

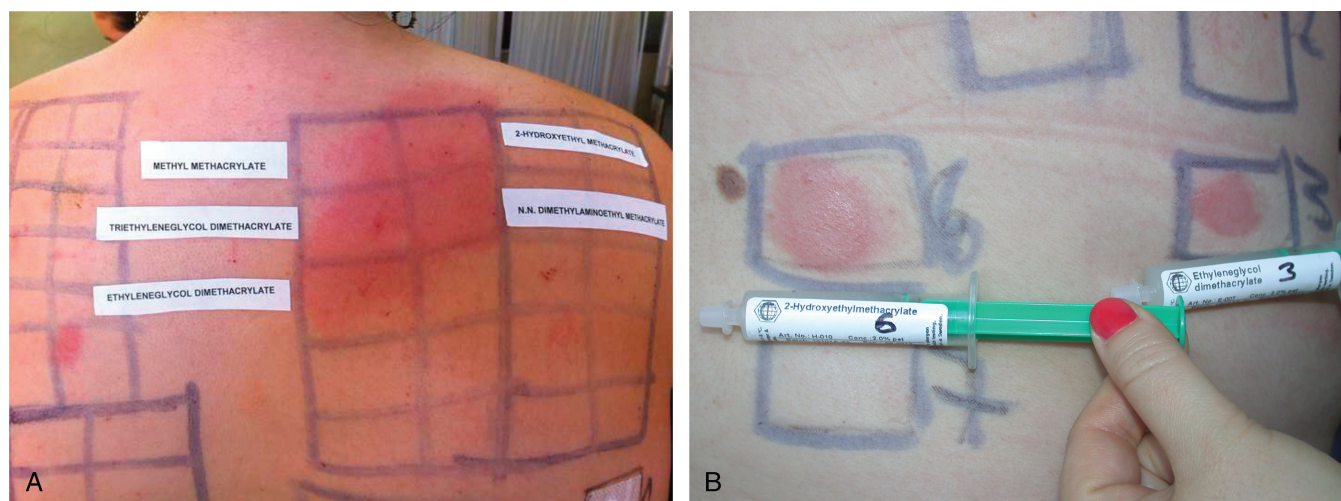


FIGURE 2. A, Positive and wide extension of the acrylates patch tests. B, After performing patch testing with the acrylates separately, positive reactions to ethyleneglycol dimethacrylate and 2-hydroxyethyl methacrylate were obtained.

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REFERENCES

1. Fisher AA. Paresthesia of fingers accompanying dermatitis due to methyl methacrylate bone cement. *Contact Dermatitis* 1979;5:56–57.
2. Sadoh DR, Sharief MK, Howard RS. Occupational exposure to methyl methacrylate monomer induces generalized neuropathy in a dental technician. *Br Dent J* 1999;186:380–381.
3. Fisher AA. Permanent loss of fingernails due to allergic reaction to acrylic nail preparation: a sixteen-year follow up study. *Cutis* 1989;43:404–406.
4. Donaghy M, Rushworth G, Jacobs JM. Generalized peripheral neuropathy in a dental technician exposed to methyl methacrylate monomer. *Neurology* 1991;41:1112–1116.
5. Sickels DW, Stone JD, Friedman MA. Fast axonal transport: a site of acrylamide neurotoxicity? *Neurotoxicology* 2002;23:223–251.

Fermented Rice Flour in Pediatric Atopic Dermatitis

To the Editor:

Atopic dermatitis (AD) is a chronic inflammatory multifactorial disease involving a genetic defect in the proteins supporting the epidermal barrier. Atopic dermatitis is the result of

impaired epidermal barrier function due to intrinsic structural and functional abnormalities in the skin epidermal barrier.¹ The current management of AD aims to relieve inflammation and prevent flare-ups. Conventional therapy for AD consists of elimination of exacerbating factors, moisturizers to maintain skin hydration, antihistamines to alleviate pruritus, topically applied corticosteroids, or topical calcineurin inhibitors to control inflammation. Severe forms of AD may need systemic corticosteroids, oral cyclosporine, and/or phototherapy. There is increasing evidence that disturbances in gut microbial composition play a role in the pathophysiology of immune-mediated disorders such as AD.^{2–5} Gut microbiota are key players in the early development of both local immune maturation and systemic immune programming. Differences in perinatal colonization patterns with both the level of industrialization and subsequent allergic outcomes⁶ provides a strong foundation for intervention studies designed to modify post-natal colonization in the prevention of allergic and immune-mediated diseases. Lactobacilli are a significant component of the Gram-positive intestinal microflora; therefore, they are frequently used as probiotics. Probiotic therapy with *Lactobacillus* and other organisms has been studied for the treatment of atopic dermatitis in infants and children, with contrasting results.⁷ Some probiotic effects have been reported even by nonviable bacteria; the benefits of the ingredient can be ascribed

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Heinz Italia SpA provided the experimental product.

The authors have no funding or conflicts of interest to declare.

DOI: 10.1097/DER.000000000000103

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TABLE 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Age >6 mo	Any other allergic diseases in acute phase/not controlled
AD moderate to severe, according to SCORAD index	Chronic diseases
	Infectious acute or chronic diseases
	Therapy with probiotics in the preceding month
	Therapy with topical calcineurin inhibitors in the preceding 3 months

to the bacterial components present in the final products (eg, DNA, cell wall) as well as other metabolites released during the fermentation process.⁸

Heat-killed probiotic lactobacilli orally administrated as a complementary therapy exhibited beneficial activities in management of AD in adults.⁹ We enrolled 10 voluntary pediatric patients (ages 6 months to 6 years; 5 male, 5 female) affected by moderate to severe AD, to evaluate clinical effects of 12 weeks intake of a fermented rice flour containing *Lactobacillus paracasei* CBA-L74. Written informed consent was obtained by parents or legal guardians. The study was approved by the local ethical committee.

Inclusion and exclusion criteria are shown in Table 1. Patients' enrollment started in February 2013; the study was completed in June 2013. We followed up the patients for 4 additional weeks.

Diagnosis of AD was made by an expert pediatric allergy specialist after careful exclusion of other possible diagnoses. At the recruitment (T0), all children underwent a complete clinical examination, including Scoring Atopic Dermatitis (SCORAD) clinical assessment. No blood tests were performed. At enrollment each patient received a 3-month supply of fermented rice. The daily dosage to be diluted in a liquid

was 7 g. Skin moisturizers were not discontinued; application of topically applied corticosteroids was permitted and strictly monitored. No other therapy was permitted and constituted reason for exclusion.

Fermented rice products in powder were provided by HJ Heinz (Heinz Italia SpA, Latina, Italy). The fermented rice was prepared from rice flour fermented by *Lactobacillus paracasei* CBA L74 (Heinz Italia SpA, Latina, Italy), International Depository Accession Number LMG P-24778. The bacterium has been selected for its ability to ferment cereals (rice, wheat, and oat) and milk. The fermentation is started in the presence of 10⁶ bacteria and is carried out at 35°C for about 20 hours. On average, the final count at the end of the fermentation process is 10⁹ CFU/g. After heating at 85°C for 20 seconds, in view of inactivating the live bacteria, the fermented rice is spray-dried. Thus the final fermented powder does not contain significant amount of living cells but bacterial bodies and fermentation products. The products used in the present study have been checked for their absence of microbiological and chemical contaminants.

Fermented rice consisted of flour powder to be used as a supplement to be dissolved in a liquid as desired. All children were compliant to the prescribed dose of fermented rice flour,

TABLE 2. Patients' SCORAD Assessments at Enrollment and at 4, 8, and 12 Weeks

Patient	SCORAD			
	T0	T4ws	T8ws	T12ws
1	28	33.3	3.5	2
2	50.1	28.3	18.6	21.3
3	28.5	18	N/A	N/A
4	62	20.2	15.3	12.5
5	50.4	35.9	31.8	26
6	70.4	7.9	7.4	0
7	53.9	33.2	37.9	18.6
8	48.1	30.7	18.2	10.3
9	66.4	45.1	39.1	N/A
10	61	20.6	5.5	0

N/A, not available.

which tastes slightly sour similarly to a yoghurt; no palatability complaint was reported. The fermented rice flour was well tolerated in all subjects, and no adverse events were reported during the whole study period. Two girls interrupted the fermented rice flour, one of them at week 4 because of a car accident and the resulting recovery period; the second girl interrupted the fermented rice flour at week 8 because of the difficulty experienced by her mother in mixing it with the food. Eight of 10 children assumed fermented rice flour for 12 weeks; their SCORADs at T0 ranged from 70.4 (severe) to 35 (moderate); they all improved at week 4. At week 8, 7 of 8 children properly consuming the fermented rice had a SCORAD assessment less than 35 (mild). At week 12, all patients' SCORADs were less than 35. All the patients reduced topical steroid application frequency; 4 of 8 suspended them. Table 2 shows patients' SCORAD assessments. After the arranged fermented rice flour suspension, we carried on the patients' follow-up for 4 additional weeks; only a mild flare-up was observed in 1 child (SCORAD <35).

Several studies have been performed to evaluate the efficacy of probiotics for prevention and treatment of AD. A 2007 Cochrane review found no evidence to recommend the addition of probiotics to infant diets in preventing AD; nevertheless, there is emerging evidence that probiotics may prevent and treat AD in children.⁷

Some preclinical data on a mouse model suggested that inactivated bacteria may be effective in protecting against intestinal inflammation⁸ and reducing contact hypersensitivity reactions⁹ and development of atopic skin lesions.¹⁰ Given the probiotic effects of nonviable bacteria in human studies^{11–13} too, their use could be more valuable than viable bacteria (reduced infectious hazards, no need for refrigerated storage, longer shelf life, chance to mix them with warm or hot liquids). For these reasons, we found it very interesting to investigate the benefits of heat-killed probiotic bacteria in the management of children with AD. In this pilot study investigating the clinical effects of a supplementary diet prepared from rice flour fermented by *Lactobacillus paracasei* CBA L74, we registered improvements in all patients; moreover, the parents' perception of their children's AD severity improved for all patients in terms of clinical outcomes and quality of life.

Our study has several limitations; the small sample size and the lack of a placebo control group that prevent statistical evaluation, the shortness of the follow-up, and the upcoming summer that could favor persistence of AD remission. A randomized controlled trial is needed to gain firm conclusions.

Our promising results in terms of steroid sparing, clinical improvement, and parent satisfaction should spur on further investigations on rice flour fermented by *Lactobacillus paracasei* CBA L74 effects in AD affected children.

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REFERENCES

1. Elias PM, Steinhoff M. "Outside-to-inside" (and now back to "outside") pathogenic mechanisms in atopic dermatitis. *J Invest Dermatol* 2008;128:1067–1070.
2. Kirjavainen PV, Arvola T, Salminen SJ, et al. Aberrant composition of gut microbiota of allergic infants: a target of bifidobacterial therapy at weaning? *Gut* 2002;51:51–55.
3. Winkler P, Ghadimi D, Schrezenmeir J, et al. Molecular and cellular basis of microflora-host interactions. *J Nutr* 2007;137:756S–772S.
4. Nermes M, Kantele JM, Atosuo TJ, et al. Interaction of orally administered *Lactobacillus rhamnosus* GG with skin and gut microbiota and humoral immunity in infants with atopic dermatitis. *Clin Exp Allergy* 2011;41:370–377.
5. van der Aa LB, Heymans HAS, van Aalderen WMC, et al. Probiotics and prebiotics in atopic dermatitis: review of the theoretical background and clinical evidence. *Pediatr Allergy Immunol* 2010;21:e355–e367.
6. Kalliomäki M, Kirjavainen P, Eerola E, et al. Distinct patterns of neonatal gut microflora in infants in whom atopy was and was not developing. *J Allergy Clin Immunol* 2001;107:129–134.
7. Lee J, Seto D, Bielory L. Meta-analysis of clinical trials of probiotics for prevention and treatment of pediatric atopic dermatitis. *J Allergy Clin Immunol* 2008;121:116–121.
8. Wagner RD, Pierson C, Warner T, et al. Probiotic effects of feeding heat-killed *Lactobacillus acidophilus* and *Lactobacillus casei* to *Candida albicans*-colonized immunodeficient mice. *J Food Prot* 2000;63:638–644.
9. Chapat L, Chemin K, Dubois B, et al. *Lactobacillus casei* reduces CD8+ T cell-mediated skin inflammation. *Eur J Immunol* 2004;34:2520–2528.
10. Sawada J, Morita H, Tanaka A, et al. Ingestion of heat-treated *Lactobacillus rhamnosus* GG prevents development of atopic dermatitis in NC/Nga mice. *Clin Exp Allergy* 2007;37:296–303.
11. Agostoni C, Goulet O, Kolacek S, et al. Fermented infant formulae without live bacteria. *J Pediatr Gastroenterol Nutr* 2007;44:392–397.
12. Indrio F, Ladisa G, Mautone A, et al. Effect of a fermented formula on thymus size and stool pH in healthy term infants. *Pediatr Res* 2007;62:98–100.
13. Moroi M, Uchi S, Nakamura K, et al. Beneficial effect of a diet containing heat-killed *Lactobacillus paracasei* K71 on adult type atopic dermatitis. *J Dermatol* 2011;38:131–139.