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EAACI Guidelines on Allergen Immunotherapy – Out With the Old and In With the New

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Occurring in both developed and developing countries and across all ethnic groups and ages allergic diseases represent a global health problem. During the last few decades, there has been an increase in the prevalence of allergic diseases and it has been predicted that by 2025 half of the entire EU population will be affected [1]. The three major management strategies are avoidance, symptom control by pharmacotherapy and allergen immunotherapy (AIT). By contrast with symptom control by pharmacotherapy AIT aims to modify the immune system via tolerance induction [2] and is potentially able to alter the course of allergic diseases [3]. The potential preventive effect of AIT is currently being explored for pollen [4].

Introduced by Noon and Freeman in 1911 for the treatment of allergic rhinitis (AR), the procedure of desensitisation using allergen extracts has been used around for more than 100 years [5]. A significant body of data accumulated regarding the safety and efficacy of AIT vaccines in adults and children both for respiratory allergy and for venom hypersensitivity and recent data look promising also for food allergy. However, AIT remains underused mainly due to lack of agreement between documented efficacy, insufficient data on its cost-effectiveness, educational level and different specialty of physicians taking care of allergic subjects, lack of awareness on AIT, scattered world-wide availability of regimens and/or products for application, varying selection of potential responders [6]. AIT studies reached to high standards during recent years, with the requirements for study design reaching a satisfactory standard with focus on solid end-points, evaluation of dose-response and optimal dosage, use of large patient cohorts, accurate statistical assessment and reporting. These standards should be followed today and GMP products with solid proof of efficacy and safety and well-defined immune mechanisms should be used to optimize the effectiveness of AIT as a key intervention in allergic diseases [6,7].

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Professional guidelines provide a practical and ethical framework for decision-making and thus instill a sense of responsibility and accountability. Numerous AIT guidelines have been developed by national and international organizations ranging from local consensus reports to international position papers. A recent evaluation using the Appraisal of Guidelines for Research & Evaluation (AGREE) II tool of 31 AIT guidelines published since 1980 showed an improvement in quality since 2010 paralleling the use of GRADE methodology. However they still comprise low scores in the stakeholder involvement, rigor of development and applicability domains. Newer guidelines scored better for rigor of development, but lower in the applicability domain since they focused more on scrupulous evaluation of the evidence and less on dissemination [8].

The EAACI AIT guidelines provide a series of recommendations and also the clinically relevant steps to be followed to move AIT for major allergic diseases closer to being embraced by the medical community. The primary audience is clinical allergists, but they are of relevance to all other healthcare professionals working across a range of clinical settings (e.g, primary care practitioners, emergency departments and other specialist doctors, nurses, and pharmacists), who may deal with allergic patients. The main aim of EAACI AIT guidelines is to provide a roadmap for this burgeoning field following a rigorous path for developing recommendations based on a well-defined methodology, while ensuring appropriate representation of the full range of stakeholders and intending to minimise the risk of bias at each step of the process. Development of the EAACI guidelines has been informed by a formal systematic review and meta-analysis [9,10,11,12]. Pragmatic evidence synthesis and real life studies were also considered where appropriate. Recommendations for clinical care were formulated using an adapted Oxford Centre for Evidence-Based Medicine approach, which included highlighting the evidence base underpinning each recommendation and other potentially relevant contextual information [13,14,15,16].

The key limitations of the EAACI AIT guidelines derive from the heterogeneity and gaps in the support literature. There are many areas for which there is no evidence or no high-quality evidence. Many gaps in the evidence base exist, particularly around AIT long-term benefit, use in the pediatric population or in polysensitised patients, rare allergens, the value of AIT for primary prevention, availability of biomarkers to select responders and evaluate the efficacy objectively or of strong cost-effectiveness analysis adjusted to socio-economical differences within and between countries, preparedness of primary care to participate in the delivery of AIT [13,14,15,16,17]. Harmonization and validation of clinical outcomes, standardization of products between companies, consistent use of the uniform classification systems for grading AIT systemic and local reactions both in clinical trials and surveillance studies will allow better comparisons and best practices for all AIT treatments [14,15,16,17,18]. Regulations on AIT have profound effects on allergy practice, allergen manufacturers, and research programs. There is a need for a standardized approach between regulatory agencies from different regions of the world [19].

Coordinated actions among regulators, industry and the scientific environment to find solutions that properly answer the health expectations of the allergic patients are thus needed and should be continuously be updated.

Even the best guideline cannot substitute for the standard of care but can serve as a starting point in the shared decision making with the patient, covering the diagnostic and treatment choices available. The EAACI AIT guidelines definitely make a step forward based on the quality and the consistency of the recommendations and on the strong focus on the applicability.

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