

Letter to the editor

Hydrolysed cow's milk formulae

In the August issue of this journal, the ESPACI position paper on hypoallergenic formulae (HF) was published (1). This report was preceded by treatises of the Scientific Committee for Foods of the EC (2) and the Committee on Nutrition of ESPGAN (3). In these reports HF were classified as partly hydrolysed (pHF) or extensively hydrolysed formula (eHF). However, clear criteria for this classification were not specified. The ESPACI report included a list of brand names of HF classified as eHF or pHF and recommended only eHF for treatment of cow's milk allergy. At present, ESPACI also recommends eHF rather than pHF for the prevention of atopy. An appropriate classification of HF is, therefore, of vital importance for their recommended use. In this letter we report data on molecular weight profiles (MWP) of these HF, contributing to a more rational classification.

The MWP of HF is an important characteristic determining the potential residual allergenic activity as this is dependent on the degree of hydrolysis and special processing of the hydrolysate, such as ultra-filtration. MWP of protein hydrolysates are usually determined by gel permeation chromatography. This technique, however, does not permit a precise definition of MWP, as slightly different protocols lead to markedly different results. This disadvantage is overcome by comparing results for HF obtained

under identical conditions (2). Our laboratory produced MWP of several samples of various products in the period 1990–1993 using the same method (experimental details will be published elsewhere, but are available on request from the authors). The data for similar or identical products originating from the same manufacturer but marketed under different brand names (Profylac®, Hypolac®, NAN-HA®, Beba HA®, Good Start®, Nativa HA®, Nutrilon Pepti®, Nutrilon Pepti Plus®) were combined.

Results are given in the table based on MWP classification limits 1500, 3500 and 6000. Peptides below MW 1500 are only very rarely immunogenic on their own, peptides below MW 3500 are unlikely to cross-link two IgE molecules attached to mast cells and thus elicit immediate type reactions, and larger peptides with MW above 6000 should definitely be considered as potentially allergenic. From the table it is clear that, compared with whey-eHF, casein-eHF have a higher proportion of small peptides (about 96% versus about 85%). The fact that casein-eHF were also found to contain small, but detectable, amounts of larger peptides (>6000) is in agreement with the rare occurrence of anaphylactic reactions associated with use of these products (1, 3). It can be seen that the MWP for NAN-HA® differs markedly from that of the other whey-HF listed. The classification of Nutrilon Pepti® as pHF

Table 1. Molecular weight profile of hydrolysed cow's milk formulae

Type Product	ESPACI classification	Molecular weight range			
		< 1500	1500–3500	3500–6000	> 6000
Hydrolysed bovine casein					
Alimentum®	eHF	96.5	2.5	0.5	0.5
Nutramigen®	eHF	95.5	3.5	0.5	0.5
Pregestimil®	eHF	97.0	2.0	0.5	0.5
Hydrolysed bovine whey					
Alfa-Ré®	eHF	88.0	8.0	1.5	2.5
NAN-HA®	pHF	54.0	20.5	7.5	18.0
Nutrilon Pepti®	pHF	84.0	12.0	2.0	2.0
Pepti Junior®	eHF	85.0	11.5	1.5	2.0
Profylac®	eHF	83.5	11.5	2.5	2.5
Mix hydrolysed bovine casein/whey					
Aptamil HA®	pHF	75.0	16.5	5.0	3.5

Letter to the editor

by ESPACI is in discordance with its MWP. This observation, combined with the large reduction (10^6) of the amount of immunoreactive bovine β lactoglobulin (Nutricia Research, unpublished), would support the classification of Nutrilon Pepti® as eHF.

We hope that our comparative data on the MWP of HF contribute to the discussion on the allergenicity and correct use of HF in treatment and prevention. A final consensus regarding the permitted claims within Europe, particularly within the regulatory bodies of the EC, is strongly desired.

REFERENCES

1. BUSINCO L, DREBORG S, EINARSSON R, et al. Hydrolysed cow's milk formulae. Allergenicity and use for treatment and prevention. A position paper of ESPACI. *Pediatr Allergy Immunol* 1993; 4: 101–11.
2. Scientific Committee for Food. Report of the scientific committee for food on infant formulae claimed to be hypoallergenic or hypoantigenic (opinion expressed on 9 December 1991), 1992.
3. ESPGAN Committee on Nutrition: AGGET PJ, HASCHKE F, HEINE W, et al. Comment on antigen-reduced infant formulae. *Acta Paediatr* 1993; 82: 314–19.

Jacques G. Bindels, Jan A. Boerma
Nutricia Research, P.O. Box 1, NL-2700 MA Zoetermeer,
The Netherlands.