

Brief communications

Increased prevalence of elevated serum IgE and IgG₄ antibodies in students over a decade

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It is generally believed that asthma and other atopic diseases in children have been increasing in many industrialized countries over the last few decades.¹ Many researchers have reported the rise of the prevalence of such diseases as determined from responses to questionnaires. These results, however, might be influenced by increased recognition of the disease by the general population. We reported a corresponding increase in the prevalence of elevated specific IgE antibodies among students in a defined area in Japan since 1978.² It seems to be the only one-population-based serologic study supporting the rise of atopic prevalence, which has been demonstrated by responses to questionnaires.

The objective of this study was to obtain further serologic evidence for this increase in atopy among students by measuring serum IgG₄ and IgE antibody levels. IgG₄ was chosen because it is well established that the existence of this kind of antibody reflects a subject's history of immunologic response to the relevant allergen.³⁻⁵

METHODS

Subjects

The catchment area was a town with a population of 15,000 in northern Japan, located in Akita Prefecture. Serum samples had been collected from 312 schoolgirls

Abbreviation used

mAb: Monoclonal antibody

in June of 1981, 1985, and 1991 for another purpose and were stored at -20°C until use. Samples were collected from more than 98% of the targeted population of 13- or 14-year-old girls, who were in the second grade of junior high school in the town.

Measurement of IgE and IgG₄ antibodies

The levels of IgE antibodies were measured by a commercially available MAST chemiluminescence assay (MAST Immunosystems, Mountain View, Calif.) according to the manufacturer's instructions. Among 16 allergens determined, the values for *Dermatophagoides farinae*, Japanese cedar pollen, and egg white were used in this study.

The levels of IgG₄ antibodies against *D. farinae* (Torii Pharmaceutical Co., Ltd., Tokyo, Japan), Cry j 1 of Japanese cedar pollen (Hitachi Chemical Co., Ltd., Ibaraki, Japan), and ovalbumin of egg white (Sigma Chemical Co., St. Louis, Mo.) were measured by ELISA with anti-human IgG₄ monoclonal antibody (mAb) as previously described.⁴ The only exception was that the peroxidase-conjugated mAb was used instead of anti-IgG₄ mAb and the subsequent peroxidase-conjugated goat anti-mouse IgG. IgG₄ standard serum for each allergen was obtained from the Special Reference Laboratory (Tokyo), and the serum samples that showed values for optical density at 490 nm that were higher than this standard were regarded as positive.

All the IgE and IgG₄ assays were performed at the same time with newly thawed serum samples and the same batch of reagents.

RESULTS AND DISCUSSION

The prevalence rates of IgE and IgG₄ antibodies detected in the sera of 312 schoolgirls are summarized in Fig. 1. The rates of IgG₄ antibody-positive sera for all the investigated allergens (i.e., house

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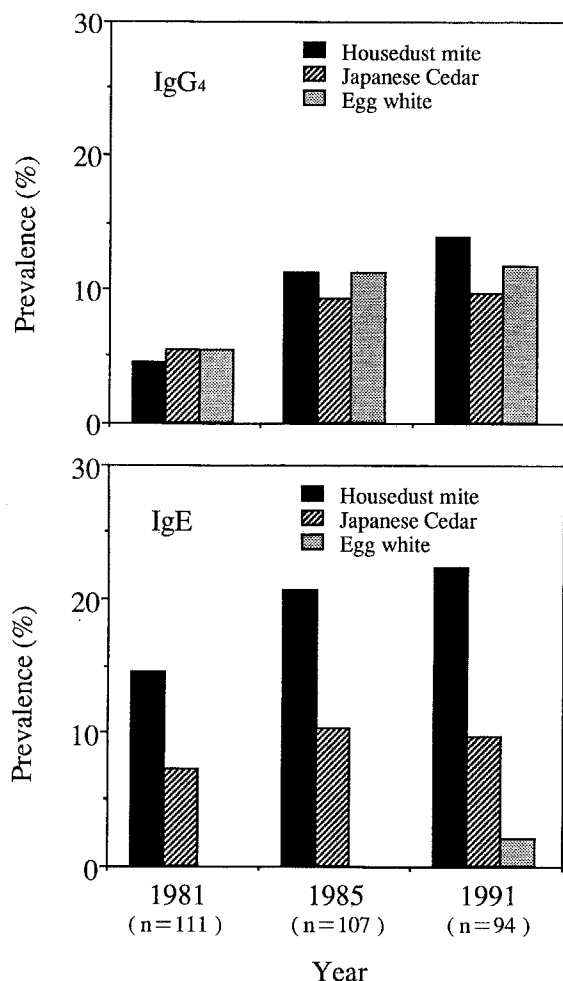


FIG. 1. The prevalence of antibody-positive sera among 312 schoolgirls in northern Japan. IgE and IgG₄ antibodies were measured by MAST chemiluminescence assay and ELISA, respectively. *n* denotes the number of schoolgirls evaluated in each year.

dust mite, Japanese cedar pollen, and egg white) were continuously increasing during the period from 1981 to 1991, and they rose dramatically between 1981 and 1985. The rates of IgE antibody-positive sera, a summary of which was previously published,² were also increased as were IgG₄ antibodies.

Whether increasing prevalence of IgG₄ or IgE antibody positivity was statistically significant was tested by using the Hoel-Yanagawa test, which extends Fisher's exact test for a 2 × 2 table.⁶ The increase in the prevalence of IgG₄ antibody positive for *D. farinae* was statistically significant (*p* =

0.02), whereas increasing trends for other allergens or for IgE antibodies were not statistically substantiated.

The number of positive samples for both IgG₄ and IgE antibodies was only two among 312 sera analyzed. They were house dust mite-positive in 1985. In addition, there was no statistical association between these two antibody levels against these three allergens.

Our data, as mentioned previously, clearly demonstrated that the prevalence of students with IgE and IgG₄ antibody positivity in a defined area in Japan is increasing over the decade, suggesting that the prevalence of allergic disease in children is increasing rapidly. The reason for this rapid increase remains unclear, but it is speculated that so-called "urbanization," including the increase in air and indoor pollution and changes in living conditions may be at least partly responsible.¹

Although the association of IgG₄ antibodies with allergic states has been noticed since 1983, their exact role as either anaphylactic or protective antibodies has not been established. However, it is generally accepted that IL-4 is essential for inducing both IgG₄ and IgE and that IgG₄ antibody levels increase after long-term allergen exposure, such as allergen-specific immunotherapy, indicating the certain biologic significance of IgG₄ antibodies in allergic disorders.^{4,5} In any event, our subjects demonstrated differences in production of IgE and IgG₄ antibodies, because there was no association between these two antibody levels, suggesting that we can evaluate the prevalence of each antibody separately as evidence of allergen exposure and provocation.

REFERENCES

1. Nakagawa T, Miyamoto T. Epidemiology of atopic disease in Japan. *ACI News* 1991;3:103-6.
2. Nakagomi T, Itaya H, Tominaga T, Yamaki M, Hisamatsu S, Nakagomi O. Is atopy increasing? *Lancet* 1994;343:121-2.
3. AAAI Board of Directors. Measurement of specific and nonspecific IgG₄ levels as diagnostic and prognostic tests for clinical allergy. *J Allergy Clin Immunol* 1995;95:652-4.
4. Nakagawa T, Kozeki H, Katagiri J, et al. Changes of house dust mite-specific IgE, IgG and IgG subclass antibodies during immunotherapy in patients with perennial rhinitis. *Int Arch Allergy Appl Immunol* 1987;82:95-9.
5. Aalberse RC, Van Milligen FJ, Van't Hob W, et al. Allergen-specific IgG₄ in atopic disease. *Allergy* 1993;48:559-69.
6. Yanagawa T, Hoel DG. Use of historical controls for animal experiments. *Environ Health Perspect* 1985;63:217-24.