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Probiotics: From anecdotes to clinical demonstration

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To the editor:

In the concise and interesting article “Childhood risk factors for atopy and the importance of early intervention,” which appeared in the April issue of The JACI, Wahn and von Mutius¹ present an updated review on recent research and hypotheses pertaining to the increasing prevalence of atopic disease. Among these, the idea that modification of intestinal flora to increase the predominance of specific beneficial bacteria and thereby to alter the intestinal milieu could be taken as an alternative to attain prophylactic or therapeutic effects in atopic diseases is mentioned. Indeed, a recent study demonstrated that differences in the neonatal gut microflora preceded the development of atopy, suggesting a crucial role of the balance of indigenous intestinal bacteria for the maturation of human immunity to a nonatopic mode.² The authors then refer as follows to the first probiotic intervention study to test the hypothesis³: “In one recently published study from Finland, which unfortunately was not blinded, infants with milk allergy and atopic dermatitis had milder symptoms and fewer markers of intestinal inflammation if their milk was fortified with lactobacilli.”

That is an unfortunate and detrimental misstatement. With respect to its design, the Finnish investigation was a randomized, double-blinded comparison of 2 groups; infants with atopic

dermatitis and challenge-proven cow milk allergy were fed either an extensively hydrolyzed formula or an extensively hydrolyzed formula containing *Lactobacillus* GG (ATCC 53103). The supplier that provided these indistinguishable products coded them independently from the researchers. There were 10 breast-fed infants who fulfilled the study criteria but were not randomized because breast-feeding continued successfully and the probiotics were given to the lactating mother; their outcomes are reported but not included in the comparison.

A significant improvement in the clinical course of atopic eczema was observed in infants given probiotic-supplemented formula, and in parallel, markers of intestinal³ and systemic allergic inflammation, as assessed in a subsequent—also randomized and blinded—study,⁴ were significantly decreased. Similar results have been obtained in milk-hypersensitive adults⁵ in another randomized, double-blinded crossover study.

I wish to make this correction to the review article of Wahn and von Mutius for 2 reasons. First, because of its clear merits, their review could find its way into the files of investigators who might not refer to the original data. Second, modification of the gut microflora forms a relatively new treatment modality for allergic disorders. The first clinical reports^{3,5} were planned to test the efficacy and safety, as well as the mechanisms, of probiotic action so as to provide backup data for larger long-term surveillance studies in different populations and with different strains. Probiotics have succeeded in evoking research interest^{6,7} only because strict methodology has been applied in the validation of specific strains both in vitro and in vivo, as well as clinically, and because important properties such as safety have been given top priority.

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