

Serum IgE in non-atopic adults and in dermatitis patients

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Total serum IgE was determined with the PRIST® technique, and specific reaginic antibodies against 10 allergens were measured in 163 healthy adults with no personal or family history of symptoms indicative of atopy (Group A). 103 non-atopic adults with a family history of atopic diseases were similarly investigated (Group B). When all subjects who at the second interview presented with a history of atopic symptoms and those with positive RAST results were excluded, the geometric mean serum IgE value for Group A was 14.5 (SD = 2) - 94.4 U/ml and for Group B 14.4 (SD = 2) - 130.2 U/ml. There was no significant difference in the IgE values between men and women. Subjects under 40 years of age had significantly higher IgE values than subjects over 40 years. In the series of 276 dermatitis patients the geometric mean IgE value for the men was significantly higher (46.8) than for the women (28.8 U/ml). There was a highly significant difference in the mean serum IgE levels between the patients with a personal history of atopic diseases and the other patients. Patients with present atopic disease had significantly higher mean IgE values than those with past atopic disease while no significant difference was discernible in the mean IgE levels between the non-atopic patients from atopic families and those with no personal and family atopy. Three years later, total serum IgE was controlled in subjects with initial IgE levels > 100 U/ml. During this time, eight subjects had developed an atopic disease. In most cases, there were only slight variations in the IgE values.

Key words: allergic contact dermatitis; other forms of dermatitis; non-atopic population; total serum IgE; age; sex.

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In countries where helminthic parasites are not prevalent, most patients with elevated serum IgE levels have atopic disorders (5). For 20 years total serum IgE levels have been used for identifying atopic subjects.

The double antibody assay (6) and the direct sandwich type assay (2) are methods accurate enough for determining low IgE levels in the non-atopic population (6, 9, 13). Using the sandwich method PRIST® (Pharmacia, Uppsala, Sweden) Zetterström & Johansson (18) obtained the geometric mean of 13.8 U/ml (SD = 2) to 114 U/ml for total serum IgE in 175 healthy non-atopic adults. They concluded that a serum IgE value above 100 U/ml in a patient is strong evidence of an atopic disease, while a

value below 20 U/ml indicates that the symptoms are due to intrinsic or infectious disease.

According to some authors males have higher IgE values than females (1, 3), but usually no significant effect of age or sex on total serum IgE levels in healthy non-atopic persons has been found (8, 13, 17, 18). Even a family history of atopic diseases has been reported to influence serum IgE levels in subjects with no personal atopic history (15, 16). Non-atopic subjects from atopic families have been excluded from many but not all IgE reference materials.

The aim of the study was 1) to establish an IgE control material consisting of non-atopic adults originating from the same population as

our patients, 2) to determine whether an atopic family history has any influence on IgE levels of healthy adults with no personal history of atopic disease, 3) to measure IgE levels in patients with various forms of dermatitis, and 4) to assess a possible correlation between anamnestic atopy and serum IgE levels in these patients.

MATERIAL AND METHODS

Population study

Group A. To collect a non-atopic control population, 236 consecutive subjects participating in a health survey, 210 blood donors, and 60 first-year students at the Turku University, were interviewed by a physician. Only those who fulfilled the following criteria were accepted:

- 1) No present or past atopic disease, including allergic rhinitis, allergic asthma or atopic dermatitis in the subject or his/her close relatives.
- 2) No recurrent ear infection, pneumonia or chronic bronchitis.
- 3) No symptoms of food or drug allergy.
- 4) No abnormal reactions to insect bites.
- 5) No symptoms of contact allergy.
- 6) No history of frequent infectious disease.
- 7) No infection in the last 2 weeks.
- 8) No specific antibodies detected in serum at RAST screening.

Group B consisted of 103 subjects who had a negative personal history of the disorders listed above but had a positive family history of allergic rhinitis, asthma or atopic eczema.

Of the 506 subjects interviewed, 240 were excluded from the material, of them 110 because of personal history of allergic rhinitis, asthma or atopic dermatitis. Only 21 % of the students and 30 % of the other subjects interviewed, fulfilled all the anamnestic criteria.

Total serum IgE was measured by the Phadebas IgE PRIST (Pharmacia Diagnostic AB, Uppsala, Sweden). Specific antibodies against

10 allergens were measured using Phadebas RAST. The allergens were cat, dog, mugwort, timothy, birch, alder, *Cladosporium*, house dust mite, and egg.

Three years later total serum IgE was controlled in subjects with initial IgE levels > 100 U/ml, their histories were rechecked and prick tests with 20 allergens were performed. The allergens were the same as used in the RAST panel plus 10 others: dandelion, white oxeye, horse, cow, feathers, *Alternaria*, *Aspergillus*, *Aureobasidium*, *Mucor*, and *Penicillium* (Allergologisk Laboratorium, Copenhagen, Denmark). To avoid seasonal variations, the blood samples for initial and control determinations of IgE were collected during October and November.

Patients

276 dermatitis (eczema) patients aged 17 to 74 years were patch tested with a standard series of allergens and other compounds indicated by a history. 180 patients were diagnosed as having allergic contact dermatitis (including 11 patients with atopic dermatitis and a relevant contact allergy), and 96 patients had other forms of dermatitis without contact allergy (atopic, nummular, seborrhoeic, irritant). The patients were divided into four groups according to their atopic history:

- 1) 47 subjects with present allergic rhinitis, allergic asthma and/or atopic dermatitis.
- 2) 43 subjects with past atopic disorders.
- 3) 53 subjects with negative personal but positive family history (parents, siblings, children) of atopic disorders.
- 4) 135 subjects with negative personal and family histories.

Only after this classification was the total serum IgE determined by the PRIST technique according to the manufacturer's protocol. Each patient was subjected to prick tests with the same 20 allergens as the prick-tested subjects of the control population. Statistical calculations were made after e-log conversation of the IgE results. Student's t-test was used for statistical analyses.

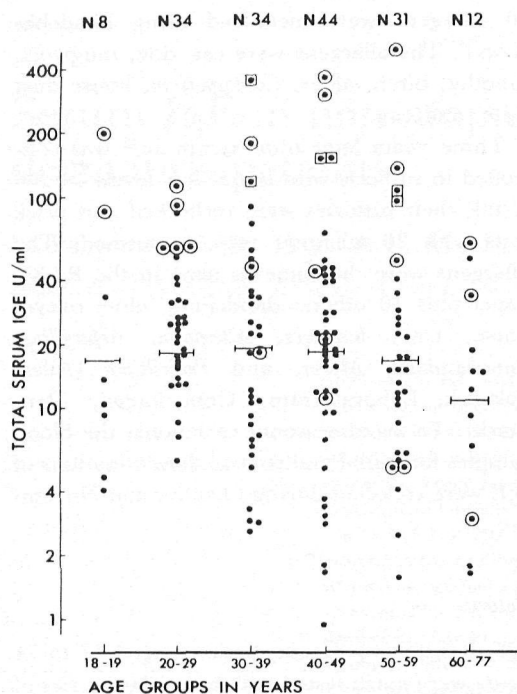


Fig. 1. Distribution of total serum IgE levels in various age groups in the initial non-atopic population. Cross bars indicate geometric means. ● RAST positive; ■ criteria for non-atopy not fulfilled.

RESULTS

Non-atopic control population (Group A)

IgE levels of the initially selected 163 subjects varied from 0.7–500 U/ml (Fig. 1). Of them 87 (57%) had IgE levels < 20 U/ml, while 13 (8%) had IgE levels $\geq$ 100 U/ml. Ten of the latter subjects presented with a history of atopic symptoms when the histories were rechecked (Table 1). During the 3-year period one man had developed allergic rhinitis and another had suffered from recurrent urticaria. There was good correlation between the RAST results and prick test responses except in two cases (Nos. 1 and 11) with negative RAST but positive prick test. The allergens causing positive prick test responses (Taraxacum/dandelion, Chrysanthemum/white oxeye) were not included in the RAST panel. In seven cases the IgE levels had

somewhat decreased during 3 years. The greatest increase was observed in a man with a yersinia infection 3 weeks before the IgE determination (Table 1).

Grade 1 RAST responses were found in 10 and grade 2 or 3 responses in 13 subjects (14%). Fig. 2 illustrates distributions of IgE concentrations in various age groups when all those with specific antibodies as well as those who did not fulfill the anamnestic criteria, were excluded. This final control population consisting of 134 apparently healthy non-atopic subjects (77 men and 57 women) aged 18–77 years, had a geometric mean serum IgE value of 14.5 U/ml. Mean + 1 SD was 37.8 and mean + 2 SD 94.4 U/ml. There was no significant difference in IgE values between the men (mean IgE 14.8) and the women (mean IgE 14.2 U/ml). 62% of the subjects had IgE levels below 20 U/ml. None had levels of 100 U/ml or above.

Non-atopic population with positive family history (Group B)

In this group IgE levels varied from 1.0 to 595 U/ml. Of the subjects 45% had IgE values below 20 and 18% above 100 U/ml. 21% had at least one positive RAST result. Grade 1 responses were found in nine and grade 2 or 3 responses in 13 subjects. At the second interview two persons reported a personal history of atopic dermatitis, two had developed allergic rhinitis and one had suffered from recurrent otitis media during childhood. All these subjects as well as those with positive RAST results were excluded. Also a woman with an initial IgE level of 345 U/ml who did not come to re-examination, was excluded. Of the remaining 75 subjects (37 men and 38 women), aged 18–74 years, 46 (61%) had IgE levels below 20, and 4 (5%) above 100 U/ml. The geometric mean IgE value was 14.4, mean + 1 SD was 43.3 and mean + 2 SD 130.2 U/ml.

In Group B, the variation in IgE levels between the age groups was greater than in Group A. Of the 209 subjects belonging to these groups, those over 40 years had significantly lower IgE values than those younger ($P < 0.05$).

In all, 75 positive (grades 1, 2 or 3) RAST

results were found in 45 subjects from Groups A and B. Two thirds of the reaction were caused by mugwort, house dust and cat epithelium. In subjects with IgE levels lower than 40 U/ml only class 1 antibodies were found, one per person. Those with IgE levels over 100 U/ml had specific reaginic antibodies of class 2 or 3, usually to two or more allergens.

Dermatitis patients

In the whole series there was a significant difference in IgE levels between men (46.8 U/ml) and women (28.8 U/ml). Women sensitive to nickel had the same mean IgE value as women

sensitive to other allergens. When those with a positive personal and family history of atopic disease were excluded, the corresponding values were 30.5 and 17.3 U/ml. Patients with allergic contact dermatitis had higher IgE levels than the other dermatitis patients - except those with atopic eczema (Table 2).

Fig. 3 shows the serum IgE levels of the 276 dermatitis patients in relation to their atopic histories. There was a significant difference in the mean IgE levels between the patients with a personal history of atopic disorders and those without ($P < 0.001$). Patients with a present atopic disease had significantly higher IgE values than those with a past atopic disease ($P < 0.01$).

Table 1

Data concerning subjects who had a negative personal and family history of atopic disease at the first interview but IgE levels ≥ 100 U/ml

Pat. No.	Sex	Age	IgE U/ml		RAST®	Prick test	History rechecked
			initial	controlled 3 years later			
1	F	50	100	88	neg	pos	ROM and urticaria in infancy
2	M	56	107	86	neg	neg	AD in infancy
3	F	37	112	140	neg	neg	urticaria since 2 yrs, hand eczema
4	F	29	115	124	pos	pos	neg
5	M	53	142	109	pos	pos	neg
6	M	42	154	88	neg	neg	ROM in infancy
7	M	43	154	264	neg	neg	ROM in infancy, recent yersinia infection, pathological liver function tests
8	F	31	184	140	pos	pos	neg
9	F	19	200	124	pos	pos	AC in infancy
10	M	42	315	400	pos	pos	AR since 1.5 yr
11	F	37	362	420	neg	pos	fish allergy in infancy, frequent sneezing in the morning
12	M	46	380	470	pos	pos	pruritic skin, urticaria episodes, allergic reaction to bee sting
13	F	51	500	470	pos	pos	frequent attacks of sneezing, daughter has developed AR

ROM = recurrent otitis media; AD = atopic dermatitis; AR = allergic rhinitis; AC = allergic conjunctivitis

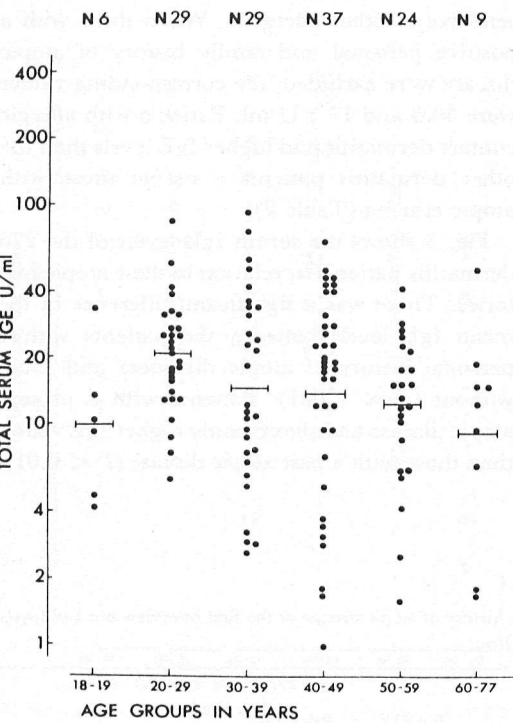


Fig. 2. Distribution of IgE levels in the final non-atopic population.

There was no significant difference in IgE values between the non-atopic subjects who had atopic disease in the family and subjects with no history of personal and familial atopic diseases. Of the dermatitis patients, anamnestically free of atopic diseases but with an IgE value above 100 U/ml, four developed allergic asthma or atopic eczema during the subsequent 3 years.

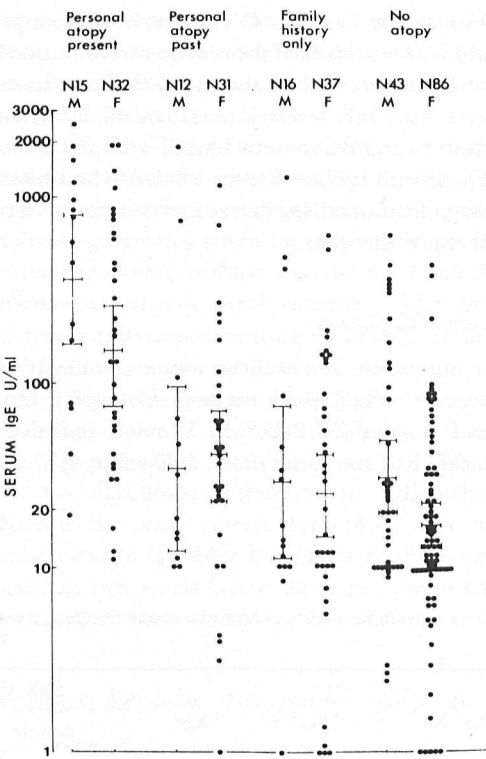


Fig. 3. Serum IgE levels in 276 dermatitis patients related to their atopic history. Cross bars indicate geometric means and 95 % confidence intervals of geometric means.

DISCUSSION

We have used very strict criteria in the selection of our reference material. It is of interest that subjects with no personal and family atopy had almost the same mean IgE values as those with

Table 2
IgE levels in 276 dermatitis patients

	No.	Geom. mean	95 % confidence interval
Atopic dermatitis			
- without contact sensitivity	9	506.6	209.8 - 1222.7
- with contact sensitivity	11	500.3	152.2 - 1644.1
Allergic contact dermatitis	169	37.8	29.7 - 48.0
- Without atopy	81	24.8	18.2 - 33.7
Other forms of dermatitis	87	27.1	19.5 - 38.5
- without atopy	42	15.3	11.4 - 33.9

a negative personal but positive family history of atopic disorders. However, four persons in Group B had IgE values above 100 U/ml, while not a single person in Group A had such a high value. Our mean total serum IgE value was very close to that of Zetterström & Johansson (18), who did not primarily exclude healthy subjects who came from atopic families.

In healthy children the IgE level has been shown to increase with age (10). In atopic adults a significant decrease in IgE levels has been observed with aging (15, 17). In non-atopic adults Johansson as well as Nye et al. demonstrated a slight but non-significant decrease in IgE levels with increasing age (8, 13). When our two non-atopic groups were evaluated together, a significant difference was found in mean IgE values between the subjects under 40 years and those over 40 years.

A tendency for males to have higher IgE levels than females could be noted already in the control population, but only in the dermatitis patients was the difference statistically significant. Earlier, Forsbeck & Wahlberg have reported that the geometrical mean IgE value for dermatitis patients was higher for men than for women (4).

Immunoglobulin E levels have been demonstrated higher in smokers than in non-smokers (7). According to Lebowitz (12) IgE levels in adults differ between the sexes because of differences in smoking habits. We have not questioned our control population and patients about smoking. However, it can hardly be the only explanation for the higher IgE levels in male dermatitis patients. It might be that men are more prone than women to respond to various specific and non-specific stimuli with IgE production.

A high IgE level is often predictive of the subsequent development of an atopic disease in children (10). Also in the present adult material, a high IgE level in some subjects was found to precede allergic disease.

An increased incidence of elevated IgE levels and a frequent history of atopic disease has been demonstrated in children with recurrent otitis media (11). Many subjects with high IgE levels, initially selected for our control population, pre-

sented with a history of recurrent otitis media when the histories were rechecked (Table 1).

We found elevated IgE values in contact dermatitis patients even after exclusion of patients with atopic symptoms. O'Loughlin made a similar observation in patients with various forms of dermatitis (14) and concluded that in these disorders IgE is a secondary phenomenon rather than a primary causative factor.

In the present investigation, a good correlation was found between atopic disorders, diagnosed on the basis of the clinical picture and anamnestic data, and serum IgE levels. Although it is impossible to identify all cases with atopic symptoms by determining the serum IgE concentration, we agree with Johansson & Zetterström that a high IgE level is indicative of atopic allergy despite an initial inconclusive case history.

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