



CME Review

An obstructive sleep apnea primer What the practicing allergist needs to know



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Overall Purpose

Participants will be able to demonstrate increased knowledge of the clinical treatment of allergy/asthma/immunology and how new information can be applied to their own practices.

Learning Objectives

At the conclusion of this activity, participants should be able to:

- Recognize patients at high risk for obstructive sleep apnea
- Recommend appropriate diagnostic tests and treatment for obstructive sleep apnea

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Target Audience

Physicians involved in providing patient care in the field of allergy/asthma/immunology

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A remarkable phenomenon associated with excessive fat in young persons is an uncontrollable tendency to sleep-like the fat boy in Pickwick.

—William Osler¹

Introduction

Obstructive sleep apnea (OSA) is a common condition that affects a large segment of the general population and is considered an underdiagnosed and undersuspected disorder. An estimated 85% of cases of sleep apnea remain undiagnosed.² The exact figures regarding its prevalence vary in different studies because of the use of a variety of indexes and definitions in making the diagnosis. Its prevalence in North America is estimated to be 14% in males and 5% in females when OSA is defined as an apnea-hypopnea index (AHI) of 5 or higher as measured on by polysomnography (PSG) and is associated with excessive daytime sleepiness. This definition is consistent with the Medicare criteria for the diagnosis of OSA (<https://www.cms.gov/medicare-coverage-database/>). The disorder is often associated with a plethora of cardiopulmonary complications, although the cause-effect relationship between sleep apnea and these sequelae is still unclear.^{3,4}

During the 20th century, several patients with obesity, heart failure, respiratory acidosis, periodic breathing, and excessive daytime sleepiness were first described. This clinical presentation was referred to as Pickwickian syndrome after a character in Charles Dickens' *The Pickwick Papers* who exhibited similar features. As understanding of sleep-related breathing disorders increased, they were broadly classified as obesity hypoventilation syndrome, central sleep apnea, and OSA. The definitions of sleep-related breathing disorders are given in Table 1. OSA occurs when airflow is compromised in the presence of continued respiratory effort, whereas in central sleep apnea respiratory effort is also reduced or absent. The severity of sleep-related breathing disorders is classified based on the AHI (Table 2), which is the number of apneas and hypopneas that occur per hour of sleep. Respiratory apnea and hypopnea are diagnosed by PSG and defined by almost

complete cessation (apnea) or reduction (hypopnea) of airflow. The diagnosis of OSA requires an AHI of 15 or higher or an AHI of 5 or higher in the presence of excessive daytime sleepiness, insomnia, or comorbid illnesses, such as hypertension, diabetes, congestive heart failure, atrial fibrillation, cerebrovascular disease, ischemic heart disease, mood disorder, or cognitive dysfunction.

Mechanism of Airway Collapse

The mechanism by which OSA occurs is repeated obstruction of the velopharyngeal and/or oropharyngeal airway during sleep. This can result from a combination of factors, such as craniofacial abnormality, airway obstruction (adenotonsillar hypertrophy, and excess adipose tissue), and increased airway collapsibility. Airway obstruction can be markedly worse during REM sleep in some individuals because of the associated loss of muscle tone. The recurrent obstruction causes disruption in airflow, which culminates in oxyhemoglobin desaturations, arousals leading to disrupted sleep, increased sympathetic activity, thoracic pressure changes, and fluctuations in blood pressure and heart rate.^{5,6}

Risk Factors

Risk factors for sleep apnea are given in Table 3. The prevalence of OSA is 2- to 3-fold higher in persons older than 65 years compared with those in middle age (30–64 years of age); however, this increase plateaus after 65 years.⁷ Male sex is an important risk factor for the development of OSA, with a male to female ratio of 3:1 in the general population.^{8,9} Current smokers are at increased risk for OSA; however, former smokers are not.¹⁰ Obesity is strongly linked with OSA, with a longitudinal follow-up revealing that a 10% increase in weight was associated with a 6-fold greater risk of developing OSA in previously healthy-weight individuals.¹¹ Nasal congestion at night, regardless of cause, has been linked to an increased risk of OSA. In the Wisconsin cohort, participants who reported nasal congestion because of allergy were 1.8 times more likely to have moderate to severe sleep-disordered breathing than

Table 1

American Association of Sleep Medicine Scoring Criteria for Sleep Disordered Breathing

Condition	Description
Obstructive Apnea	A decrease in the peak airflow signal excursion by $\geq 90\%$ of pre-event baseline for ≥ 10 seconds with continued or increased respiratory effort throughout the entire period of absent airflow.
Hypopnea	A decrease in the peak airflow signal excursion by $\geq 30\%$ of pre-event baseline for ≥ 10 seconds with an associated arousal or $\geq 3\%$ oxygen desaturation with any one of the following: Snoring Increased inspiratory flattening of the airflow signal Associated thoracoabdominal paradox.
Central Apnea	A decrease in the peak airflow signal excursion by $\geq 90\%$ of pre-event baseline for ≥ 10 seconds with absent respiratory effort throughout the entire period of absent airflow.
Hypopnea	A decrease in the peak airflow signal excursion by $\geq 30\%$ of pre-event baseline for ≥ 10 seconds with an associated arousal or $\geq 3\%$ oxygen desaturation with none of the following: Snoring Increased inspiratory flattening of the airflow signal Associated thoracoabdominal paradox.
Hypoventilation	Increase in the arterial P_{CO_2} to a value ≥ 55 mm Hg for ≥ 10 minutes or an increase in arterial PCO_2 by ≥ 10 mm Hg from awake baseline to a value > 50 mm Hg for ≥ 10 minutes.

were those without nasal congestion because of allergy.¹² Use of nasal corticosteroids in children with OSA decreases the frequency of obstructive AHI; however, such data in adults are lacking.¹³ Several studies have found an increased risk of OSA in families of patients with OSA, perhaps because of genetic or shared lifestyle factors.¹⁴ Hypertension is a known risk factor for OSA; however, some studies have found that it might also be a sequela of OSA itself. An AHI of 15 or higher was independently associated with a 3-fold increased risk of developing new hypertension when participants were evaluated 4 years after the initial sleep study.¹⁵ Comorbid conditions, such as diabetes, congestive heart failure, ischemic heart disease, cerebrovascular disease, pulmonary hypertension, and atrial fibrillation, are also associated with OSA.¹⁶ Specific conditions, such as Marfan, Down, Alpert, Crouzon, and Pierre Robin syndromes, cerebral palsy, and craniosynostosis, may be associated with a higher prevalence of sleep apnea.

Clinical Features

OSA is a common but underdiagnosed disease with significant sequelae if left untreated. All physicians should be attuned to the presenting features of OSA and have a low threshold for further evaluation. Allergists may be in a unique position to diagnose this disease because studies have found that the presence of nasal allergies and asthma is associated with an increased risk of having OSA. Common presenting features of OSA include loud snoring, gasping, choking, and respiratory pauses during sleep. Patients

Table 2

Obstructive Sleep Apnea Severity Classification

Classification	AHI
Mild	5–14 with excessive daytime sleepiness or presence of comorbidities
Moderate	15–29
Severe	≥ 30

Abbreviation: AHI, Apnea-Hypopnea Index.

Table 3

Risk Factors and Associations

Risk and predisposing factors	Associations and comorbidities
Demographic features	Inflammatory or neuroendocrine
Obesity (BMI > 35)	Metabolic dysregulation
Advancing age	Inflammatory responses
Male sex	Endothelial dysfunction
Structural factors	Hypoxemia-induced gene induction
Craniofacial abnormalities	Nuclear factor- κ B induction
Upper airway soft-tissue abnormalities	Oxidative stress
Nasal obstruction or congestion	Increased platelet aggregability
Neck circumference > 17 in men	Cytokine generation
> 16 in women	Activation of the sympathetic system
Others	Cardiovascular
Family history	Hypertension
Cigarette smoking	Congestive heart failure
	Atrial fibrillation
	Ischemic heart disease
	Neurologic
	Cognitive decline (reasoning, memory, attention, and learning deficits)
	Headache
	Depression
	Cerebrovascular disease or stroke
	Respiratory or pulmonary
	Hypoxemia
	Cough
	Asthma
	Chronic obstructive pulmonary disease
	Pulmonary hypertension
	Gastrointestinal
	Gastroesophageal reflux
	Ophthalmic
	Nonarteritic ischemic optic neuropathy
	Others
	Increased motor vehicular crashes

themselves may be unaware of these symptoms and they are sometimes brought to the attention of a health care professional at the insistence of the bed partner. Associated symptoms can include insomnia, multiple unexplained awakenings at night, nocturia, nonrestorative sleep, and morning headaches. Excessive daytime sleepiness is an important symptom of OSA.¹⁷ At times patients find it difficult to distinguish true sleepiness, which is an inability to stay awake, from fatigue, which is a perception of lack of energy.¹⁸ Questionnaires such as the Epworth Sleepiness Scale (Fig 1) can be used to aid in such a distinction.¹⁹ Patients are presented with 8 situations and asked to rate the likelihood that they would fall asleep in those situations from 0 (no chance) to 3 (high chance). A score of 10 or less is considered normal, and higher scores are associated with increased daytime sleepiness. This is an important distinction because treatment of OSA is associated with improvements in sleepiness; however, fatigue is seldom changed. Sleep deprivation attributable to poor sleep quality and hypoxia from frequent desaturations can result in impairments in memory and cognition and mood disturbances.² Motor vehicle crashes attributable to sleepy driving have been found to be 2 to 3 times more common among patients with OSA and such history should be actively elicited.²

Patients should be evaluated for known anatomical risk factors for the development of OSA, such as obesity and craniofacial and upper airway abnormalities (Table 3). Obesity can be evaluated through the measurement of markers such as body mass index and neck circumference (Table 3). The airway can be evaluated using the modified Mallampati class for which the patient sits with the head in a neutral position, the mouth opened, and the tongue protruded maximally without phonation. The class is then graded based on the visibility of the airway structures: grade I, tonsils, pillars, and soft palate are all clearly visible; grade II, the uvula,

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired?

Use the following scale to choose the **most appropriate number** for each situation:

- 0 = would **never** doze
 1 = **slight chance** of dozing
 2 = **moderate chance** of dozing
 3 = **high chance** of dozing

Situation	Chance of Dozing (0-3)
Sitting and reading _____	_____
Watching TV _____	_____
Sitting, inactive in a public place (e.g. a theatre or a meeting) _____	_____
As a passenger in a car for an hour without a break _____	_____
Lying down to rest in the afternoon when circumstances permit _____	_____
Sitting and talking to someone _____	_____
Sitting quietly after a lunch without alcohol _____	_____
In a car, while stopped for a few minutes in the traffic _____	_____

Figure 1. Questionnaires such as the Epworth Sleepiness Scale can be used to aid in distinguishing sleep disorders from generalized fatigue. A score of 10 or less is considered normal, and higher scores are associated with increased daytime sleepiness. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*. 1991;14:540–5 (PubMed abstract).¹⁹ This questionnaire is being shown with the approval of Dr M. W. Johns and obtained from MAPI (<https://eprovide.mapi-trust.org/>). For any use of this form, the reader is referred to Dr M.W. Johns and MAPI.

pillars, and upper pole are visible; grade III, only part of the soft palate is visible but the uvula is partly obscured; and grade IV, only the hard palate is visible. Higher grades are indicative of a more crowded airway, which is associated with a higher risk of OSA.²

Rhinitis is a common comorbidity in sleep apnea. Negative correlations between rhinitis scores and sleep apnea severity have been found in a previous study.²⁰ Children with allergic rhinitis and asthma, craniofacial abnormalities, or trisomy 21 are at an

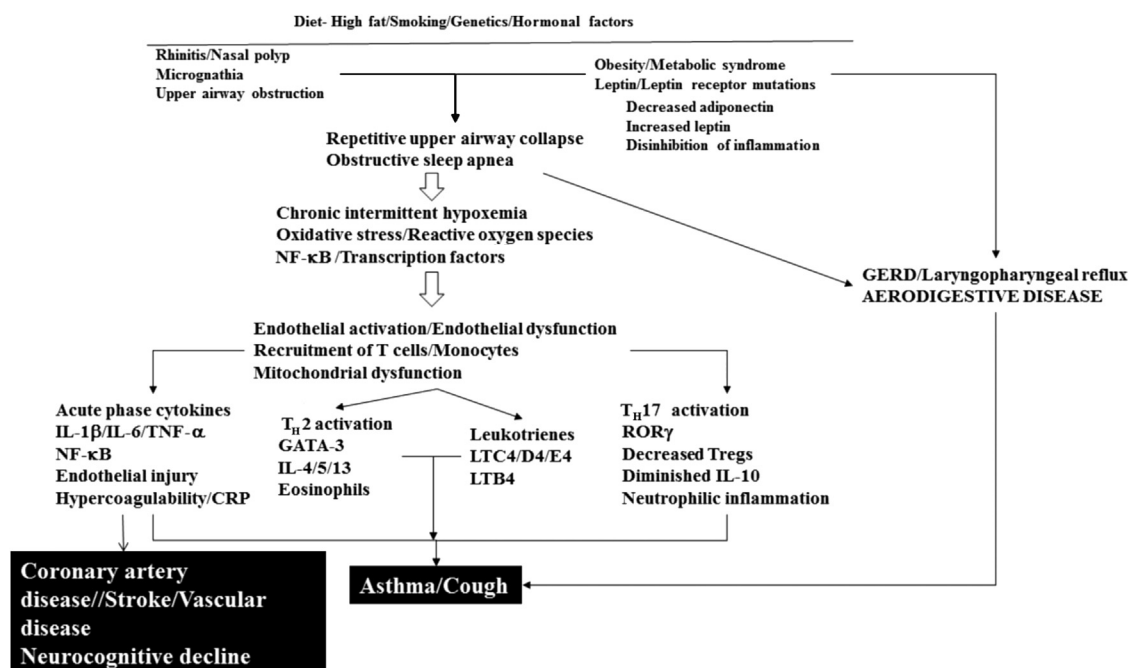


Figure 2. Showing hypothetical roles of diet, smoking, gastroesophageal reflux disease (GERD), leptin mutations, adiponectin/interleukin 10 (IL-10) defects, hypoxemia-triggered endothelial activation, cytokine generation, and leukotriene expression culminating in disinhibited inflammatory responses, leading to heart and lung disease. CRP indicates C-reactive protein; LT, leukotriene; NF-κB, nuclear factor-κB; TNF-α, tumor necrosis factor α; and Tregs, T-regulatory cells.

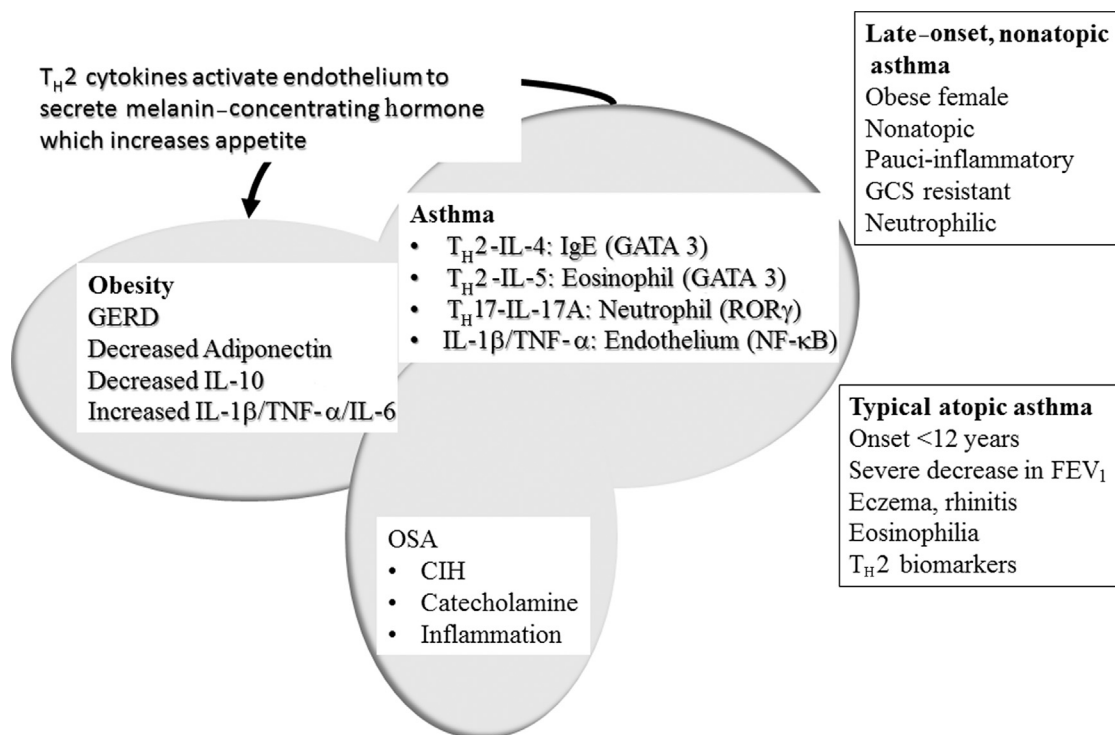


Figure 3. Hypothetical overlap of melanin concentrating hormone, cytokines, lineage-specific transcription factors, and adiposity on pathogenesis of early- and late-onset asthma in sleep apnea. Airway, obesity, and sleep apnea-related inflammatory responses contribute to inflammatory responses in various ways. Secretion of melanin-concentrating hormone by T_H2 cells and induction of this hormone in endothelial cells could contribute to obesity and sleep apnea conundrum and result in the association of these disorders with asthma. CIH indicates chronic intermittent hypoxemia; FEV₁, forced expiratory volume in 1 second; GCS, glucocorticoids; GERD, gastroesophageal reflux disease; IL, interleukin; NF-κB, nuclear factor-κB; OSA, obstructive sleep apnea; and TNF-α, tumor necrosis factor α.

increased risk for sleep apnea.²¹ Even in patients without sleep apnea, allergic rhinitis affects quality and duration of sleep.²² Mechanisms of increased sleep apnea severity in patients with allergic rhinitis include increased nasal airway resistance, the influence of mouth breathing, and secondary effects of inflammatory mediators, including histamine, leukotrienes, and interleukins (ILs), such as IL-1 and IL-4.²³ A careful evaluation for and treatment of allergic or nonallergic rhinitis should be an integral aspect of comprehensive sleep apnea management.

Comorbid Conditions and Sequelae

Conditions such as hypertension, diabetes, congestive heart failure, depression, neurocognitive dysfunction, ischemic heart disease, cerebrovascular disease, nonarteritic ischemic optic neuropathy, pulmonary hypertension, and atrial fibrillation are also associated with OSA (Table 3). The presence of these comorbidities should raise concern for the presence of OSA and prompt further evaluation. These associations are not completely understood and may be attributable to shared risk factors common to all these disorders or to direct causality possibly through development of hypertension, inflammation (Fig 2), or increased sympathetic activity.^{15,16} Hypoxemia-induced inflammatory pathways, endothelial dysfunction, platelet hyperaggregability, cytokine generation, and the metabolic dysregulation doubtlessly play important roles (Fig 2). Frequent desaturations associated with sleep disordered breathing over time can lead to neurocognitive deficits, which in turn could worsen comorbid conditions or even coexisting asthma control (because of adherence or perception issues). Several studies have found that OSA has adverse effects on reasoning, memory, attention, and learning.^{14,16} Early suspicion and intervention are pivotal to prevent or manage worsening of metabolic, vascular, inflammatory, and hypoxemic complications of the disease.

The Asthma-Cough-Sleep Apnea Conundrum

OSA is common, complicates asthma and rhinitis, and may be associated with a plethora of pulmonary, cardiovascular, and aerodigestive complications and comorbidities of relevance to the practicing allergist-immunologist (Table 3). Sleep apnea overlaps with allergic rhinitis, gastroesophageal reflux disease (GERD), and asthma, conditions that are also common in the population. A recent seminal study provided evidence for development of new-onset OSA in patients with asthma.²⁴ These investigators reported on the Wisconsin Sleep Cohort Study that began in 1988. Adult patients underwent PSG every 4 years. Patients with an AHI of 5 or higher or who were undergoing continuous positive airway pressure (CPAP) therapy were evaluated for physician-diagnosed asthma. A total of 22 of 81 participants with asthma (27%) experienced incident sleep apnea compared with 75 of 466 participants (16%) without asthma.²⁴ Duration of asthma diagnosis was related to both incident sleep apnea and habitual sleepiness. Recent studies have also found that sleep apnea can present with persistent cough, may complicate the obese-asthma phenotype, and, in the severe asthma research program, was associated with neutrophilic asthma.^{25–28}

In patients with upper airway disease, a variety of factors can contribute to sleep apnea, including rhinitis, nasal polyposis, enlarged tonsils, and adenoids, as well as structural disorders, such as micrognathia or macroglossia. In one study of patients with allergic rhinitis, more than 50% of the patients screened had an increased risk of sleep apnea, including 47% of patients with asthma.²⁹ Rhinitis was associated with a 1.44 times higher odds ratio of having OSA risk using a screening questionnaire. Participants in the Wisconsin cohort who reported nasal congestion attributable to allergy were 1.8 times more likely to have moderate to severe sleep-disordered breathing than were those without nasal congestion due to allergy.¹²

Both asthma and obesity are increasing in prevalence, and sleep apnea may provide a link between these 2 disorders in a subset of patients. In one study, the prevalence of sleep apnea in a cohort of patients with asthma was 57%, much higher than in the general population. Obesity is a risk factor for asthma, and obese patients with asthma have more difficulty to control disease.²⁷ The obese-asthma phenotype is difficult to manage because of poor response to standard antiasthma therapy, probably related to corticosteroid unresponsiveness.²⁷ Studies have found that the institution of CPAP in patients with sleep apnea results in improved cough and asthma severity.^{30–32} The plausible mechanisms underlying cardiopulmonary complications in sleep apnea are discussed below.

Inflammatory Responses in Sleep Apnea

Bidirectional interactions exist between asthma and sleep apnea, such as GERD, obesity, smoking, rhinosinusitis, and systemic inflammatory responses.²⁸ These are summarized in Figure 2 and Figure 3. Three mechanisms may relate to the coexistence of asthma, cough, and sleep apnea: mechanical factors (such as rhinitis, nasal polypsis, or structural upper airway abnormalities), reflux-associated pathologic findings, and activation of inflammatory pathways. Hypoxemia-associated activation of inflammatory and neurohumoral pathways is also incriminated in the vascular, hypertensive, and neurocognitive complications that have been described in patients with OSA (Fig 2 and Table 3).

GERD and Laryngopharyngeal Reflux

Patients with sleep apnea have a higher degree of GERD and laryngopharyngeal reflux (LPR), which contribute to cough and airway inflammation.⁴ Dixon and coworkers³³ reported that sleep apnea itself, rather than GERD, was responsible for poor asthma control in obese patients.³³ Other investigators have found an association between nocturnal GERD and poor asthma control, probably influenced by coincident sleep apnea and other anatomical or structural factors.³⁴ Persistent nocturnal GERD was associated with a heightened risk (odds ratio, 2.2; 95% confidence interval, 1.3–1.6) of new asthma. Guven et al³⁵ reported a high prevalence (74.5%) of OSA in patients with difficult to treat asthma; one-third had mild and two-thirds had moderate to severe OSA. LPR can be associated with an irritant form of vocal cord dysfunction that may also present as wheezing or make underlying asthma more difficult to treat.³⁶ LPR can induce cytokine expression in the airways, possibly by induction of nuclear factor- κ B (NF- κ B).^{37–39}

Activation of Inflammatory Pathways

Inflammatory mechanisms, including hypoxemia, superoxide radicals, and cytokines, may further contribute to airway inflammation and/or remodeling in sleep apnea.³ Figure 2 and Figure 3 show the interactions among obesity, asthma, diet, and inflammatory responses seen in asthma. Two processes are central to OSA: obesity with its proinflammatory effects and chronic intermittent hypoxemia with induction of oxidative stress (Fig 2 and Fig 3) and activation of the endothelium by chronic intermittent hypoxia (CIH), which leads to NF- κ B translocation and induction of proinflammatory cytokines that regulate acute phase responses and cellular recruitment (Fig 2). However, the association with obesity, GERD, and underlying asthma and a complex interplay of transcription factors, T cells, macrophages, neutrophils, and endothelial cells determine the degree of airway inflammation and the severity of airway and vascular inflammatory processes (Fig 3).⁴⁰

Interleukin 1 β , tumor necrosis factor α (TNF- α), chemokines, macrophage inhibitor proteins 1 α and 3 α , and activation of NF- κ B can mediate both airway inflammation and accelerated atherogenesis.⁴⁰ GERD has been associated with induction of acute-phase

cytokines, such as TNF- α . Toll-like receptor (TLR) activation (TLR2 and TLR4) on monocytes has been found in OSA.⁴¹ CPAP therapy down-regulated TLR2 and TLR4 expression after 8 weeks of continuous therapy. OSA severity has been linked to circulating serum soluble vascular adhesion molecule 1 and leptin levels.⁴² T_H17 cells and related cytokines are elevated in patients with sleep apnea.^{43,44} Pediatric patients with OSA have elevated T_H17 T-cell subsets in their tonsillar tissue.⁴³ In this study, decreased FOXP3 T-regulatory cells and elevated IL-17A, IL-1 β , IL-10, and IL-12p70 production were seen.⁴³ Cytokine gene polymorphisms, such as TNF- α single-nucleotide polymorphism (–308A), may be associated with OSA in some populations but more studies need to be performed.⁴⁵ Bouloukaki et al⁴⁶ also looked at serum cytokine levels in patients with OSA and erectile dysfunction and found elevated acute-phase response proteins and cytokines (C-reactive protein, IL-1 β , TNF- α , IL-6, and IL-8) and decreased serum adiponectin levels compared with controls. The reduced levels of adiponectin have been associated with increased proinflammatory cytokines and accelerated atherogenesis in several studies. Altered regulation of IL-6 and TNF- α appear to be correlated with daytime sleepiness.⁴⁷ It is likely that elevated leptin and proinflammatory cytokine levels are probably related more to hypoxemia-mediated immune activation in OSA rather than to obesity alone.⁴⁷

One interesting cytokine that might link the metabolic syndrome, immune responses, and sleep apnea is melanin-concentrating hormone (MCH).^{48,49} MCH is a 19-amino acid neuropeptide that stimulates hunger and may additionally regulate energy homeostasis, reproductive function, and sleep. Data suggest that T_H2 cells induce the expression of MCH by endothelial cells.⁵⁰ There is also some evidence to suggest that T_H2 cells express the orexigenic peptide, pro-MCH, confirmed by Sandig and coworkers⁵¹ in *in vitro* differentiated T_H2 cells using Western blotting, enzyme immunoassays, and reverse transcription polymerase chain reaction. Pro-MCH is processed to produce MCH, linking obesity and energy metabolism to asthma and sleep apnea⁵¹ (Fig 3).

Although changes in peripheral blood have been commonly studied, some researchers have looked at cytokine expression in the carotid body, an organ involved in chemosensitivity and respiratory regulation in response to hypoxia and hypercapnia.⁵² Fung⁵² reported on the expression of cytokine and cytokine receptors in the carotid body, which might allow for complex interactions among chemosensitivity, arterial oxygenation, and cytokine expression. Leukotrienes may also play a role in the pathogenesis of the heightened inflammatory responses, and both leukotriene B₄ and the cysteinyl leukotrienes (C₄, D₄, E₄) may be involved (Fig 2).⁵³

Transcription factors, such as NF- κ B, are central to immune regulation, cellular apoptosis, glucocorticoid sensitivity, and cytokine gene expression and are affected by hypoxemia. The T_H2 subset and T_H2 cytokines, such as IL-4 and IL-5, regulate eosinophil activation and IgE class switching in early-onset allergic asthma and are associated with transcription factor GATA-3. The IL-17 subset has been associated with transcription factor ROR γ and neutrophil-mediated asthma (Fig 2). T-cell subset and regulatory cell changes that result in reduced IL-10 and lowered adiponectin may in turn be associated with overexpression of proinflammatory cytokines important to both asthma and atherogenesis.⁵⁴ This could account for the existence of the obese phenotype asthma with a T_H17 predominance and neutrophil-mediated disease characterized by glucocorticoid resistance (Fig 3). The roles of these cytokines and subsets in asthma complicating sleep apnea are unclear and need further study.

Diagnosis of OSA

There are several proprietary screening questionnaires available that take into account symptoms, physical examination

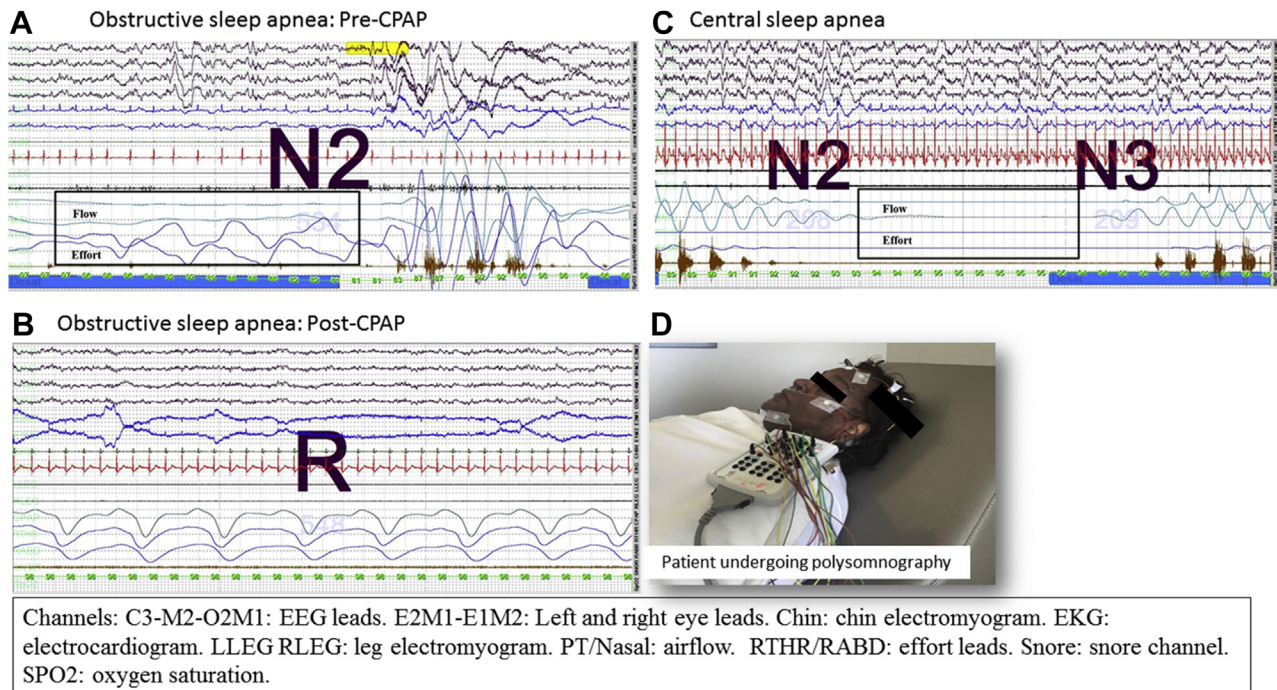


Figure 4. Polysomnography. (A) Obstructive apnea; (B) normal airflow after continuous positive airway pressure (CPAP); (C) central sleep apnea; (D) patient undergoing polysomnography. Boxes show airflow and respiratory movement abnormalities. Channels monitored are delineated.

findings, and comorbidities (as previously discussed in this article) to stratify patients into high- or low-risk groups for OSA; however, the diagnosis of OSA can only be confidently made with objective sleep testing. Diagnostic tests include in-laboratory attended PSG (Fig 4A–D), which is considered the gold standard diagnostic test for OSA and unattended home sleep apnea testing (HSAT). Figure 4A–C represents three 30-second epochs from a PSG. In Figure 4A, an obstructive apnea is seen, which is characterized by loss of airflow in the presence of continued respiratory effort. With the introduction of positive airway pressure (PAP) in Figure 4B, airflow resumes the normal pattern because of the elimination of airway obstruction. Figure 4C shows a central apnea for comparison, which is characterized by loss of flow attributable to absence of respiratory effort. Requirements for approval of PSG orders during prior authorization differ from one insurance company to the other but usually involve a face to face encounter describing symptoms and physical examination findings that raise concern for OSA along with mention of any existing comorbidities that are usually associated with the presence of OSA. Metrics, such as body mass index, neck circumference, Epworth score, and Mallampati score, should also be mentioned.

HSAT uses a portable device that incorporates at least 4 channels that usually measure flow, respiratory effort, oxygen saturation, and heart rate. Patients are instructed on how to apply the sensors and are sent home with the machine. Data are collected for 1 to 2 nights and then interpreted by sleep physicians according to the American Academy of Sleep Medicine scoring guidelines. HSAT can be used in place of PSG in individuals with a high pretest probability of having sleep apnea (as determined by symptoms, physical examination findings, and obesity) but in the absence of severe comorbidities, such as heart failure, neuromuscular disease, significant chronic lung disease, or hypoxemia. HSAT may be difficult in patients with neurocognitive impairment or reduced dexterity and may not be a good choice in such patients. HSAT can be ordered in the same way as PSG, is less expensive, and in most instances is

more convenient; however, insurance companies may prefer one over the other, depending on internal guidelines. These preferences are usually revealed at the time of obtaining prior authorization for the test. An important point is that a positive HSAT result confirms the diagnosis of OSA; however, a negative test result should prompt further evaluation by in-laboratory PSG if there is continued concern for OSA.⁵⁵

A split-night study involves introduction of PAP titration during the same night as the diagnostic PSG. This can be performed after the first 2 hours of the study if the AHI is greater than 40 and can be considered based on clinical judgment if the AHI value falls between 20 and 40.^{56,57} This is a good option when OSA is the main diagnostic concern and should be ordered as such.

Management

The approach to the treatment of OSA is multifactorial and includes lifestyle modifications, such as weight loss, avoidance of alcohol or other sedating agents, implementation of positional therapy, and interventions to improve airway patency.

CPAP as a treatment for sleep disordered breathing was first described in 1981 by Sullivan et al.⁵⁸ It provides a pneumatic splint that keeps the upper airway from collapsing. High-quality data indicate that CPAP improves AHI, decreases daytime sleepiness, and improves several other parameters, such as blood pressure, diabetes control, depression, and cognitive function.^{57,59–62} The American Academy of Sleep Medicine's Adult Sleep Apnea Task Force recommends CPAP as the treatment of choice for all severities of OSA that should be offered to all patients.⁶³ Bilevel positive airway pressure (BPAP) consists of 2 pressure settings: a higher one during inspiration and a lower one during expiration. BPAP can be used in patients who have difficulty tolerating higher continuous pressure because the lower pressure setting during expiration allows for an improved sense of comfort. It is also useful in patients with hypoventilation associated with hypercapnia, such as in patients with chronic obstructive pulmonary disease or

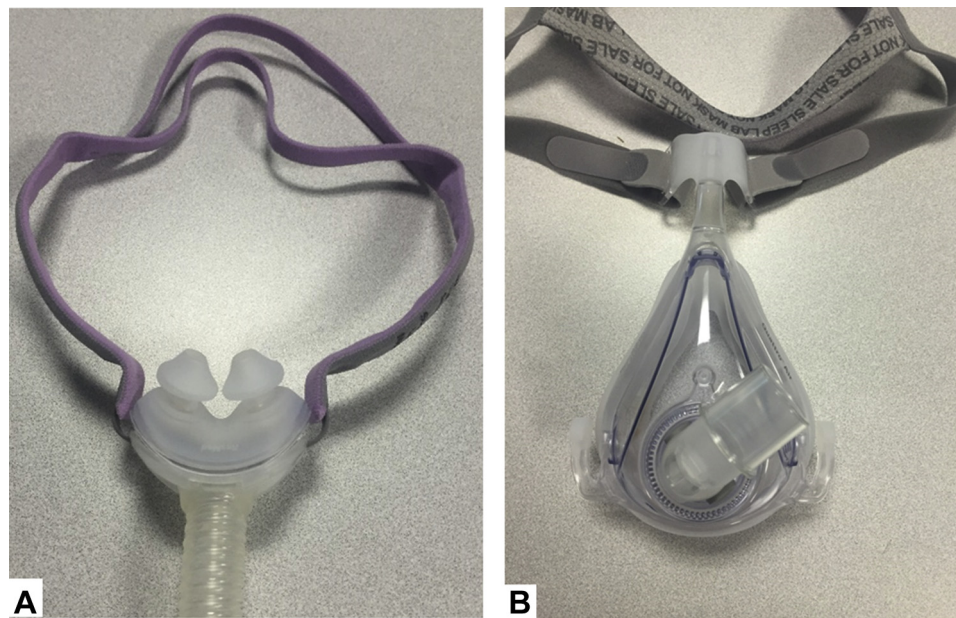


Figure 5. Therapy for sleep apnea. (A) Nasal pillows; (B) full face mask.

neuromuscular weakness.⁵⁷ There are several mask interfaces available, including full face masks (which cover the nose and mouth), nasal masks, and nasal pillows (Fig 5A and B). These masks can be individualized to patient preference. Autotitrating CPAP and BPAP machines are also available; however, the American Academy of Sleep Medicine recommends initial PAP titration in a supervised in-laboratory setting, as the preferred approach.^{63,64}

PAP use should be objectively monitored to ensure adherence.⁵⁷ Most new PAP machines contain data cards that record hours of use and residual AHI while receiving therapy. This information can be easily downloaded in the clinic and reviewed to assess adherence and effectiveness of therapy. Improvement in subjective sleep quality and reduction in the posttreatment Epworth score can also be used to gauge success.

Many pitfalls in the management of OSA can be avoided by understanding the information available through data cards. If a patient presents for follow-up after initiating PAP and continues to note daytime sleepiness, the data card can provide invaluable information. It can provide a true measure of adherence because patients usually tend to overestimate use. According to Centers for Medicare & Medicaid Services guidelines, patients need to wear the PAP machine more than 4 hours each night for more than 70% of nights in a 30-day period. In some instances, continued low adherence can result in repossession of the PAP machine by insurance companies. Low adherence should prompt discussions about barriers to use, such as problems tolerating the pressure, dryness, or mask fit. The aim of PAP therapy is to reduce the AHI to below 5. The data card also records residual AHI and amount of air leak from the mask. A residual AHI greater than 5 can result from excessive leak (in which case mask fit should be addressed and optimized) or inadequate pressure, which can prompt empiric adjustment of the pressure, changing the setting to autotitrating PAP, or obtaining a formal in-laboratory retitration. If sleepiness persists despite a normal data card download, an in-laboratory retitration can be considered before initiating alerting medications.

Insurance requires a face to face clinic visit and documentation of adherence usually by use of the data card within 30 to 90 days of initiating PAP. Close follow-up is indicated for individuals who are lagging behind in adherence or control of OSA. Yearly follow-up is recommended for optimally treated patients. Patients are eligible

for new machines every 5 years if they are adherent with therapy. Persistent lack of adherence may result in repossession of the machine by insurance.

In overweight or obese patients with OSA, weight loss improves symptoms of daytime sleepiness and the severity of OSA but normalization of the AHI is rare.^{65,66} All overweight or obese patients should be provided information on weight loss, including referrals to medical weight loss programs or bariatric surgery as clinically indicated. This should be done in conjunction with other first-line treatment options for OSA, such as PAP therapy.⁶³

PSG can identify certain individuals who have supine predominant OSA. These patients generally have less severe overall disease, and positional therapy with specially designed devices and pillows can be considered. These devices prevent patients from turning onto their backs during sleep but should not be relied on as sole therapy. They are best used in conjunction with first-line treatments or in patients who cannot tolerate PAP.⁶⁷

Studies comparing custom-made oral appliances, such as mandibular advancement or tongue-retaining devices, with CPAP have found them to be less effective at reducing the AHI and Oxygen Desaturation Index but with similar improvement in symptoms. They are also preferred by patients over CPAP, which may lead to better adherence.⁶⁸ Although CPAP is still first-line therapy, oral appliances can be considered in patients with mild disease or in those who cannot tolerate CPAP. Patients with severe OSA or significant desaturations are not considered good candidates for oral appliances.⁶⁹

Medications, such as theophylline, have been studied in patients with sleep apnea as sole therapy, but no definitive data exist to recommend their use.⁷⁰ Alerting medications, such as modafinil or armodafinil, can be used adjunctively in patients who experience excessive daytime sleepiness despite optimal correction of their sleep disordered breathing.⁶⁷ Most importantly, medications such as benzodiazepines, muscle relaxants, sedating antidepressants, sedating antihistamines, and narcotics should be avoided in patients with OSA because they worsen the severity of sleep disordered breathing.

Surgery is reserved for patients in whom PAP therapy or oral appliances fail and appears to have best results in patients with significant obstructing lesions in the upper airway. Before the

introduction of CPAP, tracheostomy was the definitive therapy for OSA. Several surgical procedures, including maxillomandibular advancement and uvulopalatopharyngoplasty, have been recommended as options for the patient intolerant of CPAP, but there is a paucity of high-quality evidence regarding their success.^{2,71} A newer device consists of an implantable hypoglossal nerve stimulator, which may have a role in patients with moderate to severe OSA; however, initial studies have revealed mixed results.^{2,71}

Conclusion

OSA is a common disorder characterized by repetitive upper airway collapse and interruptions in airflow, leading to desaturations, arousals, and increased sympathetic activity. The disease can complicate asthma because of induction of inflammatory pathways or associated esophageal reflux. Cough, neurocognitive decline, hypertension, vasculopathy (stroke or heart disease), arrhythmia, optic neuropathy, and metabolic dysregulation attributable to neurohumoral mechanisms contribute to increased morbidity associated with the illness. Early diagnosis and intervention with weight loss or CPAP can lead to improved outcomes in these patients. Whether aggressive treatment of sleep apnea improves asthma severity and risk requires further large-scale population studies.

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