
Extraordinarily high serum IgE levels and consequences for atopic phenotypes

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Background: IgE plays a central role in allergic diseases. Recent studies have postulated an association between serum IgE levels and bronchial asthma.

Objective: To examine the differences of atopic phenotypes in a group of individuals with extraordinarily high serum IgE levels ($>10,000$ kU/L) compared with children with moderately elevated IgE levels (400–1,000 kU/L).

Methods: We investigated 20 children with serum IgE levels greater than 10,000 kU/L and compared them with 56 age-matched children with serum IgE levels of 400 to 1,000 kU/L regarding prevalences of atopic dermatitis, bronchial asthma, allergic rhinoconjunctivitis, allergic sensitization, and history of anaphylaxis.

Results: The mean eczema severity score as determined by the Severity Scoring of Atopic Dermatitis Index was 56 vs 18 ($P < 0.003$), and anaphylactic reactions were reported in 20% of the group with very high serum IgE levels vs 7% in the group with moderate levels ($P < 0.02$). Sensitization to both aeroallergens and food allergens was detected in 80% of the group with very high serum IgE levels vs 32% of the group with moderate levels ($P < 0.001$).

Conclusions: Our results indicate that children with very high serum IgE levels are at risk for anaphylactic reactions and more severe atopic dermatitis.

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INTRODUCTION

Atopic phenotypes are influenced by various factors, such as atopic family background and environmental allergen exposure. Recent studies have postulated an association between serum IgE levels and atopic dermatitis¹ and asthma and forced expiratory volume in 1 second.² This association has even been found in nonallergic individuals.³ IgE levels are influenced by various factors, such as age, sex, seasonal changes, and lifestyle and genetic factors.^{4–6} This study was undertaken to examine the differences of atopic phenotypes in the group of individuals with extraordinarily high serum IgE levels ($>10,000$ kU/L) compared with children with moderately elevated IgE levels (400–1,000 kU/L).

PATIENTS AND METHODS

We investigated 20 children with serum IgE levels greater than 10,000 kU/L and compared them with 56 age-matched children with serum IgE levels of 400 to 1,000 kU/L regarding prevalences of atopic dermatitis, bronchial asthma, allergic rhinoconjunctivitis, allergic sensitization, and history of anaphylaxis. Allergic sensitization was defined as showing specific IgE levels above the detection limit (>0.35 kU/L) to at least one common aeroallergen and/or nutritional allergen. Bronchial asthma was defined as recurrent wheeze, allergic rhinoconjunctivitis, and typical nasal and conjunctival symptoms during the pollen season associated with a corresponding sensitization. Anaphylaxis was defined as a severe sys-

temic reaction with clinical symptoms of severe dyspnea and/or cardiovascular collapse. All diagnoses were made by a pediatric allergy specialist.

Patients were recruited from the sera data bank of our allergological laboratory; data were therefore analyzed retrospectively. Patients represented children whose serum samples were transferred to our laboratory for evaluation of allergy from either the primary care pediatricians of the children or our outpatient specialist department.

Total and specific serum IgE levels were measured by a fluorescence enzyme immunoassay (CAP system; Pharmacia Diagnostics, Freiburg, Germany). Specific IgE was determined for aeroallergens (birch, grass, cat, *Dermatophagoides pteronyssinus*, *Cladosporium herbarum*) and food allergens (hen's egg, cow's milk, peanut, wheat). Specific sensitization was defined as levels above the detection limit (>0.35 kU/L).

Severity of eczema was scored according to the Severity Scoring of Atopic Dermatitis Index (SCORAD), with evaluation of topography items (affected skin area), intensity criteria (extent of erythema, edema, crusts, excoriations, lichenification, and xerosis), and subjective parameters (extent of itch and loss of sleep). The maximum possible score was 103 points.⁷ Statistical significance was calculated by the χ^2 test and Yates test (SPSS statistical software version 8.0, SPSS Inc, Chicago, IL); $P < 0.05$ was considered statistically significant.

RESULTS

Twenty children (mean age, 11.4 years) were identified as having total serum IgE levels above 10,000 kU/L (mean, 29,254 kU/L). Fifty-six age-matched children (mean age, 11.5 years) with serum IgE levels between 400 and 1,000 kU/L (mean, 719 kU/L) served as controls. Comparing prev-

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Table 1. Comparison of Children with High Serum IgE Levels to Those with Moderately Elevated Serum IgE Levels

	IgE level, kU/L		P value
	>10,000 (n = 20)	400–1000 (n = 56)	
Age, mean (range), y	11.4 (2–21)	11.5 (1–19)	0.84
Sex, M/F, %	50/50	60/40	0.41
Total serum IgE, mean (range), kU/L	29,254 (10,075–213,000)	719 (420–993)	<0.001
Atopic dermatitis, %	95	50	<0.001
SCORAD points, mean (range)	56 (0–87)	18 (0–71)	<0.003
Bronchial asthma, %	60	55	0.40
Allergic rhinoconjunctivitis, %	35	45	0.67
Anaphylactic reaction, %	20	7	<0.02
Sensitized to aeroallergens solely (>0.35 kU/L), %	5	46	<0.001
Sensitized to food allergens solely (>0.35 kU/L), %	5	7	0.74
Sensitized to both (>0.35 kU/L), %	80	32	<0.001

Abbreviation: SCORAD, Severity Score of Atopic Dermatitis.

alence rates of atopic phenotypes between the 2 groups, we found significant differences in atopic symptoms (Table 1). In the group with very high IgE levels, 95% of children had atopic dermatitis compared with 50% in the group with moderately elevated IgE levels ($P < 0.001$). The SCORAD score was 56 vs 18 ($P < 0.003$), and anaphylactic reactions were reported in 20% of the group with very high serum IgE levels vs 7% in the group with moderate levels ($P < 0.02$). No differences could be detected in the prevalence of bronchial asthma and allergic rhinoconjunctivitis.

Allergic sensitization solely to aeroallergens could be demonstrated in 5% vs 46% ($P < 0.001$). Sensitization only to food allergens was found in 5% vs 7% ($P = 0.74$). Sensitization to both aeroallergens and food allergens was detected in 80% in the group with very high serum IgE levels vs 32% in the group with moderate levels ($P < 0.001$). In the group with very high serum IgE levels, there were sensitizations to 6.2 allergens compared with 3.2 in the group with moderate levels ($P < 0.02$).

We found significant differences concerning levels of specific IgE between the 2 groups: mean specific IgE levels to aeroallergens was 44.2 kU/L in the group with very high IgE levels vs 6.3 kU/L in the group with moderate levels ($P < 0.003$). Similar findings were obtained for food allergens (52.4 vs 12.8 kU/L; $P < 0.001$).

DISCUSSION

Since serum IgE levels are associated with age,⁵ we eliminated this strong influencing factor by creating age-matched groups. The primary aim was to characterize children with very high IgE serum levels. We decided to compare this group not with children with “normal” IgE levels, since marked differences are expected if extreme groups are compared. The control group was chosen with moderately elevated IgE serum levels (400–1,000 kU/L) to have “average” atopic children seen in the general practice as a control group.

The selection of patients represents a highly selected pediatric population, since the serum samples of the children were sent to our allergologic laboratory on suspicion of

IgE-mediated allergic disease. However, the aim of this study was not to compare IgE- and non-IgE-mediated allergic individuals but rather children with moderately and extraordinarily elevated IgE levels.

Among the differential diagnosis of patients with very high IgE levels is the hyper-IgE syndrome. We ruled out this diagnosis by clinical factors (such as lack of immunologic deficiencies and cold abscesses or typical physiognomy). Children with other confounding diseases were excluded from our study. Another potential confounder, atopic family history, showed no significant association with IgE levels.

One possible explanation for the similar percentage of bronchial asthma in both groups is that asthma, in contrast to atopic dermatitis, is not related to IgE serum levels.⁸ Hypothetically, this may also be true for allergic rhinoconjunctivitis, although there are no reports in the literature. Furthermore, total serum IgE levels in bronchial asthma patients can be determined by mutations in multiple genes, such as promoter polymorphisms at CTLA4 and FCεR1B.⁹

For asthma and allergic rhinoconjunctivitis, no statistical difference was found between the groups, whereas both atopic dermatitis and anaphylaxis were significantly increased in the group with very high serum IgE levels. From studies on allergy prevention, it is known that feeding a hypoallergenic formula has an impact on the development of atopic dermatitis and food allergy but not on respiratory symptoms.¹⁰ In addition, inducing a low aeroallergen environment for the infants positively influences the development of bronchial asthma and rhinoconjunctivitis. Given the fact that (1) a considerable proportion of children with atopic dermatitis have food allergy, and (2) foods are among the most common causes of anaphylaxis, and finally (3) there were more children with atopic dermatitis in the very high serum IgE group^{1,11} may explain why clinical anaphylaxis and sensitization to foods are significantly more prevalent in children with atopic dermatitis and very high serum IgE levels, whereas there is no difference for bronchial asthma and allergic rhinoconjunctivitis between the 2 groups.

The higher rate of sensitization solely to aeroallergens in the group with serum IgE levels of 400 to 1,000 kU/L can be explained by the fact that children with asthma and allergic rhinoconjunctivitis typically show moderately elevated IgE levels and sensitization to inhalant allergens and are therefore represented in our control group. The sensitization rates solely to food allergens were low in both groups, although children with atopic dermatitis have food allergy in about one third of cases. However, since children with food allergy are often polysensitized, including sensitization to aeroallergens, they are represented in the group with sensitization to both allergen groups (Table 1). In conclusion, our results indicate that children with very high serum IgE levels are at risk for anaphylactic reactions and more severe atopic dermatitis.

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