauri E, Sutas Y, Mäkinen-Kiljunen S, Oja S, Isosomppi R, Turjanmaa K. Efficacy and safety of hydrolyzed cow milk and amino acid-derived formulas in infants with cow milk allergy. *J Pediatr* 1995;127:550-7.
4. Mabin DC, Sykes AE, David TJ. Nutritional content of few foods diet in atopic dermatitis. *Arch Dis Child* 1995;73:208-10.