Breast-feeding, atopy, and asthma

To the Editor:

Recent reports by Chulada et al[1] and several others[2-4] showed a protective effect of exclusive breast-feeding of ≥4 months against asthma and atopy, though some studies did not support this conclusion.[5] What could be the reason for these controversial findings?

Normally, a balance is maintained between T_H1 and T_H2 cells. T_H1 cells produce IFN-γ, IL-2, and TNF-α, whereas T_H2 cells produce IL-4, IL-10, and IL-13 cytokines. IFN-γ is a pleiotropic cytokine that acts by binding to its receptor, which is coupled to the Jak-STAT signaling pathway. Animals that lack IFN-γ, the IFN-γ receptor, or STAT 1 display disruption of both innate and adaptive immunity. T-bet, a member of the T-box family of transcription factors, is rapidly induced in early developing T_H1 cells and is absent in developing T_H2 cells. Introduction of T-bet into T cells results in the conversion of these cells into T_H1 cells that produce IFN-γ but not IL-4 and IL-5 production.[6] Mice that lack T-bet cannot generate T_H1 response and have development of spontaneous airway hyperreactivity and asthma.[7]

Breast milk is rich in long-chain polyunsaturated fatty acids (LCPUFAs).[8] LCPUFAs, especially γ-linolenic acid (GLA), arachidonic acid (AA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), suppress immune response and the secretion of T_H1 cytokines IL-1, IL-2, and TNF-α. The inhibitory effect of EPA and DHA on the secretion of IL-1, IL-2, and TNF-α are much stronger than those exerted by GLA and AA. Synthesis and secretion of TNF-α is diminished by EPA and DHA and is unchanged or increased by AA and other ω-6 fatty acids. Furthermore, EPA/DHA supplementation enhances transforming growth factor (TGF)–β production and thus delayed autoimmune disease in experimental animals. TGF-β decreases biosynthesis and release of TNF-α and thus serves as a negative controller of TNF-α production. Some of the actions of TGF-β depend on the presence of LCPUFAs.[8] Thus, depending on the type and amounts of LCPUFAs given, T_H1 responses can be enhanced and T_H2 responses are blunted, which favor suppression of atopy and asthma. This favorable action on T_H1 and T_H2 responses may depend on the ratio between ω-3 and ω-6 fatty acids. A higher ratio of ω-6 to ω-3 LCPUFAs favors an enhancement in the T_H1 response, whereas a decrease in the ratio between ω-6 to ω-3 may favor the T_H2 response. Because breast milk is rich in ω-6 LCPUFAs, the protective effect of breast-feeding against atopy and asthma might be attributed to its high content of these beneficial fatty acids.[8] This is supported by the observation of Galli et al,[9] who showed that in newborn infants "at risk" for atopic disease, di-homo-gamma-linolenic acid and AA levels were lower in cord blood in infants who subsequently had atopic disease than in nonatopic infants. These changes were more marked in children who subsequently had atopic disease.

It is suggested that duration of breast-feeding and LCPUFA content of breast milk are two variables that may account for differences in the results reported by various investigators. It is likely that there is a linear relation between the concentrations of ω-6 and ω-3 fatty acids and TGF-β in human breast milk, which may explain the significant inverse association observed between the dose of TGF-β received through milk and wheezing.[10] Hence, in the future, not only the duration of breast-feeding but also the LCPUFA and TGF-β content and the ratio between various LCPUFAs and TGF-β in breast milk and their relation to atopy and asthma and the effect of various LCPUFAs on T-bet expression need to be studied.

Undurti N. Das, MD, FAMS, FICP
EFA Sciences LLC
Norwood, Mass

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Reply

To the Editor:

In a previous letter, we suggested that breast-feeding might protect children against environmental tobacco smoke (ETS)–related asthma and recurrent wheeze by promoting postnatal T_H2/T_H1 switching.[1] In the letter above, Dr Das[2] further suggests that high levels of ω-6 long-chain polyunsaturated fatty acids (LCPUFAs) in breast milk, namely di-homo-gamma-linoleic acid