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Title: Oral immunotherapy for food allergy: what's age got to do with it?

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Keywords:

Adult food allergy, oral immunotherapy, food allergy therapeutics, anaphylaxis

Word count: 991

References: 10

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the [Version of Record](https://doi.org/10.1111/all.15623). Please cite this article as doi: [10.1111/all.15623](https://doi.org/10.1111/all.15623)

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Conflicts of Interest:

JU reports research support/grants from Novartis, Regeneron, ALK Abello, DBV Technologies, CIHR, SickKids Food Allergy and Anaphylaxis Program, and fees from Pfizer, ALK Abello, Bausch Health, Kaleo, Astra Zeneca, and Food Allergy Canada, all outside the submitted work. TE reports recent/current positions as local PI for company sponsored trials by DBV Technologies, Greer Stallergens and sub-investigator for Regeneron and ALK Abello. He is co-Investigator or scientific lead in three investigator initiated oral immunotherapy trials supported by the SickKids Food Allergy and Anaphylaxis Program and serves as associate editor for Allergy. He/his lab received unconditional/kind contributions from Macro Array Diagnostics and ALK Abello. He holds advisory board roles for ALK Abello, Aimmune, VAMED and Nutricia/Danone and received lecture fees from ALK, Nutricia/Danone, ThermoFisher, Aimmune and Novartis. NC has no conflicts of interests to declare.

Oral food immunotherapy: what's age got to do with it?

Oral immunotherapy (OIT) is a treatment for IgE-mediated food allergy. However, evidence for the safety and efficacy of OIT has primarily been established for children with limited data in adults.² Recently in *Allergy*, Epstein-Rigbi et al.,³ present data on the clinical course, safety and efficacy of OIT in the largest adult cohort published to date.

The authors performed a retrospective analysis of 96 adults who underwent OIT to cow's milk, peanut, tree nuts, sesame, or egg over a 10-year period in a clinical setting. Outcomes in adults (≥ 17 years old, median 22.3 (IQR: 18.8–26.6)) were compared to a cohort of 1299 children aged 4–10 years (median 6.3, (IQR: 5.1–8.2)) and 309 adolescents aged 11–16 years of age (median 12.8, (IQR: 11.6–14.2)). All patients were managed with the same protocols at a single center.

Patients were considered fully desensitized if they achieved the following food protein maintenance target doses: milk: 7200mg, peanut: 3000mg, tree nuts: 3900mg, sesame: 4000mg, and egg: 6000 mg. For partial desensitization patients had to achieve at least the following food protein doses, but less than the full desensitization target: milk: 180mg, peanut: 300mg, tree nuts: 300mg, sesame: 240mg, and egg: 1500mg. These definitions were author defined and applied across all ages. An internet-based reporting system tracked doses and reactions.

The rate of full desensitization was significantly lower in adults (61.5%) compared to children (73.4%), and adolescents (69.6%). An additional 18.8% of adults were partially desensitized.

There was no difference in the rates of partial desensitization between age groups. Importantly, after controlling for factors associated with treatment failure within the study, adult age itself was no longer statistically significantly predictive of treatment failure. After adjustment, milk OIT, history of asthma, pre-OIT epinephrine use, skin prick wheal size, and single highest

tolerated dose prior to OIT remained significantly associated with treatment failure. In other words, the predictors of treatment failure are similar across all ages and just more common in older patients.

The difference in desensitization rates between adults and non-adults was driven by milk OIT. For non-milk OIT, there were no differences in rates of treatment failure between age groups (9.3% in adults, comparable to children and adolescents). The most common food allergens in adults in order of decreasing prevalence are shellfish, milk, peanut, tree nut, fish, egg, wheat, soy, and sesame.⁴ Therefore, while the reason is unclear, the difficulty observed with milk OIT is relevant to the adult population, as is the lack of shellfish OIT in this study. The similar success in adults as compared to children with foods other than milk is consistent with results from a meta-analysis of peanut OIT which concluded that OIT effectively achieves a modest degree of desensitisation independent of age.⁵

Epstein-Rigbi et al.,³ aimed for OIT to allow free consumption of the food. However, it is unclear whether free consumption of the food and expansion of the diet is what adult patients want. Little is known about patients' perspective, needs, and quality of life with regards to OIT, and even less among adults. One survey of parents of children 1-20 years old undergoing OIT demonstrated that for most families the main motivation was to reduce the risk of a fatal reaction rather than to incorporate the allergenic food into the diet. The partial desensitization doses (or lower) may align with food allergy management goals of some adults. Furthermore, these lower doses may be easier to achieve.⁷

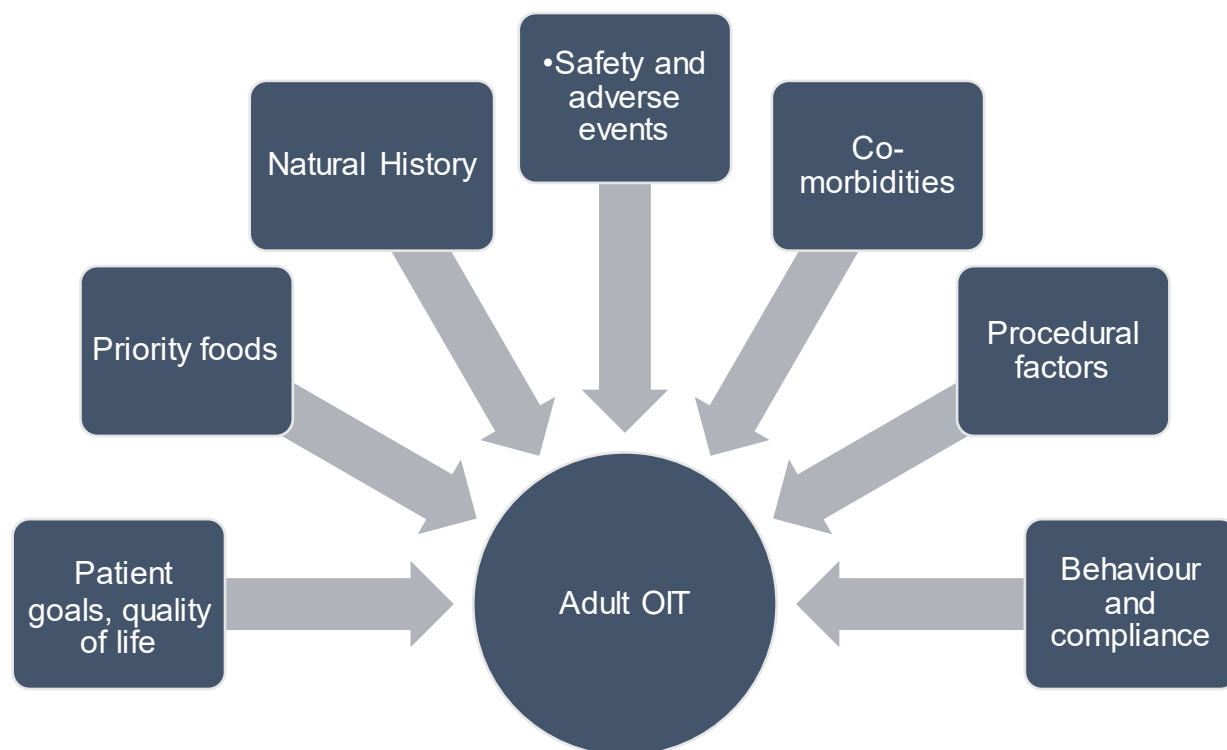
Although most adults could be desensitized, the adverse reaction rate was considerably higher in adults versus children. Almost half the adults used epinephrine during the clinic up-dosing visits (versus 15.9% of children and 26.5% of adolescents). The reactions at home were also relatively

frequent and severe. Epinephrine injection was used by 22.9% adults at home as compared to 10.5% or children and 14.2% of adolescents. Future studies should consider strategies such as lower maintenance doses, slower up dosing protocols, or adjunctive therapies such as biologics to mitigate the side effects of OIT in adults.^{2,7}

When considering offering OIT to an adult population, in addition to the patient's goals and expectations, consideration may be given to the natural history of adult food allergy. In children, there can be debate over whether to wait until older ages to start OIT given that some children on avoidance outgrow their food allergy naturally, but this is likely less relevant to adolescents and adults. Childhood-onset food allergy in adults is very likely to be persistent.⁸ Furthermore, these allergies can be severe. Approximately 50% of adults with food allergy (excluding oral allergy syndrome) reported at least one severe reaction.⁴ Additionally, young adults, especially in the second and third decades of life, are at increased risk for fatal anaphylaxis due to food.⁹ Some of this risk may be behavioural and some may be physiologic.⁹ For these reasons, adults may especially benefit from food allergy treatment with OIT, even if the adverse events and treatment failure rate may be higher. On the contrary, behavioural and system risk factors may make OIT dosing compliance and self-management in young adults and adults challenging. Gupta et al.⁴ reported epinephrine auto-injector prescriptions are low among adults with food allergies. Begin et al.¹⁰ summarized that although there is limited data, OIT in adults has consistently shown the possibility of desensitization and based on the principles of equity and of proportionality between risks and benefits it can be considered in this age group. Considerations for counseling adults for OIT are summarized in Figure 1 and broad considerations by age in Table 1.

In summary, Epstein-Rigbi et al.³ confirm that OIT can achieve desensitization in adults at similar rates to children and adolescents for many foods other than milk.. Despite comparable

efficacy, adults experienced frequent and severe allergic reactions both in clinic upon up-dosing and at home. This study provides further insight into the risks and benefits of OIT and highlights the need to reduce adverse events and to study patient-centered outcomes in adolescents and adult patients with food allergy.



- **Figure 1. Counseling adult patients for food oral immunotherapy (OIT).** Patient goals and quality specific measures for food allergy treatments have not been well studied. Milk is the second most common food allergy in adults and may be higher risk than in children. Food allergies may be more persistent and severe compared to children. Adults may also experience more adverse reactions than children during OIT. Comorbidities such as asthma and eliciting dose may further guide risk/benefit assessment. Lower maintenance doses, increased time between up-dosing, or use of biologicals may reduce adverse events. Attention to risk-taking behaviours and support/monitoring of compliance is essential.

Table 1. Age-based considerations for food oral immunotherapy (OIT).

Factors to Consider	Favours Younger	Favours Older	Notes
Food Allergy Factors			
Persistence of allergy		More persistent	
Severity of allergy		More severe	
OIT Treatment Factors			
Adverse reactions to OIT	Less adverse reactions		
Medical comorbidities	Less medical comorbidities		
Compliance	Higher compliance		Parental supervision
Quality of life			Limited data

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