

Should Clinicians Routinely Determine Rhinitis Subtype on Initial Diagnosis and Evaluation? A Debate Among Experts

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INTRODUCTION

By Martin Quan, MD

Rhinitis is one of the most prevalent conditions affecting Americans today. Twenty to 40 million Americans (10%–30% of adults and up to 40% of children) are estimated to have allergic rhinitis.¹ In recent decades, its prevalence in Western societies has increased dramatically, and studies from around the world are reporting similar trends.^{1,2} Although studies have traditionally reported a 3:1 ratio of allergic to nonallergic rhinitis, recent data suggest that as many as 87% of patients with rhinitis may have mixed rhinitis, a combination of both allergic and nonallergic rhinitis.²

Untreated or inappropriately managed rhinitis can significantly affect a patient's quality of life and ability to perform activities of daily living. It is often associated with concomitant conditions, such as fatigue, headache, sleep disturbance, cognitive impairment, and respiratory conditions, complicated by rhinitis, including asthma and sinusitis.² It is a significant cause of morbidity, health care expenditure, reduced work productivity, and absences from school.²

According to the recently released updated practice parameters, *The Diagnosis & Management of Rhinitis*, rhinitis is characterized by the presence of one or more of the following nasal symptoms:

- Congestion
- Rhinorrhea (anterior and posterior)
- Sneezing
- Itching

Inflammation is normally associated with rhinitis, but certain subtypes of the disease, such as vasomotor (increasingly known as chronic idiopathic rhinitis) or nonallergic rhinitis and atrophic rhinitis, are not predominantly inflammatory.²

The diagnosis of rhinitis may appear to be a fairly straightforward undertaking; however, rhinitis is composed of numerous subtypes and etiologies, and differentiating them can be a challenge for primary care practitioners.

Further complicating matters is the fact that many patients have both an allergic and a nonallergic component to their rhinitis. Whether or not identification of rhinitis subtype should be an integral component of initial diagnosis remains an area of controversy. While standard treatment for allergic and nonallergic rhinitis is often the same, certain subtypes of the disease do not respond well to the usual first-line treatments for allergic rhinitis. Identification of subtype, therefore, can potentially have important implications for treatment choice.

In the following section, we present a discussion between 2 members of the Respiratory & Allergic Disease (RAD) Foundation, Thomas B. Casale, MD, and Michael S. Blaiss, MD. Drs. Casale and Blaiss debate the question, “Should clinicians routinely determine rhinitis subtype on initial diagnosis and evaluation?” Each expert was randomly assigned a position to take: Dr. Casale’s views represent the “pro” argument while Dr. Blaiss was asked to speak to the “con” argument. The debate concludes with a synthesis of their arguments and final points, including important takeaway messages for the primary care practitioner. (*Clinical Cornerstone*. 2009;9[4]:54–60) © 2009 Elsevier. All rights reserved.

DEBATE

Moderator [Dr. Quan]: We will start with a fairly straightforward question that will help us frame this discussion: How common are the nonallergic subtypes of rhinitis?

Dr. Casale: Rhinitis itself is a very common problem and, depending on what type of epidemiologic study you look at, the prevalence among the American population can be as high as 15% to 20%. The different subtypes of rhinitis, however, have not been characterized. We do know that multiple nonallergic etiologies exist and are quite prevalent (**Table**). In a 2001 study by Settupane and Lieberman,¹ more than half of patients with perennial types of symptoms had either nonallergic rhinitis or mixed rhinitis; that is, they had both allergic and nonallergic rhinitis. A fairly high percentage of patients in clinical practice have this disorder, where nonallergic rhinitis plays an important role.

Dr. Blaiss: I agree with Dr. Casale regarding the Settupane and Lieberman data. In fact, Settupane published another

TABLE. NONALLERGIC RHINITIS SUBTYPES.

Vasomotor Rhinitis

- Irritant triggered (eg, chlorine, perfumes, cigarette smoke)
- Cold air
- Exercise
- Undetermined or poorly defined triggers

Gustatory Rhinitis

Infectious

- Acute
- Chronic

Nonallergic Rhinitis With Eosinophils

Occupational

- Caused by chemical respiratory sensitizers, immune mechanism uncertain
- Work-aggravated

Hormonally induced

- Pregnancy
- Menstrual cycle

Drug-induced

- Rhinitis medicamentosa
- Oral contraceptives
- Antihypertensives and cardiovascular agents
- Aspirin/NSAIDs
- Other drugs
- Atrophic rhinitis

Rhinitis Associated With Inflammatory–Immunologic Disorders

- Granulomatous infections
- Wegener granulomatosis
- Sarcoidosis
- Midline granuloma
- Churg–Strauss syndrome
- Relapsing polychondritis
- Amyloidosis

Adapted with permission from Wallace DV, Dykewicz MS, Bernstein DI, et al, for the Joint Task Force on Practice; American Academy of Allergy, Asthma & Immunology, American College of Allergy, Asthma and Immunology, Joint Council of Allergy, Asthma and Immunology. The diagnosis and management of rhinitis: An updated practice parameter [published correction appears in: *J Allergy Clin Immunol*. 2008;122:1237]. *J Allergy Clin Immunol*. 2008;122(Suppl 2):S1–S84.

article in 2003 which suggested that about 43% of the population with rhinitis had allergic rhinitis; 23% had nonallergic rhinitis; and 34% had mixed allergic and nonallergic rhinitis.² I think the underlying question here is whether or not it is really important, especially up front, to determine if a patient has an allergic or a nonallergic type of rhinitis.

Consider the practice parameters published by the Joint Task Force on Allergy, Asthma, and Immunology. For patients with symptoms that are suggestive of rhinitis, a therapeutic trial was recommended before any

evaluation other than a history.³ This would suggest that identification of subtype early on is not necessary for effective treatment.

I think one of the reasons why the rhinitis subtype really does not matter at this point is that, in most cases, whether or not you classify the patient as allergic or non-allergic is not going to affect the treatment regimen.

Dr. Casale: While I respect what Dr. Blaiss is saying, I think there are occasions when identifying the type of rhinitis a patient has will dictate specific therapy that may be more effective in managing a patient. An up-front identification, if it could be done rapidly, could certainly play a role in directing better therapies.

Moderator: You both seem to agree that many patients exhibit both allergic and nonallergic subtypes, but you disagree in regard to whether this information is important early on. In your opinion, should determining rhinitis subtype be an integral part of the initial evaluation of the patient presenting with rhinitis?

Dr. Blaiss: No, it should not. It is not efficient, and it is not necessary to routinely assess rhinitis subtype when treating a patient with rhinitis. Differentiation of allergic from nonallergic rhinitis would be important if the treatment strategies were significantly different, but in reality, they are not. The same would be true if outcomes, including prevention of complications, differed in response to various treatments, but they do not. Similar treatments are frequently employed in the same way for both allergic and nonallergic rhinitis. Therefore, identification of subtype early on really doesn't have an effect on outcomes.

A study published in the *Annals of Allergy, Asthma and Immunology* in 2008 underscores this point. Gelincik et al⁴ compared allergic versus nonallergic rhinitis to determine which, if either, is more predisposing to chronic rhinosinusitis. Notably, the authors did not find any major difference in allergic versus nonallergic patients.

Dr. Casale: I disagree that knowing rhinitis subtype early on is not important. Taking a good history and performing a physical examination goes a long way toward developing an effective treatment strategy. I think it is easy to take a relatively rapid history, for example, by utilizing the checkbox type of diagnostic worksheet that the Respiratory & Allergic Disease (RAD) Founda-

tion published in *Current Medical Research Opinion* in 2006.⁵ Such an approach enables clinicians to quickly and effectively assess patients with rhinitis and get an idea of whether or not they have allergies (**Figure**). For example, if you have a patient who is older than 35 years, with no family history of rhinitis, and if his or her rhinitis symptoms are triggered more by irritants like perfumes than by allergens like pets, then by following the worksheet you will quickly see that this patient is much more likely to have nonallergic rhinitis than allergic rhinitis.⁵

Asking some simple questions can give clinicians a very good idea of whether or not a patient has nonallergic rhinitis. For example, I will ask my patients, "Do you have persistent congestion and/or rhinorrhea or runny nose without itching and sneezing? Have you had a poor response to oral antihistamines?" The latter is an especially important question to ask, I think, because we know that nonallergic rhinitis does not respond to oral antihistamines as well as allergic rhinitis does. I also ask them, "What exacerbates your symptoms? Are they affected by strong odors, perfumes, or weather changes?" Additionally, I will inquire as to the age of onset and family history.

Suggests Nonallergic Rhinitis	Suggests Allergic Rhinitis
<input type="checkbox"/> Persistent congestion and/or rhinorrhea without itch/sneeze	<input type="checkbox"/> Sneezing
<input type="checkbox"/> Poor response to oral antihistamines	<input type="checkbox"/> Itchy nose (the "nasal salute")
<input type="checkbox"/> Symptoms exacerbated by:	<input type="checkbox"/> Seasonal symptoms
<input type="checkbox"/> Weather changes	<input type="checkbox"/> Itchy eyes/eye rubbing
<input type="checkbox"/> Temperature extremes/changes	<input type="checkbox"/> Clear rhinorrhea
<input type="checkbox"/> Foods	<input type="checkbox"/> Family Hx of allergic rhinitis
<input type="checkbox"/> Perfumes/odors	<input type="checkbox"/> Eczema
<input type="checkbox"/> Smoke/fumes	<input type="checkbox"/> Food allergy
<input type="checkbox"/> Late age of onset	
<input type="checkbox"/> Absence of cat/dog/pet trigger	

Frequent co-morbidities in pediatric patients

Ear popping, frequent upper respiratory tract infection, fatigue, headache, and sleep disturbance are among the features normally associated with both allergic and nonallergic rhinitis and, therefore, not helpful in determining the type of rhinitis.

Figure. Diagnostic worksheet for the assessment of rhinitis.⁵

Patients with allergic rhinitis often have prominent sneezing, and they may have a very itchy nose and itchy eyes, which you don't tend to see as frequently with non-allergic rhinitis. They typically will have a family history of allergic rhinitis, and there are some comorbidities, especially in children, that suggest allergic rhinitis, such as eczema or food allergy. Utilizing RAD's checkbox approach enables clinicians to elicit this important information quickly and easily and can help facilitate effective assessment of subtype.

Dr. Blaiss: Although a history and the RAD worksheet can be helpful, in some patients they can be misleading. If we rely too much on some of these criteria—such as linking seasonal symptoms to allergic rhinitis—we are probably going to miss a significant number of patients who may in fact have a year-round allergic component to their condition, such as dust mites, mold spores, and animal danders.

The other problem that we may encounter is that many patients will state they have an animal allergy, but it's more of an irritant reaction and not a true allergy/immunoglobulin (IgE)-mediated effect. If we went by history alone, these patients would be mislabeled as having allergy symptoms and might not receive effective treatment.

Moderator: Dr. Casale seems to advocate taking a history as a way to determine subtype quickly. Do patients need a radioallergosorbent test (RAST) or skin testing to confirm or make a useful diagnosis, or is history alone good enough?

Dr. Casale: I would say that you do not need to perform a skin test or RAST on every patient that you think may have allergic rhinitis. There is likely a good middle ground between doing nothing and requiring lab confirmation for diagnosing all patients. If a patient has sneezing and itchiness with clear discharge from the nose and a positive family history, and if those symptoms are exacerbated by common allergen types of exposures, like pets, or if they have a seasonal exacerbation of symptoms that coincides with pollen season, then I would not necessarily recommend allergen testing.

Dr. Blaiss: Allergy testing is an excellent diagnostic tool, but should we be testing all of our rhinitis patients? Absolutely not. I am in a private practice allergy group

and I would not recommend it. How useful would this information be in most patients? Even after following guidelines and utilizing diagnostic criteria, there is still a large overlap of patients, as stated by Setticone and Lieberman, who have mixed rhinitis.¹ We all see patients who seem to have allergy symptoms but in fact also have significant nonallergic disease.

With that said, the best objective criteria we have to help differentiate allergic versus nonallergic nasal problems is allergen skin testing or RAST. I think it is often beneficial for clinicians to put together a diagnostic worksheet and try to correlate it with an objective measure. In fact, there are studies out there that have tried to characterize rhinitis without skin testing and, unfortunately, in most cases it is just not that effective.

Dr. Casale: I would like to point out, though, that skin testing and RAST are not perfect. They do not identify all patients who may actually have an allergy. There have been some very interesting studies about local IgE production in the airways that is clinically significant based on, for example, nasal allergen challenges in patients who had a negative skin test to the allergen.⁶

While I agree that allergy testing is an important tool, I believe it is not the most important component of rhinitis assessment. If there is some confusion or some trepidation about the diagnosis, then perhaps skin testing or RAST could be useful.

Moderator: Let's assume for a moment that we are able, with either a good history, allergy testing, or both, to identify rhinitis subtype up front. Would knowing this information alter treatment decisions?

Dr. Blaiss: It could. Surely, I would not routinely recommend an oral second-generation antihistamine for patients with nonallergic rhinitis. Still, at this point in time, with several second-generation antihistamines available without a prescription, by the time a patient gets to a physician for management of chronic rhinitis, in all likelihood that patient has already tried an oral antihistamine without success.

So, if we really look at the other treatments that are available for use for our patient population with rhinitis, then there generally are not going to be any major differences as far as treatment parameters for patients with allergic versus nonallergic rhinitis.

Supporting this is a paper from the Agency for Healthcare Research and Quality of the US Department of Health and Human Services, *Management of Allergic and Nonallergic Rhinitis*.⁷ This is an evidence-based report created from a systematic review of the literature. The authors note that there have been no prospective studies to explicitly differentiate allergic versus nonallergic rhinitis. The data concerning treatment of nonallergic rhinitis are scant. No single agent has been identified as being uniformly effective for all symptoms associated with the condition.

Dr. Casale: I think you make some good points, but that would be if you are comparing run-of-the-mill allergic rhinitis with idiopathic nonallergic rhinitis, or what we used to call *vasomotor rhinitis*. There are more rhinitis etiologies than that, however, and they need to be assessed up front. One should seek to identify these other types of rhinitis because there are different recommended treatments for many of them.

Is the rhinitis, for example, due to a concomitant medication? Well, obviously treatment in such cases is going to include withdrawing that medication, if possible. Is it hormonal? If so, it is not going to respond to oral antihistamines and, for that matter, it may not respond very well to nasal steroids either. Are you dealing with nasal polyps? Is it associated with hypertrophied nasal turbinates? Is it atrophic rhinitis, which doesn't respond very well to any of the therapies that we talked about?

Clearly, there are differences in how your patients are managed. I agree that the majority of patients we see will fit into that broad category of allergic or run-of-the-mill idiopathic nonallergic rhinitis. However, we should not forget the other types of patients who can have rhinitis, either in conjunction with those more common diseases or as the primary diagnosis, and who will need an entirely different type of treatment paradigm than the standard antihistamine plus or minus a nasal steroid.

Moderator: I would like to specifically address the use of oral second-generation antihistamines. There are still a significant number of prescriptions in the United States for antihistamine monotherapy. If a patient's history suggests no allergic rhinitis, would you still support the use of antihistamine monotherapy as first-line treatment?

Dr. Casale: No, I would not. The response rates to oral antihistamines are not that good for nonallergic rhinitis, regardless of its cause. When you think about it, this makes sense; without a prominent allergic etiology, it's unlikely that histamines, or for that matter, even leukotrienes, would be important mediators in causing symptoms.

As a result, neither oral antihistamines nor oral leukotriene blockers would be very effective for such patients. In these cases, I think you have to choose medication based on your best diagnosis, and the cause of the rhinitis could certainly steer you toward a different type of treatment paradigm.

Dr. Blaiss: I agree with everything Dr. Casale said on that particular issue, but I will add that I sometimes use a first-generation oral antihistamine in nonallergic rhinitis because of anticholinergic activity, especially if there is a decongestant added to it.

Moderator: Would it be safe to say that for the great majority of patients, it is not important to determine rhinitis subtype at initial diagnosis?

Dr. Blaiss: Most patients, except for some of the exceptions that Dr. Casale mentioned, can achieve improvement in their nonallergic or vasomotor irritant rhinitis with intranasal corticosteroids and/or intranasal antihistamines. We know from the guidelines that intranasal corticosteroids are increasingly being recognized as first-line therapy, and nasal antihistamines are efficacious alone or in combination with nasal corticosteroids for both allergic and nonallergic rhinitis. So again, another reason that the diagnosis in and of itself may not be that important is because the major treatments we recommend for both conditions are the same.

Dr. Casale: I agree that intranasal corticosteroids are the single best agent that we have to treat rhinitis, regardless of the cause. I think the issue is that access to intranasal corticosteroids requires a physician encounter and a prescription. This encounter should always include taking a focused history and performing a physical examination.

Obviously, there are many choices of over-the-counter oral antihistamines available to patients. Many patients initially purchase them, but treatment is not always efficacious because they don't work well for nonallergic rhinitis. In fact, even in many patients with allergic rhini-

tis, these over-the-counter oral antihistamines are insufficient to adequately control their symptoms. Therefore, treatment success or failure with them is not necessarily a very good litmus test to determine if a patient has allergic or nonallergic rhinitis.

Moderator: You both seem to agree that intranasal corticosteroid use is supported by evidence, guidelines, and your clinical experience. Would initial empiric therapy with nasal steroids for all rhinitis patients obviate the need to make a specific diagnosis?

Dr. Casale: I think that there are exceptions to that. Those exceptions would be the types of nonallergic rhinitis that could be best managed with other types of interventions, especially, for example, surgical interventions. If you have large nasal polyps, they often do not adequately respond to nasal steroids. If a patient has a structural disorder, or any type of chronic inflammatory disease other than allergic or nonallergic rhinitis, he or she may not respond very well to intranasal steroids.

By taking a complete history and performing a thorough physical exam, clinicians should be able to rule out most of those other causes. Once that is done, then I would agree that using an intranasal corticosteroid is probably the way to go for the vast majority of patients.

Dr. Blaiss: That is a tough point to argue against. Still, when you look at the majority of patients in general, even the exceptions mentioned by Dr. Casale, once you have tried an over-the-counter antihistamine and then empiric treatment with nasal steroids and/or nasal antihistamines, you will see a reduction in symptoms for most patients. The bottom line is that early diagnosis of rhinitis subtype really is not going to change outcomes and prevention of any other chronic condition.

Moderator: Are there also considerations when it comes to the logistics of managing a patient? For example, are patients with rhinitis that is of a mixed etiology coded differently than patients with either nonallergic or allergic rhinitis alone?

Dr. Casale: In my office practice, we code for both, especially when the history is suggestive of nonallergic disease concomitant with allergic rhinitis. I think coding

for both conditions is appropriate because, in fact, the patient does have both conditions.

I think it is important to recognize that rhinitis itself can be a very complex disorder and should not be trivialized. It can result from multiple causes and it can be very difficult to treat despite our best efforts. In fact, a large percentage of patients who have significant allergic rhinitis still have significant symptoms during peak pollen times even with the use of nasal steroids and oral antihistamines or leukotriene modifiers. These patients are forced to restrict their activities and experience a diminished quality of life due to their rhinitis symptoms during these times.

Referral to an allergist and immunologist can sometimes be very beneficial because the specialist can identify what the patient is or is not allergic to and can also help with environmental control recommendations. In those patients who have a significant allergic component to their rhinitis, a specialist can recommend, prescribe, and administer allergen immunotherapy, which clearly has been shown to be effective for allergic rhinitis and to allow patients to enjoy a better quality of life with fewer medications.

Dr. Blaiss: In the primary care setting, I think that regardless of whether a patient has allergic or nonallergic rhinitis, I'm going to start them with either an intranasal corticosteroid or intranasal antihistamine empirically. If that patient does not respond to therapy, or has adverse effects associated with the therapy, then I agree with Dr. Casale: that is when I would take a closer look or have the patient referred to an allergist and immunologist. At that point, I would think skin testing would be appropriate, along with environmental control and immunotherapy.

FINAL THOUGHTS

Moderator: Gentlemen, thank you for that lively debate. Are there any final thoughts you would like to conclude with?

Dr. Casale: I would strongly advocate clinicians get into the habit of asking a few focused questions up front when assessing rhinitis. Simple questions can help guide the diagnosis, including concomitant medications that could be associated with rhinitis medicamentosa, which doesn't have to be due to an intranasal medication. There are some oral medications that can do that as well. Asking a few simple questions in conjunction with a thor-

ough physical exam will go a long way toward providing rapid and effective assessment of a patient, which can better guide therapy, including an empiric trial with an intranasal corticosteroid.

Dr. Blaiss: Even with a detailed history, in many cases one may not be able to truly distinguish a patient with allergic versus nonallergic rhinitis. The physician may be able to detect some conditions like rhinitis medicamentosa, but even in those cases, you haven't learned why the patient got hooked on the over-the-counter decongestant nasal spray in the first place. Was it because he or she had allergies or was it because he or she had nonallergic disease? The history in and of itself may not yield enough information to change the type of therapy a primary care provider is going to prescribe for patients.

Takeaway Messages

Moderator: Thank you. What are the key takeaway messages that you would like to leave our readers with?

Dr. Casale: I think taking an appropriate medical history, examining the types of symptoms, the persistence of symptoms, the seasonality of the symptoms, looking at response to medications, the triggers of those symptoms, the age of onset, and family history can all be very important steps in the initial assessment of a patient.

Performing a good physical exam, looking in that patient's nose to determine whether or not there are structural problems, a deviated septum, nasal polyps, if he or she has facial asymmetry, anything that could be causing the symptoms is another very important piece of information that can help with diagnosis and assessment.

If you are convinced that the patient most likely has allergic rhinitis or a nonallergic rhinitis not due to some of these other causes that are structural, hormonal, or gastrointestinal reflux, for example, an empiric trial of an intranasal corticosteroid can be very useful, along with some advice on avoidance of triggers.

Once these 3 things have been done and the patient returns and is still not satisfied with response to treatment, I would strongly consider referral to an allergist and immunologist because he or she can perform a more thorough assessment of the potential role of allergens

or triggers and help the patient with avoidance measures, as well as the possibility of administering allergen immunotherapy.

Finally, rhinitis is a very common disorder, but it is one that causes a significant problem in patients' quality of life. Therefore, one should not ignore it. One should ask patients about the affect on quality of life and not trivialize or ignore these types of symptoms.

Dr. Blaiss: I think another very important point is the importance of follow-up. It is important that the patient be seen again several weeks after starting treatment to determine if the medication is controlling the condition. To the point of not trivializing the disease, I would add that chronic rhinitis that is not properly treated can lead to complications, such as sinusitis, worsening asthma, and sleep deprivation.

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