

Preface

Leaps and Bounds in Allergen Immunotherapy



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Editors

It has been almost one hundred ten years since allergen immunotherapy (AIT) was first recognized as a treatment for allergic diseases by the English physicians, Noon and Freeman. However, it was applied thousands of years earlier. Snake handlers learned that if they swam in snake-infested waters, they would acquire immunity to the cobra's venom.¹ This was likely the first use of oral immunotherapy (OIT) because the snake-infested waters contained venom, and the snake handlers swallowed it as they swam.

This issue begins with an outstanding review by Komlósi and colleagues² of the mechanisms of subcutaneous and sublingual AIT. It was not until the last 3 decades that we began to understand the mechanisms of AIT. Although I, Linda S. Cox, have lectured on this subject and consider myself relatively up-to-date, every time I read a "review" of this subject, there have been 4 or 5 new regulatory cells, cytokine, or CD whatever. So, I encourage you to spend time reading and digesting this article. This article is followed by an article on novel vaccination strategies in AIT by Komlósi and colleagues³ and Sánchez-Borges' article⁴ on reducing risk with subcutaneous immunotherapy (SCIT). Not only does Sánchez-Borges' article provide guidance on clinical practice interventions that can reduce mortality and morbidity associated with SCIT but also it presents the newly revised World Allergy Organization System for classifying systemic allergic reactions due to any causative agent.⁵ The article by Smith and Freeman⁶ provides a truly "up-to-date" discussion of sublingual immunotherapy (SLIT), which covers venom large local reactions, atopic dermatitis, and food and latex allergy. Golden's article⁷ addresses many of the "unanswered" questions regarding venom immunotherapy, such as when is it really safe to stop, when can I tell a patient to stop carrying an epinephrine autoinjector, as well as the guidelines in the newest Venom Allergic Practice Parameter.⁸ The next article is

devoted to the cost-effectiveness of AIT compared with that of pharmacotherapy for the treatment of allergic rhinitis and asthma by Cox and colleagues.⁹

The field of food AIT is undergoing a dramatic development. The first published report of the allergen-specific immunotherapy dates back to 1908, when Schofield described successful oral desensitization to raw egg in a teenage boy with anaphylactic egg allergy.¹⁰ The renewed interest in food immunotherapy emerged in the first decade of the twenty-first century in response to the growing global burden of food allergy. Following the ground-breaking investigator-initiated studies that were limited in size, we have entered a stage of international clinical trials and pharmaceutical product development. Our understanding of the mechanisms of immunomodulation is also improved by Smeekens and Kulis.¹¹ OIT remains at the forefront of this progress, with the first biologic drug (AR101, Palforzia™) being currently reviewed by the Food and Drug Administration. AR101 has shown promising efficacy in desensitizing peanut-allergic children to a minimum 300-mg peanut protein (equivalent to 1 peanut kernel) following 12 months of treatment by Tang and colleagues.¹² However, concerns remain regarding the treatment-emergent adverse events (AEs), uncertainty regarding permanent tolerance development, the need for long-term treatment, and the lack of long-term safety data by Vázquez-Cortés and colleagues.¹³ SLIT has not been developed commercially, although recent long-term follow-up data from peanut SLIT demonstrate a favorable risk-to-benefit ratio and suggest that SLIT may lead to tolerance (sustained unresponsiveness [SU]) in a subset of treated patients by Waldron and Kim.¹⁴ These allergen-specific strategies pose a significant burden of long-term daily maintenance dosing and raise concerns about real-world adherence. Epicutaneous patch immunotherapy (EPIT) with Viaskin Peanut™ 250 is another commercial product evaluated in a phase 3 clinical trial in children with peanut allergy. Peanut EPIT offers superior safety compared with OIT with AEs mostly limited to local skin reactions at the site of patch application, but lower efficacy. OIT with probiotic and other adjuvants is being investigated to address the safety and efficacy concerns by Nicolaides and colleagues.¹⁵ Alternative strategies involving omalizumab and dupilumab as monotherapies or in combination with allergen-specific therapies are being investigated as means of enhancing achievement of SU as well as improving safety and adherence by Albuhairi and Rachid.¹⁶ As the OIT for other and multiple foods remains the subject of investigator-initiated studies, there is an urgent need to harmonize the international efforts regarding protocol design, efficacy endpoints, and safety reporting. Finally, it is important to determine the risk reduction afforded by therapies that induce desensitization but not SU by Remington and Baumert.¹⁷

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