The Laboratory Services Reform Programme

ADVICE NOTE

Indications for Measurement of Total IgE in General Practice and Non-specialist Settings

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Clinical Practice Guidance Document Cover Sheet

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The Laboratory Services Reform Programme offers the following advice:

1.1 Advice for Laboratory Users

1. There are few indications for the measurement of total IgE in general practice or non-specialist settings.
2. Accepted indications for the measurement of total IgE are outlined below in section 1.2 (8). Please state specific indications using these terms, or other similar terms based on local laboratory advice on each request for total IgE levels.
3. Measurement of total IgE should not be used as a screening test for allergy.
4. A raised total IgE does not diagnose an allergic disorder and is never, in isolation, an indication for specialist referral. Elevated total IgE levels are common and usually associated with but not diagnostic of the atopic diseases – asthma, eczema, allergic rhinitis and food allergy (or a past history of these conditions). Atopy can be ascertained from the history without recourse to laboratory testing.
5. Very high (>1000) IgE levels are common in eczema. High levels can also be seen in ultra-rare immunodysregulatory disorders like Hyper IgE Syndrome but are not specific for these conditions and not a defining feature.
6. A normal total IgE does not exclude an allergic disorder.
7. Measuring total IgE levels adds little to a clinical history in most settings. Unnecessary testing may result in the inappropriate initiation of a diagnostic and referral cascade and cause undue anxiety for patients. Unnecessary testing also involves the avoidable risk of needle exposure and generates unnecessary clinical and laboratory waste.

1.2 Advice for Laboratories and Users

1. The accepted indications for measurement of total IgE are

    a. In patients where allergic bronchopulmonary aspergillosis (ABPA) is suspected

    b. In patients where omalizumab (anti-IgE) therapy is being considered for indications where dosing is total IgE and weight dependent

    c. To assist in the interpretation of weakly positive specific IgE results by experienced or specialist clinicians

    d. To assist in the characterisation of T2 inflammation and endotyping of asthma by experienced or specialist clinicians

    e. In patients where very rare immunodysregulatory disorders or inborn errors of immunity are suspected

2. Repeat testing may be useful in monitoring for ABPA exacerbations or response to ABPA treatment but is otherwise not indicated

1.3 Advice for Laboratories

1. Laboratories should communicate to laboratory users the specific indications for testing of total IgE levels that are accepted by the laboratory.

2. Total IgE should be reported with an age-related reference range where required.

3. Measurement of total IgE levels 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

4. To the greatest extent that is practical, requests for total IgE levels that do not meet these requirements should be rejected.

5. If samples are rejected a report should issue to the effect that testing for total IgE was not performed because the criteria were not met

2 Background

Immunoglobulin E is one of five human antibody isotypes (IgG, IgA, IgM, IgD and IgE) produced by B cells and plasma cells. IgE has the lowest concentration of these immunoglobulins in the serum. This is because it largely exists bound to high affinity receptors on effector cells such as mast cells and basophils.

IgE most likely evolved to facilitate defence against parasitic infections. However, there is redundancy to this role. Measurement of total IgE is not helpful in the diagnosis of these conditions in Irish healthcare settings.

IgE is widely recognised as the ‘allergic’ antibody isotype due to the involvement of this molecule in the pathogenesis of allergic disorders. High levels of IgE are defining characteristic of atopy. Atopy is a genetic predisposition to produce specific IgE following exposure to an allergen, and is often characterised clinically by the presence of atopic disorders such as asthma, eczema, allergic rhinitis or food allergy. IgE represents a readily measurable readout of type 2 inflammation mediated, in part, by a predisposition to a Th2 (Type 2 CD4+ helper T cell) response.

Allergic disorders have become more common in recent times. Patients increasingly seek advice from healthcare professionals on these issues. Approaches can include testing for allergic sensitisation guided by a competent allergy focussed clinical history. Allergen skin prick testing or assessment of allergen specific IgE in serum are modalities to assess allergic sensitisation where the choice of allergen is guided by a careful, plausible exposure history. Total IgE levels contribute little to this assessment and should not be used as a general screen for allergic disorders.

Experienced user groups such as allergists, immunologists or other clinicians with an interest in allergic disorders may use total IgE to guide interpretation of specific IgE tests especially when determining the significance of low level positive results.

Results indicating high levels of total IgE are common and not specific. In Irish populations they are most often associated with the atopic diseases, the presence of which can be identified by a clinical history. Levels in atopic dermatitis may be very high (>1000kU/l) but this does not typically input into clinical decision making. Elevated IgE levels may be seen in other less common disorders but is often part of broad constellation of features rather than a diagnosis defining finding. Examples of such diseases include Hyper IgE syndrome and other rare immunodysregulatory syndromes, or vasculitic disorders such as eosinophilic granulomatosis with polyangiitis. These entities are usually diagnosed and managed in specialist settings

Elevations in total IgE are useful to aid in the diagnosis of allergic bronchopulmonary aspergillosis (ABPA). Levels of total IgE can increase during ABPA exacerbations and fall during successful therapy, making it one of the only scenarios in which serial measurement is useful. Measurement of total IgE may be useful in asthma, more generally, as it may be an easily measurable readout of type 2 inflammation that can inform choice of biologic in advanced disease management.

Measurement of total IgE may also be vital as a component of the dose calculations for anti-IgE monoclonal antibodies. There is no indication for repeat measurement when this treatment is being used.

In summary, measurement of total IgE has a very limited clinical utility outside a number of specialist settings. It should never be used as a screen for allergic disease and should never, in isolation, be a trigger for specialist referral. Laboratories and laboratory users should endeavour to ensure that measurement of total IgE is restricted to appropriate and clinically useful scenarios.

3 References

Clinical Significance of Immunoglobulin E. Commins et al. Middleton's Allergy: Principles and Practice, 2020 (9th Edition) 66, 1087-1096

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