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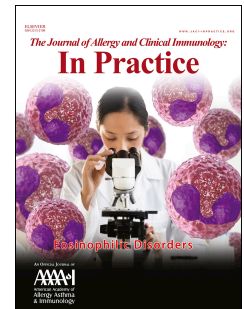
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A Pragmatic Approach Towards Sinonasal Diseases

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Disclosure:

J. H. Clark declares no relevant conflicts of interest. F. M. Barood is on the Advisory Boards of Regeneron, ALK, and Astra-Zeneca. R. M. Naclerio is on the Speakers Bureau for Optinose and Regeneron; and is a consultant for Sanofi, Lyra, TASC, AstraZeneca, TerSera, Insys, and the American Chemistry Council.

Abstract:

Sinonasal disease in its multiple forms affects billions of people worldwide. Although physicians train to precisely diagnose a patient and then treat appropriately, the sheer number of people afflicted with sinonasal disease precludes this approach. We argue that patients should first be treated with an intranasal corticosteroid for 2 weeks. Based on their perceived response, they should be triaged. Those who respond well can be instructed on how to continue to manage their disease. Those who don't would be referred to allergists or otolaryngologists for diagnosis and treatment. We believe this pragmatic approach is safe, provided first line physicians, physician assistants and nurse practitioners recognize some warning symptoms and signs of serious, but infrequently occurring, sinonasal diseases that would not lend themselves to this proposed approach.

Key words: sinonasal disease, intranasal corticosteroids, allergic rhinitis, chronic rhinosinusitis, classification

Manuscript:

Sinonasal disease is broadly defined as a pathological process involving the mucosa of the nasal cavity with or without paranasal sinus involvement. Symptoms related to sinonasal disease represent a leading cause for seeking medical care in the US.¹ Underlying pathogenesis can be broad and varied, ranging from allergy and viral upper respiratory tract infection to chronic rhinosinusitis and malignancy.² The presence of nasal symptoms has a significant adverse impact on quality of life, emotional function, productivity and the ability to perform daily activities.³ Sinonasal disease, in addition, has a significant consequence on healthcare expenditure.⁴⁻⁷

The USA spends \$3.6 trillion or 17.7 percent of the total gross domestic product (GDP) on healthcare.⁸ Recognition of this already spiraling cost is changing healthcare delivery and has created an era defined by the need to curtail cost, pressuring a transition towards a value-based healthcare model.⁹ The axiom of value-based healthcare is a focus to provide high value for patients, where value is defined as health outcomes achieved per dollar spent.¹⁰ As a result there is a need for a paradigm shift in the clinical approach to sinonasal disease.

Sinonasal disease presents multiple challenges to classification. This includes significant symptom overlap among phenotypes.² This is further complicated by the incomplete knowledge of the variable endotypes and their phenotype association.¹¹ There is also a lack of cost effective, sensitive and specific diagnostic testing. This is best illustrated when considering the diagnostic process for allergic rhinitis which frequently includes allergy testing. If you have nasal symptoms that respond favorably to an intranasal corticosteroid (INCS), do you really need to be allergy tested? Furthermore, positive allergy testing alone does not prove that the presenting nasal symptoms are the result of an allergic response.

A number of approaches to classification of sinonasal disease have been proposed based on severity, disease duration, temporal pattern, predominant symptom, disease control and apparent trigger(s).¹¹ However, no single approach has proved ideal. Accordingly, the current system incorporates multiple variables resulting in a complex and impractical classification scheme.^{12,13} Included in this issue of the journal are outstanding reviews of the phenotypes and endotypes of rhinitis and rhinosinusitis, thus we refer the interested reader to those entities for details of the differential diagnosis.¹⁴⁻¹⁶

In the United States, nasal symptoms are a leading cause to seek first line health care services.¹⁷ The average face-to-face time during these visits is 16.5 (SD 9.2) minutes.¹⁸ During this time the provider is also expected to address the patient's general health, therefore, it is unlikely that the limited encounter time will permit the comprehensive evaluation that the current classification of sinonasal disease necessitates. Lack of adherence to sinonasal guidelines is further demonstrated by an ad hoc approach to medical management among frontline providers.^{19,20} The complexity of the current classification scheme has also led to the development of instruments such as "The International Primary Care Respiratory Group (IPCRG) Guidelines Allergic Rhinitis Questionnaire".²¹

A new approach to sinonasal disease should therefore target the non-specialist and address these previous deficiencies. The specific aim of a new approach should be intuitive and provide clear medical management recommendations. Furthermore, it should help prevent patient harm and unnecessary medical investigation/cost.

Papadopoulos and colleagues have presented an approach to rhinitis, which centers on treatment based on phenotyping and on disease control.¹¹ In this model a patient presenting with rhinitis symptoms and an exam without concerning features is started on empirical treatment.

The patient then follows up and, if there has not been any response, they are referred on to a specialist. If they have responded, they continue treatment and follow up with primary care. A prospective validation of this approach, however, is needed.

The efficacy of INCS in allergic rhinitis and chronic rhinosinusitis with nasal polyps is well documented²². They also have benefits in other sinonasal diseases. Meltzer and colleagues compared the effect of placebo, mometasone nasal spray 200 mcg QD, mometasone nasal spray 200 mcg BID, and amoxicillin in the treatment of acute rhinosinusitis. They showed that mometasone nasal spray was more effective than both placebo and amoxicillin with no difference in adverse events²³. Other studies support the efficacy of INCS in other forms of sinonasal disease. The adverse events are minimal enough that INCS were approved for short term over-the-counter usage. Importantly, INCS do not make sinonasal diseases worse.

We propose that patients reporting to health care providers with sinonasal complaints undergo a history and brief physical exam. The purpose is to eliminate emergent and non-benign forms of sinonasal disease that require further evaluation. Warning signs and physical findings of such problems include severe headache, unilateral otitis media with effusion, facial numbness, dental swelling, unilateral watery drainage, high fever, periorbital swelling, interference with extraocular movement, bloody discharge, decreased sense of smell, unilateral nasal obstruction and wheezing (figure 1). Once emergent forms of the disease are ruled out, patients can be treated with INCS at their standard dose for two weeks. If there is a good clinical response as perceived by the patient, then treatment can be continued or discontinued based on the perceived duration of the problem. Those patients not, or incompletely, responsive should be referred to an otolaryngologist or allergist for further evaluation and more detailed diagnosis and treatment.

Reasons for partial or lack of response include nonadherence, dislike of the INCS, irritative effects, mechanical problems obstructing airflow such as concha bullosa, septal deviations, tumors, chronic rhinosinusitis with or without polyps, and subtypes of rhinitis that are not steroid responsive like most forms of nonallergic rhinitis, occupational rhinitis, gustatory rhinitis and the rhinitis of pregnancy. Some entities, like gustatory rhinitis, can be successfully treated with ipratropium nasal spray. Others such as a deviated septum maybe treated with surgical intervention like a septoplasty.

A specialist can perform additional testing such as nasal endoscopy and CT scans, and better evaluate overlapping processes, such as allergic rhinitis and a septal deviation. However, in our proposal the patients with both a septal deviation and allergic rhinitis who responded well to an INCS would not be referred to a specialist because the congestion secondary to allergic rhinitis was the most important contributor to symptoms. Allergy testing must always be interpreted in the presence of a detailed allergy history, something a busy primary care provider does not have time to do. For example, over 50% of the US population has positive allergy tests, but only 20% have allergic rhinitis.²⁴ Additionally, specialists can prescribe additional treatments. The patient with perennial allergic rhinitis who only partially responded to an INCS maybe a candidate for immunotherapy or combination pharmacotherapy.

What is the drawback of such a paradigm? ICD coding for initial visits could often be wrong. It might delay the referral of patients with tumors that present with bilateral symptoms, but if the 2 week rule is adhered to this would not affect prognosis. Some patients would be unnecessarily treated with INCS, but since the drug has few adverse effects, and will be used for a short period of time, this is a minor concern. The patient's response to treatment will be verbal and subjective, but could be quantified by a visual analogue scale if needed. Some patients who

appear to respond to an INCS may have responded to a placebo, but does it matter? The patient would not have an accurate diagnosis, but this inaccuracy doesn't hurt the patient since they are receiving a safe drug and it helps them by improving their quality of life, the goal of treatment. On the upside, there would be fewer referrals for INCS-sensitive disease and the referrals for corticosteroid insensitive disease would be more complicated. Moreover, a two week course of an INCS is inexpensive.

Since the vast majority of sinonasal disease primarily affects quality of life, and a safe and inexpensive treatment helps a large percentage of sufferers, why not endorse a simple paradigm. If such a paradigm was effective, then studies to develop new treatments would focus on the non-corticosteroid responsive individuals. Likewise, algorithms for the best management of those individuals failing INCS treatment could focus on the patients needing specialized care. Is it time to educate primary care providers and the public about this paradigm?

References:

1. Annual number and percent distribution of ambulatory care visits by setting type according to diagnosis group. United States, 2009-2010. :5.
2. Krouse J, Lund V, Fokkens W, Meltzer EO. Diagnostic strategies in nasal congestion. *Int J Gen Med*. 2010;3:59-67.
3. Shedden A. Impact of nasal congestion on quality of life and work productivity in allergic rhinitis: findings from a large online survey. *Treat Respir Med*. 2005;4(6):439-446. doi:10.2165/00151829-200504060-00007
4. Keith PK, Desrosiers M, Laister T, Schellenberg RR, Wasserman S. The burden of allergic rhinitis (AR) in Canada: perspectives of physicians and patients. *Allergy Asthma Clin Immunol*. 2012;8(1):7. doi:10.1186/1710-1492-8-7
5. Palmer JN, Messina JC, Bilech R, Grosel K, Mahmoud RA. A cross-sectional, population-based survey of U.S. adults with symptoms of chronic rhinosinusitis. *Allergy Asthma Proc*. 2019;40(1):48-56. doi:10.2500/aap.2019.40.4182
6. Stewart M, Ferguson B, Fromer L. Epidemiology and burden of nasal congestion. *Int J Gen Med*. 2010;3:37-45. doi:10.2147/ijgm.s8077
7. Soni A. Statistical Brief #204: Allergic Rhinitis: Trends in Use and Expenditures, 2000 and 2005. Allergic Rhinitis. 2000:6.
8. Historical | CMS. <https://www.cms.gov/Research-Statistics-Data-and-Systems/StatisticsTrends-and-Reports/NationalHealthExpendData/NationalHealthAccountsHistorical>. Accessed December 6, 2019.
9. Tsevat J, Moriates C. Value-Based Health Care Meets Cost-Effectiveness Analysis. *Ann Intern Med*. 2018;169(5):329. doi:10.7326/M18-0342
10. Porter ME. What Is Value in Health Care? *New England Journal of Medicine*. 2010;363(26):2477-2481. doi:10.1056/NEJMp1011024
11. Papadopoulos NG, Bernstein JA, Demoly P, Dykewicz M, Fokkens W, Hellings PW, et al. Phenotypes and endotypes of rhinitis and their impact on management: a PRACTALL report. *Allergy*. 2015;70(5):474-494. doi:10.1111/all.12573
12. Meltzer EO, Hamilos DL, Hadley JA, Lanza DC, Marple BF, Benninger MS. Rhinosinusitis: Establishing definitions for clinical research and patient care. *Otolaryngology - Head and Neck Surgery*. 2004;131(6, Supplement):S1-S62. doi:10.1016/j.otohns.2004.09.067
13. Wallace D, Dykewicz M, Bernstein D, Blessing-Moore J, Cox L, Khan DA, Lang DM, et al. The diagnosis and management of rhinitis: An updated practice parameter. *J Allergy Clin Immunol* 2008;122(2):S1-S84. doi:10.1016/j.jaci.2008.06.003

14. Patel G, Kern RC, Bernstein JA, Hae-Sim P, Peters AT. Current and Future Treatments of Rhinitis and Sinusitis. *J Allergy Clin Immunol Pract* 2020;XXX/
15. Cho Sh, Hamilos DL, Han D-H., Laidlaw TM. Phenotypes of Chronic Rhinosinusitis. *J Allergy Clin Immunol Pract* 2020;XXX.
16. Mullol J, del Cuvillo A, Lockey RF. Rhinitis Phenotypes *J Allergy Clin Immunol Pract* 2020;XXX.
17. Explore Primary Care Physicians in the United States | 2019 Annual Report. America's Health Rankings.
<https://www.americahealthrankings.org/explore/annual/measure/PCP/state/ALL>. Accessed December 7, 2019.
18. Young R, Burge S, Kumar K, Wilson J, Ortiz D. A Time-Motion Study of Primary Care Physicians' Work in the Electronic Health Record Era. *Family Medicine*. doi:10.22454/FamMed.2018.184803
19. Ramírez LF, Urbinelli R, Allaert F-A, Demoly P. Combining H1-antihistamines and nasal corticosteroids to treat allergic rhinitis in general practice: ALLERGY. *Allergy*. 2011;66(11):1501-1502. doi:10.1111/j.1398-9995.2011.02682.x
20. Demoly P, Concas V, Urbinelli R, Allaert F-A. Spreading and impact of the World Health Organization's Allergic Rhinitis and its impact on asthma guidelines in everyday medical practice in France. Ernani survey. *Clin Exp Allergy*. 2008;38(11):1803-1807. doi:10.1111/j.1365-2222.2008.03085.x
21. Price D, Bond C, Bouchard J, Costa R, Keenan J, Levy ML, et al. International Primary Care Respiratory Group (IPCRG) Guidelines: Management of allergic rhinitis. *Primary Care Respiratory Journal*. 2006;15(1):58-70. doi:10.1016/j.pcrj.2005.11.002
22. RR Orlandi, TT Kingdom, PH Hwang, Smith TL, Alt JA, Baroody FM, et al. International consensus statement on allergy and rhinology: Rhinosinusitis. *Int Forum Allergy Rhinol* 2016;6:S22-S209, 2016.
23. Meltzer EO, Bachert C, Staudinger H. Treating acute rhinosinusitis: comparing efficacy and safety of mometasone furoate nasal spray, amoxicillin, and placebo. *J Allergy Clin Immunol*. 116(6):1289-95, 2005 Dec
24. Salo PM; Arbes SJ Jr; Jaramillo R; Calatroni A; Weir CH; Sever ML; Hoppin JA; Rose KM; Liu AH; Gergen PJ; Mitchell HE; Zeldin DC. Prevalence of allergic sensitization in the United States: Results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006; *J Allergy Clin Immunol*. 134 (2):350-9, 2014 PMID: 24698318

231 Figure Legend: Presenting signs and symptoms of sinonasal disease that require special attention
232 by the clinician.

