



Foreword

Rhinosinusitis Diagnosis and Management: The Hoops and Hurdles



Linda S. Cox, MD, FACP, AAAAI
Consulting Editor

In my nearly 3 decades of clinical practice as an allergist/immunologist, I can think of no other condition more difficult and frustrating than chronic rhinosinusitis (CRS). Most of my CRS patients were refractory to treatment. At times, in frustration, I would “throw the kitchen sink at them” (ie, oral corticosteroids, topical and oral antibiotics, topical antifungal agents) to try to improve their quality of life. There are several reasons CRS diagnosis and management are so challenging. CRS is a complex, heterogeneous disease with several subgroups (also known as endotypes), which are defined by biomarkers that reflect their biological mechanism. As CRS endotypes may vary in their response to a specific agent, proper classification is important for determining optimal treatment. This foreword reviews the “hoops and hurdles” that a clinician must navigate to properly diagnose and effectively treat CRS.

The term rhinosinusitis infers an inflammatory process involving the sinus and passageways. It is a relatively recent term that was introduced because the majority of persons with chronic sinusitis had concurrent nasal disease. There is no billable *International Classification of Diseases, Tenth Revision (ICD-10)* code for acute or chronic rhinosinusitis. Several *ICD-10* codes are generally used to bill for CRS services. This may be partly because there is no uniform definition of CRS. The Rhinosinusitis and Nasal Polyps expert committee position paper proposed the following definition for CRS: “rhinosinusitis is defined as inflammation of the nose and the paranasal sinuses characterized by 2 or more symptoms, one of which should be either nasal blockage/obstruction or nasal discharge (anterior/posterior nasal drip)” for 12 weeks or longer.¹ The US practice guidelines on rhinosinusitis offered a less specific definition: “rhinosinusitis, defined as inflammation of at least 1 paranasal sinus, is characterized as acute when lasting shorter than 12 weeks and chronic when lasting at

least 12 weeks.”² The problem with these definitions is that they are based largely on patient symptoms. CRS is a complex disease with several variants, which can be classified according to clinical features (phenotype) or biomarkers (endotype).¹ The presence or absence of nasal polyps (NP) defines the 2 most common CRS phenotypes in “primary” CRS (see Ashley M. Bauer and Justin H. Turner’s article, “[Personalized Medicine in Chronic Rhinosinusitis: Phenotypes, Endotypes, and Biomarkers](#),” in this issue). Phenotype classification system does not account for the various biological mechanisms that have been identified in different CRS subgroups. Endotype classification is based on biomarkers that reflect biological mechanisms, such as eosinophilia, neutrophilic mediators, cytokine production, T-cell markers, and interferon-gamma. Endotype-based CRS management should result in a more personalized approach to CRS management and aid in treatment-related decisions, such as who is the best candidate for surgery, corticosteroids, antibiotics, or biologics. CRS endotype classification is a relatively new phenomenon. More research is needed to establish the predictive utility of CRS biomarkers in terms of optimal treatment and disease progression. The diagnosis of “primary” CRS requires consideration of other medical conditions or factors that impact nasal/sinus mucosal defense mechanisms (eg, immune deficiencies, autoimmune, vasculitis, immotile-cilia syndrome, sinus surgery, and cystic fibrosis; see Huwylar C, Lin SY, Liang J: Primary Immunodeficiency and Rhinosinusitis, and Okafor S, Kelly KM, Halderman AA: Management of Sinusitis in the Cystic Fibrosis Patient, in this issue).

Confirmation of CRS diagnosis can be challenging for several reasons. There are no pathognomonic signs or symptoms that definitively confirm or exclude the diagnosis,² nor are there any diagnostic tests that definitely confirm a specific CRS endotype. Sinus CT imaging can confirm the presence of sinus inflammation, but it generally cannot distinguish between a chronic or an acute process. Although Air-fluid levels may suggest an acute process, this finding can be seen after nasal irrigation. In addition, the resolution of infection-related inflammation on CT imaging may lag significantly after clinical resolution. Allergy testing only confirms the presence of allergen-specific immunoglobulin E. The clinician must determine the relevance of the positive allergy tests in terms of the patient’s CRS. Some tests may only be available at specialized centers (eg, nasal secretion analysis for cytokines, cellularity, mediators, and nasal mucosa biopsy for cilia function or local production of immunoglobulin E). The lack of test availability poses a significant barrier to making the correct CRS endotype diagnosis.

In my opinion, the greatest challenge in CRS management is determining the best treatment approach for each patient. Ideally, the treatment plan should be evidence based and “personalized” per the patient’s endotype. To warrant a “high-grade” or strong recommendation in a practice guideline, a treatment must have demonstrated efficacy in a systematic review, randomized, controlled clinical trial. Large randomized, controlled clinical trials are expensive and time consuming but a requirement for regulatory authority approval. Unfortunately, few CRS treatment interventions have not been this extensively studied. Thus, the evidence supporting many CRS interventions is largely empiric. For example, there is little evidence supporting the efficacy of topical corticosteroids, nasal saline irrigation, or oral or topical antibiotics in CRS management, but many clinicians prescribe them, likely because they recognize that the lack of evidence does not necessarily prove lack of efficacy. It may be due to lack of published studies. My primary frustration with CRS treatment is not the paucity of published evidence, but the limited effectiveness of the available treatments. The good news is there has been a breakthrough in CRS treatment with the Food and Drug Administration approval of the biologic, dupilumab, for NP. Several other

biologics have completed phase 3 trials, and more biologics for CRS treatment may soon be available (see Franzese CB: The Role of Biologics in the Treatment of Nasal Polyps, in this issue).

Once a clinician has successfully navigated the “hoops and hurdles” of CRS diagnosis and management, there remains one last “hurdle”: how should treatment success be measured and monitored (see Chowdhury N, Smith TL, Beswick DM: Measuring Success in the Treatment of Patients with Chronic Rhinosinusitis, in this issue)? This “hurdle” poses several questions. Is there a single test or tool that best reflects treatment success or failure? Should treatment success be based on the following:

- Composite or a single outcome(s) or
- Objective (eg, CT scan, nasal endoscopy) versus subjective (SNOT-22 and other quality of life questionnaires)?

This issue of *Immunology and Allergy Clinics of North America*, masterfully orchestrated by Sandra Lin, provides more in-depth and up-to-date information about the topics discussed in this foreword. In addition, this issue reviews the role of the microbiome and role of air pollution in CRS, the role of doxycycline and macrolides, and nasal irrigations in the treatment of CRS. Other topics reviewed in this issue are primary immunodeficiency, allergic fungal sinusitis, nasal polyposis and aspirin-exacerbated respiratory disease, olfactory dysfunction, odontogenic sinusitis, and cystic fibrosis. Each article has key points and a synopsis, which nicely summarize the article's important points and findings. This issue should be read cover to cover as it provides valuable information for clinicians navigating the “hoops and hurdles” of proper diagnosis and management of CRS.

Linda S. Cox, MD, FACP, AAAAI
Department of Medicine and Dermatology
1108 South Wolcott Street
Casper, WY 82601, USA

E-mail address:
lindaswolfcox@msn.com

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2. Peters AT, Spector S, Hsu J, et al. Diagnosis and management of rhinosinusitis: a practice parameter update. *Ann Allergy Asthma Immunol* 2014;113(4):347–85.