

A centennial anniversary for allergen immunotherapy: pioneering immunomodulation for atopy and beyond

I am extremely pleased and excited to introduce this issue of the *Annals*, which is designed to commemorate the 100th anniversary of the publication of the initial report of the effectiveness of allergen immunotherapy (AIT).¹ As you will read in articles written by outstanding authors, the century has been marked by both changes and consistencies in the thinking about how to perform AIT (eg, indications, dosing, duration, and patient selection) and how it works. What you will also appreciate is the extraordinary way in which the clinical design for this therapy has remained fundamentally consistent throughout the century. Although methods for testing and dosing may have evolved, the original concept remains largely intact. Allergists-immunologists understood and used the clinical principles of what became known as immune tolerance long before the concept was formally hypothesized by basic immunology researchers. In addition, given the consistent demonstrated value for AIT for atopic patients in multiple clinical settings, the principles and practices of AIT offer a model for future immunomodulatory therapies for a variety of inflammatory diseases.

The content of this issue was formed in a collaborative fashion with a special ad hoc College committee led by Dr Ira Finegold and our *Annals* editorial team. Dr Finegold and colleagues set about to bring together a comprehensive review of how AIT has been practiced during the past century,² citing the relevant literature of the day and sharing insight into the thinking of brilliant practitioners from Noon and Freeman as it related to the treatment of hay fever (now recognized as allergic rhinitis) to multiple investigators who are publishing studies that support the notion that AIT can, in the right population, delay or prevent the progression of rhinitis to allergic asthma. This holds great promise for modifying the incidence and prevalence of asthma in our society—no small feat from what began as a treatment for a disease described as lasting only 3 months of the year (grass season).

Other articles appearing for your enjoyment and education include a history of the changes in thinking regarding the mechanisms behind how AIT works written by Dr Mitchell Grayson.³ It is amazing to reflect on how the thinking has evolved as our understanding of immunology has progressed during the past century. It is important to remember that when Noon and later Freeman⁴ published their original articles on AIT in the early 20th century, no one had any idea about the structure of antibodies, B cells, or T cells or even that antigens have a protein base. This speaks to the insightfulness of those such as Noon and Freeman who developed an effective

therapy based on a sound clinical (albeit perhaps a bit naive from a mechanism perspective) rationale. There are excellent articles in this issue that describe cutting edge issues in AIT of all sorts, including better biochemical definitions of antigens, results with oral allergen therapy for foods and molds, and new methods and results of AIT in various settings, such as asthma and venom sensitivity.

The issue concludes with a perspective written by Dr Finegold and Dr John Oppenheimer that posits their opinion on the future of AIT.⁵ If their vision is accurate, we hope to see the effectiveness of AIT expand to other allergens, including foods, drugs, and more molds in patients with other allergic conditions, such as skin allergies and perhaps even anaphylaxis. The methods for AIT may continue to evolve and become even more safe and effective. This may result from AIT being combined with other immunomodulatory modalities and/or other routes of desensitization, such as enteral, as seen with sublingual immunotherapy.

Finally, as a translational clinical immunologist who has been interested in the mechanisms of immune modulation for more than 30 years, I can envision a future where the immunoregulatory principles of desensitization accomplished by AIT are applied to other clinical states, such as autoimmune, neurodegenerative, metabolic, and even cardiovascular diseases characterized by uncontrolled inflammation. Will the day come when appropriate patients can get an “allergy” shot for their coronary artery disease or rheumatoid arthritis? I am excited about the possibilities that the next century will witness, and I expect principles from allergy and clinical immunology to be at the forefront of these developments. Thanks, Drs Noon and Freeman, for helping an untold number of allergy patients with your vision and for providing the basis for helping countless more in the future—the journey has just begun.

GAILEN D. MARSHALL JR, MD, PhD
Editor-in-Chief

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