

A detailed investigation of circulating IgE levels in a normal population

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Summary

Total circulating IgE levels were measured in a carefully selected normal population, using a highly sensitive double antibody assay. The mean level of 36.3 u/ml found in this group is much lower than that reported in all previous studies. No circadian rhythm was evident, but IgE levels varied slightly from day-to-day. IgE levels in 100 serum samples were compared using the double antibody assay and the Phadebas test kit, based on a solid phase technique. A poor correlation was obtained with values below 100 u/ml, however, there was an excellent correlation for samples with IgE levels above this figure.

Introduction

The normal functions of immunoglobulin E (IgE) are not clearly understood, although the high circulating levels found in atopic individuals (Berg & Johansson, 1969; Gleich, Averbek & Swedlund, 1971; Johansson *et al.*, 1970; Johansson & Juhlin, 1970; Juhlin *et al.*, 1969; Kumar *et al.*, 1970; Salmon, 1970; Smith, Ozkaragoz & Gokcen, 1972; Stenius, Wide & Seymour, 1972) and in people with parasitic infections (Johansson, Melbin & Valquist, 1968; Ito, Sawada & Sato, 1972; Kojima, Yokogawa & Tada, 1972), has led to the suggestion that it is related to allergy and that serum IgE estimations can enable an atopic population to be distinguished from normal. Low levels are found in very young children (Johansson, 1968; Polmar *et al.*, 1972) and in certain diseases such as cancer (Augustin & Chandrasa, 1971; Jacobs *et al.*, 1972), ataxia telangiectasia (Ammann *et al.*, 1969; Biggar *et al.*, 1970; Polmar *et al.*, 1972; Polmar, Waldman & Terry, 1973), and agammaglobulinaemia (Polmar *et al.*, 1970, 1973; Stites, Ishizaka & Fudenberg, 1972). The low levels of circulating IgE found in normal subjects and in the latter group of disorders necessitate the use of radioimmunoassay for its measurement. Thus most immunodiffusion techniques (Arbesman *et al.*, 1972; Reerink-Brongers *et al.*, 1973; Rowe, 1969; Smith *et al.*, 1972; Spitz *et al.*, 1972) can be applied only if levels are raised.

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Many reports (Gleich *et al.*, 1971; Jacobs *et al.*, 1972; Johansson, 1968; Juhlin *et al.*, 1969; Leonardy & Peacock, 1972; Polmar *et al.*, 1970, 1972; Salmon, 1970) attempting to define the normal range of IgE levels by radioimmunoassay have not employed a sufficiently sensitive procedure or fulfilled certain essential criteria for such a study (including the possibility of circadian or day-to-day variations) or supplied data concerning whether some of the subjects had a past, present or family history of allergy. Establishment of a well-defined normal range is obviously essential if conclusions are to be drawn concerning the significance of high or low levels.

Table 1. Questionnaire completed by volunteers

ALLERGY QUESTIONNAIRE

NAME: AGE:
 TIME: SEX:
 DATE: HOSP. NO:
 ADDRESS: HEALTHY:
 DIAGNOSIS:

Have you ever suffered from: (please ✓ or —)

ASTHMA
 HAYFEVER
 ECZEMA
 URTICARIA
 MIGRAINE
 OTHER 'ALLERGIES' (specify)

Family History: (please ✓ if yes)

	Asthma	Hayfever	Eczema	Urticaria
Father				
Mother				
Brothers				
Sisters				
Sons				
Daughters				

Have you had any recent infection? e.g. cold, sore throat, bronchitis,
 gastroenteritis. YES / NO

Drugs List (including 'Pill')

Time of last meal: hours ago.

Materials and methods

Sources of material were as follows: Immunoglobulin E (IgE) reference standard 68/341 from the Division of Biological Standards, London, England; ^{125} I-IgE and Sephadex-linked anti-IgE from Pharmacia AB, Uppsala, Sweden; rabbit anti-IgE serum from Hoechst Ltd, Hounslow, Middlesex, England; donkey anti-rabbit serum

and unactivated horse serum from Wellcome Laboratories, Beckenham, Kent, England; human serum albumin (HSA) from Kabi AB, Stockholm, Sweden, and Tween 20 from Koch Light Laboratories Ltd, Colnbrook, Buckinghamshire, England.

Criteria for the selection of subjects were as follows. Volunteers completed a questionnaire (Table 1) with the help of the physician and only those with no past, present or family history of allergy were asked to participate in the study. The time of sample collection, of the last meal and whether they were receiving drugs were recorded. The majority were healthy hospital staff, although some were hospital inpatients.

Collection of samples

(a) Random blood samples were collected from 102 subjects (forty-seven male, fifty-five female) whose ages ranged from 18 to 83 years.

(b) To investigate the circadian rhythm, six men and five women aged 21–34 years had repeated venepuncture at 2-hourly intervals between 8 a.m. and 8 p.m., and also at midnight and 4 a.m.

(c) To assess the day-to-day variation, three men and three women aged 25–34 years provided samples three times a week for 3–4 weeks.

Table 2.

	Solid phase assay	Liquid phase assay	
		Low sensitivity	High sensitivity
Order and volume of additions			
Test sample diluted 1:2 or standard	100 μ l	100 μ l	100 μ l
^{125} I-IgE	100 μ l (1.5 u IgE)	100 μ l (0.16 u IgE)	—
Anti-IgE	1000 μ l (Sx-anti-IgE)	100 μ l (Final dilution 1:30,000)	100 μ l (Final dilution 1:120,000)
Incubation at room temperature	16 hr (with vertical rotation)	16 hr	48 hr
^{125} I-IgE	—	—	100 μ l (0.16 u IgE)
Incubation at room temperature	—	—	24 hr
Separation of bound and free fractions			
Donkey anti-rabbit serum (1:24)+ normal non-immunized rabbit serum (1:240) in distilled water	—	200 μ l	200 μ l
Incubation at 4°C	—	24 hr	24 hr
Total time required for assay	24 hr	48 hr	96 hr

Preparation of reagents

Albumin-phosphate buffer: 0.05 M phosphate buffer, pH 7.4, containing 0.3% human serum albumin, 0.5% Tween 20 and 0.05% sodium azide.

Standard diluent. Fifty per cent horse serum in albumin-phosphate buffer.

Standard solution. For the solid phase assay the IgE reference material was diluted in albumin-phosphate buffer to give standards ranging from 1.6 to 400 u/ml, and for the high and low sensitivity double antibody assays in standard diluent to contain from 0.0625 to 16.0 u/ml and from 4.0 to 200 u of IgE/ml respectively.

All other reagents were diluted in albumin-phosphate buffer.

Radioimmunoassays

(a) Liquid phase. Low sensitivity assay. The reagents were added to LP2 tubes (obtained from Luckham Ltd, Burgess Hill, Sussex, England) in the volumes and order summarized in Table 2. In addition three sets of three tubes were prepared to measure; (a) the maximum binding of ^{125}I -IgE in the system (B_0), in which the unlabelled IgE was replaced by standard diluent; (b) the blank (B_b), in which the unlabelled IgE was replaced by standard diluent and the anti-IgE by albumin-phosphate buffer; and (c) the total radioactivity (T), in which ^{125}I -IgE only was added. The tubes were vortexed, incubated at room temperature for 16 hr, and the bound and free fractions separated by the second antibody technique as outlined in Table 2. The precipitates, containing the bound fractions, were counted using an automatic gamma counter (LKB-Wallac, Croydon, Surrey, England).

(b) Liquid phase. High sensitivity assay. The reagents were added to LP2 tubes in the volumes and order summarized in Table 2. The tubes were then vortexed, incubated at room temperature for 48 hr, and the bound and free fractions separated by the second antibody technique.

(c) Solid phase. Phadebas IgE test. The assay was performed according to the instructions supplied with the kit, reagents being added to LP3 tubes in the volumes and order summarized in Table 2. The tubes were incubated with constant vertical rotation, using a rotator obtained from Chemlab Instruments Ltd, Romford, Essex, England.

Calculations

The antibody bound fraction (B_i) was expressed either as a percentage of the total radioactivity ($B_i/T \times 100$), or as a percentage of the maximum binding ($B_i/B_0 \times 100$).

The best cubic curve was computed for the standards using the method of least squares, and the amount of IgE in the test samples was interpolated automatically using a suitable computer programme and a 9100b calculator (Hewlett-Packard Company, Colorado, U.S.A.)

Results

Standard curves were obtained for the three assays in which the maximum binding of ^{125}I -IgE ($B_0/T \times 100$) was approximately 60%, 25% and 20% for the low and high sensitivity assays and for the Phadebas solid phase assay respectively. Blank values ($B_b/T \times 100$) were about 3% and 'between assay' coefficients of variation for all three assays were approximately 10% for IgE values lying on the steep part of their standard curves. It can be seen (Fig. 1) that the high sensitivity liquid phase assay is some thirty times more sensitive than the low sensitivity liquid phase assay and has a sensitivity

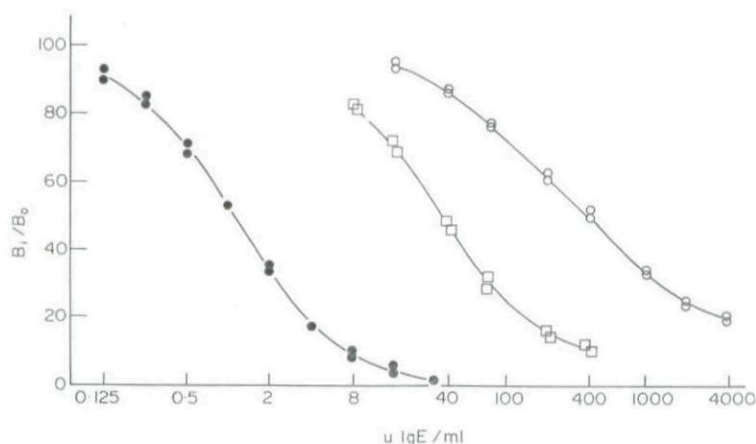


Fig. 1. Comparison of standard curves obtained using Pharmacia standards in the high sensitivity liquid phase radioimmunoassay (●—●), the low sensitivity liquid phase radioimmunoassay (□—□), and the Phadebas solid phase radioimmunoassay (○—○).

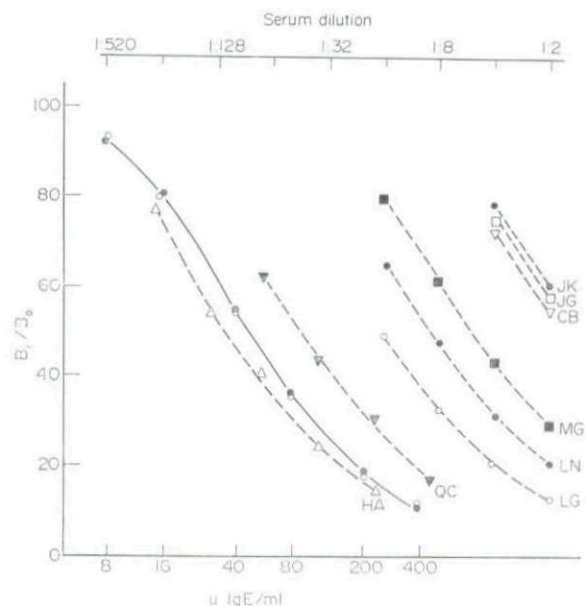


Fig. 2. Parallel inhibition of the binding of ^{125}I -IgE exhibited by serial dilutions of serum samples (---), compared with Pharmacia standards (●—●) and WHO standards (○—○).

at least 100 times greater than the solid phase technique.

Doubling dilutions of eight serum samples, measured by the low sensitivity liquid phase assay, were parallel to the standard curve (Fig. 2). The 'within assay' coefficient of variation at 25 u/ml for this method was 6%.

Comparison of solid phase and liquid phase assays

Figure 3 compares the results obtained for 100 sera measured by the two assays. A poor correlation was obtained with values below 100 u IgE/ml ($r = 0.539$) with the

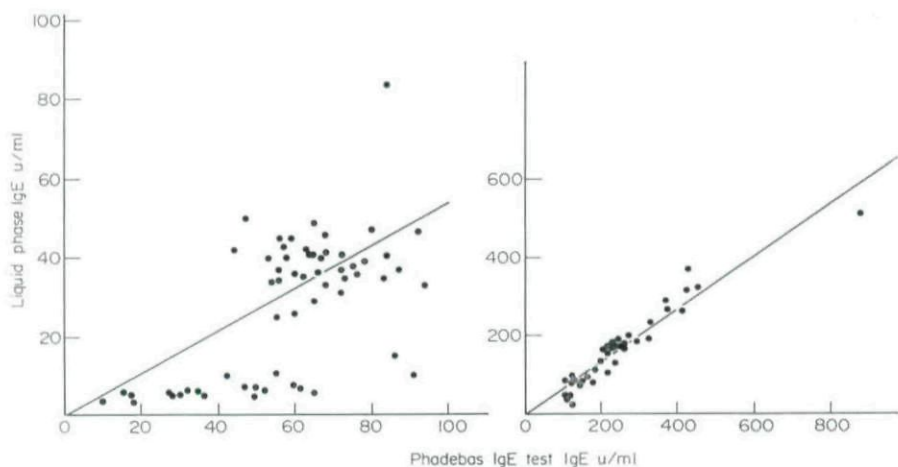


Fig. 3. Correlation between liquid phase radioimmunoassay and Phadebas solid phase radioimmunoassay. Below 100 u IgE/ml $r = 0.539$, $y = 0.464x - 0.117$; and above 100 u IgE/ml $r = 0.959$, $y = 0.680x - 3.240$.

liquid phase assays giving lower results than the solid phase technique. There was, however, a good correlation for samples with IgE values above this range ($r = 0.959$).

IgE levels obtained by the liquid phase radioimmunoassay

(a) Results for 102 normal subjects gave a skewed distribution (Fig. 4) with ninety-

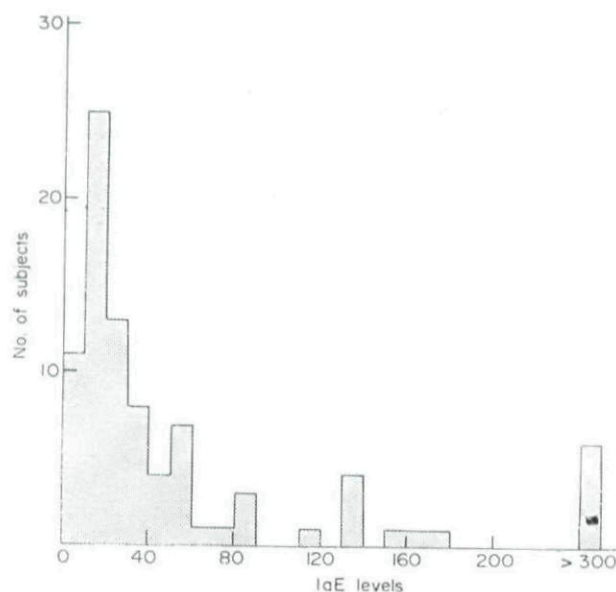


Fig. 4. The distribution of IgE levels in 102 normal subjects.

six having values within the range 1.0–178 u/ml. The other six had levels of 321, 372, 517, 2111, 2503 and 3824 u/ml, with the highest being found in a subject recently

Table 3. IgE levels measured by liquid phase radioimmunoassay in the circadian rhythm study

Subject	Age	Sex	Time throughout the day (hr)								Mean	s.d.	C.V.	Assay
			08.00	10.00	12.00	14.00	16.00	18.00	20.00	00.00	04.00			
EN	21	M	182	180	162	172	200	178	173	155	168	±12.9	7.4	L
HL	25	M	73.2	94.2	84.0	78.4	77.8	72.9	78.9	77.6	97.8	±8.8	10.7	L
CB	26	F	47.1	46.4	40.6	47.1	45.9	35.9	40.4	48.8	36.8	±4.9	11.3	L
JK	30	M	44.9	49.7	42.3	40.2	39.6	43.4	40.8	40.6	45.4	±3.3	7.6	L
JG	26	F	40.5	42.7	40.2	36.4	37.3	46.6	32.5	42.3	38.9	±4.1	10.3	L
ADH	22	M	33.3	25.6	34.7	38.2	37.2	33.6	34.5	33.7	36.4	±3.6	10.6	L
AET	21	M	24.3	29.6	23.8	28.7	22.8	30.4	25.5	27.2	24.5	±2.8	7.5	L
SD	21	F	18.9	18.7	23.3	18.7	21.2	21.0	23.7	18.5	17.9	±2.2	10.8	L
RW	34	M	3.3	5.7	5.1	5.7	5.7	5.4	3.9	5.0	4.9	±0.85	17.1	H
VC	25	F	3.3	3.2	3.0	2.8	3.2	3.3	3.4	3.8	4.3	±0.44	13.0	H
JD	23	F	3.0	2.9	2.9	3.2	2.3	2.0	2.4	2.2	—	±0.44	16.8	H

H = high sensitivity assay; L = low sensitivity assay.

Table 4. IgE levels measured by liquid phase radioimmunoassay in the day-to-day study

Subject	Age	Sex	Week 1			Week 2			Week 3			Week 4			Mean	s.d.	C.V.	Assay
			Week 1			Week 2			Week 3			Week 4						
			1	2	3	1	2	3	1	2	3	1	2	3				
PH	25	F	80.5	76.2	75.7	83.8	87.9	62.7	81.9	76.9	79.4	57.5	65.2	72.0	75.0	± 9.9	12.1	L
HHL	25	M	66.7	72.8	79.6	84.2	70.0	89.1	59.9	75.4	71.8	—	—	—	74.4	± 8.9	12.0	L
KT	28	M	45.1	43.1	43.3	53.2	48.3	46.8	40.3	51.6	34.6	39.6	—	—	44.6	± 5.6	12.7	L
SJ	25	F	11.0	10.0	12.2	10.1	10.8	10.5	9.9	7.5	10.2	10.6	10.5	9.8	10.3	± 1.9	10.5	L
KF	25	F	6.1	7.3	7.0	6.3	5.9	7.1	4.5	4.8	6.4	6.5	10.0	6.0	6.49	± 1.39	21.4	H
RW	34	M	5.5	5.8	4.3	8.3	4.4	5.4	5.2	5.4	4.0	5.0	—	—	5.33	± 1.19	22.3	H

H = high sensitivity assay; L = low sensitivity assay.

arrived from Fiji, who may have had a parasitic infection. The results were not known at the time that these subjects left hospital, and it was impossible to determine the reason for their high values which were excluded from further calculations since all other subjects had levels below 180 u/ml.

The mean IgE was 36.3 and the logarithmic mean 21.2 u/ml with the modal value lying between 10 and 20 u/ml. There was no sex difference, the numerical means being 35.4 and 37.0 u/ml for men and women respectively. When the results were divided according to the subject's age (18-29, 30-49, and 50-83 years) all groups showed a skewed distribution with modal and logarithmic mean values of approximately 20 u/ml.

(b) The results of the circadian rhythm study are shown in Table 3. The coefficient of variation for each subject was usually slightly greater than that of the method (10%), however, no definite pattern was observed.

(c) The results of the day-to-day study (Table 4) show that the coefficients of variation for the individual subjects were greater (12.0-22.3%) than that for the method and for the circadian rhythm study (7.4-17.1%) indicating that their IgE levels varied slightly although no definite pattern was evident.

Discussion

There have been many attempts to determine the normal range of serum IgE levels, some of which are summarized in Table 5. The values quoted by different workers,

Table 5. Normal range of IgE levels as reported in the literature

Author	Separation	Normal IgE levels	
		Mean	Range
Arbesman <i>et al.</i> (1972)	Radioimmunoassay	218	<20-8850 ng/ml
Ito <i>et al.</i> (1972)	Radioimmunoassay	—	25-1750 ng/ml
Smith <i>et al.</i> (1972)	Radioimmunoassay	80	Undetectable-1000 u/ml
Reerink-Brongers <i>et al.</i> (1973)	Radioimmunoassay	—	<200-410 u/ml
Johansson (1968)	Solid phase (Phadebas IgE test)	248	66-1830 ng/ml
Juhlin <i>et al.</i> (1969)	Solid phase (Phadebas IgE test)	248	61-1000 ng/ml
Leonardy <i>et al.</i> (1972)	Solid phase (Phadebas IgE test)	150	20-500 ng/ml
Jacobs <i>et al.</i> (1972)	Solid phase (Phadebas IgE test)	215	85-740 u/ml
Present study	Solid phase (Phadebas IgE test)	—	<100-273 u/ml
Bazara <i>et al.</i>	Solid phase (Bromoacetyl cellulose)	205	19.4-810 u/ml
Gleich <i>et al.</i> (1971)	Second antibody	179	1-2700 ng/ml
Present study	Second antibody	36	1-178 u/ml

even when using the same technique, are very different. In part, this may have been due to the confusion between nanogram and units. In most early studies IgE levels

were reported by mass rather than as units at a time when it was thought that 1 ng was equivalent to 1 u of IgE, whereas 2.4 ng are now thought to equal 1 u. This emphasises the importance of an international reference standard such as that prepared by the World Health Organization (Rowe *et al.*, 1970). Selection of normal subjects with respect to atopy is another problem since inclusion of atopic individuals would significantly increase the mean values obtained. Finally most of the radioimmunoassays used were operated at the limits of their sensitivity, which leads to marked imprecision (Ekins, 1974).

In an attempt to clarify the situation we developed a radioimmunoassay, using the second antibody separation technique, which was initially developed to measure IgE levels lying between 8 and 400 u/ml. Several subjects, however, had IgE levels of less than 10 u/ml and the original method was therefore modified to markedly increase sensitivity to enable the detection of as little as 0.125 u/ml. This assay is also of value in very young children and in various diseases, such as cancer, where low levels are encountered. For routine investigations, however, the less sensitive liquid phase assay has the advantage that it operates over a wider range and results can be obtained within 48 as compared with 96 hr.

The mean IgE level of 36.3 u/ml found in this study is much lower than that reported in all previous papers. Furthermore, since the data formed a skewed distribution the logarithmic mean of 21.2 u/ml is a more realistic figure as it is nearer the modal value which lies between 10 and 20 u/ml. Oprée, Krause & Stockberg (1972) measured IgE levels in a random population and found a multimodal distribution with three maxima. The proportions in each group agreed with the theoretical frequencies derived from the Hardy-Weinberg law for two alleles at a single locus, and with the frequencies for non-atopic and atopic alleles as calculated by Weiner, Zieve & Fries (1936). The three groups were, therefore, designated AA, Aa and aa and the inclusion of Aa individuals in a normal population could account for the skewed distribution found in this and other normal studies.

There was no difference in the IgE levels of men and women in agreement with previous reports (Johansson, 1968; Gleich *et al.*, 1971). Johansson (1968) suggested that there was a slight but non-significant decrease in IgE levels with increasing age in adults, and our results confirm this since, although the numerical mean for the age group 50–83 years was lower than those for the younger age groups, the logarithmic means and the modal values were approximately 20 u/ml for all groups. There was no significant variation throughout the 24 hr period but IgE levels vary slightly from day-to-day in an apparently random manner.

Comparison of the Phadebas solid phase and the liquid phase assays showed that the latter yielded lower results for IgE levels below 100 u/ml which also helps explain our lower normal range as compared with other groups employing the Phadebas technique. An excellent correlation was found above 100 u/ml ($r = 0.959$), although below this level the correlation was very poor. Bazaral, Orgel & Hamburger (1971) using anti-IgE coupled to bromoacetyl cellulose suggested that non-specific blocking factors become significant at low levels of IgE and such factors could be responsible for the poor correlation between the two methods below 100 u/ml. In a recent study Lundkvist & Merrett (personal communication) have shown that the second antibody method and a paper disc 'sandwich' technique (Ceska & Lundkvist, 1972) give similar results and neither appears to be susceptible to non-specific effects.

The Phadebas IgE test was designed to distinguish between a normal and an

atopic population and it performs this function very well. Furthermore, it is a useful routine test since it operates over a wide range (100–4000 u/ml), which obviates the necessity to prepare repeated dilutions of allergic sera, it is both simple and precise, and results can be obtained within 24 hr. Late addition of ^{125}I -IgE (Merrett, unpublished) can improve its sensitivity to measure levels as low as 10 u/ml, but, without this modification it should not be used to measure low levels of IgE.

References

- AMMANN, A.J., CAIN, W.A., ISHIZAKA, K., HONG, R. & GOOD, R.A. (1969) Immunoglobulin E deficiency in ataxia—telangiectasia. *New England Journal of Medicine*, **281**, 469.
- ARBESMAN, C.E., ITO, K., WYPYCH, J.I. & WICHER, K. (1972) Measurement of serum IgE by one-step single radial radiodiffusion method. *Journal of Allergy and Clinical Immunology*, **49**, 72.
- AUGUSTIN, R. & CHANDRASA, K.D. (1971) IgE levels and allergic skin reactions in cancer and non-cancer patients. *International Archives of Allergy*, **41**, 141.
- BAZARAL, M., ORGEL, H.A. & HAMBURGER, R.N. (1971) IgE levels in normal infants and mothers and an inheritance hypothesis. *Journal of Immunology*, **107**, 794.
- BERG, T. & JOHANSSON, S.G.O. (1969) IgE concentrations in children with atopic disease. *International Archives of Allergy*, **36**, 219.
- BIGGAR, D., LAPOINTE, N., ISHIZAKA, K., MEUVISSEN, H., GOOD, R.A. & FROMMEL, D. (1970) IgE in ataxia-telangiectasia and family members. *Lancet*, **ii**, 1089.
- CESKA, M. & LUNDKVIST, U. (1972) A new and simple radioimmunoassay method for the determination of IgE. *Immunochemistry*, **9**, 1021.
- EKINS, R.P. (1974) Basic principles and theory. *British Medical Bulletin*, **30**, 3.
- GLEICH, G.J., AVERBECK, A.K. & SWEDLUND, H.A. (1971) Measurement of IgE in normal and allergic serum by radioimmunoassay. *Journal of Laboratory and Clinical Medicine*, **77**, 690.
- ITO, K., SAWADA, T. & SATO, S. (1972) Increased serum IgE level in individuals infected with *Schistosoma japonicum*, *Wucheria bancrofti* or hook worm, and the changes by treatment in Schistosomiasis. *Japanese Journal of Experimental Medicine*, **42**, 115.
- JACOBS, D., HOURI, M., LONDON, J. & MERRETT, T.G. (1972) Circulating levels of immunoglobulin E in patients with cancer. *Lancet*, **ii**, 1059.
- JOHANSSON, S.G.O. (1968) Serum IgND levels in healthy children and adults. *International Archives of Allergy*, **34**, 1.
- JOHANSSON, S.G.O., BENNICHI, H., BERG, T. & HÖGMAN, C. (1970) Some factors influencing the serum IgE levels in atopic disease. *Clinical and Experimental Immunology*, **6**, 43.
- JOHANSSON, S.G.O. & JUHLIN, L. (1970) Immunoglobulin E in 'healed' atopic dermatitis and after treatment with corticosteroids and azathioprine. *British Journal of Dermatology*, **82**, 10.
- JOHANSSON, S.G.O., MELLBIN, T. & VAHLQUIST, B. (1968) Immunoglobulin levels in Ethiopian pre-school children with special reference to high concentrations of immunoglobulin E (IgND). *Lancet*, **i**, 1118.
- JUHLIN, L., JOHANSSON, S.G.O., BENNICHI, H., HÖGMAN, C. & THYRESSON, N. (1969) Immunoglobulin E in dermatoses. Levels in atopic dermatitis and urticaria. *Archives of Dermatology*, **100**, 12.
- KOJIMA, S., YOKOGAWA, M. & TADA, T. (1972) Raised levels of serum IgE in human helminthiasis. *American Journal of Tropical Medicine and Hygiene*, **21**, 913.
- KUMAR, L., NEWCOMB, R.W., ISHIZAKA, K. & MIDDLETON, E. (1970) Clinical correlates of serum IgE in asthmatic children. *Pediatric Research*, **4**, 435.
- LEONARDY, J.G. & PEACOCK, L.B. (1972) An evaluation of quantitative serum immunoglobulin determinations in clinical practice. *Annals of Allergy*, **30**, 378.
- OPRÉE, W., KRAUSE, H. & STOCKBERG, H. (1972) Genetic aspects of serum IgE levels in atopic families. *Acta allergologica*, **27**, 247.
- POLMAR, S.H., LISCHNER, H.W., HUANG, N.N., WALDMANN, T.A. & TERRY, W.D. (1970) IgE levels in immunological deficiency stages (abstract). *Clinical Research*, **18**, 431.
- POLMAR, S.H., WALDMANN, T.A., BALESTRA, S.T., JOST, M.C. & TERRY, W.D. (1972) Immunoglobulin E in immunologic deficiency diseases. I. Relation of IgE and IgA to respiratory tract disease in isolated IgE deficiency, IgA deficiency and ataxia-telangiectasia. *Journal of Clinical Investigation*, **51**, 326.

- POLMAR, S.H., WALDMANN, T.A. & TERRY, W.D. (1973) A comparison of three radioimmunoassay techniques for the measurement of serum IgE. *Journal of Immunology*, **110**, 1253.
- REERINK-BRONGERS, E.E., STOOP, J.W., GROEN, A.S., VAN LOOKEREN CAMPAGNE, J.G., FELTKAMP, T.W.E., VEER, M.V.D., CALLIAUW, J.O. & SANDER, P.C. (1973) IgE levels, antibodies against smooth muscle and eosinophilia in asthmatic patients and normal controls. *International Archives of Allergy*, **44**, 233.
- ROWE, D.S. (1969) Radioactive single radial diffusion: a method for increasing the sensitivity of immunochemical quantification of proteins in agar gel. *Bulletin of the World Health Organization*, **40**, 613.
- ROWE, D.S., TACKETT, L., BENNICH, H., ISHIZAKA, K., JOHANSSON, S.G.O. & ANDERSON, S.G. (1970) A research standard for human serum immunoglobulin E. *Bulletin of the World Health Organization*, **43**, 609.
- SALMON, S.E. (1970) Serum and secreted IgE globulin in man (abstract). *Clinical Research*, **18**, 432.
- SMITH, H.J., OZKARAGOZ, K. & GOKCEN, M. (1972) A simplified radioimmunoassay technique for measuring human IgE. *Journal of Allergy and Clinical Immunology*, **50**, 193.
- SPITZ, E., GELFAND, E.W., SHEFFER, A.L. & AUSTEN, K.F. (1972) Serum IgE in clinical immunology and allergy. *Journal of Allergy and Clinical Immunology*, **49**, 337.
- STENIUS, B., WIDE, L. & SEYMOUR, W.M. (1972) Clinical significance of total IgE and of specific IgE to *Dermatophagoides Spp.*, grass pollen and other common allergens. *Clinical Allergy*, **2**, 303.
- STITES, D.P., ISHIZAKA, K. & FUDENBERG, H.H. (1972) Serum IgE concentrations in hypogammaglobulinaemia and selective IgA deficiency. Studies on patients and family members. *Clinical Experimental Immunology*, **10**, 391.
- WEINER, A.S., ZIEVE, I. & FRIES, J.H. (1936) The inheritance of allergic disease. *Annals of Eugenics*, **7**, 141.

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