



# Guidance on Allergen-specific IgE

Doctors are creatures of habit; over a decade ago the Radio-Allergo Sorbent Test (RAST) was superseded by superior technologies for detecting immunoglobulin E (IgE), but “RAST” is still used most often in laboratory requests for allergy testing. “Allergen-specific IgE” is the correct term for allergy blood testing now and into the future.

IgE-mediated reactions manifest differently, depending on the nature of the allergen exposure. Airborne allergens (grass, weed, tree pollens, moulds and house dust mite) cause allergic rhinitis and asthma. Allergens delivered directly into the circulation (e.g. bee venom, IV medications) or those absorbed through the gut in food or oral medications, mediate acute urticaria, systemic symptoms and anaphylaxis.

Knowing the type of reaction usually narrows down the candidate allergens to be pursued specifically. Modern testing is highly sensitive and specific, however a number of factors influence test performance.

**Clinically “false” positives.** That is, the test is not incorrect, but rather the positive test indicates sensitisation but this is not the cause of the clinical allergy. This is particularly seen in the case of food allergens because;

- Cross reactivity occurs between antigenically related proteins in foods.
- Cross reactivity occurs due to common carbohydrate determinants in many foods.
- Some antigens are chemically altered by cooking and are therefore tolerated, but the specific IgE remains positive to the uncooked food antigen.
- An extremely high total IgE >1000kU/L may associate with low levels of allergen-specific IgE, and should be interpreted with caution.

Using large screening panels of allergens without a clear history of verified immediate reactions associated with specific exposures are usually not helpful. In the case of food allergens, false positives can lead to unnecessary and potentially harmful dietary restrictions.

**Clinically false negatives.** Allergen-specific IgE's may test negative even when true sensitisation is present.

- Levels of circulating IgE vary with time after sensitisation and allergen exposures.



*Allergen-specific IgE testing may be mechanised but interpretation isn't!*

Allergen-specific IgE levels to medications and insects, for example, may decline if tested many years after a reaction. Or testing too soon after a severe reaction (e.g. bee anaphylaxis) may miss the appearance of specific IgE, the reason why such testing is typically arranged a few weeks after reactions.

- Allergen mixes contain a limited number of component single allergens that may be irrelevant to the clinical reactions, leading to false negatives. This is again mostly applicable to food allergens. A detailed history of food ingredients preceding symptoms along with a history of ingredients known to be tolerated can help determine which likely culprit(s) should be tested as single allergen-specific IgE. The most common causes of serious food allergy are peanuts, tree nuts, fish and shellfish in adults and peanuts, milk and egg in children but there is a vast array of

potential allergens in food, underscoring the need to rely on the history to direct the testing.

- In rare cases, an allergen-specific IgE may not be detectable because of biological factors such as IgE directed to novel molecular targets in the allergen. Once again, this underscores the importance of the clinical history. If there is a very strong clinical probability of IgE-mediated allergy triggered by a specific exposure, Skin prick testing and supervised challenge in a specialised allergy clinic may be appropriate.

As a rough guide to selection of allergen-specific IgE:

**For rhinitis/allergic asthma** – if highly seasonal symptoms request grasses and trees. If perennial symptoms, consider house dust mite, molds and animal exposures as appropriate for pattern of symptoms. A standard aeroallergen panel including a mix of local grasses is not unreasonable for screening based on the high analytical sensitivity of current assays.

**For anaphylaxis** – testing must be directed by the history. Enquire about food, stinging insects and latex exposures. Medication IgE testing is limited due to the nature of drug epitopes mediating allergy. The entity of food-dependent exercise induced allergy is associated with omega-5 gliadin IgE which can be requested if clinically suggestive.

**For acute urticaria** – testing without clues in the history as to possible allergen is not useful. Enquire about food and medication exposures.

Finally, many common adverse reactions are not due to IgE-mediated allergy, including delayed skin rash on medications, local skin rash from topical creams, or headaches after takeaway meals. These entities are usually discernable from the clinical presentation (while a negative allergen-specific IgE helps exclude IgE-mediated allergy if needed). When used selectively in conjunction with clinical information, the allergen-specific IgE test is of enormous value in management of allergy (regardless of what we call it!).