

# Cytokines in Breast Milk from Allergic and Nonallergic Mothers

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## Key Words

Milk, human · Cytokines

## Background

The allergy-preventing effect of breast-feeding is controversial [1, 2]. This may be due to individual variations of the composition of human milk. Allergy is associated with a bias to production of cytokines involved in IgE synthesis, e.g. IL-4 and IL-13 [3] and the eosinophil chemotactic [4] and survival [5] factor IL-5. In contrast, IFN- $\gamma$ , which inhibits IgE synthesis [6], is downregulated [7]. Cytokines involved in IgA production, IL-6, IL-10 and TGF- $\beta$  [8, 9] have also been proposed to be involved in IgE synthesis [10–12]. Comparative investigations of cytokine levels in breast milk from allergic and nonallergic mothers have not been reported. The aim of this study was to investigate the levels of IL-4, IL-5, IL-6, IL-10, IL-13, IFN- $\gamma$ , TGF- $\beta$ 1 and TGF- $\beta$ 2 in breast milk from allergic and nonallergic mothers.

## Materials and Methods

Colostrum and mature milk, obtained at 1 month after delivery, from 49 mothers, whose children participated in a prospective study, were analyzed. The mothers considered as allergic (n = 19) had allergic symptoms and a positive allergy screen and the nonallergic ones (n = 20) had no allergic symptoms and a negative allergy screen. The cytokine levels were analyzed with commercial ELISA kits from CLB

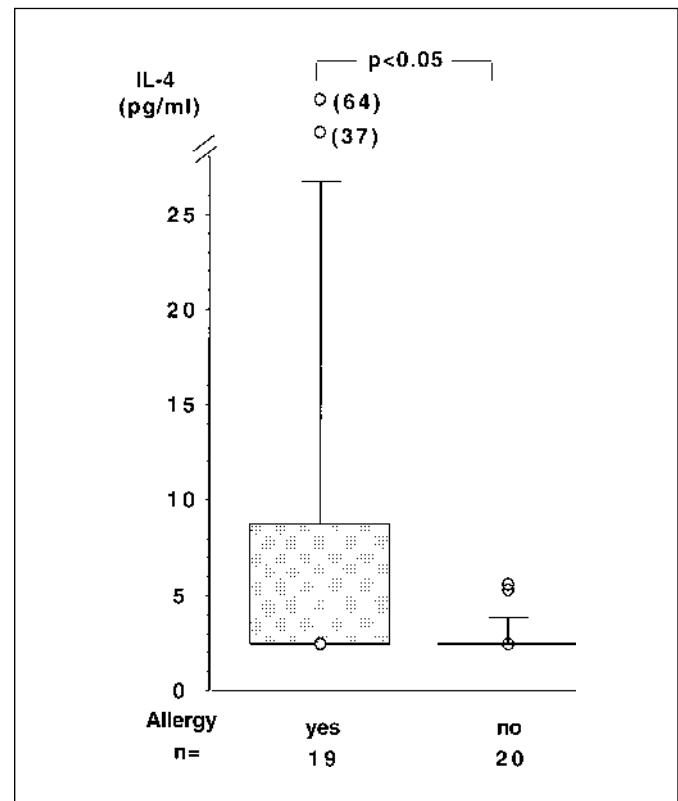


**Fig. 1.** Levels of IL-4 in colostrum from allergic and nonallergic mothers. Detection level was 5.6 pg/ml. The 10th, 25th, 50th, 75th and 90th percentiles are indicated as well as outliers (n = number of samples).

**Table 1.** Cytokine levels in human colostrum and mature milk

|                | Cutoff | Colostrum |        |            | 1 month  |        |            |
|----------------|--------|-----------|--------|------------|----------|--------|------------|
|                |        | positive  | median | range      | positive | median | range      |
| IL-4           | 5.6    | 12/49     | <5.6   | -91        | 10/49    | <5.6   | -109       |
| IL-5           | 6.2    | 4/46      | <6.2   | -11        | 1/47     | <6.2   | -11        |
| IL-6           | 5.6    | 42/49     | 19     | -279       | 31/48    | 20     | -247       |
| IL-10          | 19.2   | 6/49      | <19    | -202       | 3/48     | <19    | -139       |
| IL-13          | 3.2    | 16/48     | <3.2   | -89        | 12/47    | <3.2   | -56        |
| IFN- $\gamma$  | 66.7   | 4/49      | <67    | -113       | 1/49     | 67     | -59        |
| TGF- $\beta$ 1 | 125    | 49/49     | 325    | 152-1,165  | 48/49    | 261    | -616       |
| TGF- $\beta$ 2 | 250    | 49/49     | 1,131  | 357-16,784 | 47/47    | 787    | 166-11,696 |

The median and range for the cytokines are expressed in pg/ml. Positive samples are those above the cutoff, expressed in relation to the total number of analyzed samples. The cutoff is the lowest limit for quantitative determination shown for the different assays.

Research Diagnostic, Flanders, USA (IL-4, IL-6, IL-10, IL-13 and IFN- $\gamma$ ) and R&D Systems, Minneapolis, Minn., USA (TGF- $\beta$ 1 and TGF- $\beta$ 2). IL-5 and total IgA were analyzed with in-house ELISAs.

levels of the cytokines involved in IgA synthesis correlated and the levels of these cytokines were higher in samples with high total IgA levels.

## Results

There were large variations in the levels of the different cytokines among the mothers (table 1). However, supporting that breast milk is anti-inflammatory, the immunosuppressive cytokine TGF- $\beta$  was dominating. The allergic, as compared to non-allergic mothers had higher levels of IL-4 (fig. 1) and tended to have higher levels of IL-13 ( $p = 0.11$ ) and IL-5 ( $p = 0.13$ ) in their colostrum. The levels of the other cytokines were similar between the two groups. The

## Conclusion

The immunosuppressive [13] TGF- $\beta$  was the major cytokine in human breast milk. Levels of IgA and cytokines involved in IgA synthesis correlated. This may explain the early IgA production seen in breast-fed, as compared to formula-fed babies [14]. The higher levels of IL-4 in breast milk from allergic mothers could partly explain the controversial results regarding the protective effect of breast-feeding against atopic sensitization in the children.

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