



Editorial

Looking into the seeds of time

Are home-based OIT programs the shape of things to come for selected patients?



Peanut allergy affects 1.4% to 4.5% of children and fewer than 25% are anticipated to outgrow peanut allergy naturally, with many sufferers having severe reactions.^{1–3} Although no approved therapy is currently available, 2 products are in phase III trials, and multiple centers and offices already engage in off-label clinical oral immunotherapy (OIT) programs.⁴ Such for-profit programs boast good success but, because of their “unregulated” status, data are sparse (or possibly not even collected), making it difficult to compare such programs with formally regulated and Good Clinical Practices-compliant clinical trials for OIT, despite it already being evident that more patients have undergone “off-label” OIT than have completed formal clinical trials.^{5,6} Academic circles have long been critical of “renegades” pursuing off-label IT and have raised the question of equipoise in the matter pending further data supporting the safety and efficacy of OIT.^{7,8} It is important to not dismiss the off-label experience, but in the absence of data, this makes for rife debate and risks each camp ignoring the strengths and highlighting the weaknesses of the other’s philosophy and practice.^{5,8} In this case, it could be argued that the field and the patients potentially lose.

Although some academics are quick to dismiss the off-label OIT experience, such approaches could be the combination punch of a future combined treatment routine that maximizes the in-office and out-of-office potential of IT (whether oral, epicutaneous, or other routes) as a successful therapy for children whose allergy is not primarily prevented by early dietary introduction or other selected preventive programs.^{5,7,8} The question of how to operationalize the emerging therapies has become prominent and, given the paucity of even intermediate-term data on the efficacy or efficaciousness of OIT, it would be pretentious and unscientific to dismiss any potential strategic variation for OIT without at least rigorous dialogue.⁹

Variations currently exist between the low-dose commercial OIT strategy (300 mg maintenance, >1,000-mg cumulative tolerance end

point) and off-label strategies (which range from low to high dose, with personalized and unspecified end points), and it is unclear where the line should be drawn for further personalizing end points in patients who might demonstrate higher levels of desensitization.⁸ Moreover, this argument can extend to discussions of whether such personalization should or must occur within the context of in-office observation. Because there is no clear guidance in how one should administer and monitor office-based IT, such considerations are very relevant going forward.

Arkwright et al¹⁰ detail an interesting case series of 6 children with nonanaphylactic reaction histories who then demonstrated high threshold responses at peanut oral food challenge (reacted to the challenge but at a cumulative level >200 mg of peanut protein) and underwent an at-home OIT program on a personalized ladder starting from 25% of their oral food challenge threshold built up to a maximal goal of 15 peanut kernels at least 3 times a week (~2 g of protein). These patients were seen by their allergy provider every 3 months and instructed to contact their provider for any interim reactions and not to attempt any home dosing if more than 4 weeks of therapy had been missed. Caregivers were key stakeholders in this, because the decision to proceed with this program (and how to advance) was all tailored to family comfort and preference. All 6 successfully progressed over the ensuing 24 months of observation to tolerate up to 6 peanuts thrice weekly, without any significant reactions or need for OIT-related medical care.¹⁰

Some might consider this to be unethical human subject research, occurring without informed consent or oversight, and (gasp) allowing the parents to do this outside our guarded supervision. Others might look at this as the shape of things to come, a realistic and pragmatic extension of OIT that currently does not fit all cases of peanut allergy. This is not the first report of such a program, because Garvey et al¹¹ also reported on a similar and slightly larger cohort, but with comparable success, despite an even lower intensity of support.

Although such home dosing is a truly unsafe and a general “bad idea” in aqueous IT, home dosing is the hallmark of OIT, and the routineness of its use in OIT lends a potential strategic advantage to other families who eventually might wish to push the envelope after successful low- or lower-dose OIT programs.

Although data from the STOP II trial very clearly show that at least some parents have a distinct preference to maintain a dosing level that will buffer against an accidental exposure,¹² such preferences can shift over time as a child successfully completes a low-dose OIT program and the family decides they might want something more. Is it ethical or feasible to tell a family they have reached the limit approved by the US Food and Drug Administration and leave it to them to potentially embark on their own home up-dosing

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program without allergist supervision? What these 2 European studies show is that allergists can identify patients with peanut allergy who could be advanced to higher levels of desensitization (and possibly full tolerance) outside the office.^{10,11} It is important to recognize that such patients have always existed and to use these data for further hypothesis-generating controlled studies to enhance the practicality of this as a future strategy that we might want to incorporate into or instead of drug-grade OIT clinical practice.

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