

Symposium: Rhinitis: A Dose of Epidemiological Reality

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ABSTRACT

In the wide spectrum of medical practice, rhinitis is often incorrectly assumed to be solely allergic in etiology. Consequently, other rhinitis subtypes (nonallergic and mixed) remain under-diagnosed. This is of concern because inaccurate diagnosis may lead to unsatisfactory treatment outcome. Contributing to this under-diagnosis is the fact that primary care practitioners do not often have at their disposal the same diagnostic tools as the allergist. Tools that the allergist is more likely to use include nasal cytology, skin testing and in vitro assays for specific immunoglobulin E. Patients with pure nonallergic rhinitis have negative skin tests or clinically irrelevant positive results. Mixed rhinitis refers to the presence of both allergic and nonallergic rhinitis components within the same individual. Allergic rhinitis more commonly develops before the age of 20, whereas nonallergic rhinitis affects an older population and disproportionately more females. The type of nasal symptoms manifested by the patient usually does not differentiate allergic from nonallergic rhinitis. Vasomotor rhinitis is the most common form of nonallergic rhinitis, followed by nonallergic rhinitis with eosinophilia and others. In terms of estimated prevalence, allergic rhinitis affects approximately 58 million Americans, 19 million have pure nonallergic rhinitis and 26 million have mixed rhinitis. Thus a wide spectrum of relevant epidemiologic information can be used to assist in determining the differential diagnosis of rhinitis. Physicians are reminded to look further and consider whether a rhinitis patient truly has pure allergic rhinitis or whether a diagnosis of mixed rhinitis or nonallergic rhinitis is more appropriate. (Allergy and Asthma Proc 24:147-154, 2003)

As the incidence of atopy continues to rise worldwide, allergists are increasingly being called on to act in advisory capacities.¹⁻⁴ This is particularly the case with

respect to disorders of the respiratory tract, because most patients with rhinitis and/or asthma initially present to the primary care setting. Although, in fact, only 12% of rhinitis patients are estimated to present for treatment, 98% of those who seek medical help first present to primary care practitioners.⁵ The collective expertise of allergists in the identification, prevalence, and management of rhinitis subtypes may help primary care clinicians diagnose and treat rhinitis more effectively.

Currently, there is a great disparity between the manner in which allergists/immunologists and primary care practitioners diagnose and treat rhinitis. Typically, allergists use a variety of clinical tools to diagnose differentially the subtype of rhinitis and tailor treatment to the diagnosis.⁶⁻¹⁴ To determine the presence of atopy, allergists rely on the information provided by a thorough medical history and physical examination, combined with the results of ancillary tests that might include nasal cytology testing, skin-prick tests, nasal allergen challenge, and assays to determine specific immunoglobulin E production. By comparison, primary care clinicians, because of time constraints, often may not conduct as detailed a history or nasal examination with respect to seeking clues for the presence of atopy, and they often do not have at their disposal ancillary tests to determine definitively an allergic etiology. Ironically, because many primary care practitioners are more familiar with allergic rhinitis than any of the other rhinitis subtypes, they usually assume the rhinitis is allergic in origin, yet neglect to specifically identify the offending environmental exposure(s). Treatment, offered by primary care practitioners, often is initiated or limited to prescribing an antihistamine, which is sometimes mistakenly regarded as a panacea for rhinitis symptoms. Unfortunately, for the majority (75%) of rhinitis patients, this management approach often leads to inadequate relief.¹⁵ In fact, it is likely that a large proportion of rhinitis patients, treated with antihistamines, in the primary care setting, do not have allergies. Perhaps the most unfortunate aspect of this scenario is the consequent frustration of treatment failure, which can generate a vicious cycle of dissatisfaction with care and poor subsequent com-

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pliance even when potentially more effective treatment is eventually prescribed.

The need to ensure successful outcomes is all the more poignant because untreated rhinitis can cause complications and is considered a risk factor for asthma. In addition to the discomfort of the disease itself, rhinitis is also associated with sleep disorders including sleep apnea, fatigue, lack of productivity, facial malformations, and otitis media.^{6-8,16} Recent evidence indicates that asthma and rhinitis often coexist both in atopic and in nonatopic patients, and effective treatment of the rhinitis frequently improves the asthma.¹⁷⁻³⁰ In fact, one study has shown rhinitis to be ubiquitous in asthma patients.³¹ In another study of 690 college freshmen who had no clinical evidence of asthma, 162 subjects (21%) initially were evaluated as having allergic rhinitis.³² During the ensuing 23 years, subjects with allergic rhinitis had a threefold higher risk of developing asthma, which manifested in 10.5% of those with allergic rhinitis compared with 3.6% of nonallergic subjects.³³⁻³⁵

What accounts for the vast differences between the diagnosis and management of rhinitis by primary care practitioners and allergists?

IDENTIFICATION OF THREE RHINITIS SUBTYPES

The problem has multiple layers. Over the last 20 years, allergists have noted extensive heterogeneity in the clinical expression of rhinitis and have identified a large segment of rhinitis patients who are nonatopic.^{6,7} In contrast to pure allergic rhinitis, which is categorized as being either seasonal or perennial based on the provoking aeroallergen(s), nonallergic rhinitis represents a diverse group of syndromes related by their common symptoms and the shared absence of immunoglobulin E-mediated sensitivity.^{6,7} Because the clinical expression of allergic and nonallergic rhinitis often overlaps, patients can be diagnosed accurately only by performing ancillary tests. A diagnosis of pure nonallergic rhinitis requires negative testing to relevant allergens and the presence of additional features derived from the medical history.⁷ However, nonallergic rhinitis remains underrecognized.

Throughout the years, as clinical evidence of the different nonallergic rhinitis syndromes has accumulated, they have been referred to by a variety of terms (*e.g.*, perennial or chronic nonallergic rhinitis, idiopathic rhinitis, and vasomotor rhinitis) and classified using a variety of different schemes. For example, they can be categorized by frequency of occurrence in the rhinitis population or by etiology based on cytological or immunologic features (Tables I and II).⁷ As a consequence of this redundancy, together with the heterogeneity of nonallergic rhinitis and the relatively few organized studies that have been conducted in this population compared with allergic rhinitis, the etiology of many nonallergic rhinitis syndromes remains a mystery. This has led to considerable practice variation in the diag-

TABLE I	
Classification of Nonallergic Rhinitis Syndromes by Frequency	
Frequent	Infrequent
Vasomotor rhinitis	Hypothyroidism
Chronic sinusitis	Atrophic rhinitis
Structural abnormality	Systemic immunological disorders
NARES/BENARS	Cerebral spinal fluid rhinorrhea
Rhinitis medicamentosa	Other structural disorders
Rhinitis of pregnancy	Foreign body
	Ciliary dyskinesia
	Nasal mastocytosis
<i>BENARS = blood eosinophilia nonallergic rhinitis syndrome.</i>	

nosis and management of nonallergic rhinitis. This situation has improved considerably over the last 5 years as more information on the demographics and epidemiology of rhinitis has become available and through the efforts of the Joint Task Force on Practice Parameters in Allergy, Asthma, and Immunology. A practice guideline published by the Joint Task Force was designed to standardize the diagnosis and treatment of rhinitis by describing the clinical expression, pathogenesis, and treatment of the different rhinitis subtypes and syndromes.⁶

Knowledge of an additional third subtype of rhinitis, termed mixed rhinitis, is even in less widespread use than that of nonallergic rhinitis, leading to its extensive underrecognition. Mixed rhinitis refers to the presence of both allergic and nonallergic rhinitis components within the same individual.⁷ Because recent epidemiologic studies indicate that mixed rhinitis may be a predominant rhinitis subtype, greater awareness of its diagnosis and treatment will likely improve rhinitis outcomes. However, mixed rhinitis can be even more difficult to diagnose definitively and treat than nonallergic rhinitis. The magnitude of the mixed rhinitis population has prompted allergists to question whether a large number of rhinitis patients have received an incorrect diagnosis and to reevaluate the diagnostic criteria that distinguish the different types of rhinitis.

RECOGNIZING NONALLERGIC AND MIXED RHINITIS

How can clinicians recognize the presence of nonallergic rhinitis? Although some of the syndromes have characteristic symptoms, the hallmark of nonallergic rhinitis is symptoms of chronic duration.^{6,7} Most patients with pure nonallergic rhinitis have negative skin-prick tests. In those patients with pure nonallergic rhinitis, who do test positive, the skin tests are explained as clinically irrelevant if these patients do not develop symptoms in response to allergen

TABLE II

Etiologic Classification of Nonallergic Rhinitis Syndrome

Inflammatory	Noninflammatory	Structurally Related Rhinitis
Eosinophilic nasal disease	Rhinitis medicamentosa	Septal deviation
NARES	Reflex-induced rhinitis	Neoplastic and nonneoplastic tumor
BENARS	Bright lights and Other	Miscellaneous
Basophilic/metachromatic	Physical modalities	Adenoid hypertrophy
Nasal disease	Vasomotor rhinitis	Choanal atresia/stenosis
Infectious	Irritant rhinitis	Trauma
Chronic sinusitis	Cold air	Foreign body
Nasal polyposis	Gustatory rhinitis	Malformation
Aspirin intolerance	Metabolic rhinitis	Cleft palate
Churg-Strauss syndrome	Rhinitis of pregnancy	
Young's syndrome	Hypothyroidism	
Cystic fibrosis	Hormone replacement therapy	
Kartagener's syndrome	Acromegaly	
Atrophic rhinitis		
Immunologic nasal disease		
Sjogren's syndrome		
Systemic lupus erythematosus		
Relapsing polychondritis		
Churg-Strauss syndrome		
Sarcoidosis		
Wegener's granulomatosis		

BENARS = blood eosinophilia in nonallergic rhinitis.

exposure.⁷ Rather than being provoked by allergens, non-allergic rhinitis symptoms are exacerbated by "classic non-allergic" provocateurs, which include nonimmunogenic respiratory irritants, changes in weather conditions, and alcoholic beverages.⁷ Respiratory irritants include substances that emit strong odors or fumes such as perfume, soap, paint, hair spray, and cigarette smoke. Weather changes refer to exacerbation by drafts, cold air, dampness, and changes in humidity and temperature. These occur most commonly in the spring and fall, which is why it can be difficult to distinguish between some nonallergic rhinitis syndromes and seasonal allergic rhinitis, based on temporal expression alone.

There are other clinical clues that help distinguish among allergic, nonallergic, and mixed rhinitis (Table III). In addition to having a working knowledge of the different classification schemes, practitioners caring for rhinitis patients should be familiar with the demographic profiles of the rhinitis subpopulations. For example, allergic rhinitis more commonly develops before the age of 20 years, whereas nonallergic rhinitis generally affects an older population. In a study by Togias of 362 rhinitis patients, symptoms began before the age of 20 years in 70% of patients with allergic rhinitis, whereas disease onset began after the age of 20 years in 70% of patients with nonallergic rhinitis.³⁶

Similarly, the gender distribution appears to differ for allergic and nonallergic rhinitis. Although the genders are represented equally in allergic rhinitis, a disproportionately

large percentage (58–74%) of women were diagnosed with nonallergic and mixed rhinitis, depending on the study population.^{6,7,37,38} One reason for the gender bias may be the influence of endocrinologic effects on the development of hormonal nonallergic rhinitis, including the menstrual cycle, pregnancy, and the use of oral contraceptives or estrogen/hormone replacement therapy.

Thus, the profile of clinical features indicative of nonallergic rhinitis includes the constellation of symptoms and their temporal expression and demographic traits. The presence of any one of these features can provide clues to the allergist regarding the likelihood of nonallergic rhinitis. However, the type of nasal symptoms manifested by the patient usually does not differentiate allergic from nonallergic rhinitis. Despite this limitation, the most prominent symptoms of nonallergic rhinitis tend to be congestion and postnasal drainage, with sneezing or itching being less frequent. These perennial symptoms often are accompanied by nasal hyperreactivity that is exacerbated by nasal irritants and weather changes.⁷ Information from the medical history regarding the onset of symptoms also is important, including both the age when symptoms first appeared and their temporal expression. As stated previously, the demographics of nonallergic rhinitis suggest an increased likelihood that patients with nonallergic rhinitis will be women >20 years old.^{36,37} Nonallergic rhinitis patients also are unlikely to have close relatives with allergies or to have a history of other allergic syndromes such as atopic dermatitis. On physical examination, the absence of features typical of allergic

TABLE III

Differential Diagnosis of Allergic and Nonallergic Rhinitis

Manifestation	Allergic Rhinitis	Nonallergic Rhinitis
Age of onset	Usually <20	Usually >20
Seasonality	Seasonal or perennial	Usually perennial
Exacerbating factors	Allergen exposure	Irritant exposure, weather changes
Nature of symptoms		
Pruritus	Common	Infrequent
Congestion	Common	Common
Sneezing	Prominent	Occasionally predominates
Rhinorrhea	Common	Uncommon
Postnasal drip	Not prominent	Prominent
Other allergic symptoms	Often present	Absent
Family history of allergy	Usually present	Usually absent
Ancillary studies		
Skin-prick tests	Positive skin tests	Negative to relevant allergens
Cytologic testing		
Nasal scraping	Eosinophils usually present	Eosinophils present in 1/3 (NARES and BENARS)
Peripheral eosinophilia	Often present	Absent except for BENARS

BENARS = blood eosinophilia in nonallergic rhinitis.

rhinitis is an important clue to the possible presence of nonallergic rhinitis.⁶ These include eye irritation, itchiness of the throat or palate, and the “allergic salute” (upward rubbing of the nose with the palm of the hand in an attempt to reduce persistent itching) or the “allergic crease” (a transverse skin line above the tip and below the bridge of the nose caused by constant rubbing).⁶

Although these represent general characteristics of patients with nonallergic rhinitis, specific features of the more common nonallergic rhinitis syndromes are also worth mentioning. By far the most common form of nonallergic rhinitis is vasomotor rhinitis, which occurs in 61% of patients with nonallergic rhinitis.³⁸ Frequencies of the most prevalent nonallergic rhinitis syndromes were shown in a study of 78 nonallergic rhinitis patients conducted by Settupane and Klein.³⁸ As shown in Table IV, nonallergic rhinitis eosinophilia syndrome (NARES) and sinusitis are also common, affecting 33 and 16% of patients with nonallergic rhinitis, respectively. Blood eosinophilia in nonallergic rhinitis had a prevalence of 4% and hypothyroidism had a prevalence of 2%. Other hallmarks of vasomotor rhinitis are provocation by the spectrum of classic provocateurs and the presence of nonspecific nasal hyperreactivity. In addition to nasal irritants, weather changes, hormonal changes, and alcohol ingestion, triggers of vasomotor rhinitis include bright lights and hot or spicy foods.⁷ There are two categories of vasomotor rhinitis patients, those whose predominant symptom is rhinorrhea, referred to as “runners,” and those whose predominant symptom is congestion, referred to as “blockers,” although some patients alternate between the two.^{6,7}

Patients with NARES often present with intense nasal symptoms, complaining of perennial sneezing paroxysms, profuse watery nasal secretions, nasal itching, and loss of

TABLE IV

Frequency of Nonallergic Rhinitis Syndromes in 78 Patients

Syndrome	Patients	
	Number	Percent
Vasomotor rhinitis	44	61
NARES	25	33
Sinusitis*	11	16
BENARS	3	4
Hypothyroidism	1	2

BENARS = blood eosinophilia nonallergic rhinitis syndrome.

**Overlapping diagnoses.*

Source: Adapted from Ref. 38.

the ability to smell (anosmia).^{6,7} Smears of their nasal secretions contain high eosinophil counts. Although elevated eosinophils, sneezing paroxysms, and nasal itching are often characteristics of allergic rhinitis, allergy skin tests performed on NARES patients are definitively negative.

Symptoms of chronic sinusitis include nasal congestion and discharge, postnasal drip, facial pain or pressure, olfactory disturbances, and fever or halitosis.^{6,7} Rhinitis mediated by a cholinergic mechanism is another nonallergic rhinitis syndrome characterized by distinct nasal symptoms and triggers. The sudden onset of profuse, watery nasal secretions on ingestion of hot, spicy foods is typical of gustatory rhinitis, and a similar response to cold, dry air is characteristic of skier's/jogger's nose.^{6,7} Rhinitis of pregnancy is the most common form of hormone-associated rhinitis, the hallmark of which is nasal congestion that

TABLE V

Prevalence of Allergic Rhinitis

Investigator	Year	Subjects	Prevalence Rate
Freeman <i>et al.</i> ³⁹	1964	8th graders	22%
		12th graders	29%
Hagy and Settippene ^{32,33}	1969	College freshmen	21%
		College seniors	24%
Greisner <i>et al.</i> (follow-up) ³⁵	1985	40 years old	42%*
Broder <i>et al.</i> ²⁰	1974	16–24 years old	15%
Gergen and Turkeltaub ⁴¹	1992	18–24 years old	9% Allergic
		18–24 years old	17% Chronic
Wright <i>et al.</i> ⁴²	1994	6 years old	42%
McMenamin ⁴³	1994	NHIS and NAMCS	9%
Nathan <i>et al.</i> ⁴⁴	1997	Nationwide survey	18%

*Cumulative prevalence (ever had) of allergic rhinitis.

progresses in severity throughout pregnancy and subsides at parturition, in the absence of sneezing or itching, although some patients may have increased nasal secretions.^{6,7} Another nonallergic rhinitis syndrome, referred to as rhinitis medicamentosa, is drug induced. In this syndrome, nasal congestion can be triggered by numerous medications, including oral antihypertensive drugs, birth control pills, and some agents used for relief of urinary obstruction, although the term is used most often to refer to the rebound congestion that follows overuse of topical decongestants for >5–7 days or the abuse of cocaine.^{6,7}

Mixed rhinitis can be more challenging to recognize. These patients exhibit definitive allergic rhinitis, triggered by either seasonal or perennial allergens, and test positive on skin-prick tests. However, they also exhibit chronic rhinitis symptoms that are not entirely explained by skin test reactivity. For example, a patient might have perennial rhinitis symptoms that are triggered by “classic” nonallergic rhinitis provocateurs and, in addition, manifest a worsening of symptoms during the late summer, although skin tests are only positive for ragweed.⁷

This type of information has served the practitioner well when differentially diagnosing rhinitis. Although the field continues to evolve, one of the areas that has changed most over the last 2 years is the relative prevalence of the three rhinitis subtypes. Most epidemiologic studies have omitted the nonallergic and/or mixed rhinitis populations, significantly biasing diagnostic classification in favor of allergic rhinitis. Earlier studies that used skin tests to distinguish only allergic and nonallergic rhinitis would have eclipsed the mixed rhinitis population under the allergic rhinitis umbrella. The magnitude of the prevalence rates can help remind clinicians to consider mixed rhinitis when diagnosing rhinitis, which would likely improve treatment outcomes.

RELATIVE PREVALENCES OF RHINITIS SUBTYPES

Several epidemiologic studies have been conducted to determine the prevalence of allergic rhinitis.^{20,34,39–44} Although examining the frequency of this rhinitis subtype might seem to be more straightforward than either of the other two, even these studies were fraught with problems. Prime among these is the lack of uniformity in the criteria used to determine the presence of allergy or rhinitis, many being self-reported questionnaires that did not specify physician-diagnosed rhinitis nor confirm atopy with skin testing. Because most of the studies focused only on hay fever, neglecting other triggers of seasonal or perennial allergic rhinitis, they tended to underestimate the prevalence rates, particularly of perennial disease. There was also considerable variation in the ages and sizes of the study cohorts and their geographic locations. Such variability undoubtedly accounts for the considerable interstudy variation in the reported prevalence rates of rhinitis in the United States, as shown in Table V.

One of the earliest studies, conducted by Freeman in 1964, was based on a self-reported questionnaire given to school children in Denver.³⁹ The prevalence of seasonal allergic rhinitis (hay fever) was 16% in 8th graders and 22% in 12th graders. An additional 7.3% of 8th graders and 5.6% of 12th graders had perennial rhinitis (overall prevalence rates of 21.6 and 29.3%, respectively). Other studies conducted in children and adolescents also reveal high prevalence rates for allergic rhinitis. As mentioned earlier, a similar frequency of 21% was reported in a 1969 study of college freshmen by Hagy and Settippene, which increased 3.1% by the senior year.^{32,40} Long-term follow-up of this population by Greisner *et al.* revealed a continued increase in prevalence to 31% when the population reached 40 years of age in 1985, which represented a cumulative prevalence of 42%.³⁴

TABLE VI

Prevalences of Allergic, Nonallergic, and Mixed Rhinitis

Investigator	N	Type of Rhinitis		
		Allergic	Mixed	Nonallergic
Mullarkey <i>et al.</i> ⁴⁵	142	48%	Included in allergic*	52%
Togias ³⁶	362	83%	Not studied	17%
ECRHS ¹⁷	1412	75%	Not studied	25%
NRCTF ^{7,47}	975	43%	34%	23%
NRCTF combined allergic		77%		23%
NRCTF combined nonallergic		43%		57%

*Forty-six percent (22/48) of patients with definite allergic rhinitis had symptoms provoked by physical agents.

Several other studies also have shown that the prevalence of allergic rhinitis increases throughout childhood and peaks during adolescence, including two population-based studies of physician-diagnosed allergic rhinitis, an early one by Broder *et al.* reported in 1974, and a survey by the National Health and Nutrition Examination II reported by Gergen in 1994.^{20,41} In the Broder study of seasonal and perennial allergic rhinitis in a rural Michigan community during the mid-1960s, peak prevalence rates of 15.4% occurred in 16- to 24-year-old subjects.²⁰ In the National Health and Nutrition Examination II study, conducted in 1976–1980 on a nationwide population and which used confirmatory skin-prick tests, prevalences peaked in 18- to 24-year-old subjects who had frequencies of 9% for allergic rhinitis and 17% for chronic rhinitis (which encompassed allergic and nonallergic perennial rhinitis).⁴¹ This is in stark contrast to the high prevalence (42% by the age 6 years) of physician-diagnosed allergic rhinitis among 747 children in Tucson reported by Wright in 1994.⁴² Two other nationwide population surveys conducted in 1990 and 1993 reported overall prevalence rates for physician-diagnosed allergic rhinitis of 9 and 18%, respectively.^{43,44}

Although there is a comparative dearth of studies on the epidemiology of nonallergic rhinitis, those that have been conducted reveal even greater inconsistencies and variability than the allergic rhinitis studies. Accurate differential diagnosis of nonallergic rhinitis requires skin testing, but this verification has been omitted in most of the studies. In general, ratios of allergic to nonallergic rhinitis tend to be skewed in favor of seasonal allergic rhinitis because it is easier to identify seasonal exacerbations.

Five studies have examined the prevalence of nonallergic rhinitis, and only three of these also have measured the prevalence of the mixed rhinitis population (Table VI). The first study was conducted by Mullarkey *et al.* in 1980 on 142 physician-diagnosed rhinitis patients.^{45,46} They identified four groups of patients based on skin tests and other parameters, two groups that tested positive for allergy [48%] (one group with seasonal allergic rhinitis [33.8%], and another group with less pronounced allergy [14.8%]) and two groups with nonallergic rhinitis (52%) comprised

of vasomotor rhinitis (36.6%) and NARES (14.8%) patients. In addition, 46% of the patients classified as having definite allergic rhinitis also had symptoms triggered by physical agents.⁴⁵ This latter group of patients possesses characteristics consistent with mixed rhinitis and, consequently, has been noted as such in Table VI. Two subsequent studies, one by Togias conducted in 1990 on 362 rhinitis patients and a second by the European Community Rhinitis Health Survey (ECRHS) conducted in 1999 on 1412 rhinitis patients, only examined the frequencies of allergic and nonallergic rhinitis, reporting prevalence rates for nonallergic rhinitis of 17 and 25%, respectively, and prevalences for allergic rhinitis of 83 and 75%, respectively.^{17,36}

Two recent studies examined the prevalences of all three rhinitis subtypes in two different large U.S. populations.^{7,35,47,48} The first of these, reported in 1999 by the National Rhinitis Classification Task Force (NRCTF), was a retrospective review of 975 patients at 15 allergy centers across the country who had physician-diagnosed rhinitis.^{7,47} The prevalence rates were 23% for pure nonallergic rhinitis, 34% for mixed rhinitis, and 43% for pure allergic rhinitis. These rates compare favorably with those of the ECRHS because if the NRCTF study had omitted the mixed rhinitis group, and instead had combined it with the allergic rhinitis group, the prevalence of allergic rhinitis would have been 77% (43 + 34%). This figure closely resembles the prevalence of allergic rhinitis reported by the ECRHS (75% for allergic rhinitis and 25% for nonallergic rhinitis), and likely represents a similar pooling of the mixed rhinitis and allergic rhinitis groups because both tested positive on skin test. It also indicates that the ratio of allergic to pure nonallergic rhinitis is 3:1. Alternatively, had the mixed rhinitis group of the NRCTF been combined with the nonallergic rhinitis group, the prevalence of nonallergic rhinitis would have been 57% (23 + 34%), reflecting the large contribution of the nonallergic component to rhinitis.

How can these ratios be used to determine that actual size of the U.S. population affected by rhinitis? Based on the fact that ~20% of the U.S. population suffers from allergic rhinitis, there are 58 million individuals with allergic rhinitis in this country. Using the 3:1 ratio of allergic to pure

nonallergic rhinitis, the number of people estimated to have pure nonallergic rhinitis in the United States is 19 million. Extrapolating from the composition of the 58 million people estimated to have allergic rhinitis, 26 million would be expected to have mixed rhinitis and 32 million would be expected to have pure allergic rhinitis. Therefore, a total of 45 million (19 million + 26 million) rhinitis patients are estimated to have a nonallergic component.

More recently, a survey study of 16,860 rhinitis patients in primary care practices across the United States was conducted using a new rhinitis screening tool.⁴⁸ This rhinitis screening tool was devised to help primary care practitioners differentially diagnose rhinitis based on the history given by the patient regarding the type of trigger and the temporal expression of symptoms. Preliminary results of this study reveal what allergists have long suspected: that the magnitude of the mixed rhinitis population vastly exceeds that of the other two subtypes. The prevalence rates of the rhinitis subtypes were determined to be 77% for mixed rhinitis, 12% for pure allergic rhinitis, and 9% for pure nonallergic rhinitis. Thus, although this study was limited by being purely historical data, it does confirm a high prevalence of mixed rhinitis.

CONCLUSION

The magnitude of the mixed rhinitis population is an entirely new concept, prompting clinicians to question whether rhinitis has been diagnosed incorrectly in a large proportion of cases, both in research and in clinical practice. Because the correct differential diagnosis of rhinitis can aid in designing an appropriate management strategy and in optimizing successful outcomes, it is imperative that patients are diagnosed accurately and that both allergic and nonallergic components are addressed. However, diagnosis can be challenging, because many of the symptoms for allergic, nonallergic, and mixed rhinitis overlap. Nonallergic and mixed rhinitis are far more common than previously suspected. Although the use of ancillary tests provides additional information, it is important for clinicians to remember that positive skin tests do not exclude the possibility of mixed rhinitis; even when a relevant allergen is found to exist, there is a strong possibility (44%) of coexistent nonallergic rhinitis. Thus, a wide spectrum of relevant information can be used in the differential diagnosis of rhinitis, including the prevalence rates of rhinitis subtypes and syndromes. The presence of clinically relevant allergens merely serves as a reminder to look further and consider whether a patient truly has pure allergic rhinitis or suffers from mixed rhinitis, so that optimal treatment is prescribed.

REFERENCES

1. Sly RM. Changing prevalence of allergic rhinitis and asthma. *Ann Allergy Asthma Immunol* 82:233–252, 1999.
2. Evans R III. Epidemiology and natural history of asthma, allergic rhinitis, and atopic dermatitis. In *Allergy: Principles and Practice*, 4th

- ed. Middleton E, Reed CE, Ellis EF, et al. (Eds). St. Louis, MO: Mosby-Year Book, Inc., 1109–1136, 1993.
3. Howarth PH, and Holmberg K. Allergic rhinitis: an increasing clinical problem. *Allergy* 50(suppl 23):4–5, 1995.
4. Howarth PH. Is allergy increasing? Early life influences. *Clin Exp Allergy* 28(suppl 6):2–7, 1998.
5. Rachelefsky G. National guidelines needed to manage rhinitis and prevent complications. *Ann Allergy Asthma Immunol* 82:296–305, 1999.
6. Dykewicz M, and Fineman S (Eds). Diagnosis and management of rhinitis: complete guidelines of the Joint Task Force on practice parameters in allergy, asthma, and immunology. *Ann Allergy Asthma Immunol* 81:478–518, 1998.
7. Settipane RA, and Lieberman P. Update on nonallergic rhinitis. *Ann Allergy Asthma Immunol* 86:494–508, 2001.
8. Lieberman P. Rhinitis. In *Expert Guide to Allergy and Immunology*. Slavin RG, and Reisman RE (Eds). Philadelphia: American College of Physicians, 23–40, 1999.
9. Lund V. Allergic rhinitis—making the correct diagnosis. *Clin Exp Allergy* 28(suppl 6):25–28, 1998.
10. Urval KR. Overview of diagnosis and management of allergic rhinitis. *Prim Care* 25:649–662, 1998.
11. Storms WW. A comprehensive diagnostic approach to upper airway disease. *J Allergy Clin Immunol* 101:S361–S363, 1998.
12. Chrostowski D, and Pongracic J. Control of chronic nasal symptoms: directing treatment at the underlying cause. *Postgrad Med* 111:77–95, 2002.
13. Scadding GK. Non-allergic rhinitis: diagnosis and management. *Curr Opin Allergy Immunol* 1:15–20, 2001.
14. Settipane RA, and Settipane GA. Nonallergic rhinitis. In *Current Review, Ch 6. of Rhinitis*. Michael A. Kaliner, M.D. (Ed). Philadelphia: Current Medicine, Inc., 53–66, 2001.
15. Storms W, Meltzer EO, Nathan RA, et al. The economic impact of allergic rhinitis. *J Allergy Clin Immunol*. 99:S820–S824, 1997.
16. Spector SL. Overview of comorbid associations of allergic rhinitis. *J Allergy Clin Immunol* 99:S773–S780, 1997.
17. Leynaert B, Bousquet J, Neukirch C, et al. Perennial rhinitis: an independent risk factor for asthma in nonatopic subjects. *J Allergy Clin Immunol* 104:301–304, 1999.
18. Guerra S, Sherrill DL, Martinez FD, and Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. *J Allergy Clin Immunol* 109:419–425, 2002.
19. Sibbald B, and Rink E. Epidemiology of seasonal and perennial rhinitis: clinical presentation and medical history. *Thorax* 46:895–901, 1991.
20. Broder I, Higgins MW, Mathews KP, and Keller JB. Epidemiology of asthma and allergic rhinitis in a total community, Tecumseh, Michigan. *J Allergy Clin Immunol* 54:100–110, 1974.
21. Pedersen PA, and Weeke ER. Asthma and allergic rhinitis in the same patients. *Allergy* 38:25–29, 1983.
22. Leynaert B, Neukirch F, Demoly P, and Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. *J Allergy Clin Immunol*. 106:S201–S205, 2000.
23. Passalacqua G, Ciprandi G, and Canonica GW. The nose-lung interaction in allergic rhinitis and asthma: united airways disease. *Curr Opin Clin Immunol* 1:7–13, 2001.
24. Corren J. The impact of allergic rhinitis on bronchial asthma. *J Allergy Clin Immunol* 101:S352–S356, 1998.
25. Grossman J. One airway, one disease. *Chest* 111:11S–16S, 1997.
26. Rowe-Jones JM. The link between the nose and lung, perennial rhinitis and asthma—is it the same disease? *Allergy* 52(suppl 36): 20–28, 1997.
27. Simons FER. Allergic rhinobronchitis: the asthma-allergic rhinitis link. *J Allergy Clin Immunol* 104:534–540, 1999.
28. Vinuya RZ. Upper airway disorders and asthma: a syndrome of airway inflammation. *Ann Allergy Asthma Immunol* 88(suppl):8–15, 2002.

29. Moller C, Dreborg S, Ferdousi HA, et al. Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-Study). *J Allergy Clin Immunol* 109:251–256, 2002.
30. Jacobsen L. Preventive aspects of immunotherapy: prevention for children at risk of developing asthma. *Ann Allergy Asthma Immunol* 87(suppl):43–46, 2001.
31. Kapsali T, Horowitz E, Diemer F, and Togias A. Rhinitis is ubiquitous in allergic asthmatics. *J Allergy Clin Immunol* 99:S138, 1997 (Abs).
32. Hagy GW, and Settiple GA. Bronchial asthma, allergic rhinitis and allergy skin tests among college students. *J Allergy* 44:323–332, 1969.
33. Hagy GW, and Settiple GA. Prognosis of positive skin tests in an asymptomatic population. *J Allergy Clin Immunol* 48:200–211, 1971.
34. Settiple RJ, Hagy GW, and Settiple GA. Long-term risk factors for developing asthma and allergic rhinitis: a 23-year follow-up study of college students. *Allergy Proc* 15:21–25, 1994.
35. Greisner WA III, Settiple RJ, and Settiple GA. Co-existence of asthma and allergic rhinitis: a 23-year follow-up of college students. *Allergy Asthma Proc* 19:185–189, 1998.
36. Togias A. Age relationships and clinical features of nonallergic rhinitis. *J Allergy Clin Immunol* 85:182, 1990 (Abs).
37. Enberg RN. Perennial nonallergic rhinitis: a retrospective review. *Ann Allergy* 63:513–516, 1989.
38. Settiple GA, and Klein DE. Nonallergic rhinitis: demography of eosinophils in nasal smear, blood total eosinophil counts and IgE levels. *N Engl Reg Allergy Proc* 6:363–366, 1985.
39. Freeman GL, and Johnson S. Allergic diseases in adolescents. *Am J Dis Child* 107:549–559, 1964.
40. Hagy GW, and Settiple GA. Risk factors for developing asthma and allergic rhinitis: a 7 year follow-up study of college students. *J Allergy Clin Immunol* 58:330–336, 1976.
41. Gergen PJ, and Turkeltaub PC. The association of individual allergen reactivity with respiratory disease in a national sample: data from the second National Health and Nutrition Examination Survey, 1976–1980 (NHANES II). *J Allergy Clin Immunol* 90: 579–588, 1992.
42. Wright AL, Holberg CJ, Martinez FD, et al. Epidemiology of physician-diagnosed allergic rhinitis in childhood. *Pediatrics* 94:895–901, 1994.
43. McMenamin P. Costs of hay fever in the United States in 1990. *Ann Allergy* 73:36–39, 1994.
44. Nathan RA, Meltzer EO, Selner JC, and Storms W. Prevalence of allergic rhinitis in the United States. *J Allergy Clin Immunol* 99: S808–S814, 1997.
45. Mullarkey MF, Hill JS, and Webb R. Allergic and nonallergic rhinitis: their characterization with attention to the meaning of nasal eosinophilia. *J Allergy Clin Immunol* 65:122–126, 1980.
46. Mullarkey MF. Eosinophilic nonallergic rhinitis. *J Allergy Clin Immunol* 82:941–949, 1988.
47. Settiple R. The broad spectrum of rhinitis: etiology, diagnosis, and advances in treatment. Presented at the meeting of the National Allergy Advisory Council (NAAC), St. Thomas, US Virgin Islands, October 16, 1999.
48. Lieberman PL, Rakel RE, Hedges HH III, et al. Quantifying the incidence of mixed rhinitis with a new patient screening tool. *Ther Trends* 20:221–232, 2002. □

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