

Evaluation of IgE tests in an allergy practice

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We measured serum IgE in 264 patients seen in the course of an allergy practice during the summer of 1970. IgE values were elevated in 21 per cent of patients who had idiopathic asthma and 10 per cent of patients who had idiopathic rhinitis. The elevated IgE was of no immediate clinical help in this idiopathic group because we were unable to detect hidden allergenic factors on further review of the history and skin tests. The finding of such an elevation, however, will prompt us to a continuing search for an allergic etiology or other condition associated with elevation of IgE. In patients who had hypersensitivity to stinging insects, IgE was elevated in 9 of 29 (31 per cent), and in patients with asthma and aspirin intolerance it was elevated in one of 5. Results in small numbers of patients with several other conditions including cold urticaria, chronic urticaria, and drug allergy are also presented.

The allergist encounters many conditions that might be mediated by IgE antibodies. A test that would reliably identify those patients with IgE-mediated symptoms might prove helpful in guiding the investigation and management. The findings by Johansson and associates that patients with allergic asthma¹ and rhinitis² had higher serum IgE levels than normal subjects and that only 5 per cent of normal subjects and nonallergic asthmatic patients had elevated levels suggested that measurement of serum IgE might be such a test. This report concerns the application of this test to 264 patients seen in our allergy practice during the summer of 1970.

MATERIALS AND METHODS

Radioimmunoassay

Serum IgE was measured by a double antibody radioimmunoassay as described previously.³ The standard used in this assay was purified IgE myeloma protein prepared from PS myeloma serum. An extinction coefficient at 280 nm. of $E_{1\%}^{1\text{cm.}} = 13.5$ was assumed. By this assay, 95 per cent of nonallergic normal subjects had IgE concentrations below 540 ng. per milliliter and 51 per cent of allergic patients had concentrations of 540 ng. per milliliter or more. The coefficient of variation for measurement of IgE was 14.6 per cent. After blood samples had clotted at room temperature, serum was separated by centrifugation and frozen at -20°C . Samples were analyzed within a few days after being received in the laboratory. Sera and standards were diluted 1:11 in buffer containing one per cent bovine serum albumin, and 0.1 ml. was used in the assay. Although this procedure resulted in

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less sensitivity at the lower concentrations of serum IgE, values in the borderline region between normal and abnormal fell into the midrange of the assay where precision is greatest. Serum samples whose concentrations of IgE in the diluted aliquot were greater than the highest point on the calibration curve were simply listed as more than this value ($> 1,489$ ng. per milliliter).

Skin tests

Except for an occasional item that produced a marked reaction on the scratch test, allergens were applied intradermally to the upper arms. Animal epidermals and mold extracts were used in a concentration of 500 protein nitrogen units (PNU) per milliliter. Pollen extracts were tested in a concentration of 100 PNU per milliliter. The amount injected was sufficient to raise a barely visible bleb. This has been found by prior investigation in our laboratory to amount to approximately 0.02 ml. Results were read in 15 minutes. A wheal averaging 4 mm. or greater in diameter was interpreted as a positive result.

Patients

Serum IgE was measured in 105 patients with asthma, 85 with rhinitis, and 74 with a variety of other conditions. Patients were categorized by the following clinical criteria, and the IgE level was correlated retrospectively with the various clinical entities:

Asthma or rhinitis

Allergic. History indicating specific allergic etiology corroborated by appropriate positive skin tests.

Idiopathic. History not suggestive of any specific allergic factor and skin tests negative, or only weakly reactive to antigens that were known not to precipitate symptoms on exposure. Synonymous terms would be intrinsic asthma and vasomotor rhinitis.

Other conditions

Stinging insect allergy. Extensive local reaction or systemic reaction such as angioedema, urticaria, asthma, or anaphylaxis.

Prior hay fever. Recurrent seasonal rhinitis that had subsided spontaneously in the remote past.

Chronic urticaria. Frequently recurrent or persistent multiple urticarial lesions for 3 months or longer.

Aspirin sensitivity. Manifested by an asthmatic attack after ingestion of aspirin.

Allergy to drugs other than aspirin. Included various reactions, mainly skin eruptions.

Cold urticaria. Typical acquired type with no evidence of other systemic disease as an underlying cause.

Food allergy. Reactions occurring quickly after ingestion, including urticaria, wheezing, and rhinorrhea.

Nasal polyps. Seen in most patients with rhinitis or asthma (also included in those groups).

RESULTS

Table 1 and Fig. 1 show the IgE concentrations for patients who have asthma and rhinitis. Of 30 patients with allergic asthma, serum IgE levels were elevated in 23 (76 per cent), and of 75 patients with idiopathic asthma, serum IgE levels were elevated in 16 (21 per cent). Among patients with rhinitis, of the 48 we considered allergic, 30 (62 per cent) had elevated IgE levels, while in the idiopathic group, 4 of 37 (10 per cent) had elevated IgE.

Of the 20 patients with idiopathic asthma or rhinitis and elevated IgE levels, 2 had strong family histories of atopy, 2 recalled having had hay fever

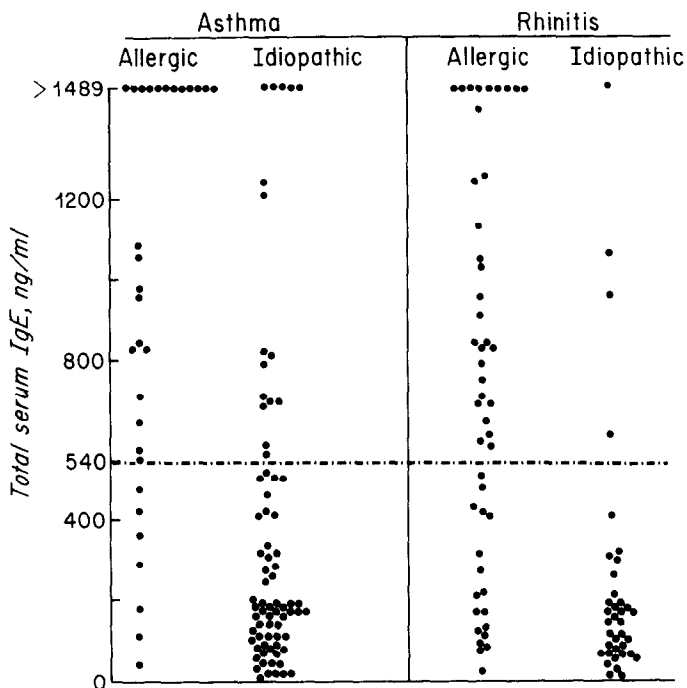


FIG. 1. Same data as in the Table I. Each dot represents an individual IgE determination.

TABLE I. Total serum IgE in patients with asthma and rhinitis

Condition	Total No. patients	IgE ≥ 540 ng./ml.	
		No. patients	%
Asthma			
Allergic*	30	23	76
Idiopathic†	75	16	21
Rhinitis			
Allergic*	48	30	62
Idiopathic†	37	4	10

*Positive allergic history and corroborative skin tests.

†Negative history for allergy and minimally reactive or nonreactive skin tests.

in the remote past, and 2 had had penicillin reactions. However, we failed to uncover any additional allergenic factors of importance by further review of their histories or by repeated skin testing in some instances.

Fig. 2 shows the IgE levels in several other conditions. The level was normal in 20 of 29 persons who had stinging insect sensitivity, most of whom were receiving hyposensitization treatment. Of the 9 with elevated levels, 6 had concomitant allergic rhinitis or eczema. None of the 4 patients with a prior history of seasonal rhinitis had increased serum IgE. Seven of 8 persons who had chronic urticaria had normal IgE levels. In the patient with increased IgE, symptoms had begun acutely 2 years earlier after an injection of tetanus toxoid. Four of 5 patients who had aspirin sensitivity had normal IgE levels. The elevated level occurred in a patient who had polymyalgia rheumatica.

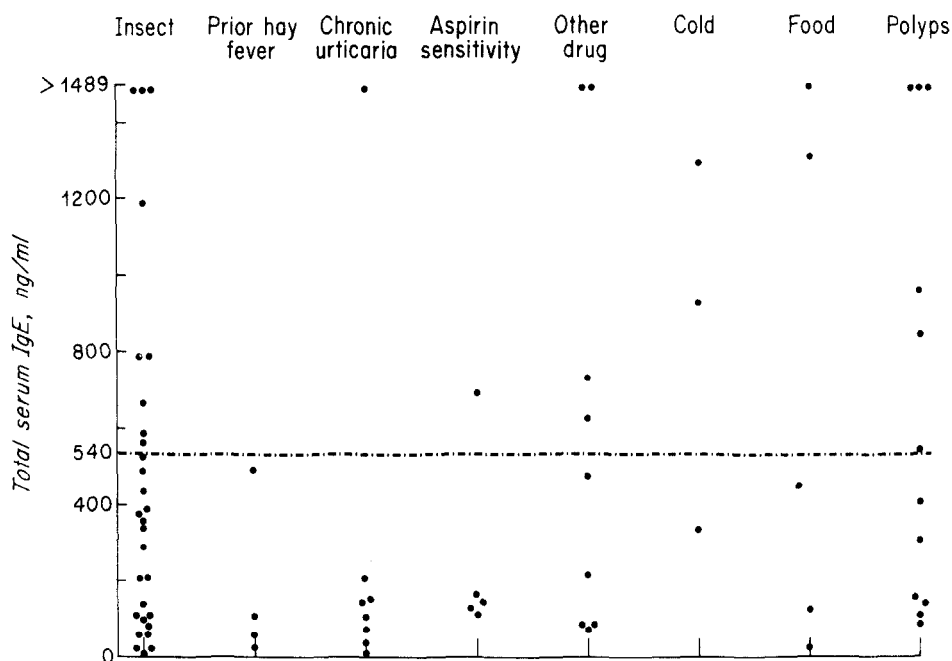


FIG. 2. Individual values of total serum IgE, nanograms per milliliter, in several conditions. See text for description of each.

On the other hand, 4 of 9 patients with a history of allergy to drugs other than aspirin had elevated IgE. Two of three patients with a history of acquired cold urticaria and a positive reaction to the ice cube test had increased IgE. Four patients with explosive reactions to foods were evenly divided between high and low levels, and 12 patients with nasal polyposis were also equally divided.

DISCUSSION

We were surprised by the elevated serum IgE in 21 per cent of patients who had idiopathic asthma. This figure differs significantly from that expected in a nonallergic sample ($p < 0.05$). We searched diligently for unrecognized allergenic factors in this idiopathic group, since such etiologic factors could be important in their management. However, we were disappointed; rechecking histories and skin tests failed to reveal any likely atopic factors or other conditions that might explain the elevations. These include parasitic infection,⁴ Laennec's cirrhosis, visceral larval migrans, celiac disease, pulmonary hemosiderosis,⁵ certain severe bacterial infections,^{6, 7} and IgE myeloma.⁸ As part of another study, many of our patients had had multiple stool examinations for parasites, all of which were negative.⁹ We wonder if continued surveillance of these patients will disclose allergic or other germane factors not yet evident.

In the allergic asthma and rhinitis groups, we found elevated IgE in 76 and 62 per cent, respectively, and these figures agree with previous reports,¹⁻³

although somewhat higher. The higher values may reflect the fact that serum samples were obtained during summer months; IgE serum levels increase following exposure to pollen.¹⁰ The number of patients who had idiopathic rhinitis and elevated IgE levels was as expected in a nonatopic sample.

The number of patients in most of the miscellaneous groups was too small to allow statistical evaluation. However, in the group with stinging insect reactions, IgE values were elevated in only 9 of 29 patients, and there were co-existing atopic conditions in 6 of these 9. The frequency of IgE elevations in this group differed from that in patients with allergic asthma and rhinitis ($\chi^2 = 11.7$; $p < 0.01$). Similarly, in the cases of aspirin intolerance, only one patient had an elevated IgE, a finding that agrees with the results reported by Vatanasuk and associates.¹¹ The implications of the normal levels of IgE in 7 of 8 patients with chronic urticaria seem apparent.

We conclude that knowledge of serum IgE level in patients seen in an allergy practice is of considerable interest but is not helpful in a directly practical manner.

REFERENCES

- 1 Johansson, S. G. O.: Raised levels of a new immunoglobulin class (IgND) in asthma, *Lancet* 2: 951, 1967.
- 2 Wide, L., Bennich, H., and Johansson, S. G. O.: Diagnosis of allergy by an in-vitro test for allergen antibodies, *Lancet* 2: 1105, 1967.
- 3 Gleich, G. J., Averbek, A. K., and Swedlund, H. A.: Measurement of IgE in normal and allergic serum by radioimmunoassay, *J. Lab. Clin. Med.* 77: 690, 1971.
- 4 Johansson, S. G. O., Mellbin, T., and Vahlquist, B.: Immunoglobulin levels in Ethiopian preschool children with special reference to high concentrations of immunoglobulin E (IgND), *Lancet* 1: 1118, 1968.
- 5 Heiner, D. C., and Rose, B.: Elevated levels of γ E (IgE) in conditions other than classical allergy, *J. ALLERGY* 45: 30, 1970.
- 6 Arbesman, C. E., and Ito, K.: A new method for measuring IgE, *J. ALLERGY* 47: 85, 1971. (Abst.)
- 7 Buckley, R. H., Wray, B. B., and Belmaker, E. Z.: Extreme hyperimmunoglobulinemia E and undue susceptibility to infection, *J. ALLERGY* 47: 108, 1971. (Abst.)
- 8 Johansson, S. G. O., Bennich, H., and Wide, L.: A new class of immunoglobulin in human serum, *Immunology* 14: 265, 1968.
- 9 Van Dellen, R. G., and Thompson, J. H., Jr.: Absence of intestinal parasites in asthma, *N. Engl. J. Med.* 285: 146, 1971.
- 10 Yunginger, J. W., and Gleich, G. J.: Seasonal changes in serum and nasal IgE concentrations *J. ALLERGY* 47: 87, 1971. (Abst.)
- 11 Vatanasuk, M., Hornbrook, M. M., and Kohler, P. F.: Serum IgE and passive transfer in aspirin intolerance, *J. ALLERGY* 47: 109, 1971. (Abst.)