

Preface

Emerging Therapies for Allergic Diseases



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Guest Editors

Allergic diseases including asthma, allergic rhinitis, atopic dermatitis, and food allergy, affect millions of adults and children. These diseases are responsible for lost days from school and work, decreased quality of life, and the spending of billions of dollars on hospitalizations and visits to emergency rooms and doctors' offices. This issue of *Immunology and Allergy Clinics of North America* focuses on emerging therapies for these allergic diseases. Many candidates that are in clinical trials or under experimental therapeutic consideration could replace the standard treatment with corticosteroids, antihistamines, and antileukotrienes. This issue is divided into two sections: therapies that are in clinical trials and therapies that are more experimental.

The first 10 articles deal with therapies that are in clinical trials, and the last two articles are on emergent therapies. Drs. Jaine Brownell and Thomas Casale describe the use of anti-IgE therapy for asthma, allergic rhinitis, and food allergies in adults and adolescents. They focus on the biology of IgE and the two therapies that have been studied in clinical trials: omalizumab, which has been approved by the Food and Drug Administration, and TMX 901, which proved to be efficacious in a double-blind, randomized, placebo-controlled trial involving patients with a history of peanut allergy. Omalizumab has been studied extensively in the treatment of asthma and allergic rhinitis and is available in the United States.

Drs. Peter S. Creticos, Yi-Shing Chen, and John Schroeder describe a novel allergen vaccine with immunostimulatory DNA coupled to a ragweed allergen for

use in patients with allergic rhinitis. This experimental vaccine is less allergenic but more immunogenic than licensed ragweed extract, and clinical trials have demonstrated its safety. This therapy has the potential to significantly improve immunotherapy for allergic disease.

Drs. K. Suresh Babu, Donna Davies, and Stephen Holgate elegantly describe the role of tumor necrosis factor- α (TNF- α) in asthma. After a thorough description of the actions, cellular sources, and immunobiology of TNF- α , including its importance in allergen challenge models of asthma, there is a complete discussion of its use in clinical trials in the treatment of rheumatoid arthritis, Crohn's disease, Behçet's disease, and sarcoidosis. They describe the preliminary trial of using a TNF- α strategy as a therapeutic modality in asthma. Although TNF- α is more of a T helper cell type 1 cytokine, they propose that it could be used in some forms of chronic asthma in which neutrophils can be the primary infiltrating cell. TNF- α blockade in this instance would be beneficial to reduce cellular trafficking and neutrophil chemotaxis and activation.

Dr. John Stankey sophisticatedly discusses the state-of-the-art of anti-interleukin 4 (IL-4) therapy. He gives a superb description of IL-4 and its signaling mechanism and describes in detail four strategies for therapeutics, three of which have failed and one, a human anti-IL-4 receptor antibody, which is still in clinical trials.

Dr. Bruce Bochner has an erudite discussion of the use of adhesion molecules as therapeutics. He describes pharmacologic targets and approaches for adhesion-molecule antagonism and a thorough discussion of cytokine antagonists, antisense oligonucleotide technology, soluble adhesion molecules, glycomimetics, small molecule antagonists, and monoclonal antibodies.

Topical treatment of atopic dermatitis is discussed fluently by Dr. Mark Boguniewicz. He offers a thorough review of the clinical disease and treatment regimens for patients and care providers. He also emphasizes the emerging new therapies for this skin disease, including the calcineurin inhibitors. There is a discussion of potentially combining calcineurin inhibitors as early intervention therapy and topical corticosteroids as rescue therapy.

Anti-IL-5 therapy for allergic diseases and hypereosinophilic syndrome is discussed elegantly by Drs. A. Barry Kay and Amy D. Klion. Although anti-IL-5 may not be the magic bullet for the treatment of asthma because of the inability to ablate tissue eosinophilia, it might be useful for decreasing levels of extracellular matrix proteins in the airway reticular basement membrane. A few small but promising studies have used anti-IL-5 in the treatment of hypereosinophilic syndrome.

Drs. Alison L. Miller and Nicholas W. Lukacs offer a thorough review of chemokine receptors that in the past have been used as targets for treating asthma, with an emphasis on potentially new targets such as C-C chemokine receptor 6 and cystein-X-cystein chemokine receptor 4.

Drs. Anna Nowak-Wegrzyn and Hugh Sampson elucidate novel and potentially exciting therapies for the treatment of food allergies. Their comprehensive

discussion includes treatments such as anti-IgE antibodies, food allergy vaccines, Chinese medical herbal preparations, and probiotics.

Drs. Gergio Canonica, Enrico Compalati, Fedrica Fumagalli, and Giovanni Passalacqua give an excellent comparison of conventional subcutaneous immunotherapy, which has been in existence for the treatment of allergic disease for a century, and other routes of immunotherapy. Sublingual immunotherapy has been in existence for only 15 years, and most of the studies on this treatment have been performed to determine its safety and efficacy. This sublingual route of administration of immunotherapy has replaced oral immunotherapy. There is a thorough discussion of the future direction that sublingual oral immunotherapy research must take to increase the translation to use in clinical practice.

The final two articles in this issue describe experimental therapeutics. Although proof of principal has been demonstrated for these treatments, they have yet to be robustly tested in clinical trials. Drs. Verena Niederberger and Rudolf Valenta expertly compare four candidate molecules for immunotherapy: unmodified, recombinant allergens, T-cell peptides, B-cell peptides, and genetically modified recombinant allergens. The potentially most exciting candidate in this group is the genetically modified allergen. One double-blind, placebo-controlled, multicenter immunotherapy trial with recombinant Bet v 1 fragments is in press. Future clinical trials will determine the efficacy of this approach as compared with the efficacy of conventional immunotherapy.

The second discussion of experimental therapeutics occurs in the article by Drs. Marco Kalliomäki and Erika Isolauri. They describe the possibility of using probiotics, which are largely microbial food ingredients that beneficially affect host health. They most often belong to the genera *Bifidobacterium* or *Lactobacillus*. Preliminary trials using probiotics as an antiallergic therapy in children with atopic eczema seem promising. Much research into the use of these molecules is still to be done before they can be used in the clinic.

We hope you find this issue stimulating. It was a pleasure to edit these exciting articles and think about the future of therapies for allergic diseases.

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