

An epidemiological study on total and specific IgE levels in Japanese schoolchildren

S. KAGAMIMORI, Y. NARUSE, M. WATANABE, S. NOHARA*
and A. OKADA*

Department of Community Medicine, Faculty of Medicine, Toyama Medical and Pharmaceutical University, Toyama, Japan

(Received 15 September 1981; accepted for publication 4 February 1982)

Summary

Total serum IgE, and specific serum IgE against mites, *Ascaris* and Japanese cedar pollen were surveyed in 251 schoolchildren by a radioimmunoassay method. These children, aged from 10 to 13 years and living in a rural Japanese town, were selected according to one-third random population sample. A high concentration of total serum IgE (700 u/ml or more) was found in thirty-one children (12.3%). The sex ratio of these children, boys to girls, was 2.1:1. The cross-sectional and 6-year follow-up study of total IgE levels showed that they decreased with advancing age.

Total IgE levels were significantly related to each of three specific IgE species investigated in this study. The levels of these three specific IgE's were also significantly related to each other. Schoolchildren with high specific IgE levels against mites have had significantly more asthmatic histories compared to children with low specific IgE levels. Such a relationship was not observed for total IgE levels and another two specific IgE species.

Introduction

Atopy is associated with many diseases in children such as extrinsic asthma, allergic rhinitis, atopic dermatitis, food allergy etc. (Collins-Williams, 1973). It has already been shown that in atopic individuals total serum IgE tends to be present in higher concentrations than in control subjects without the atopic diseases mentioned above (Johansson & Bennich, 1967). The measurement of the antigen specificity of the IgE antibodies (specific IgE) has also been performed (Wide, Bennich & Johansson, 1967) and a good agreement between the results from provocation tests on patients and their

Correspondence: Dr S. Kagamimori, Department of Community Medicine, Faculty of Medicine, Toyama Medical and Pharmaceutical University, Toyama City, Toyama Prefecture 930-01, Japan.

* Present address: Department of Public Health, School of Medicine, Kanazawa University, Kanazawa City, Ishikawa Prefecture 920, Japan

specific IgE concentration against a certain allergen was found (Berg, Bennich & Johansson, 1971).

In measurements of specific IgE levels in Japan, it has been demonstrated that house dust allergen is as commonly related to asthma as in other countries (Kurimoto & Baba, 1978). It has been proven that the main component of house dust allergen was derived from mites (Miyamoto *et al.*, 1968).

Parasite infections also important with respect to the association between IgE and atopy. Some workers have already shown that parasite infection is associated with allergy, and have emphasized infection with *Ascaris* in stimulating IgE production (Johansson, Mellbin & Vahlquist, 1968). In addition it is postulated that an elevated IgE level from parasite infection may reduce the risk of extrinsic asthma (Goldfrey, 1975).

Pollen of *Chriptomeria japonica* D. Don. (Japanese cedar pollen) has also attracted attention as a cause of allergic rhinitis in Japan (Horiguti & Saito, 1965).

We have carried out a survey of total serum IgE in Japanese schoolchildren in a rural area, and investigated the immunologic responses to mites, *Ascaris* and Japanese cedar pollen among them using an epidemiological approach. We had analysed the relationship between total IgE and specific IgEs in a cross-section of the population, and followed the total IgE concentration of some children for 6 years.

Materials and methods

Mass medical examinations for respiratory diseases in schoolchildren have been carried out in Awara-machi (town) of Fukui Prefecture, a rural district of Japan since 1972. The detail of air pollution in this town and its surroundings have been given in a previous report (Kagamimori *et al.*, 1978). Most of this area is composed of flat paddy fields, and there are no major sources of air pollution, except for two large steam power plants located in the next town. The atmospheric pollutant concentrations for the last few years have been constant; the annual mean values are around 0.02 p.p.m. for sulphur dioxides (solution conductive method), around 0.07 p.p.m. for nitrogen oxides (Saltzman method), and around 0.03 mg/m³ for suspended particulates (low-volume air sampler method) respectively. The pollen of Japanese cedar is present from March until May as Japanese cedars are planted throughout the district. There are no large areas of ragweed whose pollen has recently been emphasized as an important allergen in rural Japan.

In this study, one-third of schoolchildren aged 10 to 13 years were selected at random for a survey of IgE in 1979. Sera was collected from 251 (132 boys and 119 girls) of 253 children selected in the month of July. The mass medical examination which consisted of a questionnaire following the British Medical Research Council, assessment of skin prick reactions to allergens of house dust, *Candida* and cedar pollen (Torii Drug Company, Japan) and respiratory function tests (PFR, FVC and FEV₁) as carried out in previous years together with the IgE survey.

The concentration of total IgE was measured with a radioimmunosorbent test kit, and specific IgE with a radioallergosorbent test kit (Pharmacia Diagnostics, Sweden). In measuring specific IgE against mites, an allergen of *Dermatophagoides pteronyssinus* was chosen because the same results were found in a comparison with an allergen of *D. farinae*, common mite in our preliminary study. For the specific IgE's against *Ascaris* and Japanese cedar pollen, crude extracts of *Ascaris suum* which has a common antigen with the human parasite, *A. lumbricoides*, (Imperato, Foresi & Martinetto, 1968) were

supplied by the Department of Parasitology, School of Medicine, Kanazawa University, Japan, and the allergen of Japanese cedar pollen was obtained from the Torii Drug Company. The allergen of *D. pteronyssinus* was already attached to paper discs (Pharmacia Diagnostics) but the allergens of *A. suum* and Japanese cedar pollen were bound to the paper discs activated with cyanogen bromide.

For the skin tests the criteria of the Japanese Allergy Association were followed. Positive skin reactions had either a weal of more than 5 mm in diameter or a flare of more than 15 mm in diameter about 20 min after the test.

A total IgE of 700 u/ml or more was classified as a high level (criterion accepted in Japanese schoolchildren—Funabashi, Nishimuta & Toba, 1973). Specific IgE's with scores +1 or higher were classified as positive.

For the estimation of the correlation coefficient between each kind of IgE concentration, logarithmic transformation of counts per minute (ct/min.) calculated by a gamma counting machine were used.

Results

The prevalence of high total IgE levels at different ages are shown in Fig. 1(a). They are 15.4% for children aged 10 years, 16.9% for children aged 11 years, 9.7% for children aged 12 years and 6.7% for children aged 13 years. These percentages seem to follow a decreasing trend after 11 years. The sex ratio of children with high total IgE, boys to girls, was 2.1:1. The average concentrations transformed to logarithms show a similar trend; 2.50, 2.51, 2.43 and 2.01 for each age respectively. The prevalences of positive specific IgE against mites are shown in Fig. 1(b). They are 7.7, 11.7, 6.5 and 6.7% for

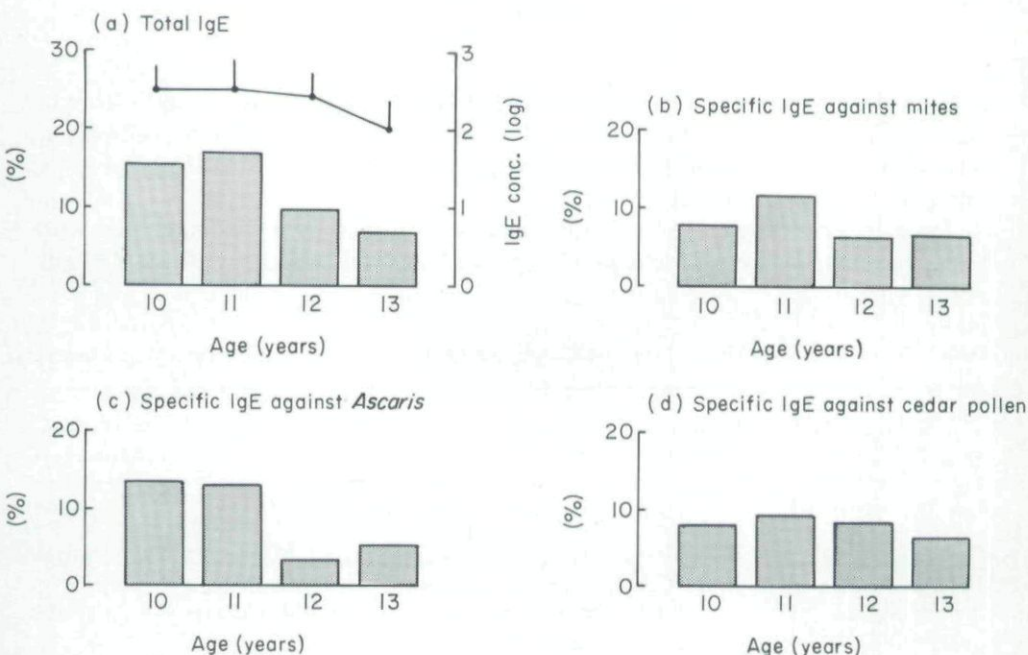


Fig. 1. The prevalences of high total IgE levels and positive specific IgE, and average concentration (log; mean $\pm$ s.d.) of total IgE in different age groups.

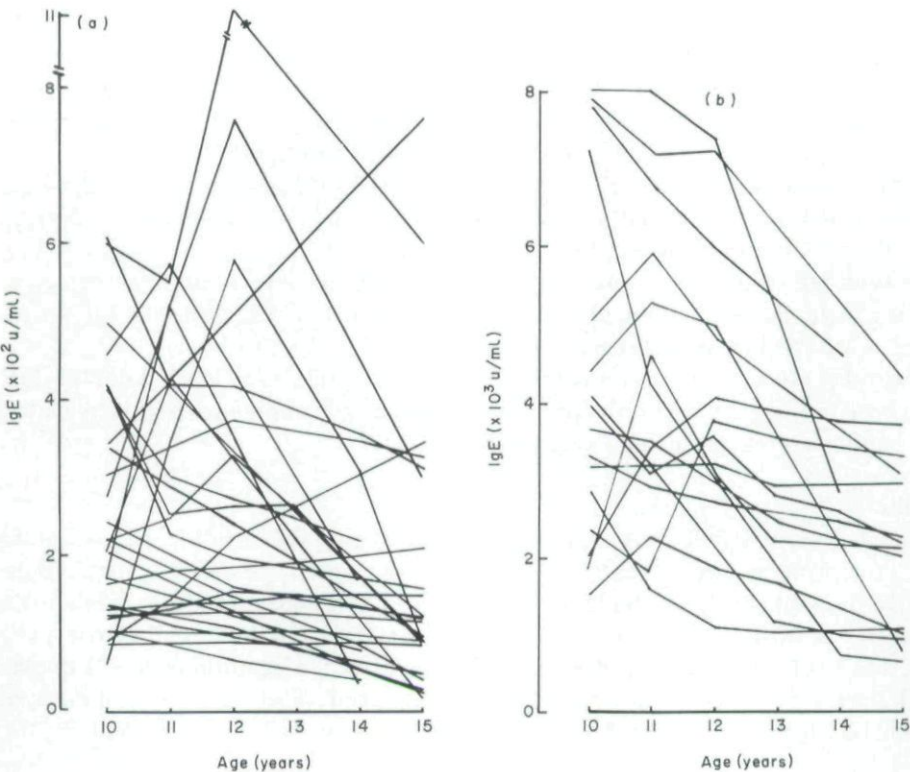


Fig. 2. Changes in total IgE concentrations in schoolchildren with (a) high levels (≥ 700 u/ml) and with (b) low levels (< 700 u/ml) followed from 10 years of age.

each age group. The prevalences of positive specific IgE against ascaris are shown in Fig. 1(c). They are 13.5, 13.0, 3.2 and 5.0% for each age group. The prevalences of positive specific IgE against Japanese cedar pollen shown in Fig. 1(d) are 7.7, 9.1, 8.1 and 6.7% for each age group.

Longitudinal changes in total IgE concentration in sixteen schoolchildren with high levels and twenty-nine schoolchildren with low levels who were 10 years of age

Table 1. The correlation coefficients between total IgE and specific IgE, and between each specific IgE species

	Correlation coefficient (<i>r</i>)		Correlation coefficient (<i>r</i>)
Total IgE-Specific IgE against mites	0.45*	Specific IgE against mites-Specific IgE against <i>Ascaris</i>	0.42*
Total IgE-Specific IgE against <i>Ascaris</i>	0.31*	Specific IgE against <i>Ascaris</i> -Specific IgE against cedar pollen	0.28*
Total IgE-Specific IgE against cedar pollen	0.33*	Specific IgE against cedar pollen-Specific IgE against mites	0.52*

* $P < 0.01$

Table 2. The relationship between specific IgE and total IgE

Total IgE	Specific IgE against mites		Specific IgE against <i>Ascaris</i>		Specific IgE against cedar pollen	
	Positive	Negative	Positive	Negative	Positive	Negative
High	12*	19	6†	25	11‡	20
Low	9	211*	16	204†	9	211‡

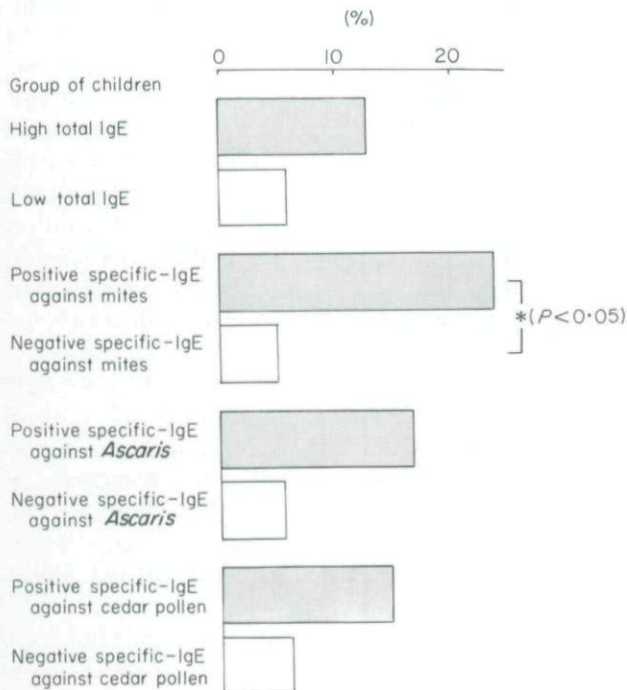
* The predictive value of positive specific IgE against mites for high total IgE = 57.1% (12/21) and of negative specific IgE against mites for low total IgE = 91.7% (211/230).

† The predictive value of positive specific IgE against *Ascaris* for high total IgE = 27.3% (6/22) and of negative specific IgE against *Ascaris* for low total IgE = 89.1% (204/229).

‡ The predictive value of positive specific IgE against cedar pollen for high total IgE = 55.0% (11/20) and of negative specific IgE against cedar pollen for low total IgE = 91.3% (211/231).

when IgE measurement started, are shown Fig. 2. In the former group their IgE levels declined in the following years, but such a trend was not so clear in the latter group.

Correlation coefficients between total IgE and specific IgE, and between each specific IgE are shown in Table 1. Total IgE level is significantly related to specific IgE's. The correlation coefficients are 0.45 ($P < 0.01$) for specific IgE against mites, 0.31 ($P < 0.01$) for specific IgE against *Ascaris*, and 0.33 ($P < 0.01$) for specific IgE against Japanese cedar pollen. The three specific IgE species discussed in this study are also

**Fig. 3.** Asthmatic history rate related to total IgE and specific IgE.

significantly and positively related to each other. These correlation coefficients are 0.42 ($P < 0.01$) between specific IgE against mites and *Ascaris*, 0.28 ($P < 0.01$) between specific IgE against ascaris and Japanese cedar pollen, and 0.52 ($P < 0.01$) between specific IgE against Japanese cedar pollen and mites.

Specific IgE level and total IgE level were divided into two categories, and their relationship are shown in Table 2. The predictive value (MacMahon & Pugh, 1970) of positive specific IgE against mites for high total IgE is 57.1% (twelve out of twenty-one), and that of the negative specific IgE for low total IgE is 91.7% (211/230). The predictive value of positive specific IgE against *Ascaris* for high total IgE is 27.3% (six out of twenty-two), and that of negative specific IgE for low total IgE is 89.1% (204/229). The predictive value of positive specific IgE against Japanese cedar pollen for high total IgE is 55.0% (eleven out of twenty), and that of negative specific IgE for low total IgE is 91.3% (211/231).

The relationship of asthmatic histories with total IgE level and the three specific IgE levels are shown in Fig. 3. A percentage of 23.8 of schoolchildren with positive specific IgE levels against mites have asthmatic histories and 5.2% with negative specific IgE levels. This difference is significant ($P < 0.05$). Except for the specific IgE against mites, the asthmatic history rate has no significant relationship with any of the IgE levels assayed in this study. Of three schoolchildren, two boys and one girl, who suffered from asthma for the last year two have both high total IgE levels and positive specific IgE levels against mites and *Ascaris*. One of the two children has also positive specific IgE level against Japanese cedar pollen.

Discussion

The cross-sectional survey to investigate the prevalence of high total IgE levels and average concentration in Japanese schoolchildren aged 10 to 13 years suggests that the levels decline with advancing age. This trend with age was confirmed in a 6-year follow-up study. The decline was mainly dependent on the changes in total IgE concentrations in schoolchildren with high levels and agrees with the report of Kjellman *et al.* (1976) in normal children. In addition, the prevalence of positive specific IgE's against mites, *Ascaris* and Japanese cedar pollen also decreased with advancing age. Our data support the theory of progressive natural desensitization (Hanneuse *et al.*, 1978). However it is possible that the prevalence of positive specific IgE against *Ascaris* decreased with advancing age, because there is also a decrease in the number of schoolchildren who are infected with *A. lumbricoides* with advancing age in the area of our study.

Although we found significant and positive correlation coefficients for total IgE levels with specific IgE levels against mites, *Ascaris* and Japanese cedar pollen, their seasonal variation should be taken into account in estimating the relationships. At the time when blood was collected, children were exposed to mites which increase in number in the bedding from June until October. This is not the case for Japanese cedar pollen whose season had finished 2 months previously. Therefore the correlation coefficient between total IgE levels and specific IgE levels against Japanese cedar pollen was probably underestimated.

The significant and positive correlation coefficients between each specific IgE level and the different properties of the allergens support the theory that IgE production is related to the genetic disposition of the host. As the predictive values of positive specific IgE levels for high total IgE levels were not significant, common allergens such

as mites, *Ascaris* and Japanese cedar pollen are probably not strongly related to total IgE production.

Only one of the specific IgE's discussed in this study against mites showed a significant relationship with the asthma histories of the children. Some reports which suggest immunosuppression caused by *Ascaris* infection (Crandall, Crandall & Jones, 1978) and the probability that increased total IgE levels due to parasitic infection reduces the risk of asthmatic incidents (Anon, 1976; Carswell *et al.*, 1977). We could not find any evidence to support such theories in this study. However the data suggest one possible mechanism that parasitic infection might exert an adjuvant-like effect on the reaginic response to other allergens (Orr, Riley & Doe, 1971; Jarrett & Bazin, 1974). Japanese cedar pollen has attracted attention as a cause of allergic rhinitis more than asthma, and allergenically active fractions were obtained from the pollen (Yasuda *et al.*, 1980). Results in this study do not show any significant relationship between specific IgE against Japanese cedar pollen and asthmatic history during childhood.

Acknowledgments

This study was partly supported by research funds from Ministry of Education, Japan.

References

- ANON (1976) IgE, Parasites and allergy. *Lancet*, **i**, 894.
- BERG, T., BENNICH, H. & JOHANSSON, S.G.O. (1971) *In vitro* diagnosis of atopic allergy; I. A comparison between provocation test and the radioallergosorbent test. *International Archives of Allergy and Applied Immunology*, **40**, 770.
- CARSWELL, F., MERRETT, J., MERRETT, T.G., MEAKINS, R.H. & HARLAND, P.S.E.G. (1977) IgE, parasites and asthma in Tanzanian children. *Clinical Allergy*, **11**, 445.
- COLLINS-WILLIAMS, C. (1973) *Paediatric allergy and clinical immunology as applied to atopic disease*, 4th ed. Churchill Livingstone, Edinburgh and London.
- CRANDALL, R.B., CRANDALL, C.A. & JONES, J. (1978) Analysis of immunosuppression during early acute infection of mice with *Ascaris suum*. *Clinical and Experimental Immunology*, **33**, 30.
- FUNABASHI, S., NISHIMUTA, J. & TOBA, A. (1973) Children with asthma and their serum immunoglobulin E. *Pediatrics*, **14**, 625 (in Japanese).
- GOLDFREY, R.C. (1975) Asthma and IgE levels in rural and urban communities of Gambia. *Clinical Allergy*, **5**, 201.
- HANNEUSE, Y., DELESPESE, G., HUDSON, D., DE HALLEUX, F. & JACUES, M. (1978) Influence of ageing on IgE-mediated reactions in allergic patients. *Clinical Allergy*, **8**, 165.
- HORIGUTI, S. & SAITO, Y. (1965) Clinical observations on Japanese cedar pollinosis. *Journal of Oto-rhino-laryngological Society of Japan*, **68**, 1225.
- IMPERATO, S., FORESI, C. & MARTINETTO, P. (1968) Comparative analysis of antigenic constitution of *Ascaris lumbricoides* var. *hominis* and var. *suum*. *Rivista dell Istituto Sieroterapica Italiano*, **43**, 235.
- JARRETT, E. & BAZIN, H. (1974) Elevation of total serum IgE in rats following helminth parasite infection. *Nature*, **251**, 613.
- JOHANSSON, S.G.O. & BENNICH, H. (1967) Studies on a new class of human immunoglobulins. I. Immunological properties. In: *Nobel Symposium 3, Gamma Globulins, Structure and Control of Biosynthesis*, p. 193, Almqvist & Wiksell, Stockholm.
- 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**, 118.
- KAGAMIMORI, S., OKADA, A., SATO, T., KATO, T. & KAWANO, S. (1978) A plant indicator of air pollution and human health in Japanese rural communities. *Environmental Research*, **17**, 33.
- KJELLMAN, N-I. M., JOHANSSON, S.G.O. & ROTH, A. (1976) Serum IgE levels in healthy children quantified by a sandwich technique (PRIST). *Clinical Allergy*, **6**, 51.
- KURIMOTO, Y. & BABA, S. (1978) Specific IgE estimations by RAST in Japanese asthmatics compared with skin, passive transfer and bronchial provocation tests. *Clinical Allergy*, **8**, 175.
- MACMAHON, B. & PUGH, T.F. (1970) Case-control study. In: *Epidemiology, Principles and Methods*, p. 262, Little, Brown and Company, Boston.

- MIYAMOTO, Y., OSHIMA, S., ISHIZAKI, T. & SATO, S. (1968) Allergic indentify between the common flour mite (*Dermatophagoides farinae*, Hughes, 1961) and house dust as a causative antigen in bronchial asthma. *Journal of Allergy*, **42**, 14.
- ORR, T.S.G., RILEY, P. & DOE, J.E. (1971) Potentiated reagin response to egg albumin in *Nippostronglyus brasiliensis* infected rats. II. Time course of the reagin response. *Immunology*, **20**, 185.
- WIDE, L., BENNICH, H. & JOHANSSON, S.G.O. (1967) Diagnosis of allergy by an *in vitro* test for allergen antibodies. *Lancet*, **ii**, 1105.
- YASUDA, H., YUI, Y., SHIMIZU, T., ENDOH, H. & SHIDA, T. (1980) Isolation studies of allergens from Sugi pollen. *Japanese Journal of Allergology*, **29**, 763 (in Japanese).

Copyright of Clinical Allergy: Journal of the British Allergy Society is the property of Blackwell Publishing Limited and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.