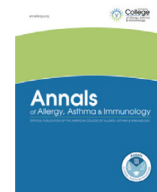




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Life in the FAST lane



Oral immunotherapy (OIT) for the treatment of food allergy represents a potential groundbreaking breakthrough in the management of food allergy.¹ The standard dogma of food allergy has been that this is a disease without treatment, other than having a variable likelihood of outgrowing the allergy to the selected foods.² Since 2006, there has been a steady increase in federally funded and other academic investigations of OIT to various foods that have been dominated mainly by studies of peanut, milk, and egg. There has been an overwhelmingly consistent conclusion of these published reports—OIT is safe and effective. However, despite these conclusions, the other key conclusion of these studies has consistently been “OIT is not yet ready for use in routine clinical practice.”^{1–4}

Within this same timeframe, there has been a parallel emergence of early adaptors offering OIT to various foods as a clinical practice.^{5–7} The enthusiasm and appropriateness of this service has been polarized by the type of lens through which the person might be viewing the issue. Prominent academics have tended to view this as inappropriate, calling for equipoise pending more definitive proof from pivotal studies that demonstrate conclusive safety and efficacy.⁴ Others have viewed these previously (and rather confidently) published conclusions as a green light and seized an entrepreneurial opportunity to become earlier adaptors who began to offer what was deemed to be an in-demand, popular, and exceptionally helpful service. Currently, it is estimated that 100 to 200 allergists offer this service, and it is likely this number will continue to increase.⁸ Regardless of the question of equipoise, the “cat is out of the bag” and OIT as a clinical service is no longer some rogue or fringe practice variant at this point.

Some might question why resistance to this practice remains. Detractors have cited that such “off-label” practices are done without consistent protocols, methods, product choices, experience in food allergy, safety safeguards, and with questionable choice of patients.^{1,4}

Proponents have consistently stated this is not the case.⁷ However, there have been few data detailing the off-label practice experience. Studies by Factor et al⁶ and Wasserman et al⁷ have offered glimpses into the experience for office-based peanut OIT, which differed methodologically from many sponsored trials but, importantly, did not denote any major differences in safety. In response to a request for more data detailing their experiences, many prominent private groups offering OIT have repeatedly stated that they are offering a clinical service and thus are not under any obligation to study their outcomes or report data and argue this is a justified opinion, given that few of us would feel obligated to report outcomes on services we deem routine.⁹

In this issue, Wasserman et al⁷ report on consensus findings from a recent meeting of a large collective of private practice allergists providing clinical OIT, titled the FAST perspective. This was a voluntarily attended conference and had representation from 68 practices and approximately 2,280 patients treated, a staggering number that is more than double the number of patients treated in any federally or commercially sponsored trial in aggregate. Although their report is not an outcome-toting piece, it is a much-welcomed glimpse into how these providers operationalize OIT as a service. Looking closely, their report is reassuring that off-label OIT is not a disorganized fly-by-night operation. These providers report using published protocols and dosing escalations, have prespecified safety standards and operating procedures, and have a process regarding who should be offered therapy and when it should be discontinued. Like any conscientious provider, this group is concerned with safety, including issues such as cofactors that might lower the threshold for reactions that require dose adjustment and ensuring that only those with experience and comfort with performing food allergy and managing food-induced anaphylaxis are engaging in OIT. There is appropriate consideration of shared decision making, setting goals of therapy, and carefully choosing the form of the food to be used. There is consensus on serologic monitoring of these patients and on understanding the necessity of a proper office set-up to handle the patient volume and potential complications. There is even description of an attempt for the collaborative effort to establish a registry to track outcomes. For any emerging US Food and Drug Administration (FDA)-approved treatments to succeed, allergists have to be able to provide what was studied in a rigorously controlled clinical trial as a clinical service. This group is describing a real-world translation of such research. More importantly, they have done so despite many years of chagrin and disapproval from a number of prominent critics.

Although not part of the conference proceedings, it is important to acknowledge that, to date, there are no reports of fatalities or catastrophic nonfatal reactions from such off-label practices.^{1,6,7} That is in

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contrast to the recent experience of OIT being conducted at Japanese academic centers, interestingly.¹⁰ Thankfully, there are no such reports from US academic centers.¹ It is understandable that there was initial resistance and calls for equipoise some 8 to 10 years ago when OIT was still new and the experience was not robustly proved. Overall, it demonstrates that practicing allergists were reading the literature, paying attention, and taking their cues accordingly. One could further question whether the initiation of pharma-based commercialization of OIT as early as 2012 was any more or less appropriate than office-based OIT based on the evidence at the time. However, that decision ultimately might have been the most crucial one in moving OIT forward.¹¹

Taking a broader view, perhaps we are applying greater scrutiny of OIT compared with the initial aero-allergy studies by Noon¹² and Freeman¹³ or even more recently by Fackler and Loveless¹⁴ and hymenoptera immunotherapy. Much has changed in the past 50 to 100 years regarding clinical research. This is well illustrated in the most recent immunotherapy to be approved—sublingual immunotherapy. The regulatory trials for sublingual immunotherapy were very well designed with regard to number of subjects and blinding. As noted by Nelson¹⁵ in his recent rostrum, the money needed to perform studies in allergy is staggering. With that said, it is important that when an intervention such as OIT is undertaken, patients and providers should feel comfortable that safety and efficacy have been maximized.^{1,5} For OIT to foods, studies in peanut have reached this threshold, although with other allergens this is potentially more questionable.¹ However, given the current funding environment, why not look more closely at the office-based experience to enrich the body of knowledge, which could result in time and cost savings in funding?

The allergy community is small, and past divisiveness over OIT has not only made it smaller but also limited the potential for what we could be learning from one another. Some knowledge is going to have to come outside a clinical trial. Likewise, not everything from a clinical trial generalizes to the real world. There needs to be a compromise, and in the future, as a field, there is a need to handle such issues with more cooperation. We are in an exciting time when academicians and practicing clinicians can work together to help a community of patients with food allergy who have a better option now—therapy. This isn't about us, it's about them. Before continuing to criticize one another, we need to consider how that would benefit the patient, especially given the lack of convincing data that the practice is unsafe. In the past, these patients would have no other option but to avoid the food to which they were allergic to and rely on self-injectable epinephrine when mistakes were made, all the while hoping that they could lose their allergy.

So, what does our future hold? It is quite likely that peanut OIT will soon be approved by the FDA.¹¹ However, approval is not the final frontier, and many questions will still need to be answered. Most of these are operational—the office set-up, optimal candidate selection, ideal shared decision making, handling nonadherence and/or treatment failure, optimal dosing and timing strategies, monitoring and duration of therapy, and uncertain long-term outcomes including when (or if) it might be appropriate for patients to potentially discontinue their prior avoidance maneuvers in daily living. More crucially, there is still no *Current Procedural Terminology* code for OIT, which, in an ironic twist, cannot occur without evidence of its use in practice.¹ In addition, we will have to determine where to go with OIT to other foods when there is not an FDA-approved option. It is important to note that the published experience for federally sponsored trials with milk is different (and less safe and successful) than with peanut, although it remains unclear whether similar challenges have been encountered with private practice milk (or other foods) OIT.¹⁰ Perhaps the past does not have to be a prologue with respect to how

these other foods are handled, and the practice experience can supply much needed information about the safety, effectiveness, and patient demand for OIT to these other allergens.

All these questions are important and need to be resolved before we can really adapt this form of therapy in the real world. There will be forthcoming guidelines on the office-based practice of OIT. This has been unanimously recognized by the American Academy of Allergy, Asthma, and Immunology, American College of Allergy, Asthma, and Immunology, and Canadian Society of Allergy and Clinical Immunology as a crucial need for the field, and there is an attempt underway to jointly approach this from a North American perspective. The FAST perspective is certainly one that can be incorporated into these broader guidelines, and it can play an important role in informing the greater allergy community as to how to operate. In considering the next steps with OIT, we would implore the field to focus on the bigger picture of a consensus on safe and effective practices and ensuring that some consistency in set-up, monitoring, and operations exists. This is paramount for the success of OIT. We have achieved this as a field with aqueous inhalant and venom immunotherapy, even with variation in brand, titration, and concentration of the extract. There is no reason to believe that we cannot achieve the same for OIT.

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