

How to Prevent Allergic Disease

I. Study of Specific IgE, IgG, and IgG4 Antibodies in Serum of Pregnant Mothers, Cord Blood, and Infants

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Abstract. We have investigated methods for decreasing the number of allergic patients and have produced the following data. We compared mothers' total IgE levels and allergen-specific IgG and IgG4 levels in 72 paired cases. In mothers with high total IgE, the cord blood levels of IgG and IgG4 specific for egg, milk, and mite allergens were significantly higher than in mothers with low IgE levels. Mothers who took over 200 ml of milk per day showed a statistically higher level of milk-specific IgG antibody. From our studies of IgE, IgG, and IgG4 antibody levels in atopic dermatitis patients, we conclude that specific IgG and IgG4 levels should be considered when eliminating offending foods. Infants with high egg-specific IgG antibody levels in cord blood were statistically more prone to develop allergic disease.

Introduction

According to our earlier study [1], about 6.8% of the 2- to 12-year-old children suffer from asthma in non-air-polluted areas of Japan. This is similar to the numbers seen in many countries. Many antiallergic drugs and many new bronchodilators have been recently produced, but such medications are mainly for controlling allergic symptoms. Since patients who suffer from allergic diseases are very difficult to cure completely, our prime concern has been to determine the best method for preventing allergic disease.

Several papers have shown that babies with elevated cord blood levels of total IgE are at increased risk of developing allergic disease [2-5].

From these data, Falth-Magnússon and Kjellman [11] suggested that the best prevention of allergic disease is maternal abstention from the major food allergens beginning the first trimester, which is a logical conclusion. But elimination of major food allergens is a very perplexing problem for the pregnant mother who requires nutrition for the embryo.

If we knew much more about the correct food to eliminate, it would benefit not only the pregnant mother, but also the physician advising food elimination. Therefore, we compared the specific antibody levels in the pregnant mother's blood, cord blood, and infant blood.

Patients and Methods

Patients

Blood from 157 women, 7-8 months pregnant, was taken and stored at -40°C. Cord blood was collected from the same patients at delivery. Blood was also collected from 72 infants for comparison. This study is based on allergy questionnaires, given to pregnant women by a tologist.

Laboratory Procedures

Serum IgE Measurement. We used a highly sensitive radioimmunoassay method (Daiichi Radio Isotope, Tokyo, Japan). This method is sensitive to 0.1 U/ml.

Radioallergosorbent Test (RAST). RAST was performed using a commercial kit (Pharmacia). RASTs with egg white, milk, soybean, and house dust mite (*Dermatophagoides farinae*) were performed by standard methods.

Specific IgG and IgG4 Antibodies. Enzyme-linked immunosorbent assay was used with polyethylene plates. Peroxidase-conjugated goat antihuman IgG (Cappel) was used for specific IgG and mouse antihuman IgG4 antibody (Yamasa, Tokyo) for specific IgG4 antibody measurement. In this experiment, we used highly specific IgG and IgG4 serum from food allergy and mite-sensitive patients for control. The results are expressed in units [6]. Serum from the mother was diluted 1/100 and the cord blood 1/50.

Correlation of Clinical Signs with IgE and IgG4 Antibody Levels. Atopic dermatitis patients (n = 196) were studied in this trial. We compared clinical signs before and after elimination of offending food. Clinical symptoms were evaluated by the following criteria: Treatment was considered effective, if clinical signs had completely disappeared or were remarkably improved as compared to before food elimination. Treatment was considered ineffective, if there was no remarkable change in clinical signs.

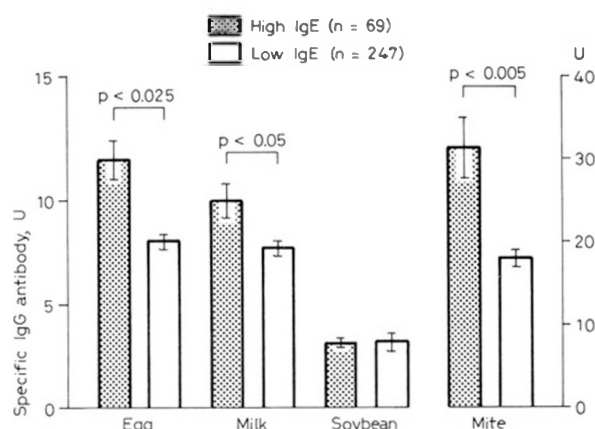


Fig. 1. Cord blood specific IgG antibody. Comparison between maternal high and low IgE values.

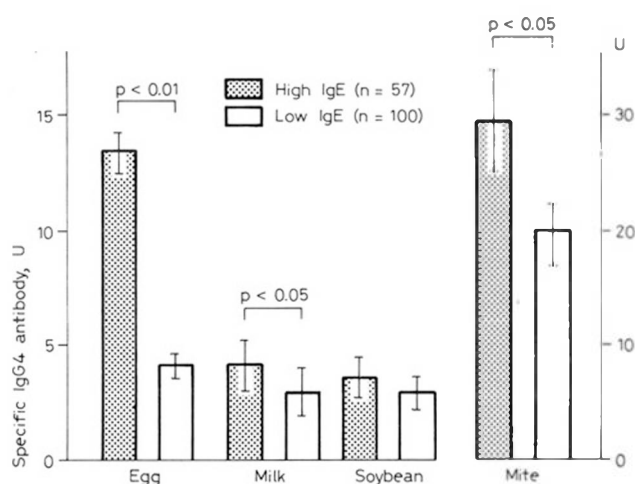


Fig. 2. Cord blood specific IgG4 antibody. Comparison between maternal high and low IgE values.

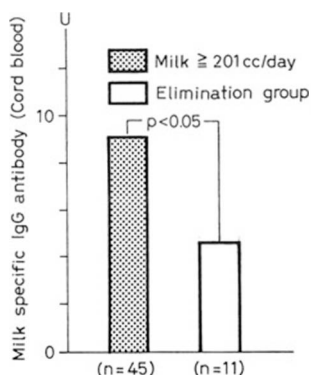


Fig. 3. Comparison of milk specific IgG in cord blood between mothers with milk intake over 200 ml per day and those that eliminated milk.

Table 1. Relationship between clinical symptoms and egg-specific IgG antibodies in infants

Clinical symptoms	Egg IgG, U		Total
	≥30	<10	
Positive	10	15	25
Negative	5	42	47
Total	15	57	72

$p < 0.01$

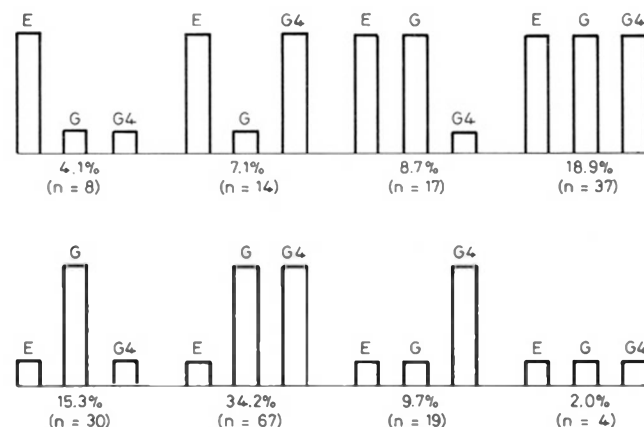


Fig. 4. Combination of IgE (E), IgG (G), and IgG4 (G4) antibody levels in elimination-effective patients. High bars indicate high antibody levels, low bars indicate low antibody levels.

Results

There was no correlation between the mother's total IgE and cord blood total IgE in 157 paired cases. Figures 1 and 2 show that the levels of IgG and IgG4 specific for egg, milk, and mite allergens were significantly higher in the cord blood of women with elevated total IgE as compared to women with low levels of total IgE. The cord blood of mothers who took over 200 ml of milk per day showed a statistically higher level of specific IgG milk antibody than those who eliminated milk (fig. 3).

Infants with high egg-specific IgG antibody levels in cord serum were statistically more prone to develop allergic disease (table 1). In only 4.1% of the subjects (the high total IgE antibody group) did clinical signs improve after the elimination of the offend-

ing food. Those patients with high specific IgG and IgG4 antibody levels showed very good improvement after the offending foods were eliminated (fig. 4).

Discussion

In allergic disease, the IgE level is very important. Human fetal cells have been demonstrated to produce IgE from the 11th week of gestation [7]. This fetal IgE is stimulated by the mother's daily life-style, especially if the mother eats highly allergenic foods, e.g., eggs and milk. In general, if the mother has an allergic disease, the child will have an increased likelihood of also suffering from an allergic disease. Methods for preventing allergic disease have been widely sought in clinical practice. For this reason, cord blood IgE studies [8] and newborn infant blood studies are very important in understanding the development of allergic disease [4]. The most important problem at present is that we are not sure what role IgE plays; however, in the studies we have described, we found that when the mother's intake of milk is excessive, the cord blood IgG and IgG4 antibody levels were very high when compared to mothers whose intake of milk was low. The important thing is whether the specific IgG and IgG4 antibody is correlated with allergic disease or not. On this point our data suggested that the cord blood specific IgG antibody is related to infants' allergic disease. The allergen-specific IgG response to specific immunotherapy for inhalant allergen is generally thought to be a blocking antibody [9]. But there is another report of food-specific IgG antibody which correlates with severe anemia and chronic bronchitis and is associated with a markedly elevated level of IgG specific for cow's milk protein [10].

The results of IgE, IgG and IgG4 antibody measurements in patients in whom food elimination was effective revealed that the specific IgG antibody is very important. Elimination of cow's milk and egg in late pregnancy has been shown to prevent atopic disease in the infant, but Falth-Magnússon and Kjellman [11] recently reported that they have not been able to show any prevention of atopy in the baby by maternal abstention from cow's milk and egg during late pregnancy. If we are to decrease the number of

allergic patients, I would like to emphasize that it is necessary to test not only IgE levels, but also IgG and IgG4 antibodies as early as possible, preferably in the cord blood.

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