

IgE Concentrations Measured by PRIST® in Serum of Healthy Adults and in Patients with Respiratory Allergy

A Diagnostic Approach

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In order to establish reference values for total serum IgE in an adult non-atopic population, 175 individuals, 17–85 years of age, were investigated. The usefulness of a sensitive method (PRIST®) for serum IgE determinations in discriminating atopy from non-atopic conditions in allergological routine diagnosis was elucidated by investigating 445 patients with symptoms of asthma, rhinitis, urticaria and eczema. Comparisons were made with case histories, *in vivo* tests and circulating IgE antibodies.

The geometric mean for serum IgE in the reference material was 13.2 kU/l with a 2 SD range of 1.53 to 114 kU/l. No significant difference between age groups or sexes was observed. In patients classified as non-atopic and pronounced atopic, the geometric mean values for IgE were 40, 123 and 458 kU/l respectively. The IgE level correlated with number of allergens positive in RAST and with skin test results.

It is concluded that IgE determinations are of great help in discriminating atopic conditions from other diseases with similar symptoms. A serum IgE value above 100 kU/l in a patient is strong evidence for the presence of an atopic disease while a value below 20 kU/l indicates that the symptoms are due to intrinsic or infectious disease.

Key words: allergens; asthma; differential diagnosis; eczema; immunoglobulin E; radioimmunosorbent test; rhinitis.

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CLINICAL ASPECTS

The results from this study confirm that determination of IgE in serum is a valuable adjunct in the diagnosis of atopic allergic diseases. A routine diagnostic procedure based on IgE determination, case history, selected skin test and *in vitro* assays of IgE antibodies in serum is reliable and time saving. Cases with weakly positive or negative skin tests or with a negative or an inconclusive case history having a total IgE level below 20 kU/l do not justify any further diagnostic investigation with regard to atopic diseases. If, on the other hand, the IgE level is high an atopic origin of the symptoms is strongly suggestive despite an inconclusive case history. In such cases extended allergological investigations are warranted.

Additionally, in clinical research knowledge of the normal value and the distribution of log IgE values in a normal population can be used as a reference in investigations of groups of subjects exposed to factors, or suffering from diseases which may affect the development of atopy. We have for instance found a high mean value and an abnormal distribution of IgE values in workers exposed to raw coffee dust.

High concentrations of circulating IgE are found mainly in patients with atopy and in subjects with helminth infections. After the first report in 1967 (11) of significantly higher IgE levels in serum of patients with extrinsic rather than intrinsic asthma, it was suggested that

measurement of serum IgE would be of value in discriminating between atopic and non-atopic disorders in the diagnosis of allergic diseases. Further studies of large, non-selected populations of allergic patients were less promising. Some patients with atopic disease had IgE values within the normal range and many patients with elevated IgE levels were easily recognized by a characteristic case history. It is possible that the diagnostic value of an IgE determination could be improved by better techniques for quantitation and a better defined non-allergic reference population.

The radioimmunosorbent test, RIST, (23) used in the original report (11) is a highly sensitive inhibition radioimmunoassay. However, it was later shown to be less accurate for determination of low IgE levels (13, 20). Nye et al. (18) using a double antibody radioimmunoassay, found that the RIST method gave less reliable values in serum with IgE concentrations below 100 units/ml. They stated that the RIST method and other previously used methods were not sensitive enough and that the normal value of IgE was much lower than previously reported.

A different principle, the direct sandwich-type radioimmunoassay was described by Wide (25). Ceska & Lundkvist (5) developed the paper radioimmunosorbent test (PRIST) and stressed its usefulness for IgE determinations. Studies using PRIST showed that, compared to RIST, and in agreement with double antibody techniques, lower and possibly more reliable results were obtained for low IgE concentrations such as those found in cord serum (14).

The aim of the present study was to establish the range of levels for circulating IgE obtained with PRIST in healthy adults to better define a non-allergic reference population. We were also interested in studying the usefulness of IgE values measured with this technique as an aid in the allergological investigation, especially with regard to distinguishing patients with extrinsic asthma and rhinitis from those with intrinsic disease and those with non-allergic diseases, e.g. emphysema or bronchitis.

MATERIAL AND METHODS

Reference group

The county of Uppsala consists of one larger and one smaller town and surrounding agricultural and forest areas and has about 250,000 inhabitants. Its demographic characteristics are comparable to the Swedish average. The Public Health Authority summons all adults for ongoing clinical investigation every third or fourth year. The frequency of participation varies somewhat between rural and urban areas, but on the average the attendance has been approximately 75%.

246 consecutive subjects participating in the Health survey during the spring of 1974 completed a questionnaire regarding previous personal and actual allergic history. A blood sample was collected and serum frozen at -20°C pending analysis. All 187 subjects denying symptoms indicative of allergic diseases were grouped together to form the prime, reference group. The serum samples were assayed for total IgE by PRIST and circulating IgE antibodies by radio-allergosorbent test, RAST, (24) using a panel of seven common allergens (horse epithelium, house dust, house dust mite, birch, timothy, mugwort and *Aspergillus*). In order to exclude all possible atopic subjects, those with a positive RAST result and/or an IgE level above the geometric mean plus 1 SD of the group, were called back for a second clinical investigation. A fresh blood sample was drawn. Fourteen subjects were recalled. Twelve of these subjects were excluded from the reference group based on the following criteria:

Five subjects had at least one positive RAST result in the second blood sample that correlated with intradermal skin testing and case history.

One patient had a pressure urticaria and another had a previous history of urticaria and severe reactions to *Hymenoptera* stings.

The remaining five subjects had two or more positive intradermal skin tests to common allergens. Four of them had atopic allergy in the family.

Two subjects with positive intradermal skin tests to extract of *Candida albicans*, but no other positive skin test, were not excluded from the study. No allergic symptoms or allergy among their relatives had been noted.

Patient group

A total of 445 patients referred to or seeking medical advice at the Allergy Clinic of the Department of Lung Medicine for the first time during 1974 were diagnosed as having asthma, rhinitis, urticaria or eczema.

All subjects were classified with regard to atopy without knowledge of the actual IgE levels. At least one of the following criteria had to be fulfilled for classifying a subject as atopic:

1. Presence of serum IgE antibodies as measured by RAST: Allergens included in the routine assay were horse-, dog-, and cat-dander, birch-, timothy-, and mugwort-pollen, house dust, house dust mite (*Dermatophagoides pteronyssinus*) and *Aspergillus fumigatus*. Allergen extract batches selected by RAST and clinical experience were used (12).

2. A positive challenge test – bronchial inhalation or intranasal – with an immediate reaction.

3. Three or more cutaneous allergen sensitivities. For the calculation of the number of cutaneous allergen sensitivities, intradermal skin tests were performed using aqueous extracts of 1/1000 w/v concentration. A skin reaction where the sum of two perpendicular diameters of the wheal exceeded 20 mm was regarded positive. Allergens known to be cross-reacting or associated with one another were recorded as one single allergen cutaneous sensitivity.

Thus positive skin tests to various grass pollens were seen as one allergen sensitivity; positive tests to birch-, alder-, oak- and hazel pollen and hazelnut as one positive test; positive reactions to pollens from weeds of the *Asteraceae* family, mugwort, *Chrysanthemum* and *Taraxacum vulgare* as one test; positive reaction to dog-, cat-, cow- and horse epithelium as one allergen sensitivity. House dust, *Dermatophagoides* and the various moulds were considered as separate al-

lergens. The same type of allergens were used in the skin test as in RAST and, in addition, two other house dust extracts and extracts of *Cladosporium*, *Candida albicans* and *Alternaria* were tested. When indicated by the patient's history, additional allergens were also used in the test.

Thirty-four subjects with one or two cutaneous allergen sensitivities but negative RAST results and/or challenge tests were classified as being atopic or non-atopic using other criteria such as type of symptom, previous allergy history and hereditary factors.

The degree of atopic involvement was classified as non-atopy, moderate atopic disease and pronounced atopic disease. The criteria for pronounced atopic disease were symptoms since childhood of at least two types (asthma, urticaria, eczema or rhinitis) with at least three clinical allergen sensitivities.

Data were collected for some other parameters which possibly could affect the IgE level. These were: heredity, allergy type and intensity of symptoms, number of positive allergens in RAST, number of positive skin tests and occurrence of eosinophilia.

Heredity for atopic-type symptoms was graded from 0–2 where 0 meant no heredity, 1 indicated at least one case of allergic disease in the family and 2 denoted two or more of first degree relatives (parents, siblings or offspring) have allergic disease.

The intensity of asthmatic symptoms was graded from 1–5 where 1 meant previous asthma, 2 slight episodic symptoms, 3 more pronounced episodic symptoms, 4 slight perennial symptoms, and 5 severe perennial asthma.

Rhinitis was classified in the same way as for asthma in five classes, while eczema and urticaria were graded from 1–3 on the basis of skin involvement.

The number of eosinophils in the blood was calculated by multiplying the percentage of eosinophils in a blood smear with the white blood cell count. This method is unprecise and of limited value in an individual case unless the patient has an eosinophilia of more than 10%. However in comparison between groups lower values can also be of interest.

IgE determinations

IgE was determined by Phadebas IgE PRIST (Pharmacia Diagnostics AB, Uppsala) following the directions for use. IgE antibodies were determined by RAST using allergen-coated filter paper discs kindly supplied by the Research Department of Pharmacia Diagnostics AB. The allergen extracts used in RAST were the same as those reported elsewhere (12). A preparation of immunosorbent purified anti-IgE with De2-specificity (2) was labelled by ^{125}I as previously described (12). The results were expressed in parts per thousand (‰) of an allergen-reagin reference system. Two ‰ corresponding approximately to twice the count rate of a normal serum, was applied as cut-off between negative and positive results.

Statistical calculations

In order to normalize the distribution of the IgE-values, each value was logarithmically transformed and geometric mean and standard deviations were calculated. Chi-square testing was used for the comparisons of frequencies in groups of subjects.

RESULTS

The reference group

The entire sample of 246 individuals from the health survey had a geometric mean serum IgE value of 16.5 kU/l. Mean + 2SD was 219 and mean - 2SD 1.24 kU/l. The 175 subjects who remained in the reference sample after the exclusions ranged from 17 to 85 years of age with an average of 46 years. They were rather equally divided over the ages comprising at least 23 subjects in each 10-year age group up to 75 years of age (Fig. 1). There were no significant differences in IgE levels between the various age groups or between the sexes.

The frequencies of the various IgE values are given in Fig. 2. The distribution is skewed towards low IgE values. 110 subjects or 63 %, had IgE levels below 20 kU/l. Only two subjects, that is 1.2 %, had levels of 100 kU/l or above. The distribution of the logarithmically transformed IgE values is shown in Fig. 3. The mean logarithm of the IgE value was 1.121 and the standard deviation ± 0.468 which represents a geometric mean of 13.2 kU/l and a ± 2 SD range of 1.53 to 114 kU/l.

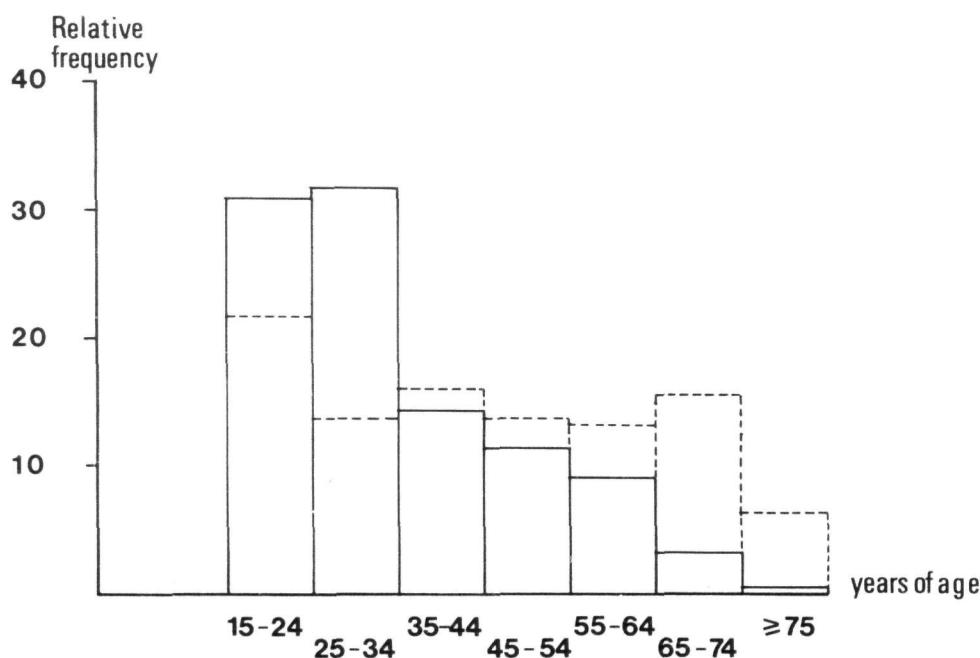


Fig. 1. The age distribution in the reference group (broken line) and in the patients referred for allergological investigation (continuous line).

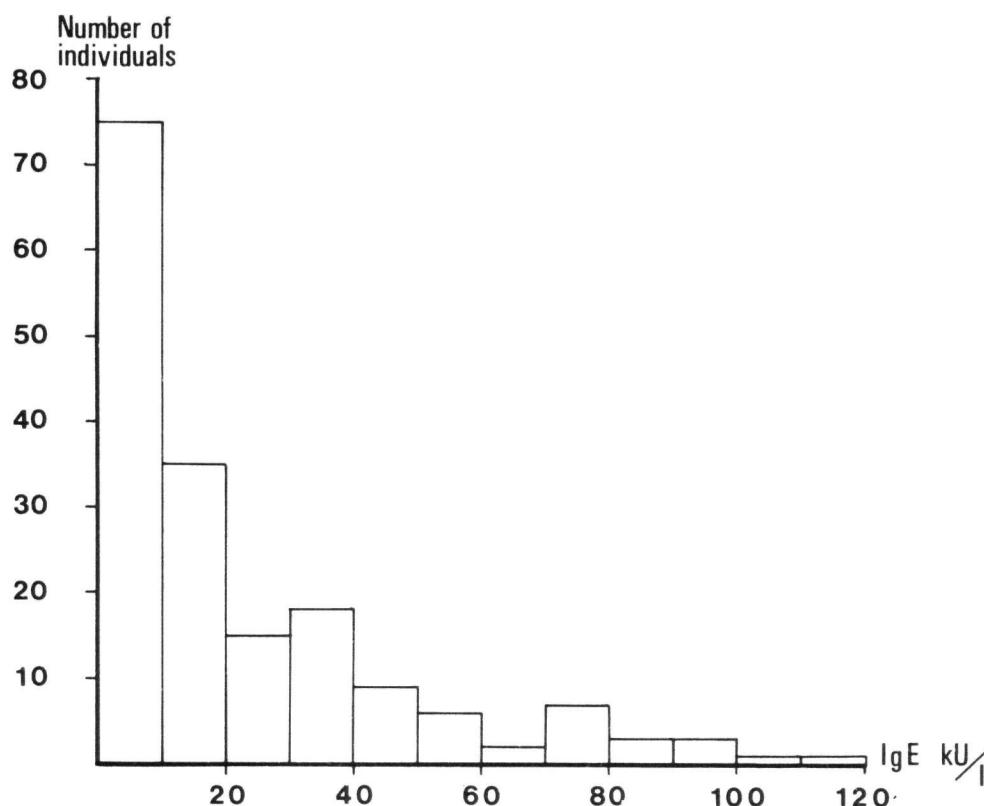


Fig. 2. The distribution of serum IgE levels in the reference material after exclusion of possible atopic subjects.

The patient group

Of the 445 patients, 224 were men and 221 women aged from 16 to 81 years. The majority were between 20 and 30 years old with an average of 35 years (Fig. 1). 179 patients were classified as being non-atopic and 266 as atopic, of whom 34 were regarded as having pronounced atopic disease.

In 40% of the patients, no hereditary factors with regard to atopy were found. 44% had some atopic disease in the family and 16% had two or more first degree relatives with an atopic allergic disease.

47% of the patients had no previous or present history of asthma. 5% had experienced childhood asthma but were presently free from symptoms. Thus 48% of the patients were classified as asthmatics. Of them, one third had episodic symptoms, and two-thirds had more or less chronic asthma.

Rhinitis was found in 80% of the patients. 37% had episodic rhinitis (mostly pollen rhinitis), and 43% had more or less perennial rhinitis.

Urticaria was found only in 14% of the patients and eczema in 11%. Only 12 of the 445 patients reported eczema in childhood.

Nasal or bronchial challenge tests were carried out in 239 patients and 49 demonstrated negative results. RAST testing was performed in 438 patients. No positive RAST results were found in 43.3%; one positive in 26.4%; two positive in 14.2% and more than two positive RAST results in 16.1%.

Skin tests were carried out in 364 subjects. 89 of them were negative. In 49 patients, one cutaneous allergen sensitivity was obtained; in 54, two sensitivities; and, in 172 patients, three or more sensitivities were observed.

The various allergen sensitivities, as evaluated from clinical history, skin and challenge tests and RAST results, showed the following specificity: 122 patients were positive to tree pollen, 130 to grass pollen, 48 to *Compositae* pollen, 116 to animal dander, 63 to house dust, 32 to *Dermatophagoides pteronyssinus* and eight subjects to moulds (*Aspergillus fumigatus*).

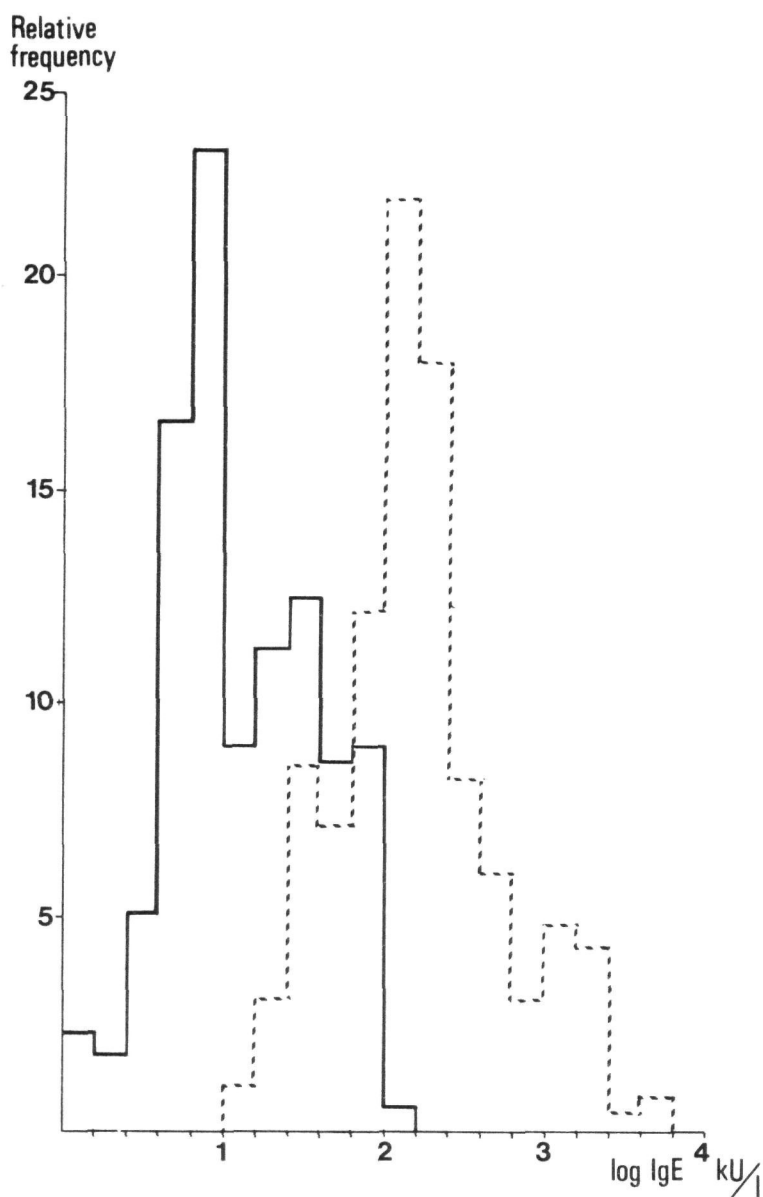


Fig. 3. The log distribution of IgE values in the reference group (continuous line) and in the atopic patients (broken line).

The eosinophil count was determined in 371 patients. The mean value was 242 cells per μ l. The distribution was skewed with most values at the lower range.

The serum IgE concentration was determined by Phadebas IgE PRIST in 412 patients of whom 160 were classified as being non-atopic, 220 as moderately atopic and 32 as pronounced atopic. The geometric mean IgE values in the groups were 40, 123 and 458 kU/l, respectively (Fig. 4).

The frequency distribution of IgE values in the healthy subjects and in the atopic patients shows that the two populations are different but also that there is an obvious overlap between the two groups (Fig. 3). The distribution of IgE values in the patients classified as non-

atopic has a bimodal appearance (Fig. 4). This finding might indicate that this group is heterogeneous and consists of one population with symptoms of a non-atopic nature and another with an atopy which we could not diagnose.

In order to define the theoretical IgE value which best discriminates normal and atopic individuals, the difference between the respective cumulative frequencies was calculated (Fig. 5). The highest difference and thus the best discrimination corresponded to an IgE-log value of 1.7 which is 50.1 kU/l. 16% of the atopic patients had an IgE level below – and 14% of the healthy subjects were above this value.

No significant correlation was found between heredity and IgE value among the patients. However, among patients classified as atopic,

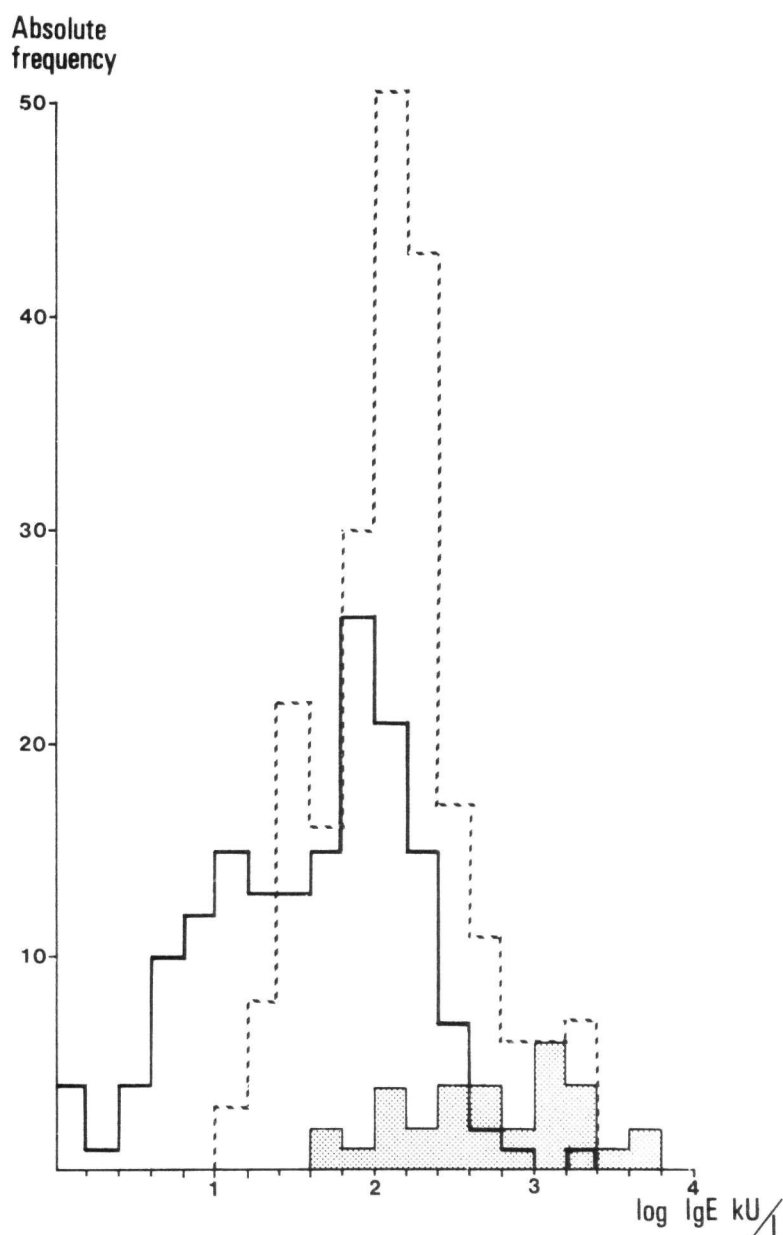


Fig. 4. The log distribution of IgE values in the three patient groups: non-atopic (continuous line), moderately atopic (broken line), and pronounced atopic (shaded area).

heredity for atopic-type symptoms was more often found than in non-atopics ($P < 0.01$).

The number of allergens positive in RAST were strongly correlated ($P < 0.001$) to the level of total IgE. Of patients with three or more positive RAST tests 87% had an IgE level above 150 kU/l. The results of skin tests also correlated strongly ($P < 0.001$) with the total IgE level.

Certain trends in the relation between the IgE levels and the clinical allergen sensitivity were seen. The values for all eight patients sensitive to *Aspergillus* were found to be above a level of 150 kU/l as well as 71% of the patients sensitive to *D. pteronyssinus* ($P < 0.01$). Monovalent pollen allergies dominated among patients with IgE

levels below 50 kU/l. All three patients with IgE levels below 20 kU/l had monovalent allergies; two of them were against pollen and one against dog dander. The latter patient had slight allergic symptoms when working as watchman exposed to dogs 3 months before the investigation.

There was no obvious correlation between IgE levels and the diagnosis of asthma, rhinitis or urticaria. However, patients with eczema had significantly higher mean IgE levels than any other group of patients. This was also true for those who had eczema in childhood but now were free of eczema symptoms.

There was also no obvious correlation between the degree of symptoms and IgE levels.

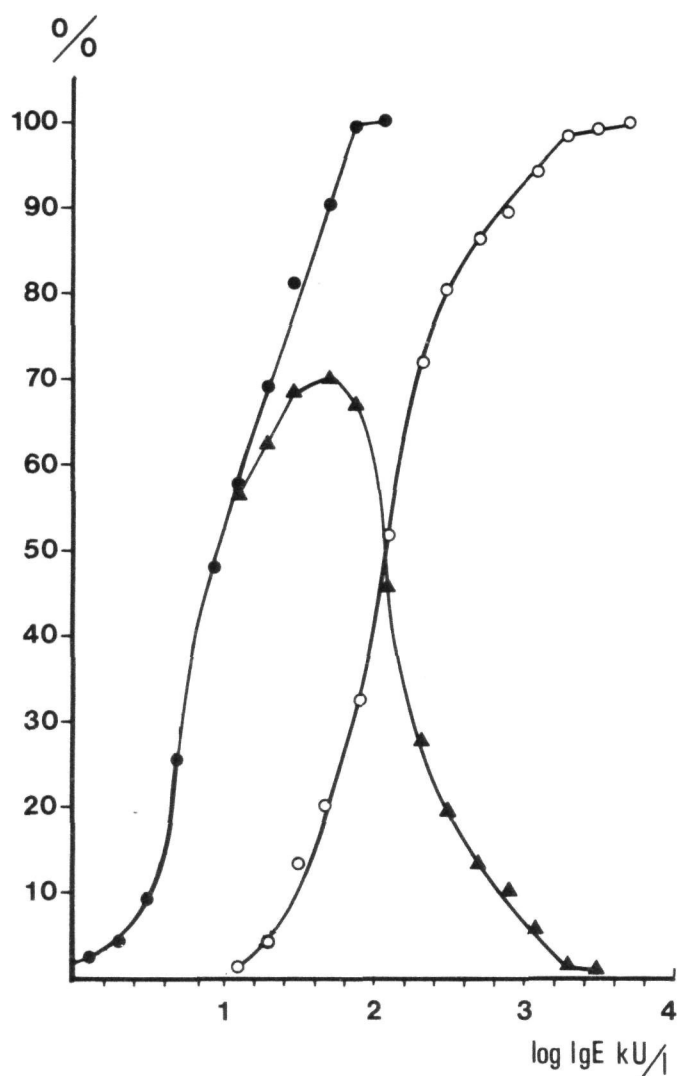


Fig. 5. Accumulated frequencies of log IgE values in the reference material (●) and in the atopic patients (○). The difference between these frequencies is a curve (▲) with a max. value at log 1.7 which is 50.12 kU/l.

Thus, atopic patients with perennial, severe asthma did not have higher IgE levels than those with weak episodic asthma or those with no asthma at all. Nor was there any correlation between the sum of the various symptoms and IgE levels. In contrast, a correlation was found between degree of symptoms and eosinophilia ($P < 0.05$). The same tendency was found in both non-atopic and atopic patients.

DISCUSSION

The first study of IgE concentrations in serum of patients with asthma and in healthy individuals was published in 1967 (2). It revealed that IgE is significantly increased in atopic asthma, a finding that laid the basis for the use of

IgE determination in the diagnosis of atopic allergy. Since then many investigations of IgE levels in normals and in patients with various diseases have been performed using several types of immunological methods. Technical difficulties, as well as problems involved in defining the healthy, reference population and selection of the patient samples have led to somewhat different results. However, in general, the original findings have been confirmed.

The actual values for the IgE concentrations vary. The first investigations tended to give higher normal values than later studies. Through investigations by Nye et al. (18), Johansson et al. (13), Gleich et al. (7) and Merrett & Merrett (17) it has been shown that a method with a sensitivity of a couple of kU/l was best suited for establishing normal values in European and North American communities. A very good correlation was found in this low level range between PRIST and double antibody radioimmunoassay (8). With the use of these methods, the mean normal values for serum IgE in Caucasian populations have been found to be low i.e. 21–42 kU/l (4, 18, 19). With the PRIST method, normal values in 13–15-year-old children were found to be about 20 kU/l (15).

The reason for the still lower normal values found in this investigation, 13.2 kU/l, is probably due to our effort to exclude any possible atopics from the reference group. That such an exclusion affects the mean values of IgE was recently shown by Sears et al. (21).

The exclusion of subjects with atopic sensitization seems to be rational when defining a healthy population. The number of subjects excluded from the healthy control population might seem high (59 out of 246, 24%) but there is a high prevalence of atopic disease in modern Western communities (1, 9).

Our hospital is the only one where allergological investigations are made in Uppsala county, so the patient material stems from the same population as the healthy subjects. The composition of the patient sample, with a dominance of respiratory allergy, is explained by the fact that there is a separate department for the investigation of skin disorders at the hospi-

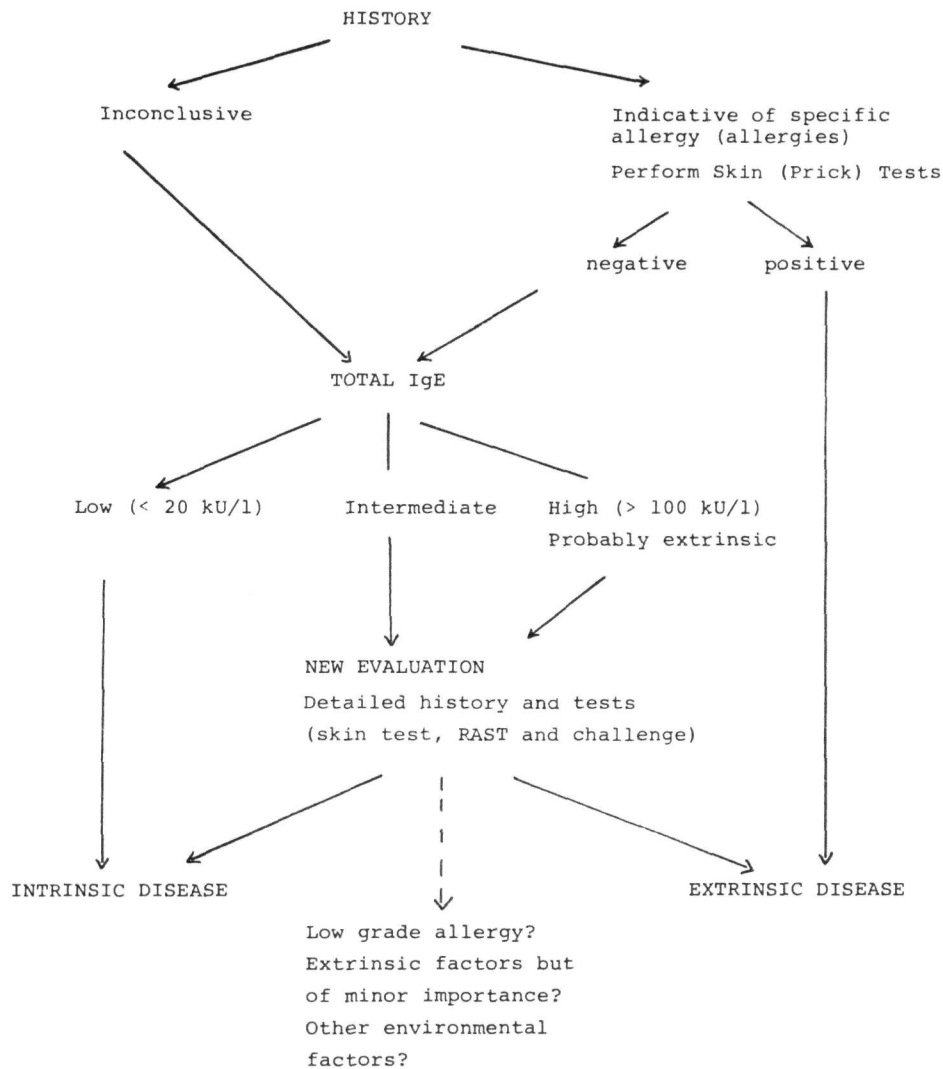


Fig. 6. Schematic diagram for routine diagnosis of patients with allergic-type respiratory symptoms.

tal, which resulted in a pre-selection of the patient material.

The relation between extrinsic and intrinsic disease in these patients with mostly respiratory symptoms is comparable to findings in other Scandinavian investigations (6). The nature of so-called intrinsic allergic disease has been discussed. Since the diagnosis of intrinsic asthma or vasomotor rhinitis is an exclusion diagnosis in subjects where no allergy has been found, it is generally agreed that at least some percentage of the intrinsic disease will eventually be diagnosed as extrinsic when our knowledge of allergens has improved. The findings of a double-peak distribution of the IgE values in the non-atopic group indicates that the group consists of patients with undetected atopic allergy as well as patients with asthma or rhinitis not mediated by IgE mechanisms. In the very first study of IgE in serum (11), patients with intrinsic asthma

were found to have lower IgE levels than the healthy control group. Similar results were found in a survey by Burr et al. (4) who reported lower IgE values in "other wheezers" than in healthy controls. In another study, patients with symptoms of allergic type but with negative skin tests had lower IgE levels than the reference population (3). This group, which could be called true intrinsics, although representing only about 20% of patients visiting our Allergy Clinic, is important to recognize.

The observation that the patients with IgE levels in the lower range of the atopic population were those with monovalent pollen allergy and having relatively mild symptoms would imply some relation between severity of disease and IgE level. The fact that we did not find any correlation between IgE concentration and degree of symptoms might be explained by the fact that other factors are probably more im-

portant for the severity of symptoms than IgE. The local "terrain" factors and the intensity of allergic inflammatory reaction as mirrored by the occurrence of eosinophilia are examples. The finding that blood eosinophilia was related to the severity of disease is in accordance with previous reports (10, 16). However, eosinophil counts cannot be used to discriminate intrinsic from extrinsic respiratory disease (22).

When handling patients with symptoms resembling allergy at an allergy clinic, the first objective is to detect those with IgE-mediated reactions to extrinsic allergens. In our opinion IgE measurement by PRIST or other sensitive and reliable methods are helpful in this important selection process. This is the case at least in areas where other causes of high IgE values, such as helminth infections, are rare. The results of this investigation suggest that an IgE value above 100 kU/l in a patient with symptoms of an allergic-type is strong evidence for the presence of an atopic disease.

The findings in this study have occasioned a change in our routine allergological investigation procedure (Fig. 6). The allergy work-up is based on a careful case history. If indications of atopic disease with allergy to one or several named allergens are obtained, a reagenic sensitization is looked for by skin prick tests. In the case of a clearly positive prick test with a valid allergen extract, in comparison with a histamine reference of 1 mg/ml, the diagnosis is considered established. If the prick tests are weakly positive or negative or an inconclusive case history is obtained, a blood sample will be drawn for determination of total IgE. An IgE level below 20 kU/l combined with a case history not suggestive of allergen sensitivity warrants no further action. In this way considerable time is saved by avoiding unnecessary allergological investigations. On the other hand, in the case of a high IgE level, atopic allergy is assumed to be present despite the original inconclusive case history. An extended interview supplemented with skin tests, RAST analyses and sometimes challenge tests is then made. Using this procedure the allergy-diagnostic work-up is simplified. Thus, the experienced allergist can place more emphasis on and

spend more time searching for allergens of a more uncommon nature or other specific environmental or occupational factors with patients having high IgE levels and negative RAST and skin tests.

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REFERENCES

1. Barbee, R. A., Lebowitz, M. D., Thompson, H. C. & Burrows, B.: Immediate skin-test reactivity in a general population sample. *Ann. Intern. Med.* **84**, 129–133, 1976.
2. Bennich, H. & Johansson, S. G. O.: Immunoglobulin E and immediate hypersensitivity. *Vox Sang.* **19**, 1–13, 1970.
3. Brown, W. G., Halonen, M. J., Kaltenborn, W. T. & Barbee, R. A.: The relationship of respiratory allergy, skin test reactivity and serum IgE in a community population sample. *J. Allergy Clin. Immunol.* **63**, 328–335, 1979.
4. Burr, M. L., Leger, A. S. St., Bevan, C. & Merrett, T. G.: A community survey of asthmatic characteristics. *Thorax* **30**, 663–668, 1975.
5. Ceska, M. & Lundkvist, U.: A new and simple immunoassay method for the determination of IgE. *Immunochimistry* **9**, 1021–1030, 1972.
6. Fagerberg, E.: Studies in bronchial asthma. I. *Acta Allergol.* **11**, 293–326, 1957.
7. Gleich, G. J., Averbeck, A. K. & Swedlund, H. A.: Measurement of IgE in normal and allergic serum by radioimmunoassay. *J. Lab. Clin. Med.* **77**, 690–698, 1971.
8. Gleich, G. J. & Dunnette, S. L.: Comparison of procedures for measurement of IgE protein in serum and secretions. *J. Allergy Clin. Immunol.* **59**, 377–382, 1977.
9. Haahtela, T., Björkstén, F., Heiskala, M. & Suoniemi, I.: Skin prick test reactivity to common allergens in Finnish adolescents. *Allergy* **35**, 425–431, 1980.
10. Horn, B. R., Robin, E. D., Theodore, J. & Van Kessel, A.: Total eosinophil counts in the management of bronchial asthma. *N. Engl. J. Med.* **291**, 1152–1155, 1975.
11. Johansson, S. G. O.: Raised levels of a new immunoglobulin class (IgND) in asthma. *Lancet* *ii*, 951–953, 1967.
12. Johansson, S. G. O., Bennich, H. & Berg, T.: *In vitro* diagnosis of atopic allergy. III. Quantitative estimation of circulating IgE antibodies by the radioallergosorbent test. *Int. Arch. Allergy Appl. Immunol.* **41**, 443–451, 1971.
13. Johansson, S. G. O., Berglund, A. & Kjellman, N.-I. M.: Comparison of IgE values as determined with different solid phase radioimmunoassay methods. *Clin. Allergy* **6**, 91–98, 1976.
14. Johansson, S. G. O., Dannaeus, A., Deuschl, H. &

- Foucard, T.: Determination of IgE and reaginic IgE antibodies in clinical routine. *Allergol. Immunopathol. Suppl. III*, 29–40, 1976.
15. Kjellman, N.-I. M., Johansson, S. G. O. & Roth, A.: Serum IgE levels in healthy children quantified by a sandwich technique (PRIST). *Clin. Allergy* 6, 51–59, 1976.
16. Lowell, F. C.: Clinical aspects of eosinophilia in atopic disease. *J. Am. Med. Assoc.* 202, 875–878, 1967.
17. Merrett, T. G. & Merrett, J.: Methods of quantifying circulating IgE. *Clin. Allergy* 8, 543–557, 1978.
18. Nye, L., Merrett, T. G., Landon, J. & White, R. J.: A detailed investigation of circulating IgE levels in a normal population. *Clin. Allergy* 5, 13–24, 1975.
19. Pauwels, R. & van der Streten, M.: Total serum IgE levels in normals and patients with chronic nonspecific lung diseases. *Allergy* 33, 254–260, 1978.
20. Polmar, S., Waldmann, T. & Terry, W. D.: A comparison of three radioimmunoassay techniques for the measurement of serum IgE. *J. Immunol.* 110, 1253–1261, 1973.
21. Sears, M. R., Chow, C. M. & Morseth, D. J.: Serum total IgE in normal subjects and the influence of a family history of allergy. *Clin. Allergy* 10, 423–431, 1980.
22. Venge, P., Zetterström, O., Dahl, R., Roxin, L.-E. & Olsson, I.: Low levels of eosinophil cationic proteins in patients with asthma. *Lancet* ii, 373–375, 1977.
23. Wide, L. & Porath, J.: Radioimmunoassay of proteins with the use of Sephadex-coupled antibodies. *Biochim. Biophys. Acta* 130, 257–260, 1966.
24. Wide, L., Bennich, H. & Johansson, S. G. O.: Diagnosis of allergy by an *in vitro* test for allergen antibodies. *Lancet* ii, 1105–1107, 1967.
25. Wide, L.: Solid phase antigen-antibody systems. In: Kirkham, K. E. & Hunter, W. M. (eds.): *Radioimmunoassay methods*. European Workshop, pp. 405–412. Livingstone Ltd., Edinburgh and London, 1971.

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