Atopy, asthma, and the elderly: A paradigm for personalized therapy

The idea for the timely topic of personalized therapy or precision medicine arose from the realization that individual patients vary, both with respect to their disease manifestations as well as the requirements for successful treatment. It follows then that, by determining these requirements for the individual patient, better outcomes can be achieved. Personalized medicine in the field of allergic disease, more specifically, brings us to the intersecting crossroads of atopy, allergy asthma, and the elderly. Each of these topics was explored by articles that are found within the pages of this issue of the Proceedings.

Between 2012 and 2050, the United States will experience almost a doubling of its elderly population (ages ≥ 65 years). Concomitant with the aging of the U.S. population is an expected increase in the number of elderly patients with asthma, which will present a significant unmet need. To address this need, in this issue, Pasha et al. provided a comprehensive review of the pathophysiology, diagnosis, and management of asthma in the elderly. Because of the importance of this article and its clinically useful implications, it was chosen for this issue’s “For the Patient” section. This segment, found in the final pages of the print version of this issue, also available online, consists of a one-page article synopsis written in a readily comprehensible fashion to help patients better understand the content of the full article.

Although the role of atopy in asthma in the elderly is poorly characterized omalizumab has been successfully used in both children and adults with asthma (including older patients) to reduce exacerbations. However, regardless of age, omalizumab has been associated with a low but significant incidence of anaphylactic events, the pathophysiologic nature of which remains unknown. To elucidate the mechanisms of this adverse drug reaction, Kowal et al. evaluated the potential pathogenetic role of anti-IgE and/or anti-IgE–IgE immune complexes to release histamine from peripheral blood basophils. In addition, they sought to determine whether anti-IgE–IgE complexes could potentially modulate allergen-mediated activation of peripheral blood basophils. The authors reported finding no evidence that humanized, monoclonal anti-IgE antibodies directly or indirectly induced histamine release from peripheral blood basophils.

Although both elevated total IgE levels and eosinophilia have been identified as classic predictive biomarkers for asthma responsiveness to omalizumab and other biologic agents, a definitive biomarker indicative of responsiveness to inhaled corticosteroid therapy has not been identified. In this issue, Manti et al. directed their investigative efforts to the role of high mobility group box 1 (HMGB1) as guidance for management of children with asthma. Their findings indicated that HMGB1 not only was a sensitive biomarker of allergic asthma in children but also that decreased HMGB1 levels provided a successful treatment response biomarker for inhaled corticosteroids.

When turning to adults with asthma, two articles in this issue investigated the association of sex and depression with asthma. When studying an asthma population in Saudi Arabia, Torchyan investigated sex differences in factors related to asthma control. The author reported that factors associated with uncontrolled asthma were different between men and women in Saudi Arabia, including factors such as stress, occupation, and obesity. In providing additional insight on this topic, Choi et al. reported finding an association between asthma and depression in Korean adults but did not find a gender association.

Another potential association with asthma is vitamin D status, which has been linked to the epidemic of atopic disease. It has been hypothesized that low 25-hydroxyvitamin D (25[OH]D) may be related to airway remodeling and eosinophilia in asthma. To investigate this hypothesis, Sypniewska et al. evaluated the association of 25(OH)D concentration with periostin, peripheral blood eosinophil counts, and IgE in children with newly diagnosed asthma. The authors reported that, in newly diagnosed pediatric asthma, 25(OH)D concentrations were significantly associated with periostin levels but not with eosinophil counts.

Vitamin D insufficiency has also been hypothesized to be associated with food allergy. To investigate this potential association, Willits et al. undertook a systematic review to assess for the association between food allergy and vitamin D status in children. As reported in this issue, this systematic review did not identify a

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significant association between vitamin D status and food allergy. Regardless of vitamin D status, the association of food allergy with eosinophilic esophagitis is well established; however, considerable controversy exists regarding optimal therapy for patients with this challenging disorder. To address this controversy, in this issue, Chehade and Sher \(^8\) summarized their lively debate held at Eastern Allergy Conference 2016 and compared the pros and cons of a medical versus dietary approach in treating eosinophilic esophagitis in children and adults.

Food allergy, in particular, the epidemic of peanut allergy, is a growing problem for the U.S. population. How patients become sensitized to peanut is not completely clear. Previous studies that measured peanut protein in house dust support the hypothesis that household peanut consumption may lead to clinical sensitization through transdermal exposure. To investigate this hypothesis, Shroba et al. \(^9\) sought to characterize peanut allergen (Ara h2) levels in house dust from homes with and without individuals with peanut allergy. The authors reported finding that, despite attempts to restrict peanuts and peanut products in the homes of individuals with peanut allergy, there is still detectable Ara h2 found in homes. In fact, Ara h2 levels in homes that completely avoided peanuts were not significantly lower than Ara h2 levels in homes that did not restrict peanuts. Possible explanations and implications of these findings are discussed.

Orthopedic surgeons, cardiologists, gynecologists, and dentists are all encountering an increasing number of patients who present with symptoms of possible hypersensitivity to biomedical metal implants. Despite a growing need for the evaluation and management of metal hypersensitivity reactions, there are few studies that provide evidence-based recommendations on how to evaluate this problem in our practices. In this issue, Rosner and Fonacier \(^10\) reviewed evidence, expert opinion, and published guidelines on pre- and postimplantation evaluation of delayed hypersensitivity reactions in patients suspected of possible metal hypersensitivity to biomedical devices.

This issue also includes the results of two pharmacologic trials. Expanding on previous studies of plasma-derived C1-inhibitor, \(^11\)–\(^14\) Fox et al. \(^15\) analyzed pregnancy data from an international hereditary angioedema patient registry. These investigators reported that administration of plasma-derived, pasteurized, nanofiltered C1-inhibitor concentrate during pregnancy was generally safe and not associated with increased treatment-related adverse events. Nayak et al. \(^16\) reported the results of a randomized, double-blind, parallel-group, placebo controlled multicenter trial that was conducted during the spring tree and grass pollen season to assess the efficacy and safety of cetirizine 10 mg syrup versus loratadine 10 mg syrup versus placebo syrup in a study of children, 6–11 years old, with seasonal allergic rhinitis. They reported that cetirizine 10 mg was statistically significantly more efficacious than placebo in the treatment of seasonal allergic rhinitis symptoms and that symptom improvement was not significantly different between the loratadine and placebo groups.

This issue’s “Patient-Oriented Problem Solving” (POPS) case presentation explored the differential diagnosis of a patient with chronic hives, intermittent fevers, and joint pain. This recurring feature of the Proceedings, as per tradition, was written by an allergy/immunology fellow-in-training from one of the U.S. allergy/immunology training programs. The purpose of the POPS series is to provide an innovative and practical learning experience for the novice allergist/immunologist in-training by using a didactic format of clinical presentation and deductive reasoning. In this issue’s POPS, Cook et al. \(^17\) led the reader through this process. This case report illustrated the complexity of the differential diagnostic process for this clinical presentation and the importance of a detailed history, physical examination, and appropriate laboratory assessment in arriving at a correct diagnosis.

In summary, the collection of articles found within the pages of this issue provide further insight into the intersecting crossroads of atopy, allergy asthma, and the elderly important to the allergic, cutaneous, and respiratory disorders that afflict patients whom the allergist/immunologist serves. These articles highlighted how both the beneficial and adverse effects of therapy continue to challenge the allergist/immunologist in decision-making and therapy. In keeping with the overall mission of the Proceedings, which is to distribute timely information regarding advancements in the knowledge and practice of allergy, asthma, and immunology to clinicians entrusted with the care of patients, it is our hope that the articles found within this issue will help foster enhanced patient management and outcomes. On behalf of the editorial board, we hope you enjoy the diversity of literature offered in this issue of the Proceedings.

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REFERENCES

1. Pasha MA, Sundquist B, and Townley R. Asthma pathogenesis, diagnosis, and management in the elderly. Allergy Asthma Proc 38:184–191, 2017.
2. Kowal K, Bielecki P, Dubuske IV, and Dubuske LM. In vitro impact of anti-immunoglobulin E monoclonal antibodies, including omalizumab on whole blood basophil histamine release: Assessment of direct induction of basophil histamine release and evaluation of modulation of allergen-induced basophil histamine release. Allergy Asthma Proc 38:204–215, 2017.
3. Manti S, Leonardi S, Parisi GF, et al. High mobility group box 1: Biomarker of inhaled corticosteroid treatment response in chil-
4. Torchyan AA. Asthma control in Saudi Arabia: Gender implications. Allergy Asthma Proc 38:e47–e53, 2017.

5. Choi S, Kim SH, and Lee JS. Association between depression and asthma in Korean adults. Allergy Asthma Proc 38:e37–e46, 2017.

6. Sypniewska G, Krintus M, Fulgheri G, et al. 25-Hydroxyvitamin D, biomarkers of eosinophilic inflammation, and airway remodeling in children with newly diagnoses untreated asthma. Allergy Asthma Proc 38:e29–e36, 2017.

7. Willits EK, Wang Z, Jin J, et al. Vitamin D and food allergies in children: A systematic review and meta-analysis. Allergy Asthma Proc 38:e21–e28, 2017.

8. Chehade M and Sher E. Medical therapy versus dietary avoidance in eosinophilic esophagitis: Which approach is better? Allergy Asthma Proc 38:170–176, 2017.

9. Shroba J, Barnes C, Nanda M, et al. Ara h2 levels in dust from homes of individuals with peanut allergy and individuals with peanut tolerance. Allergy Asthma Proc 38:192–196, 2017.

10. Rosner GA, and Fonacier LS. Hypersensitivity to biomedical implants: Prevention and diagnosis. Allergy Asthma Proc 38:177–183, 2017.

11. Farkas H, Köhalmi KV, Veszelı N, et al. Risk of thromboembolism in patients with hereditary angioedema treated with plasma-derived C1-inhibitor. Allergy Asthma Proc 37:164–170, 2016.

12. Riedl MA, Lunry WR, Li HH, et al. Subcutaneous administration of human C1 inhibitor with recombinant human hyaluronidase in patients with hereditary angioedema. Allergy Asthma Proc 37:489–500, 2016.

13. Bork K, Craig TJ, Bernstein JA, et al. Efficacy of C1 esterase inhibitor concentrate in treatment of cutaneous attacks of hereditary angioedema. Allergy Asthma Proc 36:218–224, 2015.

14. Kuhlen JL, and Banerji A. Hereditary angioedema: Special consideration in children, women of childbearing age, and the elderly. Allergy Asthma Proc 36:425–432, 2015.

15. Fox J, Vegh AB, Martinez-Saguer I, et al. Safety of a C1-inhibitor concentrate in pregnant women with hereditary angioedema. Allergy Asthma Proc 38:216–221, 2017.

16. Nayak AS, Berger WE, LaForce CF, et al. Randomized, placebo-controlled study of cetirizine and loratadine in children with seasonal allergic rhinitis. Allergy Asthma Proc 38:222–230, 2017.

17. Cook KA, Lynch MT, Weis PJ, et al. A 30-year-old woman with chronic hives, intermittent fevers, and joint pain. Allergy Asthma Proc 38:231–235, 2017.

18. Farkas H, Köhalmi KV, Veszelı N, et al. Risk of thromboembolism in patients with hereditary angioedema treated with plasma-derived C1-inhibitor. Allergy Asthma Proc 37:164–170, 2016.

19. Riedl MA, Lunry WR, Li HH, et al. Subcutaneous administration of human C1 inhibitor with recombinant human hyaluronidase in patients with hereditary angioedema. Allergy Asthma Proc 37:489–500, 2016.

20. Bork K, Craig TJ, Bernstein JA, et al. Efficacy of C1 esterase inhibitor concentrate in treatment of cutaneous attacks of hereditary angioedema. Allergy Asthma Proc 36:218–224, 2015.

21. Kuhlen JL, and Banerji A. Hereditary angioedema: Special consideration in children, women of childbearing age, and the elderly. Allergy Asthma Proc 36:425–432, 2015.

22. Fox J, Vegh AB, Martinez-Saguer I, et al. Safety of a C1-inhibitor concentrate in pregnant women with hereditary angioedema. Allergy Asthma Proc 38:216–221, 2017.

23. Nayak AS, Berger WE, LaForce CF, et al. Randomized, placebo-controlled study of cetirizine and loratadine in children with seasonal allergic rhinitis. Allergy Asthma Proc 38:222–230, 2017.

24. Cook KA, Lynch MT, Weis PJ, et al. A 30-year-old woman with chronic hives, intermittent fevers, and joint pain. Allergy Asthma Proc 38:231–235, 2017.