



EAACI Guidelines on Diagnosis of Food Allergy: What Is New?

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AN ENGAGING session presenting the newly-revised European Academy of Allergy and Clinical Immunology (EAACI) guidelines on the diagnosis of food allergy, centred around the accuracy of diagnostic tests and recommendations for practice. The session, chaired by Alberto Alvarez-Perea, Maternal and Child Hospital Gregorio Marañón, Madrid, Spain, and Eva Untersmayr-Elsenhuber, University of Vienna, Austria, was presented at the EAACI Congress 2023 in Hamburg, Germany.

DIAGNOSTIC TEST ACCURACY IN IgE-MEDIATED FOOD ALLERGY

The previous guidelines, released in 2014, were based on a meta-analysis of papers published prior to 2013. Since then, there have been numerous advances, such as the widened availability of IgE testing and the development of novel techniques, such as the basophil activation test (BAT). In order to inform the updated guidelines, the research team completed a systematic review of all the diagnostic tests available for IgE-mediated allergy. This comprehensive study aimed to overcome the limitations of prior individual studies, ensuring the production of reliable, generalisable results. Carmen Riggioni, EAACI Food Allergy Guidelines Expert Group and EAACI Research and Outreach Committee Food Allergy Group, commenced the session by summarising the recent evidence, presenting and explaining the rationale behind the updated guidelines for the main IgE-mediated food allergies.

Studies investigating participants with suspected IgE-mediated allergy to any food were included, with the sensitivity and specificity of all index tests investigated. Importantly, each study was required to use an open food challenge (OFC) in a group of participants to generate a control. Overall, 149 studies, encompassing 24,489 participants, were included. The risk of bias assessment suggested a moderate level of

heterogeneity in the studies, but overall, there was good applicability due to the use of OFC as a control.

The most accurate tests for each food allergy were summarised, with the optimal cut-offs defined in each included study analysed. This enabled the generation of median and interquartile range values for each diagnostic test. Peanut allergies were most commonly investigated by the included studies, enabling the identification of two tests that were highly specific for IgE-mediated food allergy: Ara h 2 and BAT. For Ara h 2, the median optimal value was defined as 0.44 kU_A/L, while the interquartile range was 0.30–1.30 kU_A/L, compared with a median optimal value of 5.0% and an interquartile range of 4.7–7.1% for BAT. Regarding raw egg, ovomucoid, skin prick test (SPT) with egg yolk, and SPT with ovalbumin were found to be the most specific tests, with median optimal cut-offs of 0.8 kU_A/L, 7 mm, and 10 mm, respectively. Cooked egg, ovomucoid, and SPT with ovalbumin remained accurate, with the addition of SPT with raw egg white; this is an interesting result, as allergists have been moving away from this test, more commonly opting to use extract. However, Riggioni emphasised that the results indicate that this is still a highly accurate, and thus valuable, test. Baked egg was less commonly investigated by the included studies, resulting in the generation of a broad interquartile range (6–50 kU_A/L) for IgE. Casein, SPT, IgE, and α-lactalbumin were found to be the most specific

tests for cow's milk; however, the research team were unable to perform a meta-analysis for baked cow's milk due to a lack of eligible studies. Cor a 14 and BAT were the most specific for hazelnuts and sesame, respectively, and in this case, BAT had low variability, suggesting modern tests are of a better quality. For wheat and soy, tests with good specificity and sensitivity were not identified. However, Riggioni suggested this is an expected result, since these allergies are very difficult to diagnose in clinical practice. With regards to shrimp allergy, SPT was the most sensitive. However, the included studies reporting SPT results were limited to shrimp extract, meaning these results cannot be extrapolated to the variety of SPTs used in clinical practice.

The research team then performed a subgroup analysis to ascertain whether previously defined cut-off values for different food tests remained accurate. For peanut allergies, a SPT value ≥ 8 mm and a specific IgE ≥ 15 kU_A/L still had high specificity. However, for egg allergy, the research team were unable to calculate the specificity of previously defined cut-off SPT and IgE values for egg white. Ovomucoid, on the other hand, remained specific, along with the cut-off values for SPT for cow's milk allergy and Cor a 14 for hazelnut allergy.

Riggioni then emphasised the importance of continued assessment of allergy test specificity, due to variability. For example, Ara h 2 has high specificity in Northern Europe (99%), Australia (97%), and Western Europe (92%), but in Asia the specificity is much lower (79%). Subgroup analyses, considering factors such as geographic location and age, were challenging, as included studies often failed to report this detail.

In conclusion, newly defined cut-off values for optimal sensitivity may be more useful in the screening and confirmation of the diagnosis of food allergy. Furthermore, there is strong evidence supporting the accuracy of SPT, specific IgE, and component-resolved diagnostics in aiding the diagnosis of peanut, cow's milk, egg, and tree-nut allergies. However, the diagnostic performance of the various tests is allergen-specific, and largely dependent upon the food being tested; thus, it is important to remember that no test is absolute.

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RECOMMENDATIONS FOR CLINICAL PRACTICE

Alexandra Santos, King's College London, UK, delivered the second talk regarding the EAACI guidelines update. This focused on how to implement the key updates in clinical practice, with the rationale and strength of each recommendation discussed.

Firstly, for patients with suspected IgE-mediated food allergy, a detailed allergy-focused history is recommended as the first diagnostic work-up. Key questions that need to be asked at this stage include age at symptom onset, presenting symptoms, reproducibility of reactions, and dietary history. Clinical history must be combined with the results of allergy tests to make an accurate diagnosis.

"A detailed allergy-focused history is recommended as the first diagnostic work-up."

Following this, patients with a history of suspected IgE-mediated food allergy, SPT, and/or serum specific IgE are recommended as first-line tests for the diagnosis of food allergy. This is especially relevant to patients where a possible reaction has been reported, or there is epidemiological evidence of risk for a specific food allergy. Allergens tested should be directed by clinical history, ensuring panel testing is avoided wherever possible. Santos emphasised that the previously discussed cut-offs should act as a guide during diagnosis, reminding us that they are not absolute.

The third recommendation refers to patients with suspected IgE-mediated allergy to peanut, hazelnut, or cashew nut. Ara h 2, Cor a 14, and Ana o 3, respectively, are recommended in this case, in conjunction to SPT and/or IgE extracts where available. This is most important when the history is unclear, or the results of SPT/IgE are insufficient for diagnosis. The expert panel, responsible for the guideline update, recommend concurrent testing for the component and the extract, to avoid false negative results.

It is also recommended that BATs are utilised in patients with an equivocal diagnosis of IgE-mediated allergy to peanut or sesame.

The previously discussed meta-analysis reported a high certainty of evidence regarding the value of BAT. In this case, however, it should be recognised that this testing is not available in most countries, and as such, the clinical recommendation is conditional.

Santos stressed the importance of the fifth recommendation: patients with suspected IgE-mediated food allergy should not receive the isolated use of IgG and IgG subclass tests. This is due to limited evidence, but also limited rationale for conducting these tests in clinical practice, due to ethical concerns, cost, and the unnecessary avoidance of allergens.

Recent evidence also suggests that children who have food allergies should be retested at regular intervals to test for spontaneous tolerance. Santos reminded the audience that younger children and patients allergic to milk, egg, wheat, and soya are more likely to develop spontaneous tolerance, both factors that should inform clinical decision making.

The penultimate recommendation refers to medically-supervised OFC. A high certainty of evidence suggests patients with an unclear diagnosis, despite IgE-sensitisation tests, should receive an OFC to confirm or exclude food allergy.

Finally, a double-blind, placebo-controlled food challenge (DBPCFC) is recommended only when an open OFC outcome is indeterminate. However, the certainty of evidence supporting this recommendation is low, due to a lack of studies comparing OFC with DBPCFC. The expert panel also acknowledge that an open OFC is valuable for most cases in clinical practice, while DBPCFCs should be reserved for research purposes, or for cases where subjective symptoms are expected, or the patient is highly anxious.

Santos concluded by outlining the recommended algorithm for the diagnosis of an IgE-mediated food allergy, developed based on the meta-analysis and recommendations outlined above.

CONCLUSION

Overall, these updates to the EAACI guidelines on the diagnosis of food allergy will help to optimise decision-making for physicians and healthcare professionals, contributing to improved patient care. ●