Introduction

Allergy, a hypersensitivity reaction caused by immunological mechanisms, can be IgE antibody or T cell-mediated. The majority of allergic reactions are IgE mediated and affect about 30% of the population. The causes of allergy are multi-factorial and include genetics as well as the type, dose and structure of the allergen.

Allergic conditions like allergic rhinitis, rhino-sinusitis, asthma, and urticaria, are common reasons for patients presenting to health care providers. These encounters may range in severity and frequency, and may lead to visits to general practitioners, specialists (paediatricians, ENT’s, physicians) and sometimes even to emergency rooms.

Approach to Allergy Testing

Careful history taking remains essential to the diagnosis of allergies and can identify specific triggers in the patients’ environment or diet. But in some patients where there is still uncertainty about the allergen or triggers involved in an allergic reaction, a rational and cost-effective approach to laboratory allergy testing must be adopted.

What laboratory tests can the clinician use to confirm an allergy?

Clinicians may use the following laboratory tests to assist in the diagnosis of allergic conditions;

a. Skin prick testing (SPT)

b. Specific IgE ELISA tests (originally referred to as “RAST” testing or radioallergosorbent tests but this terminology is no longer used as the methods have changed to normal ELISA platforms) for IgE mediated allergies or

c. Cellular allergen stimulation tests (CAST) for T cell mediated allergies.

An analysis of Lancet Laboratories’ data over a 4 year period (2007-2011) shows that skin prick tests (SPT’s) are used mainly by specialist ENT’s and mainly in adults (20-59 years), whereas generalists and paediatricians favour specific IgE testing (1). Although relatively cheap, SPT’s are inconvenient, may need to be done as an inpatient especially for young children, are operator and technique dependant, may sometimes be difficult to administer in very young children, and require the patient to stop using their anti-histamines and steroids for at least 3-7 days before the SPT’s are actually conducted.

In contrast, specific IgE (“RAST”) testing is more appealing because it is less time and patient intensive, does not require admission, patients do not need to stop taking anti-histamine or steroid medication, and additional specific IgE tests can be added onto an existing sample within 48 hours if necessary.

What is the most cost-effective approach for laboratory allergy testing?

Previously published local South African allergy guidelines (2, 3, 6) have emphasized the importance of history taking, the regional variability of prevailing aero-allergens and the cost-effective use of blood tests, especially those looking for groups or mixes of allergens to assist clinicians and patients to reach a diagnosis and effective treatment as quickly as possible.

The South African Rhinitis Working Group (SAARWG) recognised the need to provide new updated guidelines for the appropriate diagnosis and management of inhalant allergies in primary care and created a task force to do this. This task force, the Allergy Diagnostic Working Group (ADWG), consists of representatives from the Allergy Society of South Africa (ALLSA), the National Pathology Group (NPG) and the SAARWG.

One of the critical objectives in formulating these guidelines was to establish the most cost-effective appropriate screening test and if positive, the subsequent test selection. The emphasis was on choosing a cost-effective approach to ensure optimal patient management.
The final recommendation of the ADWG is that patients with suspected inhalant allergy may be screened using a Phadiatop® inhalant screen or a panel of inhalant skin prick tests.

If the Phadiatop® inhalant screen is positive, patients with persistent allergy symptoms may be tested for IgE antibodies to Bermuda grass, Rye grass, *Dermatophygoïdes pteronyssinus* and *Blomia tropicalis* mites, *Alternaria alternata*, *Cladosporium herbarum* and *Aspergillus fumigatus* moulds, and cat and dog allergens. If patients have seasonal exacerbations during springtime, additional testing for tree pollen IgE may be requested (appropriate tree mix screen or the individual tree pollen allergens in the environment). The following regional recommendations have been made: Western Cape/Coastal – *Epicoccum* mould spores and German cockroach; Kwazulu Natal – Oriental cockroach; Highveld, Free State and Northwest province – maize pollen, weed pollen mix (cosmos and khaki-bush) and eucalyptus tree pollen.

The following flow-diagram is a representation of the new approach to the diagnosis of inhalant allergies:

**Interpretation of Allergy Tests**

Laboratory testing for allergies is generally only useful if the patient has a specific history of allergy. Traditionally, with a suggestive clinical history, a SPT weal of $\geq 3$ mm or serum specific IgE $\geq 0.35$ kU/L support a clinical diagnosis of IgE mediated allergy.

However, if there is no suggestive history, these low positive readings are irrelevant. Large studies have shown that the specificity (the likelihood that you have a particular allergy) with a SPT wheal of $\geq 3$ mm is only 50%. The specificity of SPT’s increase with increasing wheal size and wheals of 7-8 mm have a specificity of $\geq 90\%$ for the diagnosis of an allergy.

The same applies to specific IgE testing and most laboratories consider specific IgE levels higher that 0.35 kU/L suggest allergen sensitisation, but low (class 1; 0.3-3.5 kU/L) and moderate (class 2; 3.5-17.5 kU/L) levels correlate with a low likelihood of clinical reaction.
What's new in Lab testing for allergies?

1. South African Tree Pollen test
   A cost-effective tree pollen test strip has been developed by Lancet Laboratories in consultation with one of the leading allergy test manufacturers in Germany (Euroimmun). Advice on which South African trees should be included was obtained from clinical specialists and the SAARWG. One test blot or strip will allow a screen of 18 different trees including alder, birch, oak, elm, olive, plane, willow, poplar, ash, white pine, eucalyptus, acacia (salinga), cypress, mulberry, lilac syringe, jacaranda, karee and stinkwood. This strip will be available from October 2014.

2. Molecular Allergology
   Molecular allergology is an under-utilised laboratory resource that can add considerable value to the management of allergic patients. Component testing can assess the severity of allergies. For example, for suspected food allergy, clinicians generally use the "FX5" pooled specific IgE test which includes egg, milk, fish, wheat, soybean, peanut as a screening test. If the FX5 is positive, the breakdown of the pool is done and generally would institute dietary restrictions for patients that are positive on one of the foods contained in the breakdown of a positive panel.

   However, a positive specific IgE for one of the above foods does not necessarily indicate that the patient will have an allergic reaction to this food and testing for specific components will allow the severity of the reaction to the food to be assessed. Food components that are routinely available are; egg, milk, soy, peanut, fish, wheat and milk.

   Component testing can also assist in deciding whether the patient is allergic to the raw or cooked form of the food and if for example a fish allergy can occur across certain groups of fish, or if cow's milk allergy predicts goat's or mare's milk reactions.

   Cross-reactivity may occur when a particular antigen causes an allergic reaction to an unrelated antigen. In allergy, cross reactivity occurs when 35% sequence similarity in a fragment of 80 amino acids or complete identity with a peptide of 6-8 amino acids from an allergen. Reactions to particular components like Profilin, long term storage proteins (LTP) and cross-reactive carbohydrate determinants (CCD) are found in a large number of allergens of both vegetable and animal origin, and should be tested for especially if soy/wheat and peanut specific IgE’s results are positive.

   Please contact the laboratory if you require any other component testing not listed on the request form which will then be arranged accordingly.

3. MAST cell tryptase
   Anaphylaxis is a severe, life-threatening, generalized or systemic hypersensitivity reaction that is caused by release of mediators from mast cells and basophils during degranulation, including toxic mediators such as histamine and heparin; but also proteases such as tryptase and chymase; cytokines and chemokines including interleukin (IL)-3, IL-4, IL-5, IL-13, granulocyte–macrophage colony stimulating factor, tumour necrosis factor-a, chemokine ligand 3; lipid mediators such as leukotrienes and PAF; and kinins such as bradykinin (4, 5). Foods, drugs, insect venom and latex are common triggers.

   The diagnosis of anaphylaxis is based primarily on the clinical picture and typical symptoms including cutaneous, respiratory, gastrointestinal and cardiovascular. Most commonly urticaria and angio-oedema are the initial signs (4). The management of anaphylaxis falls into either emergency treatment or resuscitation of a patient with acute anaphylaxis, or the search for a cause for the event and the formulation of a plan to prevent and treat possible further episodes of anaphylaxis. Understanding both is important in preventing unnecessary mortality from anaphylaxis.

   Measuring elevated levels of serum mast cell tryptase (in the active β-form, referred to here as “mast cell tryptase”) is diagnostic of anaphylaxis and can help distinguish it from other disorders with similar clinical symptoms. However, normal levels of serum mast cell tryptase do not exclude anaphylaxis, especially with mild reactions or in some food associated anaphylaxis reactions.

   Typically, serum mast cell tryptase peaks 1-2 hrs after onset of symptoms and remains elevated for 4-6 hours, but sometimes up to 12 hours after an episode. Mast cell tryptase is stable and may be ordered on stored blood or post mortem blood to confirm the diagnosis of anaphylaxis.

   It is also recommended that baseline levels of serum mast cell tryptase are done in individuals that are suspected of having anaphylactic reactions so that levels during an attack can be compared to their own baseline levels that may be elevated compared to the normal range.
References

6. Hawarden D. Diagnostic Testing in Allergy. April 2014. ALLSA.