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Allergy

The diagnostic process
Main examinations and interpretation

Physical examination and medical interview

As symptoms are not always typical and specific to allergic origin, **medical interviews** play an essential role in diagnosis.

They consist of researching any family and personal history of allergy and examining the circumstances under which symptoms occur. They make it possible to suspect or target the allergen or allergens responsible and therefore direct the decision on other tests to run. In the case of a food allergy, the patient may be asked to keep a food diary.

Skin tests

These reveal the presence of specific IgE antibodies bound to the surface of cutaneous mast cells.

There are different types of techniques, mainly **the skin prick test** and in some cases, **the intradermal reaction test**.

They can be carried out from a very young age, once skin is reactive. However, the development of the immune status and allergies during the first six years of life may require these tests to be repeated.

All treatments involving antihistamines must be suspended, on average, one week in advance.

When these tests cannot be run (severe atopic dermatitis, patients on antihistamines, dangerous allergens) or cannot be interpreted (dermographism), **medical tests will be required as first-line intervention**, with the search for specific circulating IgE for target allergens during the medical interview.

Total IgE antibodies

An increase in the rate of total IgE antibodies can be seen in conditions other than allergies (parasitic disease, viral infection, immunodeficiency, etc.).

A high rate of total IgE antibodies is not specific to atopy and a normal or low rate does not exclude an allergy.

Specific IgE antibodies: screening

The testing is carried out using unit tests comprised of allergen mixes of either the:

- **major airborne allergens** (Alatop®, Phadiatop®, etc.),
- **most targeted allergens**, in a more restricted number (codes gx, wx, tx, mx, ex, rx, hx for airborne allergens and fx for food allergens).

They provide general information on the presence of allergen-specific IgEs present in the mixture, without identifying the allergen involved.

Carried out as a **first-line** intervention, they allow doctors who are not specialised in allergies to assess the need to continue with a more specific investigation with an allergist.

If these tests are negative, but the symptomatic clinical picture is suggesting otherwise, further allergy investigations should be pursued. These tests, when positive, should be followed up by additional tests to indicate allergic origin.

In the absence of symptoms, positive test results merely mean sensitisation.

Specific IgE antibodies: identification

- The identification requires quantitative assay techniques for the specific IgE of **a single allergen,** targeted during the medical interview and, if possible, skin tests.

The indications are:

- dissociation of clinical data and skin tests,
- impossibility of carrying out skin tests,
- identification of rare allergens or allergens for which skin tests are ‘prohibited’,
- establishment of a reference value with the implementation of desensitisation or avoidance treatment.

- There are also tests that provide the measurement of specific antibodies to **multiple allergen components** in a single test, which explore a panel of allergens, that were not targeted during the medical interview. They must be considered in all cases as an aid to resuming diagnosis in order to identify the specific allergen(s) responsible.

The identification of allergen-specific IgE antibodies means a sensitisation towards this allergen. It does not in any way prove an allergy. A cause-effect relationship must be proven in order to declare an allergy.

The absence of specific IgE antibodies does not rule out an allergy confirmed by other tests.

- Identification is generally carried out in addition to skin tests and involves different allergen extracts to those used for skin tests.
- The assay of serum IgE antibodies does not require medical treatments to be suspended.

Cross-reactivity

Antibody immune reactions occur based on the **epitopes** present on the surface of the molecules.

These epitopes may be common to several taxonomically close substances (group I allergens common to all grasses) or diverse substances (allergens of pollen and fruit, latex and fruit, mites and snails, cats and pork, etc.).

Immunological cross-reactivity is extremely common and is being increasingly studied.

The allergens in question most often belong to the same molecular families, which are best preserved during the evolution of the species in which they play an important role, such as albumins, lipid transfer proteins (LTPs), or proteins providing resistance to illnesses, insects or stress (RPs, chitinases).

Cross-reactive carbohydrate determinants (CCDs) are also responsible for many cases of cross-reactivity *in vitro*. They are often seen in patients who are extremely sensitive to pollens. Their presence can be tested for by means of a dose of bromelain IgE or equivalent.

Cross-reactivity sensitivity is more frequent in serum dosages than in skin tests.

In vitro diagnosis today has an increasing number of molecular allergens, with well-known structures, either purified natural or recombinant, which allow the allergists to better understand these cross-reactivity reactions.

Cell tests (HL, TAB)

These consist of **studying** the response of the patient's basophils to an antigen ***in vitro***. They are not, however, predictive tests until this antigen is reintroduced.

In practical terms, the sample must be taken some time after an anaphylactoid reaction, when no antihistamine treatment is ongoing.

The test is carried out within 24 hours of the sample being taken, according to basophil function. These tests are not standardised, neither in how they are carried out nor in the selection of positivity criteria.

A positive result is not proof of an IgE-dependent mechanism and a negative result does not exclude a potential allergic reaction during a future contact.

They may be a useful in a well-documented allergy assessment, especially when the allergen does not exist coupled with the necessary support for carrying out the assay of the specific circulating IgE.

They may be useful in the study of cross-reactivity (hymenoptera venoms, curares, etc.).

Mediator-release assays

Histamine and tryptase are the main mediators sought during anaphylactic incidents.

- Histamine is released quickly *in vivo* and has a very short half-life.
- Tryptase, is released later and has a longer half-life.

The kinetics of these markers is monitored during anaphylactic reactions with two samples taken 15 to 30 minutes and one to two hours after onset of symptoms.

The baseline tryptase assay reflects the patient's mast cell mass and can be used as part of a diagnosis of mastocytosis.

It should be noted that the assay of urinary methylhistamine is no longer performed.

The assay of ECP (Eosinophil Cationic Protein) may help in therapeutic follow-up in assessing pulmonary inflammation in asthmatic patients.

The diagnosis of an allergy is based on a structured process.

Medical tests must be interpreted with the clinical context, considering case history and in particular:

- **the patient: genetics, immune system, inflammatory system;**
- **the allergen to which they are exposed: nature, frequency and degree of exposure;**
- **other factors present at the onset of symptoms: viral infection, taking of medicines, alcohol, etc.**

For more information

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