

76 received a mixture of 4 probiotics, and 74 received a placebo. CMA was diagnosed in 120 infants (52% of the study population). Thirty-seven percent of infants with CMA received *Lactobacillus* GG (n = 44), 37% received a mixture of 4 probiotics (n = 44), and 27% received a placebo (n = 32).³ There were no statistical differences at the baseline levels of cytokine secretions among different treatment groups, indicating that groups were equal at entry. The nonparametric tests were used for comparisons of all variables because of widespread dispersion of the data. Our findings of the immunologic effect of probiotics were based on the changes in cytokine concentrations (after-before) compared among treatment groups with the nonparametric Mann-Whitney *U* test. Individual changes in cytokine concentrations were analyzed with the Wilcoxon signed-rank test. We agree that the study design proposed by Niers et al¹ is the correct one and is often feasible, especially in animal studies, but not in a clinical study as ours. The diagnostic procedure to verify CMA takes a long time; the disappearance of symptoms is always required before the challenge test. In the challenge test, the short exposure to cow's milk provokes fewer symptoms, and presumably, the immunologic response is weaker than observed before treatment. Therefore, we think that randomization only after a positive challenge test result could give an erroneously negative result on the effect of treatment on both symptoms and immunologic reaction.

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Regarding "Differential control of T_H1 versus T_H2 cell responses by the combination of low-dose steroids with β_2 -adrenergic agonists"

To the Editor:

We found the article by Goleva et al¹ to be very interesting. The authors postulate that the different proliferative responses of PBMCs to suboptimal fluticasone and salmeterol between healthy controls and patients with allergy and asthma could be due to an increased expression of phosphodiesterase 4 in patients with allergy and asthma. We would like to propose an alternative hypothesis. Is it possible that this difference could be explained by β_2 -adrenergic receptor downregulation in the asthmatic population? Although we are told that β_2 agonists were withheld for 24 hours in the asthmatic cohort, we do not know how much patients were receiving before the β_2 agonists were stopped. Hayes et al² described a 22% downregulation of β_2 -adrenergic receptors after 2 weeks of albuterol treatment. McGraw and Liggett³ also reported that lymphocytes desensitized very rapidly to β_2 -agonist exposure. Such a downregulation might lead to a blunted response in the downstream cyclic adenosine monophosphate pathway. Do the authors have any insights or data regarding this?

Also, please note that fig 3 seems to be mislabeled. The text indicates that all 4 panels represent results from individuals with asthma. The y-axis labels indicate that IL-13 production is indicated in panels A and B, whereas IL-5 production is indicated in panels C and D. The legend of the figure indicates that panels A and C are results from the healthy control group and that IFN- γ and TNF- α production were measured. Any clarification on this matter would be greatly appreciated.

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