

The allergist/immunologist, the Janus gatekeeper of inflammation, COVID-19 and beyond

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In ancient Rome, the Roman god Janus was often portrayed as having two faces: one looking forward to the future, the other looking back over the past. Janus, however, had another important function to fill in the Roman pantheon. He was also the gatekeeper of Heaven and no one, not even Jupiter, could enter the celestial abode without his approval. In a metaphoric manner, the allergist/immunologist is the gatekeeper of inflammation whose domain includes the wide spectrum of reports illustrated in this issue of the *Proceedings*, which include the inflammation associated with chronic rhinosinusitis with nasal polyps (CRSwNP), the wheezing of childhood, enterocolitis of food-induced allergy, severity of atopic dermatitis, spectrum of somatoform anaphylaxis, safety of skin testing in children with penicillin allergy, allergic inflammation of the eye, and coronavirus disease 2019 (COVID-19).

As COVID-19 continues to dominate headline news in 2020, Bellanti brings the focus on the important role that the allergist/immunologist can play in the COVID-19 pandemic. He reminds us of the unique immunologic features of COVID-19 among other infectious diseases and that the inflammatory response can cause greater harm to the individual who is infected than the pathogen itself. In this comprehensive report, the pathogenesis of COVID-19 is reviewed, together with the unique influence that inflammation has on COVID-19 expression, and the potential treatment modalities.¹

In transitioning from the COVID-19 inflammatory response to the type 2 inflammatory state frequently associated with CRSwNP, Blaiss² helps us understand how biologics target the type 2 pathway and where they fit into the algorithm of treatment for CRSwNP. He recommends the use of shared decision-making in determining whether biologics should be started first instead of an initial choice of surgical intervention for patients in whom the standard of medical management has failed.² In patients for whom surgery has already failed and in patients with moderate-to-severe CRSwNP who have other type 2 comorbidities, *e.g.*, asthma, he suggested a trial of biologics as a rational

course.² 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 and 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.

The role of inflammation in childhood asthma is next addressed by Heikkilä *et al.*,³ who conducted a long-term study of health-related quality of life data in 49 young adult subjects with a history of early childhood wheezing. The authors reported that the George's Respiratory Questionnaire symptom scores were higher in the 49 cases with early childhood wheezing compared with those in the control group.³ In shifting from type 2 inflammation to non-immunoglobulin E (IgE) protein-induced inflammation, Ocak *et al.*⁴ presented unique insights that underscore the phenotypes and natural history of the food protein-induced enterocolitis syndrome (FPIES) in the east Mediterranean region. In their cohort, unlike other published series, hen's egg and fish were the two most common culprit foods.⁴ In contrast to the more restricted immune inflammatory response to a single specific protein moiety as seen in FPIES, the inflammatory mechanisms in atopic dermatitis are much more expansive. Ha *et al.*⁵ attempt to provide insight into these complex mechanisms by investigating the association of aeroallergen sensitization with severity of atopic dermatitis in school children. The authors found that the severity of atopic dermatitis correlated with the extent of allergic sensitization and eosinophilia.⁵

In transitioning from true immunologic disease to the psychogenic, Rosloff *et al.*⁶ present a case series study that reviewed an unusual cause of anaphylaxis referred to as undifferentiated somatoform idiopathic anaphylaxis. This condition is considered a psychogenic disorder because it is characterized by a lack of observable physical findings and poor response to treatment. Although failure to diagnose true anaphylaxis can have disastrous consequences, identification of undifferentiated somatoform idiopathic anaphylaxis is important to limit unnecessary expenses and health care utilization.

In moving the focus back to allergic inflammation, Kulhas Celik *et al.*⁷ investigated the safety and diagnostic value of immediate type penicillin skin test reactions in 191 pediatric patients with penicillin allergy. The authors reported that a negative predictive value of penicillin skin testing was 92.2% and that no patients experienced immediate or delayed systemic and/or local reactions in relation to the skin test procedure.⁷

In the “*Clinical Pearls and Pitfalls*” section of this issue, Bielory⁸ discusses the value of ophthalmic antihistaminic preparations in the treatment of allergic conjunctivitis. He introduced a new cetirizine ophthalmic solution 0.24%, a prescription topical ophthalmic histamine H₁ receptor antagonist recently approved by the U.S. Food and Drug Administration for the treatment of ocular itching associated with allergic conjunctivitis in adults and in children ages ≥ 2 years.

This issue’s *Patient-Oriented Problem Solving (POPS)* case presentation explored the differential diagnosis of eosinophilia and elevated IgE in a 79-year-old man that persisted despite adequate treatment for possible environmental exposures. The POPS case presentation is a recurring feature of the *Proceedings*, which, as per tradition, is 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 allergist/immunologist in-training by using a didactic format of clinical presentation and deductive reasoning. In this issue’s POPS, Brooks *et al.*,⁹ from the section of Rheumatology, Allergy, and Clinical Immunology at Yale University School of Medicine (New Haven, CT), led the reader through this learning process by illustrating the complexity of the differential diagnostic process for this clinical presentation and the importance of a detailed history and 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 provides further insight into the intersecting crossroads of inflammation and disease that manifest as allergic, immunologic, and respiratory disorders that afflict patients whom the allergist/

immunologist serve. In particular, they exemplify how the complexities of COVID-19, CRSwNP, asthma, FPIES, atopic dermatitis, anaphylaxis, drug allergy, and allergic conjunctivitis continue to challenge the allergist/immunologist. In keeping with the overall mission of the *Proceedings*, which is to distribute timely information with regard to 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 that you are able to make practical use of the diversity of literature offered in this issue of the *Proceedings*.

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