

Theme Editorial

Sinonasal Disease: An Underappreciated Entity

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Nasal and sinus diseases range from viral upper respiratory tract infections and allergic rhinitis to chronic rhinosinusitis, all of which impact the quality of life and work/school productivity and create a significant economic burden.

Rhinitis, a term for groups of upper airway diseases affecting not only the nose but also the sinuses, is primarily characterized by upper airway mucosal inflammation and symptoms of nasal congestion, rhinorrhea, sneezing, pruritus, and sometimes olfactory dysfunction. There are a variety of different phenotypes of rhinitis, the main ones of which are infectious, allergic, and nonallergic. Viral upper respiratory tract infections affect everyone, whereas allergic and nonallergic rhinitis affect approximately 600 and 200 million subjects, respectively, worldwide.¹

Mullol et al¹ describe various rhinitis phenotypes and elaborate on the different clinical signs and symptoms to assist the clinician in forming a differential diagnosis of rhinitis to further evaluate and treat this disease. Clark et al² propose a more pragmatic view to the management of various forms of rhinitis because of the enormous number of individuals who suffer from these diseases. They encourage subjects who suffer from these problems to first take intranasal glucocorticoids for at least 2 weeks. The nonresponders ideally would then be evaluated by specialists to achieve a proper diagnosis and treatment program. They indicate that this approach will greatly reduce the number of patients seeking medical evaluation. Patel et al,³ in another article in this theme issue, detail the current and future treatments of rhinitis and sinusitis.

Chronic rhinosinusitis (CRS) affects approximately 10% of the population worldwide and 38 million Americans.⁴ Chronic rhinosinusitis with nasal polyps (CRSwNP) is one of the most troublesome subgroups of CRS and can significantly impact a person's quality of life. It can result in depression, cognitive impairment, and an overall feeling of poor health status that exceeds other chronic diseases such as congestive heart failure, end-stage renal disease, and chronic obstructive pulmonary disease.⁵ Conservative estimates suggest that the total cost for CRS in the United States exceeds \$30 billion per year, \$30 billion of

which is for indirect costs.⁶ Various different CRS phenotypes and endotypes, a heterogeneous disease, are described in detail by Cho et al.⁷

Knowledge and the importance of the inflammatory process, which causes CRSwNP, continue to grow and have resulted in the categorizing of CRS by endotypes. Bachert et al⁸ outline the various CRS endotypes, in particular, the role they play in managing CRSwNP. Cho et al⁹ in a rostrum article also emphasize the importance of inflammation and CRS endotypes. In fact, they argue that CRSwNP is first a medical disease. Rowan and Naclerio¹⁰ provide a case presentation of CRSwNP treated with mepolizumab, which demonstrates that medical treatment alone can be inadequate. This patient required surgical intervention to remove obstructing polyps and control the disease. The pathology of the surgical specimen was striking in that it lacked eosinophils, not typical for CRSwNP but indicative that the pathogenesis of the polyps removed is secondary to more than just inflammation. The location of the polyps can obstruct sinus drainage.

The Food and Drug Administration has approved new treatments for CRSwNP over the last several years. These include a new device to deliver fluticasone propionate¹¹ in a more effective manner into the upper airway as well as mometasone-impregnated stents that can be inserted directly into the sinuses,¹² advancing the surgical approach to these diseases. Aspirin desensitization, after comprehensive sinus surgery, also has gained favor as has the use of budesonide and mometasone irrigation, though the evidence supporting these approaches is limited.

mAbs primarily developed to manage asthma and atopic dermatitis are now being used to treat CRSwNP because these diseases share inflammatory mechanisms. Several biologics that target components of type 2 inflammatory response, such as IgE, IL-5, the IL-5 receptor, and the IL4 receptor alpha, the latter which initiates signals for both IL-4 and IL-13, have been evaluated for efficacy in CRSwNP. Dupilumab is Food and Drug Administration—approved to treat CRSwNP.¹³ These biologics, when compared with placebo, are efficacious and illustrate the importance of type 2 inflammation in this disease. They also help to understand the heterogeneity of CRS because only a percentage of each study population improves. Importantly, these studies do not compare these biologic agents to other treatment options available to better clarify which patient will benefit the most. Future comparisons are critical for the clinician to choose the best option. Lal et al¹⁴ indicate in an editorial that severe CRSwNP should be managed by both allergists/immunologists and otolaryngologists because of the significant advances in both medicine and surgery.

The National Institutes of Health convened a multidisciplinary group of allergists/immunologists, otolaryngologists, pulmonologists, clinical trial specialists, and representatives of industry on November 4, 2019, to develop clinical trials in patients with CRSwNP to compare treatment approaches.

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Conflicts of interest: R. M. Naclerio is on the Speakers Bureau for Optinose, Sanofi and Regeneron and is a consultant for Sanofi, Lyra, TASC, AstraZeneca, GSK, and the American Chemistry Council. R. F. Lockey declares no relevant conflicts of interest.

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The results of this workshop are included in this issue of *the Journal of Allergy and Clinical Immunology: In Practice* and describe the current clinical management, questions to be addressed in the future, and recommendations for study design to answer clinical questions about CRSwNP. The National Institutes of Health hopes that investigators will use this information and submit proposals for clinical trials to improve paradigms to manage patients with CRSwNP. The National Institutes of Health, as does the journal, fully appreciates the impact of sinonasal disease on general health and the quality of life.

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