Influence of Aging and Sex on Specific IgE Antibody Production

Tsugio Nakazawa, Shinobu Houjyo*, Kunio Dobashi* and Kumiko Sato

The influence of aging and sex on specific IgE production was evaluated in a non-allergic population aged from 18 to 99 years. Specific IgE against mite antigen and Japanese cedar pollen (JCP) were measured by fluorescence enzyme immunoassay. The incidence and titer of positive anti-mite and anti-JCP IgE antibodies decreased with age, particularly in the aged group. There were slight sex-related changes in IgE production. No significant correlation was noted between anti-mite and anti-JCP IgE antibody levels in the same individual subjects. These findings suggest that the production of specific IgE, as an immunoglobulin class, declines with aging.

(Internal Medicine 33: 396–401, 1994)

Key words: mites, Japanese cedar pollen (JCP), fluorescence enzyme immunoassay (FEIA), relative fluorescence units (RFU)

Introduction

It has been suggested that aging is associated with a reduced ability to develop IgE-dependent allergic reactions. Stoy et al (1) confirmed a tendency for RAST (radioallergosorbent test) score and immediate skin reactions for some allergens to decrease with aging in allergic patients. Barbee et al (2) reported that immediate hypersensitivity is less frequent in the elderly. Hanneuse et al (3) also indicated that age and sex significantly influence IgE antibody production. A modest but significant age-associated reduction of serum IgE concentration has also been documented (2, 3).

However, most of these findings were obtained from allergic patients, and the antigens used were of one type. There are few detailed studies on specific IgE production in different age groups in a healthy non-allergic population. We have recently reported that aging decreases IgE antibody production in a healthy population (4). However, there is another report showing no relationship between these factors (1).

The present study was undertaken to investigate whether aging and sex influence IgE antibody production in a healthy population, especially in the young and the elderly.

Materials and Methods

Mite antigen (Dermatophagoides farinae) was provided by Torii Co., Ltd (Japan).

Japanese cedar pollen (JCP) antigen was prepared from Cryptomeria japonica according to a method previously described (4). Sera were obtained from non-allergic subjects who have lived in Maebashi-city in Gunma prefecture.

The elderly subjects more than 65 years of age were living in an old-age home in Maebashi. The other subjects were blood donors. Details of the study population are shown in Table 1. The young group (18–30 years old) consisted of 434 subjects and the aged group (65 years old or more) consisted of 285 subjects. Informed consent was obtained from all subjects.

Specific IgE antibody was measured by fluorescence enzyme immunoassay (FEIA) (5) and results were expressed in

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<tr>
<td>Young (18–30 year old)</td>
<td>172</td>
<td>262</td>
<td>434</td>
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<tr>
<td>Aged (&gt;65 year old)</td>
<td>130</td>
<td>155</td>
<td>285</td>
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Received for publication October 15, 1993; Accepted for publication April 25, 1994
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Relative fluorescence units (RFU).

The criteria for specific IgE positivity were set as follows. Specific IgE in all sera were measured by FEIA. RFU values were plotted on a histogram, using a personal computer program. The IgE-negative population was then determined from the curve of the histogram, and the mean value and standard deviation (SD) for the negative population were calculated. Positivity for specific IgE was then defined as any value above the cut off limit of the mean RFU value ± 3SD (Fig. 1). The antigen protein concentration was measured with a BIO-RAD kit. β-D-galactosidase-conjugated anti-human IgE antibody was obtained from Sigma Co. Ltd. All other chemicals used were of special grade and obtained from Wako Chemicals KK (Japan).

Results

**Frequency of subjects with specific IgE**

The percentage of the subjects positive for anti-JCP antibodies was about 30% in the 18 to 39-year-old age group and it gradually decreased with age. A marked decrease was found in subjects 60 years old or above. The percentage of subjects positive for anti-mite antibody gradually decreased with age, from 26.7% in the 18–19-year-old group to 15% in the 40-year-old group, and the percentage tended to increase slightly in the 50 to 60-year-old group, but was decreased markedly in the 70-year-old or above group. In the 18 to 19-year-old group, the rate of positivity for both antibodies was slightly higher in males than in females, while little difference due to sex was noted in other age groups (Fig. 2).

The aged group showed a significantly lower rate of positivity for both antibodies than the young group. The aged group showed the same rate for both antibodies, while the young group showed a slightly higher positivity rate for JCP than for mite (Fig. 2).

The percentage of subjects who had both antibodies was 12.4% in the young group and 2.5% in the aged group.

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**Fig. 1.** Distribution of specific IgE antibody.
Fig. 2. Percentage of subjects positive for specific IgE antibody in each age group (**p<0.01) (*p<0.05).

Fig. 3. Percentage of subjects with IgE antibody in young and aged groups (**p<0.01).
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Fig. 4. Anti-JCP RFU titer and aging.

Fig. 5. Comparison of specific IgE titer in young group and aged group.

Changes of IgE antibody levels

Antibody titers decreased with age when they were classified into 3 groups: 100–500, 500–1,000, more than 1,000 RFU. The 50-year-old or above groups did not produce a high titer (over 1,000 RFU) of anti-JCP IgE (Fig. 4). This tendency was more obvious when the young group and the aged group were compared although the difference was not significant (Fig. 5).

In the 18 to 40 age groups, 100–500 RFU level of IgE was slightly higher in females than in males. However, it was lower in females than that in males in over 50-year-old groups. The tendency was more frequently demonstrated in the levels of 500–1,000 RFU; no females over the age of 50 years had these high levels of antibody.

Considering the high levels of IgE antibody, marked differences due to sex were not found (Fig. 6). The results of anti-mite antibody production were similar to those as observed for anti-JCP IgE production.

Relationship between anti-mite IgE and anti-JCP IgE production in the same individual

The relationship between antibodies to both mites and JCP in the same individuals was analyzed in the young and aged groups. As shown in Fig. 7, no significant correlation was found between the levels of the two kinds of antibodies in either the young (r=0.13) or the aged group (r=0.34).

Discussion

Both total IgE and specific IgE have been reported to decrease with age in allergic patients (1–3, 6, 7). Most of the reports showed that total IgE in healthy populations also decreases with age, except two reports showing no such changes with age (2, 8–13). These findings suggest that specific IgE in healthy populations also decreases with age. Several reports supported this speculation (4–7). However, the specific IgE detected in these studies were against only one kind of allergen.

To clarify whether aging is related to a reduction of specific IgE production in a healthy population, in this study, we examined the influence of age, sex and type of antigen on specific IgE production in a healthy population using two different antigens: mite and JCP.

We found that the percentage of healthy individuals with the two kinds of specific IgE decreased with age in a similar manner.
although there were slight differences between the two antigens. The percentage of the subjects with anti-mite antibody decreased rapidly from 70 years of age, whereas that with anti-JCP IgE decreased from 60 years of age. The young group had a higher incidence of carriers with both anti-JCP and anti-mite IgE than the aged group. The number of subjects who had both antibodies was very low in the aged group. Similar results for one kind of antigen have been reported in both humans (6) and animals (14–16), but data for two or more kinds of antigens were not available. It is noteworthy that the aged group had a markedly reduced rate of IgE production to the different kinds of antigens.

IgE titer, in the present study, also decreased gradually with age and sex, and the highest titers were predominant in the young group. These findings were similar to those for the percentage of subjects who had IgE antibody and support our previous work suggesting that specific IgE production decreases with age as an immunoglobulin class (4).

A few studies have described the relationship between IgE production and sex (1–3). In the 18 to 19-year-old group, there appeared to be a higher rate of antibody positivity in males than females, while little difference between the sexes were noted in other age groups in our study. There was a slight difference between genders in IgE titer; women tended to have higher levels than men in the 18–49 age groups but the reverse was true in the 50 and above age groups. Hanneuse observed a similar phenomenon in total IgE (3). This phenomenon appears to be due to changes in estrogen or progesterone levels, since many clinical findings have suggested that allergic diseases often appear or are exacerbated during menstruation or pregnancy and disappear or subside after menopause (17, 18).

We have previously reported that there was no significant correlation between anti-mite and anti-JCP IgE levels in the same individual (4). Similar results were obtained when the present subjects were divided into young and aged groups. These findings suggest that there is no common antigenicity between the two antigens and that the production of specific IgE is affected, as a class, by age.

This study suggests that the percentage of positivity and titer of specific IgE are influenced by age and, in part, by sex, and that specific IgE production decreases with age, with the reduction being most marked in the aged group. These findings may result from an involution of the immune system; specifically, dysfunction of IgE class specific regulatory T cells, an alteration of T cells, and a change in B cell tolerance have been proposed as contributing factors for such a reduction with aging (14–16). It is of interest that IgE production is affected by age in healthy aged populations; this finding should be useful in analysis of IgE production in atopic subjects.
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Fig. 7. Anti-JCR and anti-mite antibody titers in the individuals who had both antibodies.

References