Published in final edited form as:

Curr Opin Allergy Clin Immunol. 2012 June ; 12(3): 269–270. doi:10.1097/ACI.0b013e3283535a54.

Food allergy from an avoidance to a proactive approach: a bridge too far?

Julie Wang¹ and Alessandro Fiocchi²

¹Mount Sinai School of Medicine, New York, USA

²Melloni Paediatrics, Milan, Italy

It is an exciting time for food allergy. Not only is diagnosis is being revolutionized by using a molecular approach¹, strategies of new treatment approaches are being evaluated in many studies. Among them, studies on oral tolerance are bringing a new perspective to the management of patients with food allergies².

Immunotherapy is part of the routine management of respiratory allergies and has been utilized for over a century³. One area of allergy that has not yet seen immunotherapy become part of standard practice is food allergy. Although the first report of successful immunotherapy for food allergy was published in 1923, when it was alluded to as “an attempt to increase the resistance of the patient to the offending substance”⁴, no new reports aside from single case reports emerged until the 1990s when subcutaneous immunotherapy (SCIT) for peanut allergy was reported⁵. In this double-blind, placebo-controlled trial of rush immunotherapy in peanut allergic patients, significant improvements in threshold doses at double-blind, placebo-controlled food challenge (DBPCFC) was seen for 3 subjects following treatment. Unfortunately, the study was prematurely terminated due to a fatal adverse reaction. As a handful of other attempts at SCIT for food allergy were also fraught with unacceptably high rates of systemic allergic reactions⁶, the very notion of immunotherapy as a potential treatment strategy for food allergies was all but disregarded.

In the past decade, there has been renewed interest in immunotherapy as a treatment for food allergy. With new hypotheses of oral exposures to allergens as having a tolerogenic effect, oral administration of immunotherapy has garnered significant attention. An increasing number of studies have been published in Europe and the United States demonstrating the effects of oral and sublingual immunotherapy in modulating the immune response to the major allergens, including milk, egg, and peanut. Several well-designed studies, including randomization and placebo controls, have been reporting the effectiveness of immunotherapy for increasing tolerance levels to a variety of foods, suggesting that immunotherapy is a viable option for managing food allergies^{7,8,9}. In this issue, the studies on egg¹⁰ and milk¹¹ immunotherapy are reviewed. This has led to a paradigm shift in the field of food allergy, and strict avoidance may not be the only management strategy¹².

Partial avoidance, identified as a form of oral immunotherapy, could realize “a vastly altered

approach to food allergy management”, allowing “a substantial improvement to the quality of life of milk-allergic individuals”¹³. The brilliant review published here overviews the recent studies on the possibility of introducing baked milk and egg into the diet of otherwise allergic patients¹⁴.

Results from these published studies are starting to answer several questions underlying the process and mechanisms of immunotherapy. Some questions include clinical outcomes achieved by immunotherapy (desensitization versus tolerance), optimal routes of administration (oral, sublingual), allergen type (whole protein, heat denatured protein), as well as optimal protocol (dosing, duration of treatment).

While results thus far seem promising for achieving desensitization (and tolerance at least in a subset of individuals), immunotherapy is not without risks. Severe allergic reactions requiring treatment with epinephrine have been reported⁹, as well as some cases of eosinophilic esophagitis¹⁵. Even in the case of immunotherapy with heat denatured allergens, although a significant majority of milk and egg allergic individuals can tolerate the heat denatured forms, there is no quick, easy test to determine whether a child is or is not tolerant other than oral food challenge, which must be performed with caution in a observed setting as severe allergic reactions to extensively heated milk and egg have been reported^{16,17}.

At this juncture, we do not yet have enough information to decide whether the risks and benefits tip in favor of intervention or continued avoidance¹⁸. It is important to realize that these decisions will likely depend on a number of factors, such as age of the child, severity of past reactions, and food allergen in question. For foods such as milk and egg where the most common natural history is spontaneous outgrowth in childhood, the risks of therapeutic intervention might not outweigh the benefits, particularly in young children¹⁹. On the other hand, for persistent allergies such as peanut, intervening may be the only option for the majority of patients.

For these reasons, the current standard of care continues to entail strict avoidance of the food allergen(s) and immediate availability of emergency medications in case of accidental allergic reactions, as recommended by the recently published food allergy guidelines^{20,21,22}. These guidelines were developed based on systematic reviews and metaanalyses of the existing literature as well as expert opinions from recognized leaders in food allergy. The field of food allergy has the fortune for being one of the few fields of medicine with GRADEd guidelines. It is when uncertainty is high that the clinician needs a guide to orient the patient by patient, day to day practice of evidence-based medicine. The publication of these guidelines provides an important opportunity for us to review our knowledge base and standardize our practices to ensure that we are providing optimal care for our patients²³.

In addition to providing a concise summary of current evidence-based recommendations, the guidelines identify key gaps in knowledge and highlight areas of controversy in patient management that provides a framework for us to consider future research endeavors. While great strides have already been made in the understanding of the scope of the problem of

food allergy and of the mechanisms underlying the clinical symptoms, our practice will continue to evolve as there is still much more to be learned and discovered.

References

1. Fiocchi A, Nowak-Węgrzyn A. The fascinating world of molecular diagnosis in the management of food allergy: nondum matura est. *Curr Opin Allergy Clin Immunol*. 2011; 11:200–3. [PubMed: 21467924]
2. Nowak-Węgrzyn A, Fiocchi A. Is oral immunotherapy the cure for food allergies? *Curr Opin Allergy Clin Immunol*. 2010; 10:214–9. [PubMed: 20431369]
3. Passalacqua G, Canonica GW. Specific immunotherapy in asthma: efficacy and safety. *Clin Exp Allergy*. 2011; 41:1247–55. [PubMed: 21255159]
4. Unger L. Food desensitization in bronchial asthma. *Ill Med J*. 1923; 44:40–6.
5. Oppenheimer JJ, Nelson HS, Bock SA, Christensen F, Leung DYM. Treatment of peanut allergy with rush immunotherapy. *J Allergy Clin Immunol*. 1992; 90:256–62. [PubMed: 1500630]
6. Nelson HS, Lahr J, Rule R, Bock A, Leung D. Treatment of anaphylactic sensitivity to peanuts by immunotherapy with injections of aqueous peanut extract. *J Allergy Clin Immunol*. 1997; 99(6 Pt 1):744–51. [PubMed: 9215240]
7. Niggemann B, Staden U, Rolinck-Werninghaus C, Beyer K. Specific oral tolerance induction in food allergy. *Allergy*. 2006; 61:808–11. [PubMed: 16792577]
8. Staden U, Rolinck-Werninghaus C, Brewe F, Wahn U, Niggemann B, Beyer K. Specific oral tolerance induction in food allergy in children: efficacy and clinical patterns of reaction. *Allergy*. 2007; 62:1261–9. [PubMed: 17919140]
9. Longo G, Barbi E, Berti I, Meneghetti R, Pittalis A, Ronfani L, Ventura A. Specific oral tolerance induction in children with very severe cow's milk-induced reactions. *J Allergy Clin Immunol*. 2008; 121:343–7. [PubMed: 18158176]
10. Vickery BP. Egg oral immunotherapy. *Curr Opin Allergy Clin Immunol*. 2012 (add reference details – in this issue).
11. Passalacqua G, Landi M, Pajno GB. Oral immunotherapy for cow's milk allergy. *Curr Opin Allergy Clin Immunol*. 2012 (add reference details – in this issue).
12. Slomski A. Treatment rather than avoidance may be within reach for children with food allergies. *JAMA*. 2012; 307:345–6. [PubMed: 22274676]
13. Skripak JM. Mammalian milk allergy: avoidance strategies and oral desensitization. *Curr Opin Allergy Clin Immunol*. 2009; 9:259–64. [PubMed: 19365261]
14. Huang F, Nowak Węgrzyn A. Extensively heated milk and egg as oral immunotherapy. *Curr Opin Allergy Clin Immunol*. 2012 (add reference details – in this issue).
15. Sánchez-García S, Rodríguez Del, Río P, Escudero C, Martínez-Gómez MJ, Ibáñez MD. Possible eosinophilic esophagitis induced by milk oral immunotherapy. *J Allergy Clin Immunol*. 2012 Jan 9. e-pub ahead of print.
16. Nowak-Węgrzyn A, Bloom KA, Sicherer SH, Shreffler WG, Noone S, Wanich N, et al. Tolerance to extensively heated milk in children with cow's milk allergy. *J Allergy Clin Immunol*. 2008; 122:342–7. [PubMed: 18620743]
17. Lemon-Mulé H, Sampson HA, Sicherer SH, Shreffler WG, Noone S, Nowak-Węgrzyn A. Immunologic changes in children with egg allergy ingesting extensively heated egg. *J Allergy Clin Immunol*. 2008; 122:977–983. e1. [PubMed: 18851876]
18. Prescott SL, Bouygue GR, Videky D, Fiocchi A. Avoidance or exposure to foods in prevention and treatment of food allergy? *Curr Opin Allergy Clin Immunol*. 2010; 10:258–66. [PubMed: 20431373]
19. Brozek JL, Terracciano L, Hsu J, Kreis J, Compalati E, Santesso N, Fiocchi A, Schünemann HS. Oral immunotherapy for IgE-mediated cow's milk allergy: a systematic review and meta-analysis. *Clin Experim Allergy*. 2012 in press. 10.1111/j.1365-2222.2011.03948.x
20. Fiocchi A, Brozek J, Schünemann H, Bahna SL, von Berg A, Beyer K, et al. World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy

(DRACMA) Guidelines. *Pediatr Allergy Immunol*. 2010 Jul; 21(Suppl 21):1–125. [PubMed: 20618740]

21. Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol*. 2010 Dec; 126(6 Suppl):S1–58. [PubMed: 21134576]
22. Centre for Clinical Practice at NICE (UK). Diagnosis and assessment of food allergy in children and young people in primary care and community settings. 2011. <http://guidance.nice.org.uk/CG116/Guidance>
23. Venter C, Arshad SH. Guideline Fever: An overview of DRACMA, US NIAID and UK NICE guidelines. *Curr Opin Allergy Clin Immunol*. 2012 (add reference details – in this issue).