Identification of allergic trigger is essential for the appropriate treatment of allergic diseases. This clinical report focuses on the in vitro tests available to paediatricians that can be used for the identification of allergen-specific immunoglobulin E (sIgE).

Tests Available for Specific Immunoglobulin E Detection

Availability of new enzymatic assays based on anti-IgE antibodies has replaced the radioallergosorbent test. Quantification of laboratory results in terms of sIgE concentration is becoming more common. Although the Food and Drug Administration (FDA) has approved 3 commercial detection systems for detecting IgE population, the results may vary from system to system. Skin prick test (SPT) offers immediate results at low cost compared with serum sIgE tests. However, while performing SPT, a rash-free skin is required and the drugs with antihistamine properties need to be withheld.

Test Selection and Interpretation

The tests for the identification of trigger allergen need to be selected so as to confirm the specific allergen. A positive test indicates sensitised state but is not equivalent to the clinical diagnosis. Therefore, a detailed knowledge about the clinical history of the children, disease characteristics and local aerobiology, while selecting and interpreting the tests, will avoid irrelevant testing. The patients should not be considered as allergic solely on the basis of skin test or the serum
Issues Specific to Food Allergy

In case of food allergy, testing for sIgE to foods might be considered for confirmation of allergic trigger, to substantiate the diagnosis or to monitor the allergy resolution. However, knowledge about the medical history and results from oral food challenge may help in the better diagnosis of food allergy. If the previous medical history or results from oral food challenge are not convincing, the initiated elimination diets should not be maintained.

The key observations from the diagnostic and management processes for food allergy reviewed in various guidelines (NIAID-sponsored guidelines for the diagnosis and management of food allergy in the United States, and for applications in the paediatric population and American college of allergy, asthma and immunology), are summarised below:

- Sensitisation without clinical allergy is common in food allergy. Hence, screening without considering the medical history should be avoided.
- The diagnosis of food allergy cannot be completely excluded by a negative SPT or serum sIgE test results.
- Cross reactivity among proteins may lead to positive tests often without clinical allergy.
- Strong positive results are associated with more likelihood of clinical allergy; however, the results may vary with age, nature of disease and other factors.
- Serum sIgE concentrations or SPT wheal size do not accurately predict the severity but do reflect the possibility of an allergic reaction with variable intensity.
- Test for total IgE, immunoglobulin G (IgG) and intradermal testing is not recommended.
- Food protein-induced enterocolitis and proctocolitis do not give positive IgE tests.

Issues Specific to Other Allergy

Other allergic reactions may be caused by medications, insect venom, vaccines and latex. Tests for drug allergy are not standardised and serum IgE test is not relevant in this case. SPT and intradermal test can be used for penicillin allergy. In case of venom allergy, isolated, localised swelling at the sting site and general urticaria without other anaphylactic symptoms in children of 16 years or younger does not identify a risk for anaphylaxis. Hence, testing is not required. However, systemic anaphylaxis in any age and general urticaria in case of adolescents older than 16 years require testing. SPT and intradermal tests are standard diagnostic tools in this case and these can also be performed for vaccines suspected of producing allergic response. However, proper dilution should be taken care of to avoid irritant reactions.
Evolution in Immunological Methods Used in Research and in the Clinical Diagnosis and Management of Human Allergic Diseases*

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The term hypersensitivity refers to an exaggerated or inappropriate adaptive immune response. The special issue of the Journal of Immunological Methods reviews a series of reports on humoral and cellular immunological methods that provide tools to study the mechanisms of allergic reactions and various methods for the diagnosis and management of patients with IgE-mediated hypersensitivity reactions.

Cellular Modulation of Allergic Responses

The relation between cellular (T cell, B cell and dendrite cell) and humoral (IgE and IgG antibody and cytokines) immune response in allergic patients has been well characterised (Lund et al and Frischmeyer-Guerrerio and Schroeder [in press]). IgE antibody-facilitated allergen presentation and T-cell activation play a role in the maintenance of sensitisation level and effector cell mediator release. The concentration and specificity of IgE antibody and allergen along with their interaction with the IgE receptors influence both mast cell and basophil activations as well as antigen uptake. These receptors include high-affinity receptors on mast cells and basophils and low-affinity receptors on B cells. Dendritic cell responses also play a role in sensitisation state and altering allergic disease manifestations through cytokine-mediated immunomodulation.

Immunological Methods in Food Allergy and Eosinophil-Related Diseases

Allergic response is generated when immunologically naive individuals are repetitively exposed to the allergen. This happens due to the increased concentration and affinity of allergen-specific IgE antibodies towards the IgE receptors on effector cell surfaces in tissue (mast cells) and in circulation (basophils). The point where allergen exposure causes sufficient IgE antibody aggregation, vasoactive mediators may be released which can lead to the expression of allergic responses.

Positive clinical history of allergic symptoms is usually substantiated by examining the allergen-specific IgE antibodies in the skin or blood of the patient. In case of a conflict, the clinician may use the provocation process to clarify the diagnosis. Oral food challenge, a gold standard for diagnosis of IgE-mediated food allergy can also be used for the diagnosis of non-IgE-mediated food allergy (enterocolitis), and mixed IgE and non-IgE-mediated food allergy (atopic dermatitis and eosinophilic gastroenteropathies). It is also used for monitoring the patient for the development of tolerance or loss of sensitivity towards the food.

Reference:
An immunological assay for detecting soluble Siglec-8 in blood has been reported by Na et al (in press). Soluble Siglec-8 can act as a serological marker of eosinophilic involvement and is suggested to help in discrimination between patients with different eosinophilic-associated diseases.

Management of Allergy

Avoidance of Allergen Exposure

Avoidance involves separation of allergic patient from the trigger allergen. For this, it is essential to know the present level of allergens in the given environment. Indoor aeroallergens released from dust mites, cats, dogs, rodents, cockroaches and fungi are assessed by using monoclonal antibody-based assays, whereas immunologic, spectrophotometric and nucleic acid-based assays are used for outdoor airborne allergens like pollens.

Pharmacotherapy and Immunotherapy

In case the allergen avoidance is not helpful in managing the allergic symptoms, antihistamines and steroids can be used for immediate relief. However, these do not address the underlying cause of the disease. Immunotherapy is the other option for allergic disease management in which the offending allergen is injected for producing desensitised state.

Anti-Immunoglobulin E Therapy

In 2003, the Food and Drug Administration approved humanised monoclonal anti-IgE therapy, which binds to the IgE antibodies and prevents their interaction with the high-affinity IgE receptors. This therapeutic strategy was aimed at reducing the amount of free IgE in the body and thus preventing the allergic response. The article by Hamilton (in press) examined the Law of Mass Action considerations for designing immunological methods for quantitative estimation of free IgE in serum after anti-IgE therapy. This served as the rationale for a surface plasmon resonance assay as an alternative to ELISAs. Basophil mediator release methods are also useful for monitoring changes of basophil allergen reactivity after anti-IgE therapy.

Conclusion

In conclusion, this article emphasises the progression in immunological methods for better investigation, diagnosis and treatment of patients with allergic diseases. The author concluded that automation, improved immunological methods specific for antibody detection as well as identification of mechanistic pathways involved in induction and blocking of mediators release from mast cells and basophils, will improve the effective management of allergic patients.

Reference:


Further Reading

Further details about cellular and humoral immune response in allergic patients, detection of soluble Siglec-8 in blood and the Law of Mass Action considerations can be found in the following articles.


