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Probiotics may be unsafe in infants allergic to cow's milk

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Key words: masked allergens; milk proteins; probiotics.

Differences in the intestinal microflora of atopic and nonatopic infants have been shown; atopic children have fewer bifidobacteria and lactobacilli (1–3). Beneficial immunoregulatory effects of probiotic flora have been confirmed by preventive and therapeutic studies with probiotics in infants at high risk of atopy and in those presenting with cow's milk allergy (CMA) and atopic eczema/dermatitis syndrome (AEDS) (3, 4). We report a case supporting the hypothesis that residual milk proteins at risk of reactogenicity may be present in different probiotic brands that are marketed as health supplement products.

Probiotics used as health supplements may contain milk proteins eliciting allergy in cow's milk allergic children.

A 11-month-old infant, with AEDS and CMA was fed an aminoacid formula (Neocate®; SHS International Ltd, Liverpool, UK). He presented with *Escherichia coli* colitis, so a probiotic (Bacilor®; Lab Lyocentre, Aurillac, France) was prescribed. Within 15 min, he presented with generalized erythema and laryngeal discomfort. A prick-test to Bacilor® was positive, as was a prick-test to milk (Table 1).

Three other children, aged from 3 to 10 years, with persistent milk allergy were tested to three probiotic brands: Bacilor®, Imgalt® (Lab Jaldes, Gigean, France) and Ditopy® (Lab Ducray, Boulogne, France). The prick-tests were positive to Bacilor® and Imgalt® (Table 1).

Bacilor® contains only *Lactobacillus casei*, of the *rhamnosus* variety, Imgalt® also has *L. rhamnosus*, *L. acidophilus*, *Bifidobacterium bifidum* and *B. longum*, Ditopy® contains *L. rhamnosus* and *L. acidophilus*.

The manufacturers of these preparations were questioned about the medium used for the growth of these strains: the medium used for Bacilor® and Imgalt® flora includes lactoserum proteins and casein. No control tests for residual milk proteins are carried out on these medicinal products. The culture medium of Ditopy® flora is hydrolyzed soy protein. The immediate clinical reaction in the infant, as well as positive-prick tests in these four children, support the hypothesis of residual milk proteins, the level of contamination being clinically relevant in some milk allergic infants, at risk of anaphylaxis (5).

Despite previous encouraging results, therapeutic results of probiotics were not particularly marked in a recent study (6, 7). No information was provided about the culture medium. In the event of marked allergy to milk proteins, ingestion of probiotics containing small amounts of residual milk proteins could explain sustained AEDS.

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References

1. Bjorksten B, Naaber P, Sepp E, Mikelsaar M. The intestinal microflora in allergic Estonian and Swedish 2-year-old children. Clin Exp Allergy 1999;**29**:342–346.
2. Bjorksten B, Sepp E, Julge K, Voor T, Mikelsaar M. Allergy development and the intestinal microflora during the first year of life. J Allergy Clin Immunol 2001;**108**:516–520.
3. Kalliomaki M, Kirjavainen P, Eerola E, Kero P, Salminen S, Isolauri E. Distinct patterns of neonatal gut microflora in infants in whom atopy was and was not developing. J Allergy Clin Immunol 2001;**107**:129–134.

Table 1. Prick-tests to milk and to three brands of probiotics

	Age	Clinical features	Cap System Rast to milk	Prick-tests/mm			
				Milk	Bacilor®	Imgalt®	Ditopy®
Infant 1	11 months	AEDS immediate reaction to Bacilor®	49 kIU/l	7	7	nd	nd
Child 2	3 years	AEDS	73 kIU/l	11	11	8	4
Child 3	10 years	Persistent milk allergy, eviction diet	1.5 kIU/l	4.5	4	4.5	0
Child 4	8 years	Persistent milk allergy, eviction diet	72 kIU/l	14	4	5	0

AEDS, atopic eczema/dermatitis syndrome; nd, not determined.

4. Kalliomäki M, Salminen S, Arvilommi H, Kero P, Koskinen P, Isolauri E. Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial. Lancet 2001;**357**:1076–1079.
5. Moneret-Vautrin DA, Morisset M, Flabbee J, Beaudouin E, Kanny G. Epidemiology of life-threatening and lethal anaphylaxis: a review. Allergy 2005;**60**:443–451.
6. Kalliomaki M, Salminen S, Poussa T, Arvilommi H, Isolauri E. Probiotics and prevention of atopic disease: 4-year follow-up of a randomised placebo-controlled trial. Lancet 2003;**361**:1869–1871.
7. Viljanen M, Savilahti E, Haahtela T, Juntunen-Backman K, Korpela R, Poussa T et al. Probiotics in the treatment of atopic eczema/dermatitis syndrome in infants: a double-blind placebo-controlled trial. Allergy 2005;**60**:494–500.

The new Hev b 7.02 iso-allergen from *Hevea brasiliensis* is an important allergen for health care workers and spina bifida patients

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Key words: allergen; health care worker; *Hevea brasiliensis*; isoform; latex.

Knowledge of the sensitization to single latex allergens is, besides of its diagnostic relevance, important for evaluation of cross reactivity reactions between latex proteins and food allergens (1, 2). The recombinantly produced Hev b 7.02 is a new patatin-like protein isoform.

Hev b 7.02 is of intermediate relevance for health care workers.

Total RNA from *Hevea brasiliensis* leaves was transcribed into cDNA using Hev b 7-specific primers. After sequence analysis the Hev b 7.02 coding DNA fragment was cloned into *Escherichia coli* with the pMal-c2 vector and expressed as fusion protein with maltose binding protein (MBP). The purified protein was coupled to ImmunoCAPs (3).

Sera of 60 healthcare workers (HCW), 40 from Germany, 20 from Portugal, with symptomatic latex allergy as well as sera from 10 Portuguese patients with multiple surgeries (MS) and from 15 spina bifida patients (SB) were examined with the UniCAP 100 system regarding their rHev b 7.02-specific IgE reactions. MBP coupled to ImmunoCAPs served as negative control.

DNA sequencing revealed that the analysed DNA fragment of 1167 bp was the gene coding for a Hev b 7.02 isoform, differing from the sequence published by Sowka et al. (EMBL Acc. No. AJ223038) in three positions (4). Only one of these leads to an exchange in the deduced amino acid sequence (alanine to valine at position 208). The sequence of our new Hev b 7.02 isoform was submitted to the EMBL database (Acc. No. AJ617735).

In total, 28% (17 of 60) of the HCW sera and 33% (five of 15) of the SB sera showed Hev b 7.02-specific IgE, whereas all MS sera were negative. The median values of the positive specific IgE to rHev b 7.02 (> 0.35 kU/l) clearly differed depending on the patient group [HCW Germany (n = 14): 4.63 kU/l, HCW Portugal (n = 3): 0.5 kU/l, SB: 2.27 kU/l]. In all HCW sera with positive IgE-response to rHev b 7.02 additionally nHev b 2- and nHev b 13-specific IgE (native allergens kindly provided by Dr Yeang, Rubber Research Institute of Malaysia) as well as specific IgE against at least one of the following latex allergens: rHev b 1, rHev b 5 and rHev b 6.01 were found. In contrast, all rHev b 7.02-positive SB sera showed specific IgE against rHev b 1, nHev b 2 and rHev b 5 as well as rHev b 3 and/or rHev b 6.01. No mono-sensitization to Hev b 7.02 was detected. Seventy percent of the HCW from Portugal (14 of 20) reported allergic reactions when eating fruit ('latex-fruit syndrome', LFS), predominantly chestnut. Only three of the HCW/LFS patients showed Hev b 7.02-specific IgE reactions (0.41, 0.50, 19.89 kU/l). All three patients reported severe reactions when eating chestnut, one additionally mentioned peach, another one also peach, mango, banana and manioc.

Inhibition experiments with either rHev b 7.02 coupled to ImmunoCAP or ImmunoCAP k82 were used as solid phase and two different latex glove extracts as well as rHev b 7.02 and/or latex C-serum as inhibitors (negative control: PBS) revealed that Hev b 7.02 can be found in latex milk- and some latex glove-extracts but cannot be detected in sufficient amounts in latex ImmunoCAP k82.

The new rHev b 7.02 isoform presented here is a latex allergen of intermediate importance regarding its sensitization potential (≥20, < 50% positive specific IgE reaction) in HCW and SB patients. The detection of Hev b 7.02 in latex glove- and latex milk-extracts supports a sensitization by contact with these products. The relevance of (r)Hev b 7.02 seems to be higher in German than in Portuguese HCW. We suggest that (r)Hev b 7.02 should be considered to be present in diagnostic tools for latex sensitization detection in sufficient amount.

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References

1. Schmidt MHH, Raulf-Heimsoth M, Posch A. Evaluation of patatin as a major cross-reactive allergen in latex induced potato allergy. Ann Allergy Asthma Immunol 2002;**89**:613–618.
2. Seppala U, Alenius H, Turjanmaa K, Reunala T, Palosuo T, Kalkkinen N. Identification of patatin as a novel allergen for children with positive skin prick test responses to raw potato. J Allergy Clin Immunol 1999;**103**(1 Pt 1):165–171.