

Letter to the Editor

High-titer IgE antibody specific for pollen allergens in northern California is associated with both wheezing and total serum IgE

To the Editor:

In spite of the accepted relationships (1) between increased total IgE and asthma and (2) between having allergen specific IgE and asthma, considerable confusion remains regarding the relationship between specific IgE and total IgE.^{1,2} In 1975, Gleich and Jacob³ provided striking evidence that IgE antibodies to ragweed allergen could make a major contribution to total IgE. We have reported a similar relationship between specific IgE to mite allergens and total IgE in the serum of children with wheezing in New Zealand.⁴ By contrast, specific IgE antibodies to cat and dog allergens were lower in titer and appeared to make little or no contribution to total IgE in sera with high total IgE (ie, ≥ 200 IU/mL).⁴ Taken together, these data suggest that differences between mammalian allergens and other allergens could explain the variation in antibody responses.

Previously we reported that specific IgE to rye grass pollen was associated with acute asthma among patients presenting to an emergency department during pollen season.⁵ At that time, IgE was measured by using a semiquantitative RAST assay. New-generation assays, such as ImmunoCAP, quantify IgE as international units per milliliter and allow direct comparison between specific IgE antibody titers and total IgE. Our objective in the present study was to use the currently available technology to investigate the relationship between specific IgE and total IgE in the previously studied population of symptomatic wheezing patients living in an area with very high grass pollen counts (ie, northern California).

Originally, sera were obtained from 60 adult patients presenting with wheezing and 59 controls evaluated for a nonrespiratory complaint at Travis Air Force Hospital, Fairfield, Calif, within 2 weeks of the peak grass pollen counts.⁵ Sera from 60 patients with wheezing and 57 controls were available for further analysis. Total IgE and specific IgE antibody to dust mite, cat, ryegrass, and biotinylated ryegrass allergen Lol p 1 (using streptavidin CAP) were measured by using CAP FEIA (Phadia Inc, Uppsala, Sweden). IgG antibodies to Lol p 1 were measured by using radioimmunoprecipitation.⁶

The prevalence of sensitivity to ryegrass was higher among wheezing patients (56/60 [93.3%]) than controls (18/57 [31.6%]) (odds ratio, 30 [CI, 9.5-97]) (Table I). Among sensitized subjects, the geometric mean titer of specific IgE to ryegrass was greater than 20-fold higher than that to dust mite or cat (Fig 1). Furthermore, the levels of ryegrass specific IgE were elevated among

wheezing patients compared with controls ($P < .001$, Mann-Whitney U test). There was a strong correlation between specific IgE to grass and total serum IgE (Spearman rank $r_s = 0.86$; $P < .001$; Fig 2). Among the subjects with detectable IgE antibody to ryegrass pollen, the quantity of specific IgE antibody was estimated to be $\geq 15\%$ of the total serum IgE in 60 of 75 (80%) cases. Furthermore, specific IgE to Lol p 1 was correlated closely with IgE to ryegrass ($r_s = 0.87$; $P < .001$). Serum IgG antibodies to Lol p 1 correlated with both IgE to ryegrass and IgE to Lol p 1 ($r_s = 0.53$ [$P < .001$] and 0.63 [$P < .001$], respectively). In keeping with this, 64 of 73 sera with IgG antibody to Lol p 1 also had IgE antibody to grass. Of the 9 subjects who had IgG without IgE, 1 reported wheezing.

In an area of high grass pollen exposure, having IgE antibody to grass is related to acute asthma. The additional data and analysis presented here reveal 2 important characteristics of the immune response to grass pollen. First, specific IgE antibody titers to grass are strongly related to total IgE. Second, immune tolerance, as judged by IgG antibody without IgE antibody, is infrequent even with extremely high levels of pollen exposure. We have previously reported that titers of IgE antibody produced in response to dust mite can make a major contribution to total IgE.⁴ High exposure to pollen (ie, in northern California) is also associated with dramatically elevated titers of specific IgE that correlate with increased total IgE. In addition, our results show that for grass pollen, specific IgG antibody responses to Lol p 1 are part of the allergic response. The major allergens of grass pollen and dust mite are both proteins with a molecular weight of 30 kDa and share some biologic properties that may relate to the similar immune response observed. Group 1 allergens of grass, to which 95% of patients react, are papain-related cysteine proteases.⁷ Der p 1, also a major allergen, is a cysteine protease that has been shown to cleave epithelial tight junctions, CD23, and CD25.⁸

We believe the relationship between specific IgE antibody titers and total IgE provides a distinguishing feature that can be used to establish a hierarchy of inhalant allergens. Dust mite and grass share similar features with respect to the immune response they induce. By contrast, the highest exposure to cat and dog allergens is related to decreased prevalence of sensitization, modest or low titers of IgE antibody, and a significant number of subjects making IgG antibody without IgE antibody.^{6,9} These differences, between dust mite, cockroach, or pollen allergens as a group and mammalian-derived proteins, may reflect the biological properties of the proteins or relate to the fact that many of the proteins of dust mite and grass have little homology with those found in human beings because of relatively greater (>600 million years) evolutionary

TABLE I. Characteristics of IgE antibody responses to relevant allergens among wheezing subjects (W) and controls (C)

Allergen*	Prevalence		Titer (IU/mL)†		Relationship to wheezing‡	Multiple regression
	W	C	W	C		
Ryegrass	56	18	130	5.4	30 (9.5-97)	$P < .001$
Mite	23	7	3.0	1.9	4.4 (1.7-11)	$P = .3$
Cat	14	7	3.0	5.6	2.2 (0.80-5.9)	$P = .5$

*Allergen levels were measured in dust samples from 15 homes.⁵ All homes had >2 μ g Lol p 1/g dust. Comparable levels were seen for Fel d 1 in homes with a cat.

†Geometric mean titers of specific IgE antibody among sensitized subjects.

‡For univariate analysis, odds ratios and 95% CIs are given to describe the relationship between allergic sensitivities and wheezing. Multiple regression analysis was used to determine the combined effect of allergic sensitivities on wheezing prevalence. All statistics were performed by using SPSS (Chicago, Ill).

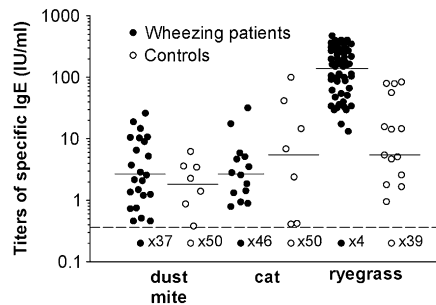


FIG 1. Titers of specific IgE antibodies to relevant inhalant allergens among wheezing patients (*solid circles*) and controls (*open circles*). Among sensitized subjects, the geometric mean titer of specific IgE to each allergen is depicted by a *solid line*.

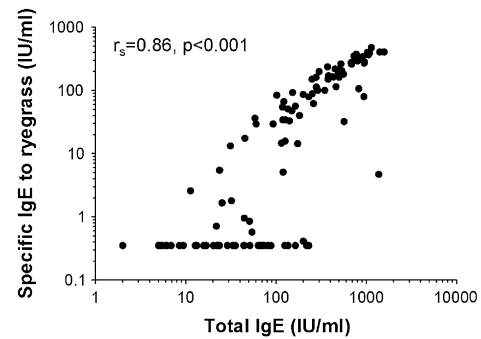


FIG 2. Specific IgE antibody to ryegrass in each individual compared with total IgE in the same patient. Spearman rank correlation is given.

distance.¹⁰ Knowledge of the differences in the immune response to individual inhalant allergens is integral to understanding the relationship between allergic sensitivity and the prevalence and mechanisms of allergic diseases.

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