
CME review article

This feature is supported by an unrestricted educational grant from AstraZeneca LP

Allergic rhinitis and its effect on sleep, fatigue, and daytime somnolence

Carah B. Santos, MS; Ellen L. Pratt, MD; Chris Hanks, MS; Jeffery McCann, MS; and Timothy J. Craig, DO

Objective: To examine the adverse effects of sleep impairment on the quality of life of patients with the disorder and how these effects can be treated with therapies targeted at the underlying problems that influence sleep.

Data Sources: Medline and Ovid search for sleep and rhinitis.

Study Selection: All literature on this topic were reviewed, and, if significant, were incorporated into this review.

Results: Intranasal corticosteroids used as treatment for allergic rhinitis have been shown to reduce the nasal congestion characteristic of the disorder. Data on sleep-related end points from clinical trials on intranasal corticosteroids also reveal that the treatment's effectiveness in alleviating nasal congestion leads to better sleep, reduced daytime somnolence, and improved quality of life.

Conclusion: Further research, specifically using sleep measurements as primary end points, is needed to definitively show that intranasal corticosteroids reduce nasal congestion, thereby improving sleep and, consequently, quality of life in patients with allergic rhinitis. These future trials will serve to identify the most effective therapies that target the adverse effects of sleep impairment in this disorder.

Ann Allergy Asthma Immunol. 2006;97:579–587.

Off-label disclosure: Drs Santos, Pratt, Hanks, McCann, and Craig have indicated that this article does not include the discussion of unapproved/investigative use of a commercial product/device.

Financial disclosure: Dr Craig has indicated that in the last 12 months he has worked as an advisory board member for Sanofi-Aventis, was on the speakers' bureau for Merck, Genentech/Novartis, GlaxoSmithKline, Pfizer, Alcon, and Schering Plough, and received research support from Schering Plough, Merck, GlaxoSmithKline, Methapharm, AstraZeneca, Boehringer-Ingelheim, Novartis/Genentech, Dyax, Lev Pharmaceuticals, ZLB, Centacore, Sanofi-Aventis, Pharming, and Altana. Drs Santos, Pratt, Hanks, and McCann do not have any conflicts of interest.

Instructions for CME credit

1. Read the CME review article in this issue carefully and complete the activity by answering the self-assessment examination questions on the form on page 586.
2. To receive CME credit, complete the entire form and submit it to the ACAAI office within 1 year after receipt of this issue of the *Annals*.

INTRODUCTION

Patients with allergic rhinitis often experience impaired sleep. A recent survey of allergic rhinitis patients revealed that 68% of respondents with perennial allergic rhinitis (PAR) and 48% with seasonal allergic rhinitis (SAR) reported that their condition caused significant sleep disturbances.¹ One of the major symptoms of the disorder, nasal congestion, in addition to such underlying disease processes as the release of inflammatory mediators, can cause the sleep impairment associated with allergic rhinitis.

The symptoms of allergic rhinitis include rhinorrhea; sneezing; pruritus of the eyes, nose, and throat; and nasal

congestion. Nasal congestion stands as one of the most prominent and bothersome symptoms of the disorder, especially since it is linked to sleep-related problems associated with allergic rhinitis, such as sleep-disordered breathing, sleep apnea, and snoring.^{2–5}

The prevalence of allergic rhinitis makes the sleep impairment associated with this disorder a common problem. Allergic rhinitis reportedly affects approximately 25% of the world's population,⁶ and its prevalence has continued to increase.⁷ It has been estimated that the disorder affects 20 million to 40 million people in the United States, which includes approximately 40% of the nation's children.⁸ In Europe, the prevalence of allergic rhinitis is estimated as 23%.⁹

Those with allergic rhinitis often cannot escape the socioeconomic burdens associated with living with the disorder. In 2000, patients spent more than \$6 billion on prescription

Allergy Research, Hershey Medical Center, Penn State University, Hershey, Pennsylvania.

Received for publication September 27, 2006.

Accepted for publication in revised form October 5, 2006.

medications for allergic rhinitis.¹⁰ Along with this overwhelming cost of treatment, patients must face the secondary cost of poor productivity, which stems from the negative impact of the disorder's symptoms on patients' lives, as well as the use of inappropriate therapies. The detrimental effect of allergic rhinitis on patients' quality of life has been demonstrated by generic health-related quality-of-life questionnaires, such as the Medical Outcomes Study 36-Item Short-Form Health Survey, and disease-specific measures, such as the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ).¹¹⁻¹⁶ This adverse impact on patients may result from the sleep impairment associated with the disorder.

Although studies have shown that treatments for allergic rhinitis, particularly those that improve symptoms of nasal congestion, can improve patients' sleep and quality of life, further research is needed to elaborate these limited existing data. This review explores the sleep impairment associated with allergic rhinitis and the adverse effects of disturbed sleep on patients' quality of life. This review also examines how these effects are altered by therapies that target the disorder's underlying problems that influence sleep. A search of the literature was conducted using Medline and Ovid. All manuscripts found on "Sleep and Rhinitis" were reviewed, and if the manuscripts added significantly to the medical literature they were included into this review.

EVIDENCE OF SLEEP IMPAIRMENT IN ALLERGIC RHINITIS

Allergic rhinitis is generally associated with sleep impairment, daytime somnolence, and fatigue. Of the multiple symptoms of allergic rhinitis, nasal congestion, in particular, detrimentally affects sleep.^{5,17} The Allergic Rhinitis and Its Impact on Asthma guidelines (Table 1) serve to classify allergic rhinitis severity and provide a measure for this degree of sleep impairment.⁶ The sleep disturbances allergic rhinitis patients experience include microarousals and sleep-disordered breathing, which includes snoring, obstructive sleep apnea, and/or hypopnea.^{18,19} Contrary to results from previous studies, however, Kramer et al²⁰ proposed that allergic rhinitis is not a major risk factor for obstructive sleep apnea syndrome. Chronic excessive daytime sleepiness or chronic non-

restorative sleep have been demonstrated as more likely disturbances in patients with frequent nighttime symptoms than in those with rare or no such symptoms.⁵ Further examples illustrating that sleep impairment is a major concern for allergic rhinitis patients include a study that showed that allergic rhinitis leads to snoring in children²¹⁻²³ and another study that demonstrated that concomitant allergic rhinitis independently relates to difficulty sleeping and daytime sleepiness in bronchial asthma patients.²⁴

MECHANISMS OF SLEEP IMPAIRMENT

To alleviate the symptom of sleep impairment in patients with allergic rhinitis, the mechanisms involved in this problematic issue must first be identified. Recent studies have proposed that the reduced sleep quality and daytime fatigue characteristic in allergic rhinitis patients may consequently arise from sleep impairment secondary to symptoms of the disorder, particularly nasal congestion,^{5,18,25} or to the effects of the disorder itself, such as the underlying pathophysiological changes associated with allergic rhinitis.²⁶

Nasal Congestion

Nasal congestion, which results when the cavernous tissues of the nasal turbinates swell after dilation of the capacitance vessels, is a common and bothersome symptom that affects numerous allergic rhinitis patients. Its mechanism involves the reduction in the internal nasal diameter and the increase in airway resistance to nasal airflow, and the symptom can also cause nasal obstruction.²⁷ Subjective, clinical assessments of nasal congestion severity exist, as well as objective measures of nasal airflow, such as peak nasal inspiratory flow, assessments of airway resistance and conductance (rhinomanometry), and acoustic rhinometry, which assesses the volume and area of the nasal cavity by analyzing reflected sound waves.²⁸⁻³⁰

The symptom of nasal congestion worsens at night and first thing in the morning, presumptively because of the posture change when an individual first lays down³¹ and the normal decrease in serum cortisol levels overnight. Landstra et al³² demonstrated the latter in asthma patients, in whom they concluded that lower cortisol levels lead to greater nocturnal airway obstruction. A study on allergic rhinitis patients concluded that congestion worsens overnight and peaks at approximately 6 AM, showing a large-amplitude, circadian variation.²⁷

Results from an Internet survey of 2,355 individuals with allergic rhinitis or the parents of children with allergic rhinitis further reinforced the complaints of those with the disorder. A total of 85% of the respondents or their children reported experiencing nasal congestion, and 40% of all respondents, the greatest proportion of participants who rated the severity of various symptoms, considered their nasal congestion severe (Fig 1).³³ Approximately 50% of the respondents reported that nasal congestion was their most bothersome symptom and that it woke them during the night and made it

Table 1. ARIA Guidelines for the Classification of Allergic Rhinitis⁶

Symptoms	Description
Intermittent	Present <4 days per week or <4 weeks
Persistent	Present 4 days per week and >4 weeks
Severity	
Mild	No impairment of sleep, daily activities, leisure or sport, or school or work; no troublesome symptoms
Moderate to severe	One of more of the following are present: impairment of sleep; impairment of daily activities, leisure, or sport; impairment of school or work; troublesome symptoms

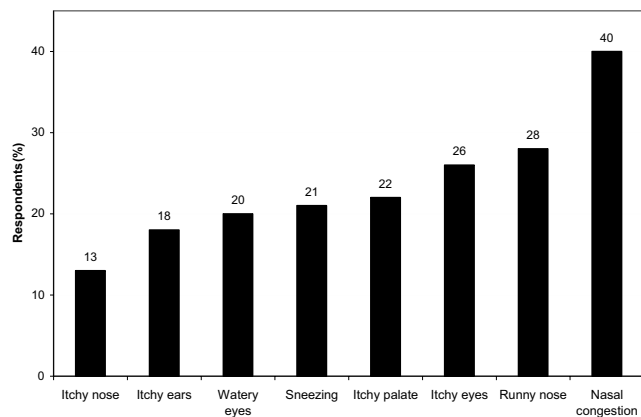


Figure 1. The severity of nasal congestion in individuals with allergic rhinitis.³⁴ Results are expressed as a proportion of all survey respondents who experienced a particular symptom who rated it as severe.

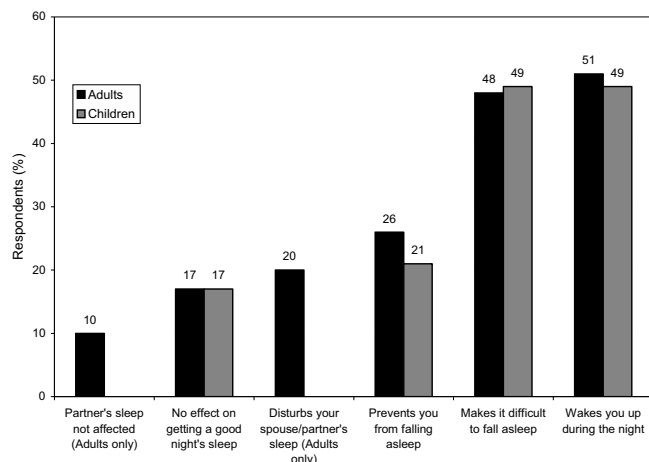


Figure 2. Effects of nasal congestion on sleep in individuals with allergic rhinitis³⁴ in response to the question, "In what ways, if any, has the nasal congestion affected you/your child during the night?"

difficult to fall asleep (Fig 2).³³ A total of 20% of adult respondents claimed that their partner's or spouse's sleep was adversely affected by their nasal congestion, and the degree of sleep impairment correlated with the severity of their congestion.³³ Furthermore, the survey revealed that nasal congestion negatively affected the individuals' or their children's emotions and ability to perform daily activities, all of which may result from the detrimental effects of nasal congestion on sleep.³³

Studies on treatments for the nasal congestion associated with allergic rhinitis, such as one by our group on treatment with topical nasal corticosteroids, propose that the poor sleep and daytime somnolence characteristic of the disorder is predominantly attributed to the symptom of nasal congestion.²⁵ It has been shown that subjecting healthy individuals to nasal occlusion leads to increased sleep apnea and transient

arousals.^{2,3} Previous studies that objectively evaluated the sleep patterns of allergic rhinitis patients demonstrated that their symptoms of nasal congestion led to increased microarousals¹⁹ and episodes of apnea at night.¹⁸ Further, in individuals with allergic rhinitis, congestion either caused or worsened their sleep impairment, which included obstructive sleep apnea.^{28,34} According to Canova et al,³⁵ patients with obstructive sleep apnea syndrome posed a higher risk of having PAR than having obstructive pulmonary disorder. To support this finding, Juniper et al³⁶ developed the Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire (NRQLQ), which led them to discover that allergic rhinoconjunctivitis patients who complained of impaired sleep due to nighttime symptoms found nasal and sinus congestion to be among their most bothersome and troublesome symptoms.

A population-based study on the role of acute and chronic nasal congestion in sleep-disordered breathing, which studied 4,927 patients with a history of nasal congestion and impaired sleep, showed that patients with frequent nocturnal rhinitis symptoms, compared with those with rare or no symptoms, were more likely to complain of habitual snoring, chronic nonrestorative sleep, and excessive daytime fatigue.⁵ Additionally, the study illustrated that patients with allergic rhinitis-associated nasal congestion were 1.8 times more likely to have moderate-to-severe sleep-disordered breathing compared with patients with allergic rhinitis and no reported nasal congestion.⁵

A population-based cohort study (n = 4,916) by Young et al⁴ investigated and confirmed the role of nasal congestion as a risk factor for habitual snoring. It has been suggested that the switch to oronasal breathing after nasal congestion, which compromises the airway and leads to sleep-disordered breathing, stands as the major element that explains the correlation between nasal congestion and snoring.⁵ Furthermore, the review by Chen and Kushida³⁷ advised that nasal obstruction must be considered in patients with sleep-associated breathing disorders as an adjunct to other surgical and nonsurgical treatment.

Other Symptoms

Additional symptoms of allergic rhinitis that may cause the poor sleep and increased sleep disturbance characteristic of the disorder include sneezing, rhinorrhea, and nasal pruritus.³⁵ During their establishment of the NRQLQ, Juniper et al discovered that allergic rhinitis patients considered rhinorrhea one of the most troublesome symptoms that interfered with their sleep.³⁶ The survey by Camhi et al³⁸ of children with sleep disturbances illustrated that respiratory symptoms serve as risk factors for disorders of initiating and maintaining sleep, snoring, and excessive daytime sleepiness. Additionally, the study characterized wheezing as a risk factor for disorders of initiating and maintaining sleep and cough and sputum production as risk factors for snoring and excessive daytime sleepiness.³⁸

Immune Response Mediators

Histamine and cytokines are examples of inflammatory mediators released in the process of an allergic reaction, and such mediators may directly influence the central nervous system and result in the disturbed sleep daytime somnolence characteristic of allergic rhinitis.^{39–41} Histamine helps regulate the sleep-wake cycle and arousal,³⁹ whereas the higher levels of the cytokines interleukin (IL) 1 β , IL-4, and IL-10 seen in patients with allergies, compared with healthy individuals, correlate with increased latency to rapid eye movement (REM) sleep, decreased time in REM sleep, and decreased latency to sleep onset.⁴¹ It is postulated that any such disruptions in REM sleep may cause daytime fatigue, difficulty concentrating, and poor performance in allergic rhinitis patients.⁴¹ Inflammatory cells and mediators exhibit evident circadian variation, with its highest levels in the early morning hours,⁴² thus possibly explaining why the peak of allergic rhinitis symptoms frequently occurs on waking and why nighttime sleep is detrimentally affected in the disorder.

SLEEP IMPAIRMENT AND QUALITY OF LIFE

The Effects of Sleep Impairment

Patients with allergic rhinitis often must face adverse consequences of sleep disturbances, such as impaired cognitive function and decreased productivity and performance in the workplace.^{43–45} In children with allergic rhinitis, learning ability and school performance are affected.^{46,47} Although symptoms of the disorder may lead to these consequences, the sleep impairment caused by allergic rhinitis is the likely cause of aggravation.^{5,47,48} Sleep-disordered breathing and sleep impairment have been known to correlate with decreased quality of life in the general population.⁴⁹ Specifically, it has been shown that experimentally induced sleep fragmentation in healthy patients leads to impaired mental flexibility and attention, increased daytime fatigue, and impaired mood.^{50,51} Children and adolescents with allergic rhinitis also experience impaired sleep, which has been shown to result in problems doing school work and poor school performance, compared with controls.^{52,53}

A survey across 5 European countries of patients with allergic rhinitis or urticaria showed that a considerable proportion of respondents reported snoring or poor sleep and not feeling rested in the morning.⁶ Of these respondents, 29% to 79% and 28% to 56%, respectively, depending on the country, considered these problems either disruptive or extremely disruptive.⁵⁴ Patients with allergic rhinitis also frequently complain of daytime fatigue, difficulty concentrating, and impaired psychomotor performance.^{15,44,55} Results from an Internet survey of 1,322 individuals with rhinitis showed that both PAR and allergic rhinitis interfered with sleep (68% and 51% of respondents, respectively) and daily routine (58% and 48%, respectively).¹ Additionally, the sleep impairment experienced by allergic rhinitis patients has been linked to reduced psychological well-being.⁵⁶

Measuring Sleep Impairment and Impact on Quality of Life

Studies on the subjective and objective measurements of sleep impairment and its influence on patients' quality of life particularly emphasize the major impact of this problem on patients with allergic rhinitis. In patients with this disorder, most studies have used subjective measures, such as questionnaires or daily scoring of symptoms, sleep problems, daytime somnolence, and fatigue. Juniper's RQLQ uses quality-of-life measures that are disease specific and includes a domain that assesses the effects of disease and/or treatment on patients' sleep.^{57,58} Such questionnaires emphasize the problems and symptoms patients commonly complain of and seek help for and are thus more sensitive to alterations in patients' quality of life than generic health-status questionnaires.¹³ The NRQLQ focuses on the functional impairments of patients with nighttime symptoms and assesses problems and symptoms during sleep time, as well as on waking hours.³⁵ The Epworth Sleepiness Scale,⁵⁹ Pittsburgh Sleep Quality Index,⁶⁰ Calgary Sleep Apnea Quality of Life Index,⁶¹ and University of Pennsylvania Functional Outcomes of Sleep Questionnaire⁶² serve as general questionnaires that examine quality of sleep and daytime somnolence. However, these questionnaires may be inadequate in their analysis of the mild-to-moderate sleep impairment characteristic of allergic rhinitis because of their poor sensitivity.

Studies on allergic rhinitis that objectively evaluate sleep by using polysomnography are few.^{4,5,18,19,26,41,63,64} One such study observed 25 patients with SAR and 25 healthy volunteers, all of whom underwent 2 consecutive nights of polysomnography before and during the pollen season, and results showed statistically significant differences between the 2 groups in sleep parameters, which included increases in the apnea index (number of apneas per hour), hypopnea index (number of hypopneas per hour), apnea-hypopnea index, snoring time, amount of REM sleep, and sleep latency.²⁶ However, parameter values were within normal limits, preventing the changes from showing clinical relevance. Statistical significance was also reported in daytime sleepiness, which was subjectively measured using the Epworth Sleepiness Scale, in SAR patients compared with healthy patients.²⁶ These results thus point toward a weak correlation between subjective and objective measures of sleep impairment.

EFFECTS OF THERAPY

Treatments aimed at reducing nasal congestion may alleviate sleep disturbances and daytime somnolence and consequently improve the quality of life of those with allergic rhinitis. However, the multiple treatments for the disorder vary in their efficacies.

Sedating antihistamines are contraindicated in patients who complain of daytime sedation, fatigue, and functional impairment; such treatment is also not recommended for most patients with allergic rhinitis. Common treatment for allergic rhinitis includes nonsedating oral antihistamines, which alleviate nasal symptoms such as rhinorrhea, sneezing, and pru-

ritus but may be less effective in reducing nasal congestion.¹⁷ Two studies by Murray et al⁶⁵ and Golden et al⁶⁶ suggest that treatment using oral or topical antihistamines results in improved quality of life and sleep. Oral decongestants are successful in improving nasal congestion but may detrimentally affect sleep because of their stimulatory effects and, additionally, may result in systemic adverse effects, such as tachycardia and urinary retention.¹⁷ Topical decongestants may improve sleep in patients with nasal obstruction⁶⁷ but should not be used for extended periods because of the risk of rhinitis medicamentosa or “rebound” congestion.¹⁷ Data, though limited, show that the anticholinergic agent ipratropium bromide may improve sleep and quality of life.⁶⁸ However, ipratropium bromide appears to be unsuccessful in the relief of nasal congestion.¹⁷ Studies have shown that either leukotriene receptor antagonists as monotherapy^{69,70} or a combination of an antihistamine and a leukotriene receptor antagonist⁷¹ effectively improves sleep and quality of life in allergic rhinitis patients and in those who have sleep-disordered breathing. Intranasal corticosteroids alleviate congestion and other nasal symptoms of allergic rhinitis and are used as first-line therapy when nasal obstruction is a predominant symptom in patients.¹⁷

The Role of Intranasal Corticosteroids

Intranasal corticosteroids have been shown to effectively relieve the nasal symptoms of allergic rhinitis, such as congestion.^{72,73} The effectiveness of intranasal corticosteroids in relieving nasal congestion may have a positive effect on sleep, daytime somnolence, and quality of life in patients with allergic rhinitis. Three studies on adults and children with PAR support the hypothesis that this form of treatment decreases nasal congestion, subjective daytime sleepiness, and fatigue and improves sleep and quality of life.^{63,74,75} Another study that used subjective measures demonstrated that intranasal corticosteroids appeared to improve nasal congestion and sleep impairment in PAR patients compared with placebo, although the study did not find significant improvement in daytime somnolence and fatigue.²⁵ A study by Berlin et al⁷⁶ showed that intranasal corticosteroids are more effective than azelastine nasal spray in improving nasal congestion, sleep, and daytime somnolence in patients with PAR. Another study on PAR concluded that treatment with intranasal corticosteroids leads to considerable improvement in subjective assessments of sleep and decreased daytime somnolence and fatigue by more than 10%, although this last result did not show statistical significance.⁶⁴ In children with SAR, intranasal corticosteroids displayed efficacy in the improvement of nasal symptoms and quality of life, as well as verbal memory.⁷⁷ This mode of treatment was also proven to alleviate allergic rhinitis associated with obstructive sleep apnea syndrome and to consequently lead to both significantly lower frequencies of apnea and/or hypopnea episodes and subjective improvements in nasal congestion

and daytime alertness, although snoring noise and sleep quality showed no statistical significance compared with treatment with placebo.⁷⁸ A study by Milgrom et al⁶⁸ found that intranasal corticosteroids alleviate nasal congestion and improve quality of life in children with PAR or non-allergic rhinitis, consequently decreasing the detrimental impact of rhinorrhea on mood, concentration in school, and sleep. Two studies in allergic rhinitis patients, one using the RQLQ⁷⁹ and the other using the NRQLQ and the Pittsburgh Sleep Quality Index,⁸⁰ revealed that treatment using intranasal corticosteroids improves both nasal congestion and health-related quality of life, including sleep.

These studies therefore support the notion that treatments that focus on the nasal symptoms of allergic rhinitis may reduce sleep impairment and improve patients' quality of life. However, this hypothesis has been supported primarily by subjective assessments in studies where sleep-related outcomes stood as secondary end points, and no study has definitively shown that the reduction of nasal congestion by an intranasal corticosteroid correlates with improvements in daytime somnolence and fatigue, snoring, or objective sleep measures. Thus, further studies, specifically large, well-designed clinical studies that subjectively and objectively evaluate the outcomes of intranasal corticosteroid use in allergic rhinitis patients with impaired sleep quality, daytime somnolence, and impaired daytime functioning, are needed.

CONCLUSIONS

The quality of life of patients with allergic rhinitis is detrimentally affected by the sleep impairment associated with the disorder. One of the key causes that leads to sleep disruptions and sleep-disordered breathing is nasal congestion, one of the most common and bothersome symptoms of allergic rhinitis. Recent research has led to the use of therapeutic agents that specifically target the nasal congestion associated with sleep impairment. Intranasal corticosteroids stand as effective treatment that significantly reduces nasal congestion in allergic rhinitis. Clinical trials using this treatment suggest that this reduction in nasal congestion correlates with decreased sleep impairment, reduced daytime somnolence, and improved quality of life.

REFERENCES

1. Blaiss M, Reigel T, Philpot E. A study to determine the impact of rhinitis on sufferers' sleep and daily routine [abstract 787]. *J Allergy Clin Immunol*. 2005;115:S197.
2. Suratt PM, Turner BL, Wilhoit SC. Effect of intranasal obstruction on breathing during sleep. *Chest*. 1986;90:324–329.
3. Millman RP, Acebo C, Rosenberg C, Carskadon MA. Sleep, breathing, and cephalometrics in older children and young adults, part II: response to nasal occlusion. *Chest*. 1996;109:673–679.
4. Young T, Finn L, Palta M. Chronic nasal congestion at night is a risk factor for snoring in a population-based cohort study. *Arch Intern Med*. 2001;161:1514–1519.

5. Young T, Finn L, Kim H. Nasal obstruction as a risk factor for sleep-disordered breathing: The University of Wisconsin Sleep and Respiratory Research Group. *J Allergy Clin Immunol.* 1997;99(suppl):S757–62.
6. Bachert C, Van Cauwenberge P, Khaltaev N. Allergic Rhinitis and its Impact on Asthma (ARIA) in collaboration with the World Health Organization: Executive Summary of the Workshop Report, 7–10 December 1999, Geneva, Switzerland. *Allergy.* 2002;57:841–855.
7. Aberg N, Sundell J, Eriksson B, Hesselmar B, Aberg B. Prevalence of allergic diseases in schoolchildren in relation to family history, upper respiratory infections, and residential characteristics. *Allergy.* 1996;51:232–237.
8. Dykewicz MS, Fineman S, Skoner DP, et al. Diagnosis and management of rhinitis: complete guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology and American Academy of Allergy, Asthma, and Immunology. *Ann Allergy Asthma Immunol.* 1998;81:478–518.
9. Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Respir J.* 2004;24:758–764.
10. Ray NF, Baraniuk JN, Thamer M, et al. Direct expenditures for the treatment of allergic rhinoconjunctivitis in 1996, including the contributions of related airway illnesses. *J Allergy Clin Immunol.* 1999;103:401–407.
11. Leynaert B, Neukirch C, Liard R, Bousquet J, Neukirch F. Quality of life in allergic rhinitis and asthma: a population-based study of young adults. *Am J Respir Crit Care Med.* 2000;162:1391–1396.
12. Bousquet J, Bullinger M, Fayol C, Marquis P, Valentin B, Burtin B. Assessment of quality of life in patients with perennial allergic rhinitis with the French version of the SF-36 Health Status Questionnaire. *J Allergy Clin Immunol.* 1994;94:182–188.
13. Juniper EF. Quality of life in adults and children with asthma and rhinitis. *Allergy.* 1997;52:971–977.
14. Juniper EF. Measuring health-related quality of life in rhinitis. *J Allergy Clin Immunol.* 1997;99:S742–749.
15. Meltzer EO, Nathan RA, Selner JC, Storms W. Quality of life and rhinitic symptoms: results of a nationwide survey with the SF-36 and RQLQ questionnaires. *J Allergy Clin Immunol.* 1997;99:S815–S819.
16. Majani G, Baiardini I, Giardini A, et al. Health-related quality of life assessment in young adults with seasonal allergic rhinitis. *Allergy.* 2001;56:313–317.
17. The Allergy Report. American Academy of Allergy, Asthma & Immunology. Available at: <http://www.theallergyreport.com/reportindex.html>. Accessed April 20, 2006.
18. McNicholas WT, Tarlo S, Cole P, et al. Obstructive sleep apneas during sleep in patients with seasonal allergic rhinitis. *Am Rev Respir Dis.* 1982;126:625–628.
19. Lavie P, Gertner R, Zomer J, Podoshin L. Breathing disorders in sleep associated with “microarousals” in patients with allergic rhinitis. *Acta Otolaryngol.* 1981;92:529–533.
20. Kramer MF, De La Chaux R, Derher A, Pfrogner E, Rasp G. Allergic rhinitis does not constitute a risk factor for obstructive sleep apnea syndrome. *Acta Otolaryngol.* 2001;121:494–499.
21. Chng SY, Goh DY, Wang XS, Tan TN, Ong NB. Snoring and atopic disease: a strong association. *Pediatr Pulmonol.* 2004;38:210–216.
22. Sogut A, Altin R, Uzun L, et al. Prevalence of obstructive sleep apnea syndrome and associated symptoms in 3–11 year-old Turkish children. *Pediatr Pulmonol.* 2005;39:251–256.
23. McColley SA, Carroll JL, Curtis S, Loughlin GM, Sampson HA. High prevalence of allergic sensitization in children with habitual snoring and obstructive sleep apnea. *Chest.* 1997;111:170–173.
24. Janson C, De Backer W, Gislason T, et al. Increased prevalence of sleep disturbances and daytime sleepiness in subjects with bronchial asthma: a population study of young adults in three European countries. *Eur Respir J.* 1996;9:2132–2138.
25. Craig TJ, Teets S, Lehman EB, Chinchilli VM, Zwillich C. Nasal congestion secondary to allergic rhinitis as a cause of sleep disturbance and daytime fatigue and the response to topical nasal corticosteroids. *J Allergy Clin Immunol.* 1998;101:633–637.
26. Stuck BA, Czajkowski J, Hagner A-E, et al. Changes in daytime sleepiness, quality of life, and objective sleep patterns in seasonal allergic rhinitis: a controlled clinical trial. *J Allergy Clin Immunol.* 2004;113:663–668.
27. Reinberg A, Gervais P, Levi F, Smolensky M, Del Cerro L, Ugolini C. Circadian and circannual rhythms of allergic rhinitis: an epidemiologic study involving chronobiologic methods. *J Allergy Clin Immunol.* 1988;81:51–62.
28. Nathan RA, Eccles R, Howarth PH, Steinsvåg SK, Togias A. Objective monitoring of nasal patency and nasal physiology in rhinitis. *J Allergy Clin Immunol.* 2005;115:S442–S459.
29. Houser SM, Mamikoglu B, Aquino BF, Moinuddin R, Corey JP. Acoustic rhinometry findings in patients with mild sleep apnea. *Otolaryngol Head Neck Surg.* 2002;126:475–480.
30. Mamikoglu B, Houser SM, Corey JP. An interpretation method for objective assessment of nasal congestion with acoustic rhinometry. *Laryngoscope.* 2002;112:926–929.
31. Rundcrantz H. Postural variations of nasal patency. *Acta Otolaryngol.* 1969;68:435–443.
32. Landstra AM, Postma DS, Boezen HM, van Aalderen WM. Role of serum cortisol levels in children with asthma. *Am J Respir Crit Care Med.* 2002;165:708–712.
33. Shedden A. Impact of nasal congestion on quality of life and work productivity in allergic rhinitis: findings from a large online survey. *Treat Resp Med.* 2005;4:439–464.
34. Jessen M, Malm L. Definition, prevalence and development of nasal obstruction. *Allergy.* 1997;52:3–6.
35. Canova CR, Downs SH, Knoblauch A, Andersson M, Tamm M, Leuppi JD. Increased prevalence of perennial allergic rhinitis in patients with obstructive sleep apnea. *Respiration.* 2004;71:138–143.
36. Juniper EF, Rohrbach T, Meltzer EO. A questionnaire to measure quality of life in adults with nocturnal allergic rhinoconjunctivitis. *J Allergy Clin Immunol.* 2003;111:484–490.
37. Chen W, Kushida CA. Nasal obstruction in sleep-disordered breathing. *Otolaryngol Clin North Am.* 2003;36:437–460.
38. Camhi SL, Morgan WJ, Pernisco N, Quan SF. Factors affecting sleep disturbances in children and adolescents. *Sleep Med.* 2000;1:117–123.
39. Tashiro M, Mochizuki H, Iwabuchi K, et al. Roles of histamine in regulation of arousal and cognition: functional neuroimaging of histamine H1 receptors in human brain. *Life Sci.* 2002;72:409–414.
40. Mullington JM, Hinze-Selch D, Pollmacher T. Mediators of

- inflammation and their interaction with sleep: relevance for chronic fatigue syndrome and related conditions. *Ann N Y Acad Sci.* 2001;933:201–210.
41. Krouse HJ, Davis JE, Krouse JH. Immune mediators in allergic rhinitis and sleep. *Otolaryngol Head Neck Surg.* 2002;126:607–613.
42. Aoyagi M, Watanabe H, Sekine K, et al. Circadian variation in nasal reactivity in children with allergic rhinitis: correlation with the activity of eosinophils and basophilic cells. *Int Arch Allergy Immunol.* 1999;120:95–99.
43. Marshall PS, O'Hara C, Steinberg P. Effects of seasonal allergic rhinitis on selected cognitive abilities. *Ann Allergy Asthma Immunol.* 2000;84:403–410.
44. Wilken JA, Berkowitz R, Kane R. Decrements in vigilance and cognitive functioning associated with ragweed-induced allergic rhinitis. *Ann Allergy Asthma Immunol.* 2002;89:372–380.
45. Kessler RC, Almeida DM, Berglund P, Stang P. Pollen and mold exposure impairs the work performance of employees with allergic rhinitis. *Ann Allergy Asthma Immunol.* 2001;87:289–295.
46. Vuurman EF, van Veggel LM, Uiterwijk MM, Leutner D, O'Hanlon JF. Seasonal allergic rhinitis and antihistamine effects on children's learning. *Ann Allergy.* 1993;71:121–126.
47. International Conference on Allergic Rhinitis in Childhood. Allergic rhinitis in childhood. *Allergy.* 1999;54:7–34.
48. Simons FE. Learning impairment and allergic rhinitis. *Allergy Asthma Proc.* 1996;17:185–189.
49. Baldwin CM, Griffith KA, Nieto FJ, O'Connor GT, Walsleben JA, Redline S. The association of sleep-disordered breathing and sleep symptoms with quality of life in the Sleep Heart Health Study. *Sleep.* 2001;24:96–105.
50. Martin SE, Engleman HM, Deary IJ, Douglas NJ. The effect of sleep fragmentation on daytime function. *Am J Respir Crit Care Med.* 1996;153:1328–1332.
51. Martin SE, Wraith PK, Deary IJ, Douglas NJ. The effect of nonvisible sleep fragmentation on daytime function. *Am J Respir Crit Care Med.* 1997;155:1596–1601.
52. Juniper EF, Guyatt GH, Dolovich J. Assessment of quality of life in adolescents with allergic rhinoconjunctivitis: development and testing of a questionnaire for clinical trials. *J Allergy Clin Immunol.* 1994;93:413–423.
53. Urschitz M, Guenther A, Eggebrecht E, et al. Snoring, intermittent hypoxia and academic performance in primary school children. *Am J Respir Crit Care Med.* 2003;168:464–468.
54. Bousquet J, Neukirch F, Bousquet PJ, Gehano P, Klossek JM, Le Gal M, Allaf B. Severity and impairment of allergic rhinitis in patients consulting in primary care. *J Allergy Clin Immunol.* 2006;117:158–162.
55. Spaeth J, Klimek L, Mosges R. Sedation in allergic rhinitis is caused by the condition and not by antihistamine treatment. *Allergy.* 1996;51:893–906.
56. Kremer B, den Hartog HM, Jolles J. Relationship between allergic rhinitis, disturbed cognitive functions and psychological well-being. *Clin Exp Allergy.* 2002;32:1310–1315.
57. Juniper EF, Guyatt GH. Development and testing of a new measure of health status for clinical trials in rhinoconjunctivitis. *Clin Exp Allergy.* 1991;21:77–83.
58. Juniper EF, Ståhl E, Doty RL, Simons FER, Allen DB, Howarth PH. Clinical outcomes and adverse effect monitoring in allergic rhinitis. *J Allergy Clin Immunol.* 2005;115:S390–S413.
59. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep.* 1991;14:540–545.
60. Buysse DJ, Reynolds CF III, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.* 1989;28:193–213.
61. Flemons WW, Reimer MA. Measurement properties of the Calgary Sleep Apnea Quality of Life Index. *Am J Respir Crit Care Med.* 2002;165:159–164.
62. Weaver TE, Laizner AM, Evans LK, et al. An instrument to measure functional status outcomes for disorders of excessive sleepiness. *Sleep.* 1997;20:835–843.
63. Mansfield LE, Diaz G, Posey CR, Flores-Neder J. Sleep disordered breathing and daytime quality of life in children with allergic rhinitis during treatment with intranasal budesonide. *Ann Allergy Asthma Immunol.* 2004;92:240–244.
64. Craig TJ, Mende C, Hughes K, Kakumanu S, Lehman EB, Chinchilli V. The effect of topical nasal fluticasone on objective sleep testing and the symptoms of rhinitis, sleep, and daytime somnolence in perennial allergic rhinitis. *Allergy Asthma Proc.* 2003;24:53–58.
65. Murray JJ, Nathan RA, Bronsky EA, Olufade AO, Chapman D, Kramer B. Comprehensive evaluation of cetirizine in the management of seasonal allergic rhinitis: impact on symptoms, quality of life, productivity, and activity impairment. *Allergy Asthma Proc.* 2002;23:391–398.
66. Golden A, Teets SJ, Lehman EB, et al. Effect of topical nasal azelastine on the symptoms of rhinitis, sleep, and daytime somnolence in perennial allergic rhinitis. *Ann Allergy Asthma Immunol.* 2000;85:53–57.
67. McLean HA, Urton AM, Driver HS, et al. Effect of treating severe nasal obstruction on the severity of obstructive sleep apnea. *Eur Respir J.* 2005;25:521–527.
68. Milgrom H, Biondi R, Georgitis JW, et al. Comparison of ipratropium bromide 0.03% with beclomethasone dipropionate in the treatment of perennial rhinitis in children. *Ann Allergy Asthma Immunol.* 1999;83:105–111.
69. Goldbart AD, Goldman JL, Veling MC, Gozal D. Leukotriene modifier therapy for mild sleep-disordered breathing in children. *Am J Respir Crit Care Med.* 2005;172:364–370.
70. Kheirandish L, Goldbart AD, Gozal D. Intranasal steroids and oral leukotriene modifier therapy in residual sleep-disordered breathing after tonsillectomy and adenoidectomy in children. *Pediatrics.* 2006;117:197–198.
71. Moinuddin R, deTineo M, Maleckar B, Naclerio RM, Baroody FM. Comparison of the combinations of fexofenadine-pseudoephedrine and loratadine-montelukast in the treatment of seasonal allergic rhinitis. *Ann Allergy Asthma Immunol.* 2004;92:73–79.
72. van Cauwenberge P, Bachert C, Passalacqua G, et al. Consensus statement on the treatment of allergic rhinitis: European Academy of Allergy and Clinical Immunology. *Allergy.* 2000;55:116–134.
73. Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H₁-receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. *BMJ.* 1998;317:1624–1629.
74. Hughes K, Glass C, Ripchinski M, et al. Efficacy of the topical nasal steroid budesonide on improving sleep and daytime somnolence in patients with perennial allergic rhinitis. *Allergy.* 2003;58:380–385.
75. Craig TJ, Hanks CD, Fisher LH. How do topical nasal cortico-

- steroids improve sleep and daytime somnolence in allergic rhinitis. *J Allergy Clin Immunol.* 2005;116:1264–1266.
76. Berlin JM, Golden SJ, Teets S, Lehman EB, Lucas T, Craig TJ. Efficacy of a steroid nasal spray compared with an antihistamine nasal spray in the treatment of perennial allergic rhinitis. *J Am Osteopath Assoc.* 2000;100:8–13.
77. Bender BG, Milgrom H. Comparison of the effects of fluticasone propionate aqueous nasal spray and loratadine on daytime alertness and performance in children with seasonal allergic rhinitis. *Ann Allergy Asthma Immunol.* 2004;92:344–349.
78. Kiely JL, Nolan P, McNicholas WT. Intranasal corticosteroid therapy for obstructive sleep apnoea in patients with co-existing rhinitis. *Thorax.* 2004;59:50–55.
79. Potter PC, Van Niekerk CH, Schoeman HS. Effects of triamcinolone on quality of life in patients with persistent allergic rhinitis. *Ann Allergy Asthma Immunol.* 2003;91:

368–374.

80. Mintz M, Garcia J, Diener P, Liao Y, Dupclay L, Georges G. Triamcinolone acetonide aqueous nasal spray improves nocturnal rhinitis-related quality of life in patients treated in a primary care setting: the Quality of Sleep in Allergic Rhinitis study. *Ann Allergy Asthma Immunol.* 2004;92:255–261.

Requests for reprints should be addressed to:

Timothy J. Craig, DO

Department of Medicine and Pediatrics

Hershey Medical Center

500 University Dr

MSHMC-UPC

Hershey, PA 17033-0850

E-mail: tcraig@psu.edu

Objectives: After reading this article, participants should be able to demonstrate an increased understanding of their knowledge of allergy/asthma/immunology clinical treatment and how this new information can be applied to their own practices.

Participants: This program is designed for physicians who are involved in providing patient care and who wish to advance their current knowledge in the field of allergy/asthma/immunology.

Credits: ACAAI designates each Annals CME Review Article for a maximum of 2 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity. The American College of Allergy, Asthma and Immunology is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

CME Examination

1–7, Santos CB et al. 2006;97:579–587.

CME Test Questions

- What is the most bothersome sleep-related symptom associated with allergic rhinitis?
 - rhinorrhea
 - sneezing
 - nasal congestion
 - pruritus
 - postnasal drainage
- Inflammatory cells and mediators peak at what time of the day?
 - 6 AM
 - noon
 - 4 PM
 - before bed
 - midnight
- Nasal congestion peaks at what time of the day?
 - 6 AM
 - noon
 - 4 PM
 - before bed
 - midnight
- Which investigational tool is used as an objective measurement of the severity of nasal airflow by assessing the volume and area of the nasal cavity by analyzing reflected sound waves of the nasal cavity?
 - peak nasal expiratory flow
 - peak nasal inspiratory flow
 - anterior rhinomanometry
 - acoustic rhinometry
 - acoustic rhinomanometry
- Elevation of which group of cytokines correlates with decreased latency to sleep onset, increased latency to rapid eye movement (REM) sleep, and decreased time in REM sleep in patients with allergic rhinitis compared with healthy control subjects?
 - interleukin (IL) 4, IL-5, and IL-9
 - IL-4, IL-9, and IL-13
 - IL-1 β , IL-4, and IL-5
 - IL-1 β , IL-10, and IL-13
 - IL-1 β , IL-4, and IL-10
- Which class of pharmacologic agent is recommended as first-line therapy when nasal obstruction is the predominant symptom?
 - oral decongestant
 - intranasal corticosteroid
 - oral antihistamine
 - topical antihistamine
 - leukotriene receptor antagonist
- Which questionnaire focuses on the functional impairments of patients with nighttime symptoms and assesses problems and symptoms during sleep time, as well as on waking?

- a. Juniper's Rhinoconjunctivitis Quality of Life Questionnaire
b. Epworth Sleepiness Scale
c. University of Pennsylvania Functional Outcomes of Sleep Questionnaire
d. Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire

e. Pittsburgh Sleep Quality Index

Answers on page 671.

U.S. Postal Service
Statement of Ownership, Management, and Circulation
(Required by 39 U.S.C. 3685)

Publication Title: Annals of Allergy, Asthma & Immunology

USPS Publication Number: 0003-4738

Filing Date: 10/02/06

No. of Issues Published Annually: 12

Annual Subscription Price: \$95.00

Complete Mailing Address of Known Publication Office: 85 W. Algonquin Rd., Suite 550; Arlington Heights, IL 60005

Complete Mailing Address of Headquarters or General Business Office of Publisher, Editor and Managing Editor:

American College of Allergy, Asthma & Immunology; 85 W. Algonquin Rd., Suite 550; Arlington Heights, IL 60005

Editor: Gailen D. Marshall, MD, PhD
U of MS MED CTR
DIV of ALL/IMM
2500 N. State St.
Jackson, MS 39216

Publication Mgr.: Mary L. Callaghan;
ACAAI; 85 W. Algonquin Rd., Suite 550;
Arlington Heights, IL 60005

Owner: American College of Allergy, Asthma & Immunology; 85 W. Algonquin Rd., Suite 550; Arlington Heights, IL 60005

Known Bondholders, Mortgages, and Other Security Holders Owning or Holding 1% or Mortgages, or Other Securities: None

Issue Date for Circulation Data Below: October 2006

Extent & Nature of Circulation		Average No. Copies Each Issue During Preceding 12 Months	Actual No. Copies of Single Issue Publ. Nearest Filing Date
a.	Total No. Copies (Net Press Run)	5,471	5,318
b.	Paid and/or Requested Circulation		
	1. Paid/Requested Outside-County Mail Stated on Form 3541 (include ad proofs & exchange copies)	3,883	3,840
	2. Paid/In-County Subscriptions Stated on Form 3541 (include ad proofs & exchange copies)		
	3. Sales Through Dealers and Carriers, Street Vendors, and Counter Sales and other Non-USPD Paid Distribution	907	903
	4. Other Classes Mailed via USPS		
c.	Total Paid and/or Requested Circulation [Sum of 15b(1), (2), (3), and (4)]	4,790	4,743
d.	Free Distribution by Mail (Samples, Complimentary, and Other Free)		
	1. Outside-County as Stated on Form 3541	174	123
	2. In-County as Stated on Form 3541		
	3. Other Classes Mailed via USPS		
e.	Free Distribution Outside the Mail (Carriers or Other Means)	12	11
f.	Total Free Distribution (Sum of 15d and 15e)	186	134
g.	Total Distribution (Sum of 15c and 15f)	4,976	4,877
h.	Copies Not Distributed	495	441
i.	Total [Sum of 15g, 15h(1), and 15h(2)]	5,471	5,318
	Percent Paid and/or Requested Circulation (15c/15g x 100)	96.26%	97.25%

Mary L. Callaghan

Signature

Publications Manager
Title

10/02/06
Date