World Allergy Week Workshop
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Allergy Diagnostic Tests (Handout)

Elham Hossny
Professor of Pediatrics
Pediatric Allergy & Immunology Unit
Ain Shams University

Objectives
To know when to order and how to interpret results of the following:

- Skin prick testing
- Specific IgE assay
- Allergen challenge testing

Atopy
Atopy is a personal and/or familial tendency, usually expressed anytime in life from childhood into maturity, to become sensitized and produce IgE antibodies in response to ordinary exposures to allergens, usually proteins. As a consequence, atopic persons can develop IgE-mediated allergic diseases including asthma, rhinoconjunctivitis, or eczema.
**Allergen**

An antigen causing an allergic disease is called an “allergen”. Most allergens initiating an IgE-mediated allergic reaction are glycoproteins with a molecular weight of 5 to 100 kD, most around 20 kD.

**The essential components of allergy diagnosis**

- Clinical history and physical examination: symptoms versus exposure
- Diagnostic confirmatory test: SPT – Specific IgE assay
- Provocation test: oral, nasal, or bronchial challenge

**Food allergy and asthma**

The incidence of FA in asthmatic children (6-8%) is lower than that in atopic eczema (35%) but when a child has asthma and atopic eczema, the likelihood of FA rises. In some patients, the manifestations of FA can be limited to subclinical bronchial hyper-reactivity (BHR) which would be difficult to recognize.

In other words, the chronic ingestion of a food to which one is allergic may result in increased BHR despite the absence of acute symptoms on ingestion.

**Skin Prick Test (SPT) in the diagnosis of atopy**

Skin allergy testing is a method for diagnosis of sensitization that attempts to provoke a small, controlled, allergic response. A minute amount of an allergen is introduced into the patient's skin by prick or scratch.

**SPT Technique**

- 1st generation short-acting antihistamines (sedating antihistamines) should be stopped at least 3 days before testing.
- 2nd generation antihistamines should be stopped at least 5 days before testing.
- Potent topical steroid should be avoided at the site of the test for at least 2 weeks.
- The patient should wait for at least 20 minutes before interpretation of the results.
- Largest and orthogonal diameter of any resultant swelling (wheal) and erythema (flare) are measured.
- Any pseudopod formation (lateral extension of the central wheal) denotes a significantly positive reaction.
- Epinephrine ampoule should be ready for any possible systemic reaction.
Suppression of skin tests by medication

- Most antihistamines and anti-depressants suppress skin tests for 3-7 days.
- H2 antagonists have no, or a very minor, effect.
- Bronchodilators do not affect skin tests.
- Data on corticosteroids vary; better avoid.

Not all allergens are available as a skin test extract: Sometimes we use fruit and vegetable prick-prick test.

Recording SPT results:

- Positive or negative
- 0 to 4+
- A superior method is to measure the reaction in mm of the wheal and flare (the most accurate way to present results).
- Any pseudopodia (lateral extension of the central wheal) denote a significantly positive reaction.

Interpretation of the results

- 0: Same size as negative control
- 1+: Induration very small; erythema present = weak reaction (mild)
- 2+: 50% of histamine control = moderate sensitivity
- 3+: Same as histamine control = definitely positive
- 4+: Larger than histamine control or with pseudopodia = strongly positive

Another system:

- Negative: Same size as negative control
- Just positive: 3 mm more than negative control but less than 8 mm (needs oral challenge if food allergen)
- Definitely positive: 8 mm or larger (may preclude oral challenge)
- Highly positive: Pseudopodia (do not do an oral challenge)

A negative skin prick test may exclude an IgE-mediated reaction (good negative test) but many patients with a positive test do not react upon food ingestion

Serological Tests in the Diagnosis Allergy

- Allergen-specific IgE
- Total Serum IgE (omalizumab: anti-IgE; ABPA)
- Multi-allergen screen IgE (define atopy)
- Mast Cell Tryptase (indicator of anaphylaxis)
- Eosinophil Cationic Protein (eosinophil activation marker)
- Precipitin-IgG antibody (Hypersensitivity pneumonitis)

**Serum total IgE in allergy**

1. Patients with allergic asthma may have increased total serum IgE concentrations, but this is not an allergy-specific finding
2. Measurement of total serum IgE may be of value in:
   - Gastrointestinal symptoms/eosinophilic esophagitis
   - Allergic Bronchopulmonary Aspergillosis (ABPA)
   - Allergic Fungal Sinusitis
3. Total serum IgE may be measured to determine the dosage of omalizumab

**Some disorders with elevated total serum IgE levels**

- Helminth infestation e.g. Ascaris, Schistosoma
- Infections with Staphylococcal strains containing enterotoxins, so called “super-antigens”
- Virus infections, e.g. cytomegalovirus (CMV)
- ABPA and allergic fungal sinusitis
- Graft versus host disease (GVHD)
- Hyper-IgE syndrome
- Wiskott Aldrich syndrome

**Serum Allergen Specific IgE in the Diagnosis of Allergy**

- Serum specific IgE result interpretation should be guided by history.
- It does not diagnose cell mediated allergy (e.g. GIT manifestations of cow’s milk allergy)
- It is expensive

**Allergen specific-IgE antibody is recommended when In-Vivo tests cannot be done:**

- The patient is taking anti-histamines or other confounding medications for skin tests
- Immediately (up to 6 weeks) following an anaphylactic event
- Patient is morbidly afraid of skin testing
- The patient has severe eczema or dermographism
Interpretation of allergen-specific IgE antibody results

Presence of allergen-specific IgE antibodies in serum indicates sensitization. “It does not equal clinical symptoms”

Predictive values for specific IgE versus challenges

95 % predictive value
- Egg: 7 Ku/L (2 Ku/L*)
- Milk: 15 Ku/L (5 Ku/L*)
- Peanuts: 14 Ku/L
- Fish: 20 Ku/L

* Infants and young children

No laboratory tests can help identify cell-mediated food reactions.
- In the pathogenesis of gastrointestinal manifestations, cell-mediated hypersensitivity predominates making standard allergy tests such as skin prick and specific IgE tests of no diagnostic value.
- Skin patch test results are controversial. It is mainly used in allergic contact dermatitis (ACD).

In-Vivo Provocation Tests
- Provocation tests involve the challenge of the affected organ by serial dilutions of an allergen extract or by the actual, suspected allergen source material, e.g. food or drug.
- A provocation test is time-consuming.
- It can result in dangerous clinical reactions and should only be performed by experienced persons with access to lifesaving equipment.

Oral food challenges in the diagnosis of food allergy:
- The food elimination-challenge testing is still the gold standard for the diagnosis of FA and is the best available test to evaluate non-IgE mediated food allergies.
- Open or single-blind oral food challenges are often used as a screening tool especially in children.

Take Home Message
- History is the most important tool in allergy diagnosis
• A positive test of sensitization (SPT or specific IgE) does not necessarily mean that the person will react on exposure
• SPT is a good negative test
• A physician should be aware of the levels of positivity that have a 95% positive predictive value for a specific allergen before interpretation of the results of SPT and specific IgE
• Elimination challenge test is important in confirmation of allergy and is the only reliable test in cell-mediated types
• Most GIT food allergies are not IgE-mediated and cannot be diagnosed by SPT or specific IgE assays
• The value of serum total IgE in the diagnosis of allergy is very limited
• Specific immunotherapy in food allergy is still experimental
• Avoidance is so far the only approved treatment of food allergy
• Wearing medical alerts help avoidance in infants and children
• Any person who experienced anaphylaxis once should have a written emergency plan, and carry epinephrine all the time e.g. filled syringe or self auto-injector pen (epipen)