

Allergen-specific IgE testing: Testing for food and inhalant allergies November 2022

Introduction

Adverse reactions to food and to inhaled substances can arise by a variety of mechanisms and these may be immune- or non-immune mediated. The usefulness of measuring IgE antibodies in Type I hypersensitivity reactions is now well established as a means to identify the allergens responsible for this immune-mediated reaction [1], which can be triggered by very small amounts of antigen.

Immune-mediated hypersensitivity reactions were classified by Coombes and Gell [2] into four types:

- Type 1 (immediate hypersensitivity) reactions are mediated by IgE antibodies; examples are hay fever and nut allergies.
- Type 2 (antibody-dependent, cytotoxic) reactions are mediated by IgG and IgM antibodies, as well as complement; for example Goodpasture's disease.
- Type 3 (immune complex) reactions are mediated by IgG and complement; for example SLE (systemic lupus erythematosus).
- Type 4 (delayed hypersensitivity) reactions are mediated by T cells; for example the contact dermatitis that characterises nickel hypersensitivity.

Over one third of the UK population has been diagnosed with asthma, eczema or hay fever [3]. The consensus is that this is largely Type I hypersensitivity. There has also been a continuous growth in anaphylactic allergic events presenting in Accident and Emergency Departments. In particular the prevalence of Type I peanut allergy is increasing [4].

Clinical manifestations of Type I (immediate hypersensitivity) diseases are caused by the release of pro-inflammatory mediators (such as histamine, leukotrienes and prostaglandins) from IgE-sensitized effector cells (mast cells and basophils) when cell-bound IgE antibodies interact with the allergen. Thus *in vitro* serum testing for IgE antibodies provides an indication of the immune response to the allergen(s) that may be associated with the disease.

While the definitive test for proving a suspected food allergy is a food challenge, this carries a significant risk to the patient and is, in most cases, impractical, so confirmation of a positive result of an allergen-specific IgE test can be made by skin prick testing (which is widely available). In most cases total IgE measurement is of relatively little value, since approximately one third of atopic adults have a total serum IgE of less than 120 kU/L, which is within the reference range for non-atopic individuals (as determined by most laboratories). However, for very high levels of total IgE, allergic disease is more likely [5]. There is also evidence to suggest that in infants a raised total serum IgE is predictive allergy in later life [6].

Antigen-specific IgE tests

Testing for IgE antibodies may be useful to establish the diagnosis of an allergic disease and to define the allergens responsible for eliciting the signs and symptoms observed. Testing also may be useful to identify the allergens responsible for an anaphylactic episode, or to confirm sensitization to particular allergens prior to beginning immunotherapy.

The presence of an IgE antibody in the serum indicates that the patient has been sensitized to a food or inhalant allergen, i.e. has generated an immune response resulting in the production of an antibody.

There are no international standards for specific IgE assays, which are instead calibrated using the WHO reference preparation for total serum IgE (75/702) [7].

There are two panels available:

1) An inhalant panel for detecting antibodies to grass pollens, tree pollens, weed pollens, dander and epithelia, mites & cockroaches and moulds & yeasts.

2) A food panel for detecting antibodies to cereals & seeds, egg & milk, fruits, legumes & nuts, meat, seafood, spices and vegetables.

A total IgE level is included in all reports.

Samples are currently referred to Bio-Diagnostics (UK) for analysis.

Interpretation of results

The level in serum of IgE antibody to each allergen is expressed in luminometry units (LU), which can be equated to a class score or kU/L, as shown below:

Class	KU_A/L	Interpretation:
0	0 – 0.34	Negative or uncertain
1	0.3 – 1.0	Low IgE level
2	1 – 5	Moderate IgE level
3	5 – 15	High IgE level
4	>15	Very high IgE level

Detection of IgE antibodies in serum at Class 1 level or greater indicates an increased likelihood of allergic disease as opposed to other aetiologies and also defines the allergens that may be responsible for eliciting the signs and symptoms.

Testing for IgE antibodies is not useful in patients previously treated with immunotherapy to determine if residual clinical sensitivity exists, or in patients in whom the medical management does not depend upon identification of a specific allergen [8].

Some individuals with clinically insignificant sensitivity to allergens may have measurable levels of IgE antibodies in serum (Classes 0/1), and results must be interpreted in the clinical context.

False-positive results for IgE antibodies can occur in patients with markedly elevated total serum IgE (>2500 kU/L) due to nonspecific binding to allergen solid phases. There are also “panallergens”, for example birch pollen, which have similar epitopes in proteins from different species and are thus a potential cause of false-positive reactions.

Patient preparation: no special preparation is necessary and the patient can continue taking supplements prior to venipuncture.

Specimen requirements: the following blood specimen is required - 1 clotted SST (serum separator, yellow top) tube or a finger-prick, capillary blood sample (special kit available on request).

Turn around time: 4 working days.

References

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4. Grundy J, Matthews S, Bateman B et al. Rising prevalence of allergy to peanut in children: data from 2 sequential cohorts. *J Allergy Clin Immunol* 2002;110:784-789.
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8. Homburger HA. Allergic diseases. In: *Clinical Diagnosis and Management by Laboratory Methods*. 21st edition. Editors: McPherson RA, Pincus MR. WB Saunders, Publishers, New York, 2007;Chapter 53, Part VI, pp. 961-971.