

EDITORIAL

Objective assessment of allergenicity of infant feeding formulae

It is now widely accepted that food allergy defined as a form of food intolerance in which there is evidence of an abnormal immunological reaction to the food [1,2] occurs as an important clinical problem in infancy and early childhood [3]. Simplistically in children the clinical problems can be broadly divided into three main groups related to timing of the onset of symptoms after food ingestion namely: (i) quick onset syndromes (within an hour of food ingestion); (ii) slow onset syndromes; (iii) combination of quick and slow onset of symptoms (usually associated with multiple food allergy) [4]. There is evidence that such allergic reactions may be mediated via IgE mediated or T cell mediated reactions [5,6].

Whatever their pathogenesis such syndromes are treated by food elimination diets and they are characteristically temporary in duration. Cows' milk allergy is by far the commonest food intolerance clinically evident. Food elimination is best achieved by means of prescription of a food substitute. In this case protein hydrolysates are usually recommended by most authorities as other protein based formulae such as soy-protein may themselves also produce symptoms of allergy [7].

Various hydrolysates are used in clinical practice based on casein hydrolysates, whey hydrolysates, soy-collagen hydrolysates and beef-soy hydrolysates. Indeed the introduction of partially hydrolysed formula (better flavour than complete hydrolysates), which may be of prophylactic value for atopy, has made this question of objective evidence for hypoallergenicity of feeding formulae to be particularly topical [8,9].

Modern adapted milk based formulae are themselves processed in such a way to render them less allergenic than whole cows' milk. This is usually achieved by heat denaturation during manufacture but an alternative is to use enzymatic hydrolysis of the protein *in vitro*. The allergenicity of normal formula feeds and these hydrolysates has been tested by their sensitizing capacity *in vivo* in guinea pigs [10,11].

An *in vitro* rat model has also been developed using peritoneal mast cells [12]. The allergenicity of cows' milk formulae was assessed by their ability to trigger prelabelled ³H-serotonin release from normal rat mast cells sensitized passively with rat reaginic anti-cows' milk protein antisera.

Another method used has been to immunize rabbits with either intact proteins or protein hydrolysates [13].

Casein and soy protein hydrolysates were investigated in this way. IgG antibody specific for the immunizing protein hydrolysates and the corresponding intact proteins were studied. The hydrolysates had lower immunogenicity than the whole protein.

Such animal studies show that hydrolysed formulae are significantly less allergenic than are standard infant formulae. However these tests are intrinsically artificial as they are based on animal studies either *in vivo* or *in vitro* and are largely testing IgE mediated sensitivity.

Thus despite such studies and also despite considerable study of the molecular weights of the residual peptides in these hydrolysates as Sampson *et al.* [14] have indicated, the only certain way that these infant feeding formulae can be shown to be 'hypoallergenic', is by means of testing their clinical effectiveness in patients. Hence the importance of the study reported by Rugo *et al.* [15] in this issue who used a variety of techniques including skin prick tests, RAST, RAST substitution and provocation tests to study comparatively, six protein hydrolysates in children with evidence of IgE mediated quick onset cows' milk allergy. Of particular interest and importance was that analysis of single blind titrated challenge with cows' milk and the hydrolysates showed that a significant number of children who reacted to cows' milk also reacted to one of the whey hydrolysates. None of the eight children challenged reacted to casein hydrolysates.

Whilst *in vitro* testing is clearly of importance in analysis of the formula, *in vivo* testing is of vital significance and may give different results.

It must be noted however that this study is entirely of children with quick onset IgE mediated sensitivity and not of children with slow onset probably T cell mediated sensitivity such as cows' milk-sensitive enteropathy and cows' milk-sensitive colitis. These are distinct entities and the findings found in the former should not be extrapolated to the latter.

References

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