Relationship between total and specific IgE in patients with asthma from Siberia

To the Editor:

Erwin et al. compared levels of total IgE and specific IgE to dust mite and cat, prevailing allergens in New Zealand and Sweden, respectively, in children with wheezing and found a significant correlation of mite-specific IgE with high total IgE (≥200 IU/mL) in New Zealand, whereas cat-specific IgE did not contribute significantly the high total IgE in either country.

Previously we demonstrated that cat is a major allergen in patients with asthma from Siberia, other important allergens being dog, dust mites (Dermatophagoides pteronyssinus and Dermatophagoides farinae), and birch. Prevalence of wheezing (based on International Study of Asthma and Allergies in Childhood [ISAAC] questionnaires) and asthma (diagnosed according to Global Initiative for Asthma [GINA] guidelines) in children from Siberian cities is 11.4% and 3.1%, respectively, similar to Sweden. Because of the importance of findings of Erwin et al., we investigated the relationship of the prevailing specific IgEs and total IgE in patients with asthma from the cities Tomsk, Thumen, and Irkutsk (Siberia, Russia). We determined total IgE and specific IgEs to cat, dust mites, and birch in 127 patients with bronchial asthma (mean age, 11.5 years; range, 4-18 years, male/female ratio, 0.72/0.28) by using the IgE-EIA-BEST strip (VECTOR-BEST, Novosibirsk, Russia) and the EUROLINE system (EUROIMMUN; Medizinische Labordiagnostika GmbH, Lübeck, Germany), respectively. Relationship between total and specific IgEs was evaluated by nonparametric Spearman correlation (STATISTIKA for Windows 5.0; StatSoft, Inc, Tulsa, Okla.).

The geometric mean of the total IgE in patients with asthma from Siberia (193.0 kU/L) was lower than in New Zealand, but almost 3 times higher than in patients from northern Sweden. In Russian patients with asthma, we observed a higher correlation between levels of total IgE and specific IgE to cat, birch, and dog allergens than to mite allergens (Table I). However, the subgroup of 70 patients with total IgE ≥200 IU/mL showed a weak tendency to correlation only between birch-specific and total IgE. Thus, similar to data from Sweden, cat-specific IgE did not contribute significantly to high total IgE even though cat is a major allergen in Siberia. This might reflect the mechanism of sensitization to cat allergens or climatic similarities between Siberia and northern Sweden.

It would be interesting to compare levels of specific and total IgE in other regions where dust mites are dominant allergens in asthma such as Virginia to see whether correlation of mite-specific IgE to high total IgE is a common or a region-specific phenomenon. Because IgE reactivity to individual birch pollen allergens varies between 6 European populations, the response to individual dust mite allergens might also differ in different countries, causing a different contribution of mite-specific IgE to total IgE.

The data of Erwin et al. have an additional important implication not emphasized in the article. Genetic linkage or association studies of allergic diseases using total IgE levels might fail to reveal some of the critical genes, if levels of specific IgE to the major allergen do not correlate with total IgE. Information about the relationship between total IgE and specific IgE to the most prominent allergens can provide clues about operation of IgE-controlling genes in different human populations.

Table I. Correlation between total and specific IgE in patients with asthma from Siberia

<table>
<thead>
<tr>
<th>Allergen</th>
<th>All patients (n = 127)</th>
<th>Total IgE &gt;200 IU/mL (n = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P value</td>
</tr>
<tr>
<td>Cat</td>
<td>e1</td>
<td>0.36</td>
</tr>
<tr>
<td>Dog</td>
<td>e2</td>
<td>0.26</td>
</tr>
<tr>
<td>Birch</td>
<td>t3</td>
<td>0.28</td>
</tr>
<tr>
<td>D. pteronyssinus</td>
<td>d1</td>
<td>0.20</td>
</tr>
<tr>
<td>D. farinae</td>
<td>d2</td>
<td>0.19</td>
</tr>
</tbody>
</table>

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REFERENCES


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Reply

To the Editor:

We thank Gusareva et al. for sharing data relating specific IgE antibody measurements and total IgE among their patients with asthma in Siberia. It is interesting to compare their data with our own. The Russian cities where the children live, Tomsk, Thumen, and Irkutsk, are all south of the cities in northern Sweden (ie, below 60°N latitude). Although the climate of western Siberia would be similar to northern Sweden and not New Zealand, the prevalence of dust mite sensitivity was strikingly lower in northern Sweden. Gusareva et al. previously reported that among children with asthma living in the areas they studied, the prevalence of sensitization to cat allergen was highest (57%), followed by dog and dust mite (30% to 40%). In Sweden, among wheezing

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children (n = 69), the prevalence of sensitization to cat, dog, and dust mite was 46.4%, 47.8%, and 11.5%, respectively.3

Further analysis of specific IgE titers and their relationship to total IgE in the 2 areas with similar climates, Siberia and northern Sweden, reveals parallels. In Sweden, high titer of specific IgE antibody (>50 IU/mL) to any allergen was uncommon. In Siberia, high titers of specific IgE to cat and dog were also relatively uncommon. High titers of specific IgE to birch in Siberia appear to be as frequent as lower titers. It is possible that this observation is explained by the time of year that some serum samples were collected (March, April, and May, although not in the same year).4 In both regions, only a modest correlation was observed between specific IgE antibody titers to cat, dog, and relevant pollen (birch in Siberia and birch and grass in northern Sweden). The relationship between dust mite and total IgE was not significant in northern Sweden (Table I).

The current analyses of Gusareva et al1 reinforce our previous suggestion that the relationship between specific and total IgE is directly dependent on the relevant environmental allergen. Allergens that induce high levels of specific IgE antibody can be related to increased total IgE. This concept may seem simple, but it implies that a ranking of antibody responses to specific allergens is possible that predicts total IgE and prevalence of wheezing. We have previously suggested that titers of IgE antibody produced in response to dust mite are higher than titers of IgE to cat in New Zealand.5 In turn, higher titers of IgE to dust mite are related to higher total IgE and an increased prevalence of wheezing in New Zealand.5 Combining the results of Gusareva et al1 with our own, northern Sweden, Siberia, and New Zealand can be ranked according to prevalence of wheezing and increased total IgE on the basis of dust mite exposure.

We agree with Gusareva et al1 that it would be interesting to look at the relationship between specific IgE antibody and total IgE in other areas. Previously, the overlap in total IgE between allergic and nonallergic persons has complicated large epidemiologic studies. We would argue that examining a single area has been an underlying problem because allergen exposure would be the same throughout the region. By simultaneously studying areas with different allergen exposures, the allergen-specific effects can be observed.

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To the Editor:

We read with interest the article by Drs Litonjua and Weiss1 on a link between vitamin D deficiency and the incidence of asthma. Indeed, several studies suggest that vitamin D deficiency is an underappreciated public health problem. The prevalence of hypovitaminosis D is dependent on the parameters used to define the need for vitamin D, a steroid hormone that only loosely fits the definition of a vitamin. Low vitamin D, as defined by levels of serum 25-hydroxy vitamin D3 (25D3), is the result of insufficient dietary intake and/or inadequate UV exposure. Theoretically, increasing time spent indoors and the rising use of sunscreen or UV protective clothing have contributed to the growing problem of inadequate vitamin D. However, it is well established that UV is a major risk factor for skin cancer and photodamage. Thus, there is a pressing need to understand optimal vitamin D status to inform recommendations for adequate dietary supplementation but maintain efforts to prevent UV-induced disease.

Recently, several studies have demonstrated that vitamin D is an important regulator of adaptive and innate immune responses in addition to its role in calcium homeostasis and bone health. T cells, monocytes, dendritic cells, and other cells essential to innate immune defense, such as epithelial cells, express the vitamin D receptor.2 On activation of the vitamin D receptor in these cell types, the expression of an array of target genes is altered. This, in turn, can modify inflammation and immune defense.3,4 As the authors suggest, it may not be a coincidence that behaviors leading to lower serum vitamin D levels are associated with an increase in immune disorders characterized by a disturbed Th1/Th2 cytokine balance. Although there is no evidence that these suboptimal levels of vitamin D result in classic disorders associated with hypovitaminosis D such as rickets or osteomalacia, the recent mechanistic connections between vitamin D and the immune system make it tempting to link immunologic disorders prevalent in industrialized societies with lower vitamin D levels.

Although an intriguing suggestion, the link between vitamin D deficiency and the asthma epidemic is premature. In contrast with infectious pulmonary disease, where a clear association has been demonstrated,5 the data for asthma are less clear.6 As mentioned by Drs Litonjua and Weiss,7 comprehensive multidisciplinary studies are necessary to determine the role of vitamin D in asthma pathogenesis. Large trials of infant and maternal supplementation will be required. Appropriate dosing will be key to ensure a benefit and also avoid toxicity. Currently, it is a matter of debate what vitamin D status is sufficient for optimal health.