The Laboratory Services Reform Programme

ADVICE NOTE

Indications for the Measurement of Allergen Specific IgE in General Practice and Non Specialist Settings

Version 1 Issued 23/07/2024

CDI/0102/1.0/2024

Clinical Practice Guidance Document Cover Sheet

Document Type	Advice Note
Document Title	Indications for the Measurement of Allergen Specific IgE in General Practice and Non Specialist Settings
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Approved by:	Professor Martin Cormican
Unique Identifier Number(UID):	CDI/0102/1.0/2024
Version Number:	1
Publication Date:	23/07/2024
Recommended Revision Date: *	23/07/2026
Electronic Location:	https://www.hse.ie/eng/about/who/cspd/lsr/resources/advice.html

Version	Revision Date	List Section Numbers Changed	Author

The Laboratory Services Reform Programme offers the following advice:

1.1 Advice for Laboratory Users

1. Specific IgE tests are laboratory tests for allergic sensitisation. Allergic sensitisation is the presence of IgE antibodies to allergens that are ingested, absorbed or inhaled.
2. Accepted indications for the measurement of specific IgE are outlined in Section 1.2. Please state these specific indications using relevant terms, or other similar terms based on local laboratory advice, on every request for assessment of specific IgE
3. Specific IgE tests are often referred to as 'allergy tests'. This is a misnomer as sensitisation and allergy are not the same thing. Individuals can be sensitised (have detectable allergen specific IgE) but not allergic (tolerate exposure without symptoms).
4. Specific IgE testing does not replace an allergy clinical history
5. Specific IgE tests should not be ordered without consideration of an allergy clinical history
    a. In the case of food allergy a careful history should examine for a clear temporal (usually within minutes, but almost always within 2 hours of exposure) relationship between symptoms consistent with IgE mediated allergy (urticaria, angioedema, anaphylaxis with or without acute gastrointestinal disturbance) and exposure to a particular food.
    b. Symptoms will not occur if the food is avoided
6. Specific IgE tests should never be ordered as 'screening' tests
7. Specific IgE tests to food mix panels should not be used. Tests should be directed to specific allergens that are related to compatible symptoms based on the clinical history
8. Specific IgE tests are not useful in the investigation of food intolerance symptoms, irritable bowel syndrome, coeliac disease or other non-IgE mediated disorders and should not be used to guide dietary manipulation in such settings
9. Specific IgE tests are not useful in the investigation of contact dermatitis
10. Specific IgE tests to foods are not useful in the management of asthma or rhinitis
11. Specific IgE tests are not helpful in the assessment of patients with a clinical history consistent with chronic spontaneous urticaria.
12. IgE mediated food allergy is frequently associated with other atopic diseases including eczema. However, Specific IgE tests are not useful in directly guiding the management of eczema.
13. Specific IgE test results are not affected by antihistamine therapy.
14. In the presence of very high levels of total IgE, (such as in eczema) low level positive specific IgE results are common. These are often clinically irrelevant and not associated with any history of IgE mediated allergy. Caution should be used when interpreting such results and expert advice should be sought if required. Measurement of total IgE in this setting may help clarify results.
15. Weak positive specific IgE results are less likely to be clinically relevant than strong positive specific IgE results.

16. The strength of positivity of a specific IgE result does not predict the severity of an associated allergic reaction.
17. Specific IgE test results should not be used to guide dietary manipulation for people where there are no IgE mediated symptoms in relation to a tested food. Applying inappropriate food avoidance in individuals who are sensitised but tolerant can cause harm.
18. Specific IgE directed against medications, such as antibiotics including penicillin, have low positive and negative predictive values and should not be used outside specialist settings
19. Analysis of specific IgE responses to single-plex or multiplex recombinant allergens should be restricted to users with experience in the use and interpretation of these tests. These tests are unsuitable for use in general settings.
20. RAST (RadioallergoSorbent Test) refers to outdated technology. This terminology should not be used.
21. Where there is uncertainty about selection of specific IgE tests or interpretation of results users should consider discussion with the laboratory team or with local allergy or clinical immunology services.
22. Unnecessary testing results in substantial costs, avoidable risks of needle exposure and generates unnecessary clinical and laboratory waste. Misinterpretation of specific IgE results can result in inappropriate dietary restrictions that are a source of harm and may initiate an inappropriate referral cascade that causes undue anxiety for patients.

1.2 Advice for Laboratories and Users

1. The accepted indications for the measurement of specific IgE against an allergen are:
    a. In the assessment of patients with symptoms compatible with allergic rhinitis, allergic conjunctivitis or asthma, specific IgE against aeroallergens may be indicated.
    b. In the assessment of patients with symptoms compatible with an IgE mediated reaction to an allergen ie urticaria, flushing, angioedema, asthma, anaphylaxis where selection of the allergen is guided by a plausible exposure history to a specific allergen.
    c. In the assessment of paediatric patients at high risk of developing food allergy to guide modifying interventions in specialist settings
2. Repeat food allergen sensitisation testing may be indicated in children on an annual or biannual basis to support clinical monitoring for resolution of food allergy. Otherwise, previously negative food specific IgE should not be repeated unless new symptoms develop that are temporally related to the food in question.
3. Repeat testing for sensitisation to aeroallergens is not helpful and is only required if new symptoms develop.

1.3 Advice for Laboratories

1. Laboratories should communicate to laboratory users the indications for testing of specific IgE sensitisation that are accepted by the laboratory
2. Measurement of specific IgE levels against an allergen should be performed when relevant and legible clinical details and requestor information are provided on the request (electronic or paper) accompanying the sample and where the sample received is suitable for analysis
3. To the greatest extent that is practical, requests for specific IgE that do not meet these requirements, where the clinical information is incompatible with an IgE mediated reaction or where information is inadequate, should be rejected
4. If samples are rejected a report should issue to the effect that testing for specific IgE was not performed because testing criteria were not met. Individual laboratories may wish to retain samples for a defined period of time, as per local practice, to allow users to update a request with appropriate information.

2 Background

Reactions mediated by allergen specific IgE is one of several pathological mechanisms that can result in clinical allergy. IgE mediated allergy is also known as Type 1 hypersensitivity. In this type of reaction histamine and other mediators are released when specific IgE, bound to receptors on the surface of mast cells and basophils, encounters the allergen to which it is directed. The clinical manifestations of IgE mediated allergy may be localised, for example allergic rhino conjunctivitis with aeroallergens such as grass pollen or house dust mite, or systemic such as anaphylaxis to a food or to insect venom allergen.

Tests for sensitisation can be used to support the clinical assessment of allergic disease. IgE sensitisation refers to the presence of IgE antibodies directed against a specific allergen. Such antibodies are found at low levels in the circulation and are also found bound to IgE receptors on effector cells such as mast cells or basophils. Skin prick testing to an allergen can be used to identify sensitisation in vivo. However, skin prick testing is semiquantitative, requires training to perform and is not widely available. Measurement of specific IgE in serum is the mainstay of assessment for sensitisation in many settings. It is vital that users ordering these tests have a basic understanding their utility and are aware of the primacy of the allergy clinical history in guiding test selection in patients with suggestive symptoms.

The identification of sensitisation is not the same as confirming clinical allergy. Allergy is a clinical outcome that may relate to sensitisation. Allergy cannot be diagnosed by assessment of specific IgE or skin testing alone. The allergy clinical history links symptoms consistent with features of IgE mediated allergy (allergic rhinitis, conjunctivitis, urticaria, angioedema, allergic asthma, anaphylaxis with or without acute gastrointestinal disturbance) to a plausible exposure. Exposures to IgE mediated aeroallergens may be persistent such as house dust mite or intermittent such as grass and tree pollens. Avoidance is often difficult. Exposures to allergens such as insect venom or drugs may be related to clearly defined instances. IgE mediated food allergy typically causes symptoms within minutes of an exposure. With uncommon exceptions, symptoms occur every time the food is eaten and are not present when the food is avoided. In most settings a suspect food can be dismissed as the cause of IgE mediated allergy where onset of symptoms is more than 2 hours after exposure.

An allergy history should carefully examine the allergen exposures that will guide test selection. Screening approaches where a battery of specific IgE tests are ordered without recourse to the clinical history is ill advised, expensive and will not inform patient management. Testing in scenarios where the pre-test probability is low, such as in settings where IgE mediated allergy is not the primary driver of symptoms is not recommended. This includes non-IgE mediated conditions like irritable bowel syndrome, food intolerance, coeliac disease, eosinophilic oesophagitis, chronic urticaria and atopic eczema. Specific IgE testing does not inform the management of these disorders.

Specific IgE results may be reported as an absolute value or as an absolute value with a grade. Weak positive results are less likely to be clinically relevant and must be considered in the context of the allergy clinical history. Strong positive results are more likely to be clinically relevant. However, it is important to recognise that the strength of positivity of the specific IgE result does not predict the severity of reaction – rather how likely it is that the detected sensitisation is clinically relevant. For certain allergens, such as peanut, nomograms can be used to calculate post test probability from a positive test in the setting of a defined pre test probability. Such charts are of limited use in day-to-day clinical practice and are not available for all allergens. In practical terms, it is important to improve pre-test probability by testing only in settings of IgE mediated allergy and only to allergens implicated in the clinical history.

Interpretation of specific IgE results is often very straightforward when the clinical history is used to guide test selection and to aid result interpretation. If users lack experience in allergy history taking, test selection or interpretation they may wish to discuss the investigative strategy with their local immunology or allergy service before embarking on testing.

New technologies such as testing with recombinant protein allergens and using multiplex allergen arrays have been developed over recent years. The place of such approaches in routine clinical settings is not well established. These tests are not a replacement for clinical history-based test selection and should not be used as a screening tool. They can be helpful in risk management decisions or in certain uncommon clinical scenarios such as food-exercise reactions. They should only be used by healthcare professionals with experience in allergy or immunology.

In summary, specific IgE tests are tests that are used to identify sensitisation to allergens. These tests should be selected on the basis of a careful allergy clinical history. These tests should never be used to investigate or manage non-IgE mediated diseases and should never be used to ‘screen’ for allergies. Laboratories and laboratory users should endeavour to ensure that measurement of specific IgE is restricted to appropriate and clinically useful scenarios.

3 References

A new framework for the interpretation of IgE sensitization tests. Roberts et al Allergy 2016 Nov;71(11):1540-1551. doi: 10.1111/all.12939. Epub 2016 Aug 15

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