

ALLERGY DIAGNOSTICS AND THE ALLERGIST'S LONELINESS

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In Italy the management of allergy is mainly assigned to specialists and independent professionals (less than 1,500) operating within the national healthcare service in full autonomy. There are a few allergy Department (only ten positions of head physician) with a few doctors for a potential more of 10 million patients. How does the allergist perform his/her diagnostic activity? The complete and accurate anamnesis he does provides him with very good indications and then, when specified, he carries out skin testing. His role very often stops at this point, unless prescription and, when possible, immunotherapy are required. The allergist is alone before his/her patients and his/her skin tests.

What discriminating capacity must the doctor have if a diagnostic reagent deteriorates and is no longer successful in a patient with multiple sensitization? Let us take the example of a North-Italian patient who is polysensitized to graminaceous (grass) pollen and parietaria (wall pellitory) showing almost similar pollination peaks. If one of the two diagnostic extracts does not work or, worse, if the patient's skin has not been pricked appropriately (to err is human), how can the allergist realize he has made a mistake? He may label the patient as monosensitized to one or the other of the two allergens without fear of being wrong, as in the case of a clinical history of pollinosis in agreement with the observed positivity. Also, considering the patient's assumed monosensitization, he may prescribe specific immunotherapy, which is still more advisable.

While diagnostic testing applied in the laboratory has intra- and inter-assay control tools that are routinely used for measuring specific IgE, the allergist does not have the same crucial devices. He can only evaluate whether the patient is reactive or not to histamine (positive control) or to glycerinated saline solution (negative control). On the other hand, any specific IgE assay can express the coefficient of variation. Furthermore, the IgE assay includes intra-assay

assessment where values, which are expressed in KUa/l and are therefore convertible in nanograms of the serum specific IgE, are compared with the control serum. The same procedure is then repeated among different sessions (inter-assay control) so as to provide as reproducible and accurate results as possible in time.

Besides these two types of control methods, the laboratory participates in an external quality assurance program among different laboratories, thus assuring homogeneity of results in different laboratories as well. What can the allergist do? He can perform intra-assay evaluation by testing the same allergen with two different lots (which are not always superimposable since the concentration of the major allergen is only rarely specified and only for a few of them). However, this method does not have incontestable validity as the different manufacturers adopt their own "in-house" standardization which is not comparable with that of the other manufacturers. As regards external quality assurance, at most, the allergist can check with a colleague to make out whether there is an increase or a decrease of the diameter of a wheal with a certain type of reagent. Obviously, he will not suggest that his/her patient should consult his/her colleague to have his/her undergo the same skin test. The allergist is alone with his good anamnesis, which is an irreplaceable diagnostic tool and the pivot of his diagnosis, and his skin tests with negative and positive control evaluation. That is all.

We personally have experienced several allergy services and in many cases anamnesis was not performed by the allergist, but by the nurses who had to fill in a pre-arranged questionnaire.

Still, was anamnesis not the cornerstone of allergy diagnostics? As to positive control, the erythematous reaction evoked by the skin test is the result of a provocation test that with the degranulation of mast cells releases various pre-formed and newly-formed mediators (histamine, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, IL-10, IL-13, serotonin, heparin, IFN-gamma, TGF-beta, chymase, tryptase, PAF, cathepsin G, leukotriene and so on). The positive control test is only carried

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out with histamine, which is certainly the major mediator but does not reproduce the complete event of allergic flogosis.

Are the two *in vivo* and *in vitro* tests comparable as to the quality of the information they give? Do they provide the same data in terms of diagnosis and prognosis? Through quantitative reporting the *in vitro* test allows the formulation of diagnosis and prognosis (see works by Sampson, Boyano- Martinez). As regards the skin test, the greater the wheal diameter, the greater the possibility that the patient should be sensitized (with the exception of the cases of dermatographism). Skin testing is still performed with the allergen extract and does not provide any information on the sensitizing molecules. Furthermore, it does not specify the positivity due to cross-reactions since with the introduction of recombinant allergens it has added the utmost specificity to *in vitro* diagnostics. At present molecular diagnostics, which is only available for the

IgE specific assay to recombinant allergens, is essential to prescribe correct immunotherapy since it indicates whether the patient is sensitized to the allergens present in the immunotherapy extract.

Greater integration between the allergist and the clinical laboratory is therefore mandatory in order to obtain an unquestionable, reliable and reproducible diagnostic aid. With the exception of a number of selected cases, such as monosensitized patients with a completely concordant clinical history, the laboratory is indispensable to make the allergist quit his loneliness and introduce him in a reliable "diagnostic circuit".

References

1. Boyano-Martinez T., Garcia-Ara C., Diaz-Pena J.-M., Esteban Manuel M. - Prediction of tolerance on the basis of quantification of egg-white specific IgE antibodies in children with egg allergy. *JACI* 2002;110:304-309.
2. Sampson H.-A. - Utility of food-specific IgE concentration in predicting symptomatic food allergy. *JACI* 2001;107:891-896.

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