

Recent advances in immunotherapy: the active treatment of food allergy on the horizon

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“The clinical trials have shown that oral immunotherapy can successfully desensitize a large number of individuals without major morbidity or mortality; at the end of the all of the studies, the greater part of patients can tolerate more of the food than at the start.”

Allergen specific immunotherapy (AIT) represents the time honoured treatment which has disease-modifying effects on respiratory allergy: allergic rhinitis and allergic asthma. This is in contrast to the symptomatic relief obtained with anti-allergic drugs, such as antihistamines, or topical or oral corticosteroid treatment [1,2]. Currently, there are two available main routes of administrations: subcutaneous route (SCIT) and sublingual route (SLIT).

The demonstration of clinical and immunologic tolerance to seasonal pollens: persistence of benefit for several years after discontinuation of immunotherapy [3] and the possibility that immunotherapy prevent new sensitizations in children monosensitized to house dust mites [4], gives AIT a true different pharmacological profile from drugs. These data demonstrate the efficacy of AIT, not only as a therapeutic agent, but also as a preventive strategy which should be introduced earlier in the course of allergic disorders. Altogether, immunotherapy should be considered earlier and not just confined to patients in whom pharmacotherapy fails.

Recently, in other allergic disorders that are beyond the respiratory disease spectrum, such as IgE-mediated food allergy, the evidence is beginning to emerge that these diseases also will respond to immunotherapy. The current

standard of care for food allergy focuses on two elements: strict avoidance of the allergen and emergency therapy in cases of accidental exposure. Several studies have reported a wide range of prevalence of food allergy. Uncertainty in estimating the incidence and the prevalence of food allergy is due to changing definitions, imprecision in terminology, potential different dietary habits in different continents and varied clinical phenotypes. Therefore, the exact incidence of food allergy is yet to be established. Food allergy is the correct diagnosis if the symptoms resulting from the ingestion of a food are due to an immune mechanism. Immune reactions to foods can be IgE-mediated, cell-mediated or result from a combination of IgE and non-IgE mechanisms. In this context the risk to overestimate the prevalence of food allergy represents a pitfall. Therefore, a food challenge may be necessary to confirm the diagnosis either in IgE mediated diseases, or in the assessment of non-IgE mediated food allergy where the diagnostic uncertainty is quite frequent.

In spite of everything, there is little doubt that food is a common problem, especially in childhood. Different factors have been hypothesized as risk factors or protective factors for food allergy, namely hereditary factors, microbial factors and allergen exposure.

**EXPERT
REVIEWS**

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Recently an increase of severe systemic reactions caused by foods was reported: these data demonstrated that acute reactions to foods are a burden for patients and their families [5].

Other reports indicate that children need longer to outgrow their milk and egg allergy, with most developing tolerance in their teenage years rather than in early school age as previously thought; in addition a quite low rate of children with either peanut allergy or tree nut allergy will develop spontaneous tolerance [6].

Therefore, a need clearly exists for active therapies that will allow food – allergic individuals to tolerate their specific – food allergens. Moreover the paradigm that delaying introduction of foods such as egg or peanuts may protect against allergy is currently under revision. Therefore, a new approach on both secondary prevention and treatment of food allergy is underway.

During the recent EAACI, WAO Congress 2013, Milan, Italy, the possibility of new active treatment of IgE-mediated food allergy was deeply discussed by means of lectures, oral abstracts presentations, posters: the studies have been carried out for milk, egg or peanut allergies. Currently, oral immunotherapy (OIT), SLIT and epicutaneous immunotherapy represent the investigated routes for the treatment of IgE-mediated food allergy, although reports on OIT thus far have been more extensive.

In addition to a number of studies, review articles [7–9], five meta-analysis on immunotherapy for food allergy have been published [10–14], including two recent Cochrane report specifically addressed on peanut OIT or cow's milk OIT [13,14]. A further therapeutic approach consisting on omalizumab oral desensitization combination therapy in significant and severe IgE-mediated food allergy [15]. Omalizumab is a recombinant humanized monoclonal IgE-blocking antibody; it decreases or prevents the allergic response triggered by IgE molecules, by binding receptors on basophils and mast cells and therefore reducing IgE mediated mast cell and basophile degranulation on allergen exposure.

The clinical trials have shown that OIT can successfully desensitize a large number of individuals without major morbidity or mortality; at the end of the all of the studies, the greater part of patients can tolerate more of the food than at the start. The natural history of allergy sensitization(s) usually develops in this exposure order: food, indoor allergens and outdoor allergens. In children without food allergy, sensitization to mites or pets firstly is diagnosed by allergists. In the light of this follow-up evidence, it should be argued that early

therapeutic interventions represent effective strategies in order to treating IgE-mediated allergies.

The immunotherapy's triad can be, on this field, an effective tool. Moreover, due to the complexity of IgE-mediated disorders each component of triad: SCIT, SLIT or OIT could be considered as complementary or synergic therapy. Currently, the challenge is represented by the possibility to defeat the reluctance to encourage the implementation of early intervention in IgE-mediated allergic diseases with the goal of achieving either secondary prevention or long-lasting benefit through immunotherapy, which is the only antigen-specific immunomodulatory treatment routinely available. These effects are of particular relevance in pediatric population in order to impair the natural history of allergic diseases. While the ultimate goal is to extend OIT protocols to the general public as a standard medical therapy; so far it could be performed in specialized medical centers because of safety concerns. Adverse events are largely unpredictable and they can occur either during up-dosing regimen of OIT or during maintenance regimen at previously tolerated doses in the setting of exercise [16], viral illness and sub-optimally controlled asthma [17]. The possibility of achieving both desensitization and tolerance, in patients with IgE-mediated food allergy, represent the goals of OIT. Of note, the milestone, of allergen immunotherapy in any route or form, is its ability to induce long-term tolerance (i.e., clinical efficacy after its discontinuation).

Nowadays, in real life, it appears that tolerance to food(s), afterwards OIT, can be maintained without a mandatory daily consumption [18].

Therefore, promoting and evaluating post-desensitization strategies will be fruitful for the success of the active treatment of IgE-mediated food allergy. OIT portend progress for the next years with the aim of improving the quality of life of patients and their families.

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References

- Bousquet J, Lockey R, Mailling HJ. Allergen immunotherapy: therapeutic vaccines for allergic diseases. A WHO position paper. *J. Allergy Clin. Immunol.* 102 (4 Pt 1), 558–562 (1998).
- Cox L, Nelson H, Lockey R *et al.* Allergen immunotherapy: a practice parameter third update. *J. Allergy Clin. Immunol.* 127(1 Suppl.), S1–S55 (2011).
- Durham SR, Walker SM, Varga EM *et al.* Long-term clinical efficacy in grass pollen-immunotherapy. *N. Engl. J. Med.* 341(7), 468–475 (1999).
- Pajno GB, Barberio G., De Luca F *et al.* Prevention of new sensitizations in asthmatic children monosensitized to house dust mite by specific immunotherapy. A six-year follow-up study. *Clin. Exp. Allergy* 31(9), 1392–1397 (2001).
- Rudders SA, Banerij A, Vassallo MF *et al.* Trends in pediatric emergency department visit for food-induced anaphylaxis. *J. Allergy Clin. Immunol.* 126(2), 385–388 (2010).
- Prescott S, Allen KJ. Food allergy: riding the second wave of the allergic epidemic. *Pediatr. Allergy Immunol.* 22(2), 155–160 (2011).
- Nowak-Węgrzyn A, Sampson HA. Future therapies for food allergies *J. Allergy Clin. Immunol.* 127(3), 558–573 (2011).
- Passalacqua G, Landi M, Pajno GB. Oral Immunotherapy for cow's milk allergy. *Curr. Opin. Allergy Clin. Immunol.* 12(3), 271–277 (2012).

- 9 Sheikh SR, Burks AW. Recent advances in the diagnosis and therapy of peanut allergy. *Exp. Rev. Clin. Immunol.* 9(6), 551–560 (2013).
- 10 Fisher HR, du Toit G, Lack G. Specific oral tolerance induction in food allergic children: is oral desensitization more effective than avoidance?: A meta-analysis of published RCTs. *Arch. Dis. Child* 96(3), 259–264 (2011).
- 11 Brozek JL, Terracciano L, Hsu J *et al.* Oral Immunotherapy for IgE mediated cow's milk allergy: a systematic review and meta-analysis. *Clin. Exp. Allergy* 42(3), 363–374 (2012).
- 12 Sheikh A, Nurmatov U, Venderbosch I *et al.* Oral immunotherapy for the treatment of peanut allergy: systematic review of six case series studies. *Prim. Care Resp. J.* 21(1), 41–49 (2012).
- 13 Nurmatov U, Venderbosch I, Devereux G *et al.* Allergen-specific oral immunotherapy for peanut allergy. *Cochrane Database Syst. Rev.* 9, CD009014 (2012).
- 14 Yeung JP, Kloda LA, McDevitt J *et al.* Oral immunotherapy for peanut allergy. *Cochrane Database Syst. Rev.* 11, CD009542 (2012).
- 15 Nadeau KC, Schneider LC, Hoyte L *et al.* Rapid oral desensitization in combination with omalizumab therapy in patients with cow's milk allergy. *J. Allergy Clin. Immunol* 127(6), 1622–1624 (2011).
- 16 Caminiti L, Passalacqua G, Vita D *et al.* Food-exercise-induced anaphylaxis in a boy successfully desensitized to cow milk. *Allergy* 62(3), 335–336 (2007).
- 17 Narisety SD, Skripak JM, Steele P *et al.* Open-label maintenance after milk oral immunotherapy for IgE-mediated cow's milk allergy. *J. Allergy Clin. Immunol.* 124(3), 610–612 (2009).
- 18 Pajno GB, Caminiti L, Salzano G. *et al.* Comparison between two maintenance feeding regimens after successful cow's milk oral desensitization. *Pediatr. Allergy Immunol.* 24(4), 376–381 (2013).

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