Acta Dermatovener (Stockholm) 54: 193–202, 1974

IMMUNOGLOBULINS IN ATOPIC DERMATITIS

With Special Reference to IgE

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Abstract. The serum levels of IgG, IgA, IgM, IgD and IgE were studied in 90 adult patients with atopic dermatitis. In 128 children with this disease, the serum IgE concentrations were determined. The geometric mean values of IgG, IgM and IgE were elevated. compared with normal controls, whereas the mean value of IgD was lower. Both children and adults with a history of asthma or allergic rhinitis in addition to their dermatitis had a higher mean serum IgE value than the patients with atopic dermatitis only. Patients with more extensive skin changes had a higher mean serum IgE level than those with a mild dermatitis. There was no pronounced variation in the serum IgE levels when monitored during the course of a year.

An increased tendency to form reaginic antibodies is a well-known characteristic of the atopic patient. We know that in many cases of bronchial asthma and allergic rhinitis, the reagins are involved in the pathogenesis of the disease. Their role in eliciting atopic dermatitis is still subject to discussion.

In 1967 Ishizaka et al. and Johansson & Bennich independently described the reagins, or skinsensitizing antibodies, as belonging to a new class of immunoglobulins, IgE (10, 13). Increased serum levels of IgE have subsequently been reported in patients with asthma, hay fever, and atopic dermatitis (1, 3, 11, 16, 19, 23) and also in patients infested with intestinal parasites (1).

In several studies the concentrations of the other immunoglobulin classes have been investigated in atopic subjects. The results here are less consistent. Varelzidis et al. (27) found a significant rise in the level of IgG in a study of adults and children with atopic eczema. Berg & Johansson (2) also found higher IgG levels in children with various types of atopy. High serum levels of IgA in atopic subjects have been described by Ortiz (24). Kohler & Farr (18) reported significantly higher IgD levels in atopic sera. They found, as have several others, no significant differences in the concentrations of IgG, IgA and IgM in atopic patients, as compared with normal controls (5, 8, 9, 21, 25).

Hitherto, no complete study has ever been made of all the immunoglobulin levels in a large group of adults with atopic dermatitis. Nor has there been any report of a more extensive study on serum IgE levels in children with this disease. In the following we report our findings from a study of these groups where due emphasis has also been paid to various clinical data. A year-round study of the serum-IgE levels in adults with atopic dermatitis was also made.

MATERIAL AND METHODS

Patients

Between January and June, 1969, 255 patients with a diagnosis of atopic dermatitis visited the outpatient clinic of the Department of Dermatology, University Hospital, Uppsala. Of these, 221 (87% attendance) took part in the study. These included 64 boys and 64 girls under 15 years of age (89% attendance). Their age distribution is shown in Fig. 1. The adult group, those over 15 years of age, consisted of 35 men and 58 women (84% attendance). Their age distribution is shown in Fig. 2. The majority of those who did not take part could not be contacted, due to change of address. The criteria used for the diagnosis atopic dermatitis were the same as given by Pillsbury et al. (26).

A detailed case history was obtained from all the patients, in which special attention was given to allergic manifestations such as asthma, allergic rhinitis and urticaria. Those with any previous or present history of asthma and/or allergic rhinitis will be referred to as "mixed" and the patients with atopic dermatitis only will be referred to as "pure". The severity of the atopic dermatitis was also graded as mild, moderate, or severe.

In order to minimize any possible seasonal influence on the serum level of IgE, nearly all of the patients were studied during the latter part of 1969. They were all examined by one of the authors.

Repeated IgE determinations were made during one year in 20 patients with high serum IgE values (> 1 000 ng/ml) and

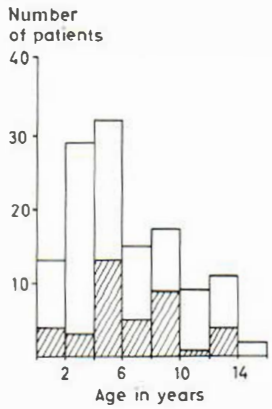

Fig. 1. Age distribution in children with atopic dermatitis. □, patients with only dermatitis ("pure"); ▨, patients with dermatitis + asthma and/or allergic rhinitis ("mixed").

in 16 patients with normal values (125 to 500 ng/ml). Those with a high IgE value were 10 men and 10 women, aged 17 to 35 years, 19 of whom also had had symptoms of asthma and/or allergic rhinitis during the previous 3 years. The group with serum IgE levels within normal limits consisted of 4 men and 12 women, aged 16 to 37 years. Seven of them had had symptoms of asthma and/or allergic rhinitis during the previous 3 years. On average, five IgE determinations were made, representing the periods October–December, February–April, end of May–middle of June (mainly birch pollen season), July–August (mainly grass pollen season), and September–October. On every occasion the severity of the patient's atopic dermatitis was graded as described previously and symptoms of asthma or allergic rhinitis were recorded.

Immunoglobulin determinations

Capillary blood samples were taken from the children and, in the adults, the determinations were carried out on venous blood. The serum was separated after 2 to 3 hours at room temperature and stored at −20°C until analysed.

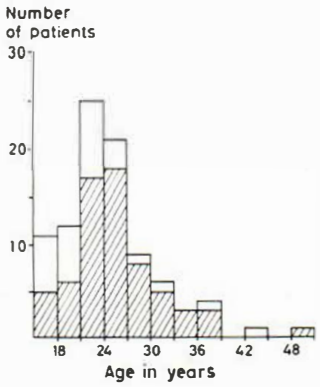

Fig. 2. Age distribution in adults with atopic dermatitis. □, patients with only dermatitis ("pure"); ▨, patients with dermatitis + asthma and/or allergic rhinitis ("mixed").

The concentrations of the immunoglobulins G, A, M and D in the adult group of patients were determined by single radial diffusion in agar gel according to the method of Mancini et al. (20) but with some modifications (15). The IgE concentrations in adults and children were estimated according to the radioimmunosorbent technique (RIST) of Wide & Porath (29) as applied to IgE determinations by Johansson et al. (14). IgE concentrations as low as 5 ng/ml could be measured. The error of the method calculated as the standard deviation (S.D.) for duplicate analysis of samples is about 15%. By this method, the mean value of IgE in serum from healthy adults has been found to be 248 ng/ml with a 95% confidence interval of 60 to 1 000 ng/ml (12).

Some problems have been encountered with the standardization of the IgE levels and we have reason to believe that the normal values published previously are somewhat high (2, 12). With an improved technique, we seem to be better able to discriminate between the very low values.

After the present investigation was completed the Immunoglobulin Reference Center of WHO distributed reference sera to facilitate comparisons between different laboratories. It was also recommended that the IgE values should be given in units instead of nanograms per ml. Analyses of WHO sera, which are now under way, will make it possible to transform earlier reported nanogram values to WHO standard units.

Statistical calculations

The frequency distribution of serum immunoglobulin values in healthy persons is skewed to the right when arithmetic values are used but are rather normally distributed when using logarithmic values. The calculations, therefore, have been done using logarithmically transformed values. IgD amounts of less than 1 mg/100 ml have been calculated as 0.5 mg/100 ml. In children the IgE level is known to rise slowly with age (2); this can be seen in Fig. 4 where the regression line for healthy children (log IgE on age) is superimposed on all the actual values for the children in this study. As a consequence of this age-dependent increase of the IgE concentration, we have, for statistical reasons, preferred to express the IgE value in children as a "deviation from the expected mean value for the age" transformed logarithmically to base 10. This is called the residual value (R.V.) (see Fig. 3). The expected mean value for the age has been calculated from the formula $^{10}\log \text{IgE} = 2.10016 - 0.0223 \times$ age in years (2).

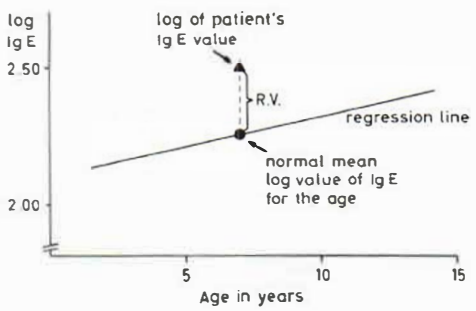

Fig. 3. Calculation principle of residual value (R.V.) of log IgE in children.

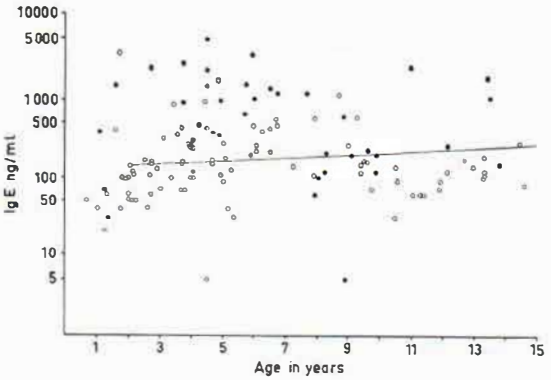

Fig. 4. Serum IgE values in 128 children with atopic dermatitis. ○, children with only dermatitis ("pure"); ●, children with dermatitis + asthma and/or allergic rhinitis ("mixed"). The regression line used for calculation is superimposed.

RESULTS

A. *Immunoglobulins G, A, M and D*

Determinations of the levels of IgG, A, M and D could be made in only 90 of the 93 adult patients. The results are summarized in Tables I, II and III. In Table I figures are also included from concurrent determinations on 104 healthy blood donors. Their ages ranged from 19 to 58 years.

The geometric mean values of IgG and IgM for the total group of adults with atopic dermatitis were significantly increased ($p < 0.01$) compared with the mean values of the normal controls. No such difference could be found for IgA. The mean value of IgD was significantly lower ($p < 0.01$) than that of the controls. There was no significant difference between the mean values of IgG, A, M and D of those with atopic dermatitis only ("pure") and those with additional symptoms of asthma and/or allergic rhinitis ("mixed"). Nor was there any significant difference between those with a mild dermatitis and those with more extensive involvement of the skin.

In Table III the patients are grouped according to their serum levels of IgE. No significant difference in the other immunoglobulin levels could be found between the groups with high or normal IgE Values.

B. *Immunoglobulin E*

Since special attention was devoted to this part of the study, the report here will be somewhat more detailed.

Atopic dermatitis and combinations with asthma and allergic rhinitis

Children. Fig. 4 shows the individual IgE values in the children with atopic dermatitis. The geometric mean value and mean of residual values (R. V.) for the entire group are given in Table IV. Here, patients are also divided into groups with or without symptoms of bronchial asthma or allergic rhinoconjunctivitis, that is, into "mixed" and "pure" groups.

The children with "pure" atopic dermatitis had a mean R.V. of IgE in serum slightly below zero. From our definition of R.V. it follows that the normal mean of IgE (2) corresponds to a R.V. of zero.

In children who had a "mixed" atopic dermatitis, the mean R.V. of IgE was elevated above zero ($p < 0.001$) and it differed significantly ($p < 0.001$) from the mean of children with a "pure" atopic dermatitis. Patients with atopic dermatitis and asthma had the highest mean, followed by the group with atopic dermatitis and both asthma and allergic rhinitis, and finally the children with atopic dermatitis and only allergic rhinitis. An analysis of variance showed no significant difference between these last three subgroups.

Essentially, the same findings were obtained when the children were grouped according to what symptoms of asthma and allergic rhinitis they had displayed during the previous 3 years. The mean R.V. became somewhat larger for the "mixed" group and also for the subgroup dermatitis plus asthma.

Adults. In Fig. 5 the individual IgE values are shown for the adult patients. In Table V the geometric means of the actual IgE values are given, expressed as nanograms per ml. The mean IgE value of the patients who, in addition to their dermatitis, had a history of asthma and/or allergic rhinitis ("mixed" group) was higher ($p < 0.01$) than in the group with only dermatitis ("pure" group). The highest mean was recorded in patients with both asthma and allergic rhinitis.

A grouping according to what symptoms of atopy the patients had shown during the previous 3 years gave very similar results.

History of urticaria

A history of urticaria at some time during their life was obtained in 7% of the adults with a "pure" atopic dermatitis and 9% of the children. Only one of the 8 children with a "pure" dermatitis and a previous history of urticaria had an elevated serum IgE value. In the adults, the 2 patients with a

Table I. *Mean values of serum IgG, M, A and D in adults with atopic dermatitis*

		IgG				IgM			
	No. of patients	Geometric mean (mg/100 ml)	Arith. mean	10_{log} Mean	S.D.	Geometric mean (mg/100 ml)	Arith. mean	10_{log} Mean	S.D.
Total	90	1 388.7	1 425.3	3.1426	0.0991	151.6	172.1	2.1807	0.2885
Male	35	1 464.7	1 504.7	3.1658	0.1021	144.2	176.3	2.1589	0.4103
Female	55	1 342.4	1 374.7	3.1279	0.0940	156.6	169.4	2.1946	0.1693
Normal Controls	104	1 219.0	1 238.2	3.0860	0.0776	171.6	184.3	2.2346	0.1660

Table II. *Mean values of serum IgG, M, A and D in adults with atopic dermatitis with regard to atopy coexisten*

		IgG				IgM			
Form of dermatitis	No. of patients	Geometric mean (mg/100 ml)	Arith. mean	10_{log} Mean	S.D.	Geometric mean (mg/100 ml)	Arith. mean	10_{log} Mean	S.D.
"Pure"	26	1 463.7	1 496.0	3.1655	0.0922	161.0	168.1	2.2069	0.1287
"Mixed"	64	1 359.2	1 396.5	3.1333	0.1001	147.9	173.7	2.1701	0.3317
Mild	54	1 353.2	1 386.6	3.1314	0.0967	144.9	168.9	2.1610	0.3432
Mod.-Severe	36	1 443.8	1 483.3	3.1595	0.0999	162.3	176.9	2.2104	0.1734

Table III. *Mean values of serum IgG, M, A and D in adults with atopic dermatitis with regard to serum IgE level.*

		IgG				IgM			
Amount of IgE	No. of patients	Geometric mean (mg/100 ml)	Arith. mean	10_{log} Mean	S.D.	Geometric mean (mg/100 ml)	Arith. mean	10_{log} Mean	S.D.
> 1 000 ng/ml	33	1 336.5	1 370.3	3.1260	0.0953	160.2	173.5	2.2046	0.1692
< 1 000 ng/ml	57	1 419.9	1 457.1	3.1523	0.0998	146.9	171.2	2.1669	0.3383
< 125 ng/ml	26	1 397.0	1 427.5	3.1452	0.0912	130.7	165.5	2.1163	0.4571

"pure" dermatitis and a history of urticaria had normal IgE levels in serum.

In the "mixed" group, urticaria had occurred in 30% of the adults and 26% of the children. Most patients had had only a few episodes of urticaria.

Severity of atopic dermatitis

Children. When a comparison was made on the basis of severity of the atopic dermatitis, it was found that children with a mild dermatitis had a mean R.V. of IgE very close to zero (Table VI). When pooled together, the groups with moderate or severe dermatitis had a significantly higher mean R.V. ($p < 0.05$) than those with mild dermatitis. To avoid the influence of asthma and/or allergic rhinitis, the same grading system was used for children with a "pure" atopic dermatitis. In this case no significant differences could be found between the groups with mild, moderate or severe dermatitis.

Adults. As can be seen from Table VII, the mean IgE value increased considerably with increasing severity of the atopic dermatitis when all patients were considered ($p < 0.01$). When patients with only atopic dermatitis were analysed, those with a moderate and severe dermatitis had a higher mean IgE value than those with a mild dermatitis ($p < 0.01$).

Food intolerance, heredity, and age of onset

There was no significant difference between the mean IgE values of patients with and those without

gA				IgD			
Geometric mean mg/100 ml)	Arith. mean	10_{log} Mean	S.D.	Geometric mean (mg/100 ml)	Arith. mean	10_{log} Mean	S.D.
95.5	103.5	1.9799	0.1771	1.64	2.37	0.2145	0.3519
91.6	98.1	1.9620	0.1620	1.80	2.42	0.2550	0.3346
98.0	106.9	1.9912	0.1854	1.54	2.33	0.1887	0.3601
76.7	74.0	1.8244	0.2020	2.29	3.23	0.3603	0.3727

with dermatitis and to severity of dermatitis

gA				IgD			
Geometric mean mg/100 ml)	Arith. mean	10_{log} Mean	S.D.	Geometric mean (mg/100 ml)	Arith. mean	10_{log} Mean	S.D.
96.0	105.6	1.9822	0.1948	1.59	2.37	0.2017	0.3886
95.3	102.6	1.9789	0.1696	1.66	2.37	0.2197	0.3357
91.2	98.8	1.9602	0.1764	1.51	2.06	0.1800	0.3292
02.2	110.5	2.0094	0.1743	1.85	2.83	0.2663	0.3776

gA				IgD			
Geometric mean mg/100 ml)	Arith. mean	10_{log} Mean	S.D.	Geometric mean (mg/100 ml)	Arith. mean	10_{log} Mean	S.D.
99.8	98.4	1.9535	0.1852	1.81	2.84	0.2588	0.3767
98.9	106.4	1.9951	0.1706	1.54	2.09	0.1888	0.3340
97.7	101.9	1.9898	0.1303	1.75	2.51	0.2424	0.3745

a stated food intolerance. Nor could any difference be found between those with a family history of atopy and those without. Also, no correlation was found between reported age of onset of dermatitis and the actual IgE value.

In both children and adults, those with a stated food intolerance had a significantly lower median age of onset ($p < 0.01$) as compared with those without food intolerance.

The children with a moderate or severe type of dermatitis also had a significantly lower median age of onset ($p < 0.05$) as compared with those with a mild form. In the adult group no such difference could be found.

C. *Seasonal Variation of IgE Levels in Serum*

The mean IgE values for the different periods are given in Table VIII. During the course of a year there was no pronounced variation in the serum IgE level in either group. In patients with a normal serum IgE level, this was lower in May–June than that in February–April ($p < 0.05$) when calculated on the difference between logarithmically transformed values, and in patients with a high serum IgE level, this was lower in July–August than that in September–October ($p < 0.01$). No other significant differences were found between the IgE values of two consecutive periods. Neither were the slightly lower IgE values in the summertime significantly

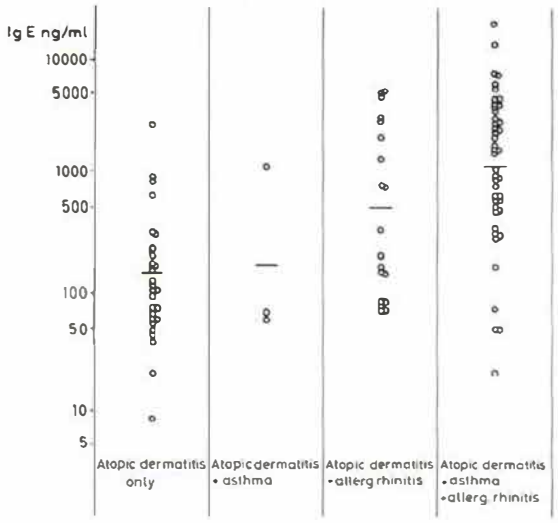

Fig. 5. Serum IgE values in 93 adults with only atopic dermatitis and combinations with asthma and/or allergic rhinitis.

different from those taken in the winter. When the mean IgE values were calculated in patients with a positive reaction to pollen on intradermal testing and/or RAST (Radioallergosorbent test (28)), we did not find any significant change in IgE levels from winter to summertime.

The atopic dermatitis was more pronounced in the wintertime and improved during the summer.

Table IV. *Mean values of serum IgE in children with atopic dermatitis*

Atopy coexistent with dermatitis	No. of patients	Geometric mean[b] of IgE (ng/ml)	R.V.[a] Mean	R.V.[a] S.D.
None ("Pure")	89	141	−0.0835	0.4421
Asthma and/or allergic rhinitis ("Mixed")	39	452	+0.4071	0.6449
Asthma	19	585	+0.5468	0.7187
Allergic rhinitis	8	269	+0.1545	0.5203
Asthma and allergic rhinitis	12	424	+0.3543	0.5800
Total	128	201	+0.0660	0.5579

[a] R.V. = residual value of IgE, expressed in ^{10}log. The residual value of IgE is the difference between the patient's ^{10}log IgE value and the normal mean value of ^{10}log IgE for the age measured in ng/ml.
[b] Not corrected for age.

As shown in Figs. 6 and 7, the degree of severity of atopic dermatitis roughly paralleled the IgE curve during the year.

DISCUSSION

For a study of this type, it is a problem to find a group of patients which represents a true cross section of the disease. Some patients with minor symptoms will never see a doctor. Other patients are seen by doctors other than hospital dermatologists; often because they are under care for other major diseases. Since there are no dermatologists in the Uppsala area except at our hospital, a large proportion of the patients with atopic dermatitis are seen at our outpatient clinic. The patients studied might therefore be considered as fairly representative of the actual panorama of atopic dermatitis.

Thirty per cent of the children seen by us had displayed symptoms of asthma and/or allergic rhinitis ("mixed" group), as compared with 71 % of the adults. One explanation could be that the children represent a selection if the pediatricians also treat the dermatitis of those with asthma and allgergic rhinitis. Another possibility is that an increased number of children will develop symptoms of asthma or allergic rhinitis later in life [7]. Still another possibility could be that the presence of asthma or allergic rhinitis would lead to a more persistent dermatitis if the patient is prone to have skin changes.

It is evident that different compositions of the patient material with regard to age, diagnosis and severity of atopy, as well as the various techniques

Table V. *Mean values of serum IgE in adults with atopic dermatitis*

Atopy coexistent with dermatitis	No. of patients	Geometric mean of IgE (ng/ml)	^{10}log IgE Mean	^{10}log IgE S.D.
None ("Pure")	27	144	2.1573	0.4792
Asthma and/or allergic rhinitis ("Mixed")	66	830	2.9190	0.7055
Asthma	3	171	2.2321	0.7227
Allergic rhinitis	19	496	2.6952	0.7086
Asthma and allergic rhinitis	44	1 154	3.0625	0.6646
Total	93	499	2.6979	0.7330

Table VI. *Mean values of serum IgE in children with regard to severity of atopic dermatitis*

Severity of atopic dermatitis	All children				Children with "pure" atopic dermatitis			
	No. of patients	Geometric mean[b] of IgE (ng/ml)	R. V.[a] Mean	S.D.	No. of patients	Geometric mean of IgE (ng/ml)	R. V.[a] Mean	S.D.
Mild	86	171	−0.0087	0.5220	69	134	−0.1117	0.4408
Moderate	29	290	+0.2264	0.5610	17	161	−0.0004	0.4705
Severe	13	262	+0.2020	0.7129	3	217	+0.0931	0.3040
Total	128				89			

[a] R. V. = residual value of IgE expressed in ^{10}log. The residual value of IgE is the difference between the patient's ^{10}log IgE value and the normal mean value of ^{10}log IgE for the age measured in ng/ml.
[b] Not corrected for age.

Table VII. *Mean values of serum IgE in adults with regard to severity of atopic dermatitis*

Severity of atopic dermatitis	All adults				Adults with "pure" atopic dermatitis			
	No. of patients	Geometric mean of IgE (ng/ml)	^{10}log IgE Mean	S.D.	No. of patients	Geometric mean of IgE (ng/ml)	^{10}log IgE Mean	S.D.
Mild	55	261	2.4166	0.6520	20	112	2.0481	0.4720
Moderate	18	683	2.8342	0.6199	4	237	2.3754	0.4048
Severe	20	2 232	3.3487	0.5977	3	393	2.5948	0.3492
Total	93				27			

used in different laboratories, will make it difficult to compare the results from different studies of immunoglobulin levels. Kaufman & Hobbs (17) have also suggested that the discrepancies in the results might be due to an increased frequency of both subnormal and high immunoglobulin values in atopic patients.

We have found in our study higher levels of IgG and IgM in patients with atopic dermatitis. This is in agreement with some of the previous reports (2, 27) in atopic patients. The different results in other studies (5, 8, 9, 21, 25) might very well be explained by some of the reasons mentioned above. We were unable to ascertain any special feature which may be responsible for the elevated values of IgG and IgM as no difference in this respect could be found between those patients with atopic dermatitis alone and those with additional symptoms of asthma and/or allergic rhinitis. Nor was there any difference between those with mild or more extensive skin changes. Likewise, a comparison between the patients with high IgE levels and those with normal or rather low values did not show any significant difference in the concentration of the other immunoglobulins. It is still very difficult to say whether or not the elevated IgG and IgM values would reflect an abberant immunologic response in analogy with the tendency to form reaginic antibodies. The hypothesis exists that these differences in IgG and IgM might merely reflect a higher incidence of infections in these patients. It should also be pointed out that atopic manifestations can occur in individuals lacking IgA and in various immunoglobulin deficiencies (1, 6).

Table VIII. *Mean serum IgE values during one year in adult patients with atopic dermatitis*

The figures shown are the geometric mean of IgE in ng/ml

	Patients with high serum IgE values	Patients with normal serum IgE values
October–December	3 398	216
February–April	3 169	227
May–June	2 863	193
July–August	2 760	188
September–October	3 538	202

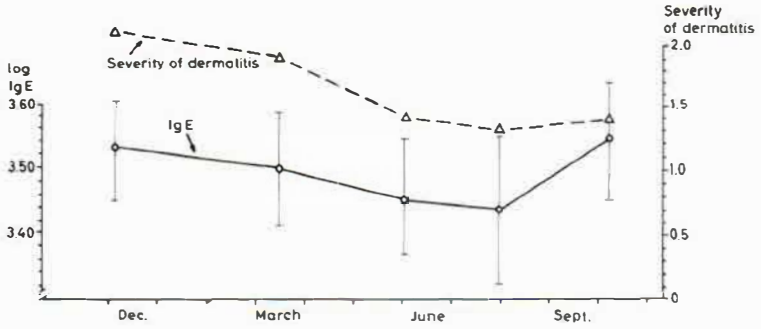

Fig. 6. Means of serum IgE value and of severity of dermatitis during one year in adult patients with atopic dermatitis and high serum IgE values. The vertical range bars indicate ± S.E. of the mean. The severity has been graded as: mild = 1, moderate = 2, severe = 3.

The IgE values in healthy subjects with no history of allergy have been estimated by Johansson & Berg (2, 12). The same technique has been used in the present study, but since these IgE determinations were not made at the same time as those in our patients, we have been careful when drawing conclusion from comparisons with these reported IgE levels in healthy subjects. We have reason to believe that the technique now has improved when estimating IgE values below 100 ng/ml. Since our calculations are based on the geometric means, a decrease of 20 to 40 ng/ml at this level will have a comparatively great influence on the mean. This might explain why the mean IgE level of our adult patients with "pure" dermatitis, i.e. without asthma and allergic rhinitis, is slightly lower than the previously given normal geometric mean. For the higher IgE values the method seems less sensitive to minor methodological changes.

For both the children and the adults with asthma and/or allergic rhinitis in addition to their dermatitis, the mean IgE value was found to be higher than for those with atopic dermatitis alone and also higher than the previously reported normal mean values for healthy children and adults. Previous studies have shown increased serum IgE levels in patients with asthma and allergic rhinitis (3, 11). It is therefore possible to link the common finding of a higher IgE value in the "mixed" group to the concomitant symptoms of asthma and/or allergic rhinitis. We know that symptoms of asthma or allergic rhinitis may be elicited when reagins react with their antigens. It is possible, however, to have a few circulating allergen-specific reagins which will not be detected as an increased IgE value, and not all allergens might stimulate the IgE production to the same extent. Also, we know very little about to what extent the circulating IgE might reflect local concentrations in various organs, e.g. the skin. The normal IgE value found in patients with dermatitis alone therefore gives no clue as to whether reagins are involved in the pathogenesis of the dermatitis.

In many of the patients with atopic dermatitis and a previous history of urticaria, this dated far back and was often a single episode. None of our patients were studied for IgE during an acute attack. However, in patients with acute or chronic urticaria without atopic dermatitis, asthma or allergic rhinitis, the IgE level was not increased (16). This and our own findings do not lend any support to the possibility that a history of urticaria would influence the IgE level.

When studing the severity of the atopic dermatitis it was found that, on the whole, those with more extensive involvement of the skin also had a higher

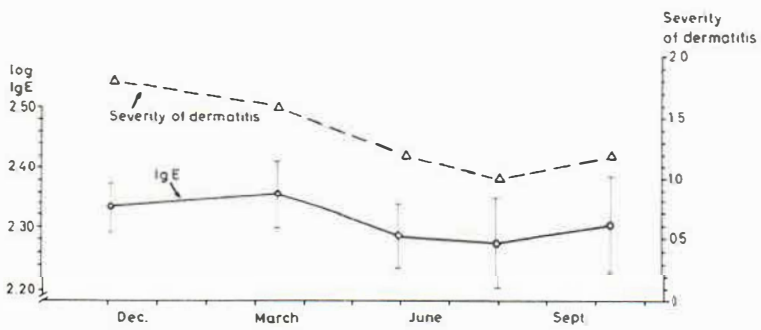

Fig. 7. Means of serum IgE value and of severity of dermatitis during one year in adult patients with atopic dermatitis and normal serum IgE values. The vertical range bars indicate ± S.E. of the mean. The severity has been graded as: mild = 1, moderate = 2, severe = 3.

mean IgE value than those with a milder type of dermatitis. This would indicate that the reagins actually are involved in eliciting the skin changes. One must, however, take into consideration here that a grading of the severity of atopic dermatitis is a crude method with a certain amount of subjectivity included and is influenced by treatment and sudden flare-ups. In a recently published study of 23 patients with varying degrees of atopic dermatitis, Ogawa et al. (22, 23) also found a correlation between serum IgE levels and the severity of the dermatitis.

The fact that in a previous study (16) no correlation was found between the severity of dermatitis and the IgE level could probably depend on the material consisting mainly of patients treated on the wards for severe skin changes. Under such circumstances a relationship would be difficult to detect.

In our children with only asthma and atopic dermatitis, the mean IgE value was higher than in the other "mixed" groups. In a previous study of children with atopic diseases (3), the same tendency was also found. One explanation could be that the presence of dermatitis might in some way enhance the reagin response in these children. Why the children with asthma and rhinitis in addition to their dermatitis have a less elevated IgE is uncertain, but the rhinitis could be the dominant symptom in this group because patients with allergic rhinitis alone have a less increased mean IgE level. The finding in children could not be reproduced in adults, possibly because we only had 4 patients in the group with dermatitis and asthma, and their asthma attacks were few and minor during recent years.

In patients with symptoms of asthma or allergic rhinitis elicited by pollen, an increase in the IgE level has been reported during or after the pollination season (4). The rise in pollen-specifc IgE was then more pronounced than the increase in the total IgE concentration. There is much evidence for believing that the reagins are here involved in the pathogenetic mechanisms. Whether the same is also true for patients with atopic dermatitis is more difficult to prove. One reason is the lack of a good provocation test for atopic dermatitis. Indirect evidence, such as a higher serum IgE level in patients with a more severe type of dermatitis, would favour a role of the reagins in at least some patients with atopic dermatitis. Another indirect evidence would be the findings in this study that the IgE level in serum to some extent paralleled the severity of the dermatitis during the year, but too much emphasis cannot be put on this as the variations in IgE levels were very small. It is interesting to note, however, that even if the patients with a positive test for pollen in our study were considered as a group, they had the same tendency as the entire group to slightly, but not significantly, lower values in the summer. This is in contrast to the increase in serum IgE level during the pollination season reported in patients with allergic rhinitis or asthma (4). The pollen-specific reagin titres were not determined during the season. It is therefore possible that in some of our patients an increase of the pollen-specific reagins did occur although they did not influence the total serum IgE level.

In our studies of the serum concentrations of IgG, IgA, IgM, IgD and IgE in a rather unselected group of patients with atopic dermatitis, we have found a slight, but statistically significant, rise in the levels of IgG and IgM and a pronounced increase in the IgE concentration. The changes in IgE reflected, to some extent, the severity of the disease; this was especially true for the patients with concomitant symptoms of asthma or allergic rhinitis. These last two indications of the atopic constitution were, at the time of the study, of a rather moderate degree in relation to the IgE level when compared with the IgE levels of patients with asthma alone, or allergic rhinitis and no atopic dermatitis. It could be that the skin changes seen in atopic dermatitis to some extent potentiate the IgE response in bronchial asthma and allergic rhinitis. The etiologic role of IgE in atopic dermatitis still remains obscure but the relationship is sufficiently interesting to stimulate continued studies of IgE as one of several factors influencing atopic dermatitis.

ACKNOWLEDGEMENTS

This investigation was supported by the Swedish Medical Research Council (grant no. B72-16X-105-08), the Medical Faculty of Uppsala University, and the Jörgen Schaumann Foundation.

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Received August 28, 1973

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