

Relationship between Serum IgE Concentration and Occurrence of Immediate Skin Test Reactions and Allergic Disorders in Young People

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We studied serum IgE concentration by the PRIST® method in 157 adolescents (71 boys) aged 15–17 years. This group was randomly drawn from a larger unselected population of 708 young people. The geometric mean IgE for the 157 subjects was 37.6 U/ml. After careful exclusion 77 subjects without any signs or symptoms of atopy were found. The mean IgE for them was 16.8 U/ml and the upper reference limit, calculated as mean $\pm$ 2SD of the logarithmic value, was 160 U/ml. Nineteen per cent of the population had an IgE concentration higher than 160 U/ml and 30% had a value below 20 U/ml. Positive skin test reactions were strongly associated with increased IgE values. Atopic eczema and allergic rhinitis also raised the IgE level, but the effect of bronchial wheezing was insignificant.

We conclude that IgE concentrations above 160 U/ml during adolescence suggest atopy and correlate with positive skin test reactivity and/or clinical symptoms. An IgE value below 20 U/ml almost certainly excludes the possibility of positive skin reactions and somewhat less certainly the possibility that symptoms are due to atopy.

Key words: adolescent; asthma; eczema; epidemiology; immunoglobulin-E; rhinitis; skin prick tests; wheezing.

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CLINICAL ASPECTS

Previously, we have reported data on skin prick test reactivity, allergen-specific IgE antibodies and allergic disorders in an unselected population of adolescents living in southeast Finland. The present article gives information on total IgE concentrations in a subgroup of the same population.

We found that IgE concentrations above 160 U/ml suggest atopy and correlate with positive skin test reactivity and/or clinical symptoms. An IgE value below 20 U/ml almost certainly excludes the possibility of positive skin reactions and somewhat less certainly the possibility that symptoms are due to atopy.

Skin prick testing with careful clinical examination is usually sufficient for judging whether the patient's symptom is atopy related or not. Determination of the total serum IgE level is a useful aid in diagnostic work. If skin testing cannot be done, IgE assay may serve as the first screening procedure for atopy.

High serum immunoglobulin-E (IgE) concentrations are encountered in patients with allergic disorders caused by immediate hypersensitivity (atopy) and in patients with some parasitic infections. Thus it has been possible to use IgE levels as an aid when the decision between

atopic and non-atopic disease is not obvious (2, 15, 16). It should immediately be stated that the assay has its limitations, since many patients with atopic disease have IgE levels within the reference (normal) range, and many patients with high serum IgE concentrations are easily

recognized as atopics on the basis of clinical history and results from simple skin tests without further laboratory studies.

The interpretation of a laboratory test such as the serum IgE level is dependent on knowledge of the ranges in healthy persons and in patients with a disorder affecting the measured quantity. We have made a thorough study of the occurrence of allergic disorders in a group of 708 unselected adolescents in Imatra, Finland (7, 8, 9). In the present paper we describe the serum IgE concentrations in a randomly taken subpopulation of 157 adolescents. We will describe how the serum IgE concentrations observed were related to the occurrence of symptoms and signs of atopy and positive skin test reactions.

SUBJECTS AND METHODS

The subjects consisted of 157 students (71 boys) aged 15–17 years and living in Imatra, a small industrialized town in southeast Finland. This group was randomly drawn from a larger population of 708 students (316 boys). Skin prick tests with 16 extracts of 12 common allergens and a physical examination were carried out on each subject. This was done at the same time as the larger population was surveyed. The biological activities of the 16 allergen preparations from Bencard, U.K. and Dome Laboratories, U.K. were calculated from the skin test results of the whole population and expressed in HEP units (7). The allergen potency of the extracts used varied from 0.6 to 21.8 HEP units and showed no correlation with concentrations reported by manufacturers (PNU/ml or % units).

Information on allergic disorders in the subjects and the occurrence of atopic symptoms in parents or siblings was obtained through a questionnaire and a personal interview (6). The methods and the population characteristics of the original population have been described in previous articles (7, 8).

Positive skin test reactions occurred in 41% of the subjects (49% in the group of 708 adolescents). Cumulative prevalences of different allergic disorders were 12% for bronchial wheez-

ing, 25% for allergic rhinoconjunctivitis (seasonal and perennial rhinitis) and 20% for atopic dermatitis (eczema). The figures are closely similar to those we reported for the larger group of young people, 12, 24 and 27% respectively.

Serum total IgE concentrations were determined with the Phadebas IgE PRIST radioimmunoassay (Pharmacia Diagnostics, Uppsala, Sweden). Concentrations below 0.5 U/ml could not be measured. Coefficient of variation within and between assay ranged, according to the level of IgE, from 6.2% to 16.6%. Venous sampling was performed at the time of clinical examination and skin testing in the spring.

Distribution of the IgE values was assumed to be log-normal, and therefore usual linear model techniques and F-test procedures are applicable after logarithmic transformation.

RESULTS

The geometric mean IgE concentration for all the adolescents aged 15–17 years was 37.6 U/ml, 40.5 for the boys and 35.4 for the girls. The difference between sexes was not significant.

In our reference group (non-atopic individuals) we included subjects without symptoms or signs of allergy and without positive skin tests. Seventy-seven such subjects were found and the geometric mean IgE concentration for them was 16.8 U/ml. Only 6% in the reference group had an IgE value of 70 U/ml or more. The upper reference value for IgE was 160 U/ml calculated as mean + 2SD of the logarithmic values. In the total population 19.1% of the subjects had an IgE value higher than 160 U/ml. Thirty per cent of the values were below 20 U/ml. The IgE assay with a cutoff limit of 160 U/ml has high specificity but low sensitivity for the various allergic disorders (Table 1). The sensitivity is somewhat better in males (Fig. 1).

The IgE values in different subgroups are shown in Fig. 1. Positive skin test reactions are most clearly associated with increased IgE values. The mean IgE was 116.3 U/ml in the skin test positive and 16.9 U/ml in the skin test negative subjects. Report of at least one symptom also increased IgE values ($P < 10^{-4}$). This

Table 1

Sensitivity and specificity of the serum IgE assay in various allergic disorders. The cutoff limit used was 160 U/ml

Serum IgE (U/ml)	Symptom							
	Wheezing		Rhinitis		Eczema		Any symptom	
	Present		Present		Present		Present	
	Yes	No	Yes	No	Yes	No	Yes	No
160–	4	26	15	15	13	17	20	10
0–159	15	112	24	103	18	109	36	91
All values	19	138	39	118	31	126	56	101
Sensitivity ¹	21 %		38 %		42 %		36 %	
Specificity ²	81 %		87 %		86 %		90 %	

¹ Percentage of true-positives detected by the test.
² Percentage of true-negatives rejected by the test.

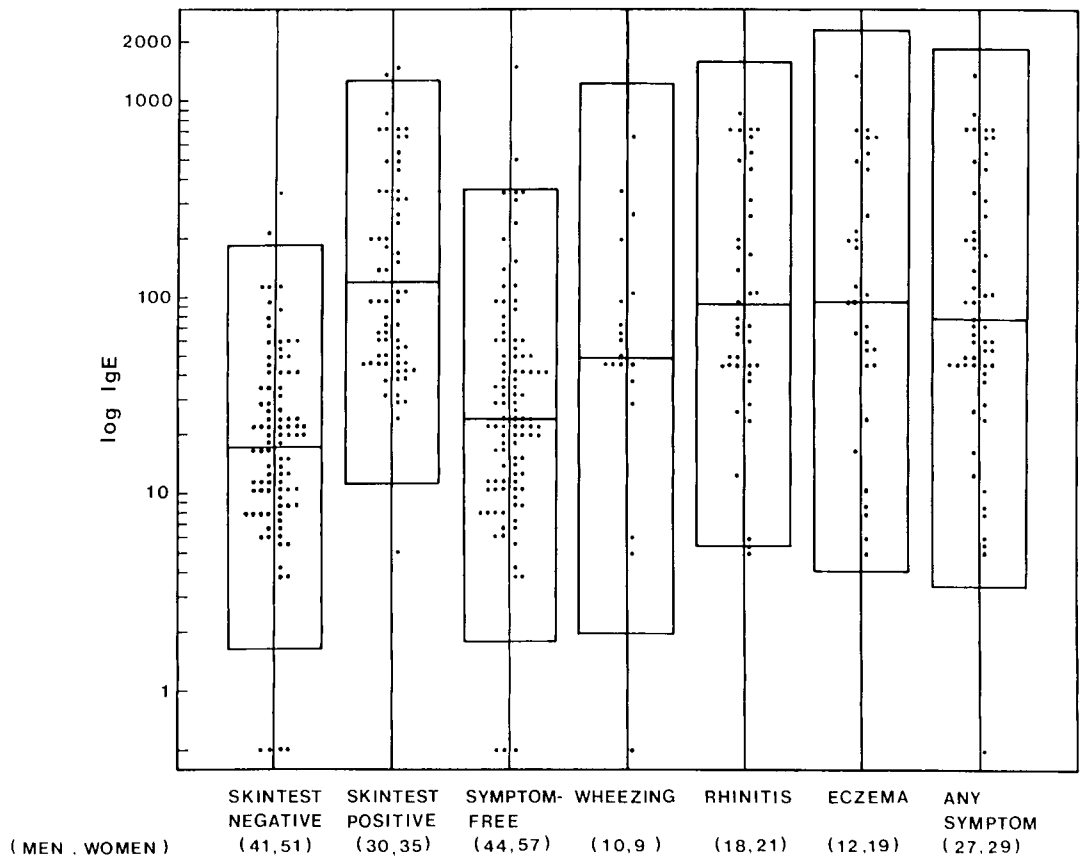


Fig. 1. Distribution of IgE values in the different subgroups (logarithmic scale). For each group the geometric mean $\pm$ 2 SD is drawn. The number of subjects belonging to each group is also indicated.

association was clear in the allergic dermatitis and rhinitis groups ($P < 0.001$) but non-significant in the subjects with bronchial wheezing.

The three symptom groups indicated in Fig. 1 partly overlap because one subject could report several symptoms. We tried to single out the effects of different symptoms and signs by regressing logarithmic IgE values on variables indicating presence or absence of the symptom in question and assuming zero cross-effects. The following equation was obtained:

$$\begin{aligned} \log \text{ IgE} = & 1.168 + 0.068 S + 0.051 H + \\ & (0.82) \quad (0.59) \\ & 0.820 T - 0.600 W + 0.242 A + \\ & (8.56) \quad (-3.81) \quad (0.88) \\ & 0.161 F + 0.104 P + 0.212 E \\ & (1.04) \quad (0.85) \quad (1.91) \end{aligned}$$

In the equation, S is sex, H heredity, T skin test, W wheezing, A asthma, F hay fever, P perennial rhinitis and E eczema. These variables are defined as one when reported positive (sex is one when male), otherwise zero. The figures in parentheses are t-values corresponding to the test that the particular coefficient is zero. From the equation it can be seen that the effect of positive skin tests dominates and also eczema raises the logarithmic IgE values significantly. A curious fact is that the coefficient of bronchial wheezing, excluding asthma, is negative and almost significant ($P < 0.057$).

Close examination of Fig. 1 reveals that the distribution of log IgE values in girls reporting wheezing and eczema is more dispersed than in boys having the same symptoms. This lowers the magnitude of corresponding coefficients.

DISCUSSION

The population sample in this study was random and not chosen to include or exclude allergic individuals. In previous papers (7, 9) we described a high rate for the occurrence of allergic skin reactivity as well as allergen-specific IgE antibodies in the adolescent population from which the present subgroup was drawn.

The wealing reactions produced by skin tests are largest and also most prevalent in young adults (1). The decline of skin reactivity has generally been attributed to the fall in serum IgE that begins in early adulthood (4). Highest IgE levels occur among 6- to 14-year olds (2). Kay (11) suggested that IgE levels reach a peak just after puberty, when the thymus begins to atrophy.

The geometric mean IgE for the present young population was 37.6 U/ml which may be compared with the 32.1 U/ml in the population sample of all ages surveyed by Barbee et al. (2). According to them males have higher IgE levels than females at any given age. The sex difference is also reported by Delespesse et al. (4), Pauwels & Van Der Straeten (14) and Freidhoff et al. (5). Zetterström & Johansson (16) did not find serum IgE concentrations to be sex dependent in their non-atopic healthy population. In the present study the mean IgE concentration was slightly higher in boys. Previously, we have reported that adolescent boys have significantly more often positive skin tests than girls (7), more often allergen-specific IgE antibodies (9) and more respiratory allergy (8). We know of no explanation for the sex difference.

With paper radioimmunosorbent test (PRIST) the mean values for serum IgE in reference groups have been shown to be markedly lower than was assumed previously on the basis of assays with older methods. Kjellman et al. (12) reported mean values for 13–15-year-old children to be 20 U/ml and Zetterström & Johansson (16) found a mean value of only 13.2 U/ml for their non-atopic adult population. The PRIST method was used in both studies. The lower values may in part reflect a better exclusion of allergic subjects from the reference groups. We found the mean IgE concentration to be 16.8 U/ml in non-atopic adolescents, which is close to the Swedish observations. The upper reference value for IgE was 160 U/ml; calculated as mean + 2SD of the logarithmic value. The cutoff limit of 160 U/ml had a high specificity, but a low sensitivity for the various allergic disorders. For instance, only 15 out of 39 subjects with allergic rhinitis had an IgE value of more than

160 U/ml (low sensitivity), but 103 out of 118 subjects without rhinitis had an IgE value lower than the cutoff limit (high specificity) (see Table 1). It is well known that patients with a clear-cut atopic symptom, e.g. hay fever, often have normal IgE concentration. Johansson et al. (10) stated that only 20–30% of patients with allergic rhinitis and 40–60% of patients with allergic asthma have raised IgE levels.

Positive skin tests were strongly associated with increased IgE values. Subjects with positive skin test results, when defined to include anyone with a 3 mm wealing reaction in prick testing with 16 allergen extracts, had a geometric mean IgE concentration of 116.3 U/ml compared to 16.9 U/ml in the skin test negative subjects. Only one skin test positive subject had an IgE value below 20 U/ml while 46 subjects in the skin test negative group had such low values. Brown et al. (3) stated that skin prick test reactivity correlated with both total and allergen-specific IgE, and increasing IgE levels were positively correlated with increasing skin reactivity. In our study, the grade of skin test positivity had an insignificant effect; the “jump” to a much higher IgE level happened as soon as any 3 mm wealing reaction in skin testing was demonstrated.

Symptoms suggestive of allergy also tended to link with increased IgE levels. Eczema raised the IgE values more than respiratory allergy. Öhman & Johansson (17) made the same observation and also noted that the IgE level is especially high when eczema is combined with respiratory allergy. In our study we made the rather unexpected finding that bronchial wheezing, manifest asthma excluded, had a lowering effect on the IgE level. This could happen by chance alone, but some of our “wheezers” with low IgE could be at risk to develop intrinsic asthma later on. Childhood asthma is certainly associated with atopy, but adult asthma is frequently intrinsic or cryptogenic, i.e. not atopy related.

The distribution of IgE values in a general population is very skewed. Many persons have an IgE level below 20 U/ml. Barbee et al. (2) reported that almost 40% of the IgE values were below that limit. We found the corres-

ponding figure in adolescents to be about 30%. On the other hand, a general population includes individuals with IgE values up to several thousands. The wide dispersion of IgE values in groups with various symptoms and signs is also shown in Fig. 1.

According to Zetterström & Johansson (16) a serum IgE value above 100 U/ml in adults is strong evidence for the presence of atopy. Orgel et al. (13) reported that IgE levels above 100 U/ml at any age below 6 years strongly suggest the possibility of atopic disease. We conclude that IgE concentrations above 160 U/ml during adolescence suggest atopy and correlate with positive skin test reactivity and/or clinical symptoms. An IgE value below 20 U/ml almost certainly excludes the possibility of positive skin reactions and somewhat less certainly the possibility that symptoms are due to atopy.

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