

Maximal rise in IgE antibody following ragweed pollination season

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Patients allergic to ragweed pollen who did not receive immunotherapy had an increase in ragweed-specific IgE antibodies associated with seasonal exposure. Of 17 such patients, 15 reached peak levels between mid-September and mid-October. Two had peak values after mid-October; the levels were only slightly higher than earlier values. Our study shows that serum obtained in mid-October reflects approximately the maximal IgE antibody level attained by ragweed-sensitive patients in our area and that this value can be used as a baseline in monitoring the subsequent decline in antibodies. In addition, our data support an earlier observation that the magnitude of seasonal rise in IgE antibody is related to the preseasonal value. The significantly positive correlation of the results of carefully performed skin tests (end point titration) with radioallergosorbent test (RAST) values suggests the possibility that the RAST can be employed as a reliable diagnostic aid, perhaps even replacing the skin test.

We have used the radioallergosorbent test (RAST) to measure IgE antibody to ragweed antigens. In ragweed pollen-sensitive patients, we¹⁻³ have found (in agreement with others⁴⁻⁶) an antibody level increase associated with the seasonal exposure in untreated patients. In the present study, we have analyzed the relationship between the time of pollination and the time that peak IgE antibody levels are reached. Determination of the timing of the peak could reduce the number of bleedings required in future investigations. We also have compared initial RAST values with the seasonal rise in individual cases, and we have correlated RAST values with the results of skin test end point titrations.

MATERIALS AND METHODS

Patients

Seventeen patients (12 men and 5 women), whose ages ranged from 17 to 49 years (mean, 32 years), participated in the study. All 17 had clear-cut histories of annually recurrent symptoms of typical hay fever during the ragweed season for 10 to 30 years (mean, 19 years), and all had had unequivocally positive skin tests to ragweed extract. None was receiving immunotherapy, and treatment during the season consisted only of antihistamines, as needed.

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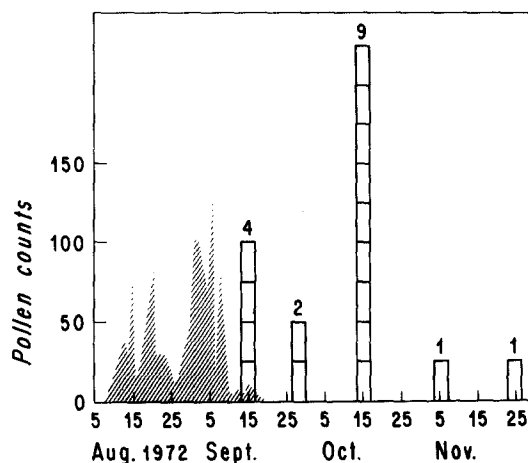


FIG. 1. Occurrence of peak antibody levels in 17 untreated patients (1972 ragweed pollen season). The numbers over the rectangles indicate the number of patients whose maximal IgE antibody was found on the given date.

Material

Bleedings were made preseasonally and at 2- to 3-week intervals from mid-September to December, 1972. Samples were stored at -20°C . and all were analyzed for IgE antibody levels in the same assay at the conclusion of the study.

Measurement of IgE antibody

IgE antibody levels were measured by the RAST, as described in detail elsewhere.^{1,7} Antigen is bound to solid-phase carrier and incubated with the serum, washed, and exposed to radiolabeled antibody to IgE. The radioactivity associated with the solid-phase antigen represents IgE antibody level and is expressed as a ratio of counts bound to counts added. The antigen in the study was prepared by coupling 26 mg. of partially purified short ragweed protein to 500 mg. of microcrystalline cellulose. The details of the production of the partially purified ragweed protein have been presented previously.⁸

Ragweed pollen counts

Pollen was collected in a sampler (Durham), and the counts were expressed as granules per square centimeter per 24 hours.

Skin tests

Each patient was tested with 5 commercially available extracts titrated to the end point, as detailed elsewhere.⁸ Briefly, this consisted in using serial fivefold dilutions and identifying the dilution that caused a 6 by 6 mm. wheal 15 minutes after the intradermal injection of an amount sufficient to produce a 3 by 3 mm. wheal and interpolating when necessary. The reciprocal of the dilution factor was regarded as the measure of potency, to which we assigned the term "skin test units." For example, an extract producing a positive test in a 1:2,500,000 dilution would be regarded as having 2,500,000 skin test units.

RESULTS

Nine of the 17 patients had peak antibody values in mid-October, 6 had peak values during September, and 2 had peak values in November (Fig. 1). The 2

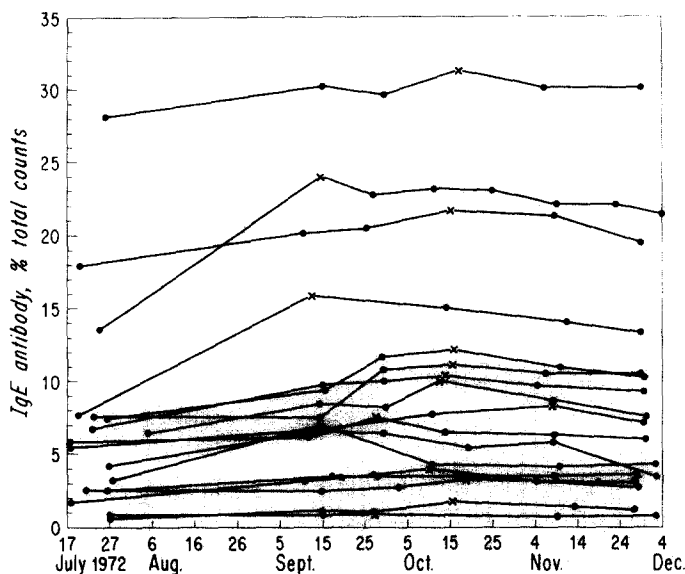


FIG. 2. Seasonal changes in IgE antibodies to ragweed in 17 untreated patients (x denotes the peak value for each). IgE antibody to ragweed is expressed as the radioactivity (associated with the affinity chromatography purified sheep anti-IgE) bound to the solid-phase ragweed divided by the total added radioactivity and multiplied by 100. Normal serum and fetal calf serum used as controls yielded 0.3 per cent counts bound. Low values for allergic serum were 0.7 and 0.8 per cent, respectively.

TABLE I. Comparison of preseasonal antibody values with skin test results (end point titration)

Extract*	r
A	0.58 (p < 0.05)
B	0.59 (p < 0.05)
C	0.71 (p < 0.01)
D	0.61 (p < 0.01)
E	0.79 (p < 0.001)

*Five different commercial extracts of short ragweed pollen.

patients whose values did not peak until after October 15 had earlier values within 10 per cent of their respective peaks (Fig. 2). The increase in the IgE antibody level was related positively to the preseasonal level (Fig. 3). There was also a significant correlation between skin test results with each of the extracts and preseasonal RAST values (Table I). The highest correlation coefficient for any one extract was + 0.79 (Fig. 4).

DISCUSSION

During the 1970 ragweed season, we measured IgE antibody to partially purified antigen E in 14 patients not receiving immunotherapy and in 10 non-allergic persons.¹ Bleedings were taken in July, at the end of August, in mid-October, and in January. The normal persons had lower initial values and dem-

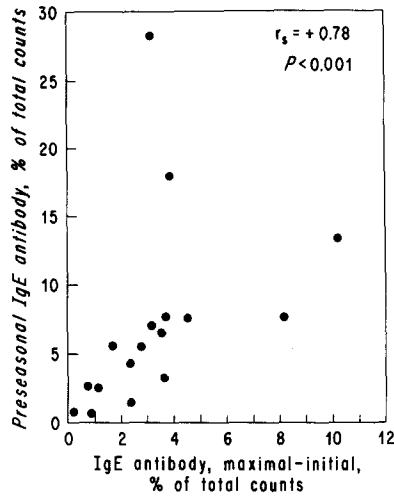


FIG. 3. Relationship between initial and final IgE antibody levels in 17 untreated patients (1972 ragweed pollen season).

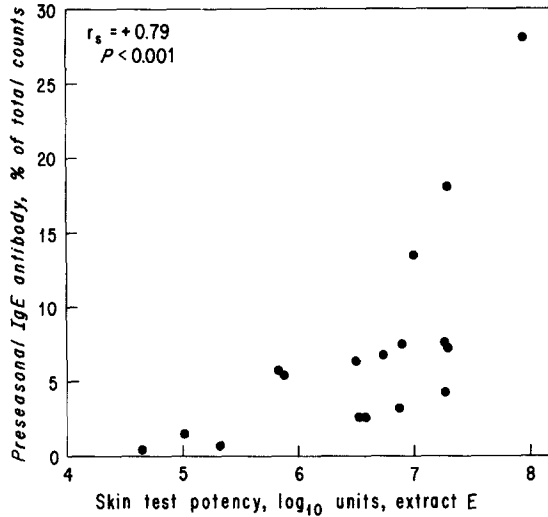


FIG. 4. Relationship between initial IgE antibody levels and skin test results with a commercial extract of short ragweed by end point titration in 17 patients.

onstrated no seasonal increase. The allergic patients demonstrated an increase in antibody that reached a peak in October and declined by January. Wondering if we had missed earlier peaking, we checked 7 patients in 1971 on July 15, August 20, September 2, September 17, and October 20.² We found that some antibody levels started increasing after August 20 but did not peak until mid-September and that other levels peaked at the time the last sample was taken in mid-October.

This brought up the possibility that some patients reached their peak levels

after mid-October and that this timing would be missed if sampling was discontinued in mid-October. The current study, however, suggests that the critical period is the 6 to 7 weeks from early September to mid-October, with no significant increase in antibody content occurring after that date.

This information is of importance in studies of immunotherapy and its effects on IgE antibody production. Because the levels increase and then decline, bleedings must be taken at or near the peak of the rise. Measurement of IgE antibody on these samples allows one to measure the maximal increases in IgE antibody as a result of pollen exposure as well as to begin measurements of the declines in IgE antibody that follow during the months from October to July of the next year. Earlier we found that immunotherapy did not suppress rises in IgE antibody to ragweed AgE when the changes in the untreated and treated groups were compared as a function of their initial levels.¹ In the same study, we noted that by January, 13 of 14 of the untreated group still had IgE antibody levels higher than the July values. In contrast for the high-dose treated group, only 12 of 26 had values higher in January than in July. These results in the two groups differed significantly ($p < 0.01$; χ^2 test, with Yates continuity correction). Although we could not show a significant difference in declines of IgE antibody between our groups, the results emphasize the need to analyze the effects of immunotherapy both on the rises in IgE antibody (July to October) and on the declines after October. The results of the present study indicate that serum should be obtained in mid-October in order to determine the maximal rise in IgE antibody level and that the level in mid-October then serves as a baseline in the measurement of the decline of IgE antibodies.

The relationship between initial IgE antibody levels and the amount of seasonal rise agreed with our observations on the 14 untreated patients in the 1970 study ($r = +0.64$, $p < 0.02$).¹

The relationship between carefully performed skin tests and RAST values that we demonstrated has been noted by others^{9, 10} and may herald a new approach to the management of the allergic patient. The histamine release test has provided an in vitro method of demonstrating the degree of allergic sensitivity, but the technique does not lend itself to mass clinical practice. The RAST, as Norman, Lichtenstein, and Ishizaka¹⁰ have pointed out, is convenient for both patient and physician and can be performed on stored serum. In addition, many tests can be run on one sample. Furthermore, the direct skin test, although giving immediate results, is time-consuming if carried to end point titration, necessitating several dilutions for each item tested. Although we have found that the RAST correlates with ragweed and grass pollen skin tests, whether this relationship prevails for other pollens, mold spores, and epidermals remains to be shown.

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Select the ONE best answer for the following question from the Allergy Foundation of America Self-Assessment Program:

Question 2. An overdose of aminophylline does NOT usually produce

- (A) bloody stools
- (B) vomiting
- (C) hypotension
- (D) somnolence
- (E) convulsions

The correct answer and bibliographic reference will be found on page 48 of this Journal.