Is It Necessary to Incorporate IgE Antibody Measurements to Look for Allergic Subjects in Multiphasic Health Checkup Systems?

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ABSTRACT

Number of subjects suffered from allergic diseases including bronchial asthma, allergic rhinitis and atopic dermatitis has increased dramatically in recent years, as to reach 30–40% of the whole population. It is quite important to identify newly-onset allergic patients and/or subjects with high-risks to develop diseases, which in turn early introduction of preventive measures and of optimal medications possible. From this point of view, an attempt will be made in this brief communication, to propose that IgE antibody measurements to search and determine causative allergen(s) should be incorporated in multiphasic health checkup systems.

Key Words Allergen; Allergic Disease; IgE Antibody

INTRODUCTION

Allergic (atopic) diseases, symptoms of which are initiated by the interactions between allergen(s) and IgE antibodies on mast cells and basophilic leukocytes, are quite common in Japan, and it is generally assumed that approximately one-thirds of the entire population is affected. It is also accepted that the prevalence of these disorders, including bronchial asthma, allergic rhinitis and atopic dermatitis, has increased considerably in recent years, a trend which has also been experienced in Western countries. This increase was confirmed not only by the responses to questionnaires, but also by the serological evaluations. In this brief communication, an attempt will be made to propose that IgE antibody measurements should be incorporated in multiphasic health checkup systems, based upon this recent increase, in order to search and determine causative allergen(s) which in turn can make early intervention possible.

CURRENT PREVALENCE OF ALLERGIC DISEASES IN JAPAN

As mentioned above, current prevalence of allergic diseases in Japan is estimated to be more than 30%.

Bronchial asthma

The majority of asthma surveys in Japan have been carried out since the late 1950s. In the past three to four decades, it was widely believed that the incidence of asthma in the adult population has shown 3-fold increase, and at the moment it is assumed that the nation-wide prevalence is around 4%. No difference is found in males and females; the rate is relatively high both in subjects aged 15–29, and also in elderly subjects.

A similar increase has also been observed in childhood asthma. It was believed that the incidence in children was around 1% in the 1960s, but recent epidemiological studies demonstrated that the percentage has gone up to between 4% and 8%, significantly higher than that of adults (Table 1). Moreover, this rate goes up to between 10% and 15% when wheezing bronchitis is incorporated to asthma as evaluated and reported by the “ISAAC program”. It should be noted that the majority of these patients are sensitive to house-dust mite, and the reason of the increase of incidence will be described later in “atopic dermatitis” section.

Atopic rhinitis involving pollinosis

The prevalence of perennial allergic rhinitis is generally assumed to be in the 20–25% range throughout Japan. House-dust mite and pollens from the Japanese cedar/cypress trees are the most important causative allergens; the former affects mainly younger people including school children, while the latter affects mostly adults. However, recent studies indicate the dramatic increase of pollinosis in younger generations.

At the moment, current prevalence of perennial allergic rhinitis is estimated to be around 15–20%, while that of Japanese cedar pollinosis (seasonal allergic rhinitis) is assumed to be 13.5–16.2%. It should be noted that area difference exists in terms of prevalence of Japanese cedar pollinosis; for example 26.9% in Yamanashi as the highest, 0.6% in Okinawa as the lowest and around 20% in Tokyo, Chiba and Kanagawa areas.

Japanese cedar pollinosis was first reported in 1964, and it was generally accepted to be quite rare until the late 1960s. However, the incidence has risen markedly since the 1970s. This explosive increase is partly attributed to the rise in the number of diesel-powered cars in Japan, because diesel exhaust particulates have been shown to enhance allergic reactions by promoting IgE antibody synthesis and eosinophilic inflammation.

Atopic dermatitis

The prevalence of atopic dermatitis in children is also increasing decade by decade, and this trend is particularly prominent in urban areas. For example, Ueda and his colleagues in Nagoya city investigated the incidence of atopic dermatitis, defined by the dermatologists; the incidence of atopic dermatitis was 2.8% in 1981, 3.62% in 1985, 4.2% in 1988, 6.6% in 1992 and 1999, respectively. It was confirmed by each survey that its incidence

Table 1 Trends in prevalence of bronchial asthma in Japan.

<table>
<thead>
<tr>
<th>Year</th>
<th>Childhood</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>1950s</td>
<td>—</td>
<td>1.0–1.2%</td>
</tr>
<tr>
<td>1960s</td>
<td>0.5–1.2%</td>
<td>1.2–4.0%</td>
</tr>
<tr>
<td>1970s</td>
<td>1.2–4.5%</td>
<td>0.9–5.0%</td>
</tr>
<tr>
<td>1980s</td>
<td>1.7–6.8%</td>
<td>0.5–3.1%</td>
</tr>
<tr>
<td>1990s</td>
<td>3.9–8.2%</td>
<td>1.6–4.4%</td>
</tr>
</tbody>
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was in the order of urban > suburban > rural areas; for example
6.63%, 3.37%, 2.54% in 1988, respectively. It should be noted here that its precise prevalence in older children and adolescents is still unclear, but the trend of increase is also observed.

The main causative allergen for atopic dermatitis is house-dust mites. It is widely accepted that the number of house-dust mites has increased year by year in house dusts collected from individual homes. This may be due to the increase of newly-built unwooden, tightly-closed houses and of usage of carpets and curtains, particularly common in urban areas.

FUTURE TRENDS IN PREVALENCE

It is generally accepted that prevalence of allergic diseases in Japan will increase further in the 21st century. This assumption was drawn by the evidences that positivity of IgE antibodies in sera of children has increased markedly, as reported earlier. According to the survey by the Tokyo Metropolitan Office which was performed in 2000, for example, 55% of school children aged 11–12 showed positive IgE antibody response to house-dust mite, while 42% positive to Japanese cedar pollens. It was also shown that positivity went up grade by grade, from the 4th to the 6th grade in the elementary schools (Department of Health, personal communication). It may be possible that prevalence of allergic diseases will exceed 50% of whole population some day in the near future.

METHODS TO DETERMINE CAUSATIVE ALLERGENS

To determine causative allergens, which induce asthmatic, rhinitic, and/or eczematous symptoms, is the key initiator of the diagnosis and treatment of allergic diseases, since allergen avoidance is the first step to prevent the occurrence of the diseases. In vivo and in vitro various methods, as shown in Table 2, are clinically employed for this purpose at present.

In vivo methods

Skin tests including prick, scratch and intradermal tests, as well as provocation tests via various routes are employed as the in vivo methods to determine causative allergen(s). The former has been applied for clinical practice for long time but needs well-trained medical stuffs to perform. The positive response in the latter provides conclusive answers, but it sometimes suffers from serious adverse events such as asthmatic attacks, especially after bronchial provocation test.

In vitro methods

Recently, instead of in vivo methods mentioned above, serum IgE antibody measurements and histamine release tests (HRT) have been widely used clinically. As the methods to evaluate IgE antibodies in the serum samples, CAP RAST, MAST (multiple antigen simultaneous test), AlaSTAT, LUMIWARD, QAS (Quidel allergy screen), and newly developed DiaPack with Oriton IgE are employed for this purpose. Usually CAP RAST, AlaSTAT, LUMIWARD and DiaPack are employed for single allergen determinations, while MAST and QAS for multiple allergen determinations for the purpose of screenings of the cause. Each method has advantages and disadvantages in terms of time needed, automated or not, sensitivity or specificity of the tests, etc., as the summary of them are shown in Table 3.

HRT Shionogi use whole venous blood as the sample to measure released histamine from peripheral basophilic leukocytes upon the interactions between IgE antibodies and relevant allergen(s) on their surfaces. The specificity of HRT is demonstrated to be superior to serum IgE antibody measurements, but this test needs longer time and has lower sensitivity, as compared to the latter. It should be noted here that approximately 10% of the subjects are non-responders to various stimuli in HRT and show false-negative even if this subject possesses allergen-specific IgE.

PRINCIPAL ALLERGENS IN JAPAN

Then what allergens are important in patients with allergic diseases in Japan? Figure 1 shows the results of IgE antibody determination in 100 allergic subjects, samples of them were obtained from departments of internal medicine, pediatrics, otorhinolaryngology and dermatology at five institutes located in metropolitan area. It is evident from the figure that house-dust, house-dust mite (Dermatophagoides farinae), Japanese cedar, timothy, cat and dog dander as the aeroallergens, and egg white, soy been, milk and cheese as the food allergens exhibit extremely or relatively high positive rates among these subjects. Similar tendencies of high positive rates among 406 allergic patients of house-dust, house-dust mite, Japanese cedar and cypress, etc as the aeroallergens were reported by the evaluation utilizing LUMIWARD.

PROPOSAL AND CONCLUDING REMARKS

From the data mentioned above, one can conclude that number of subjects suffered from allergic diseases including bronchial
Fig. 1 Frequency of positive response to 26 allergens evaluated by MAST-26 in sera of 100 allergic subjects (adapted from reference [9]).

Asthma, allergic rhinitis and atopic dermatitis has increased dramatically in recent years as to reach 30-40 % of the whole population. Based upon the socio-economical points of view and quality of life (QOL) of the affected persons, it is quite important to identify newly-onset allergic patients and/or subjects with high-risk to develop diseases in the near future, which in turn early introduction of preventive measures and of optimal medications possible. It seems reasonable, based upon the recent increase and necessity to find out relevant subjects, to propose that multiphasic health checkup institutes in Japan incorporate IgE antibody measurements in their procedures to accomplish this task. House-dust, house-dust mite, Japanese cedar/cypress, timothy, cat and dog dander or epithelium can be nominated as the allergens which should be searched in the system. As the methods to employ, CAP RAST, LUMIWARD or DiaPack with Oriton IgE may be recommended, since the process needed is short enough to carry out within one hour and the possibility of automation. Consideration and appropriate adaptation of this proposal in each health checkup institute will be appreciated in advance, for the promotion of health-related QOL, both in mental and physical condition.

ACKNOWLEDGEMENTS

The author would like to appreciate Ms. Naomi Sato for her excellent secretarial assistances.

REFERENCES