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Obstructive Sleep Apnea

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CASE PRESENTATION

A 61-year-old obese male presents to a new primary medical doctor for a regular check-up with continued complaints of fatigue and drowsiness. The patient reports he often falls asleep during the day while watching television and recently fell asleep while driving. The patient’s wife comments she has noticed her husband snores loudly. The patient’s past medical history is significant for hypertension diagnosed 7 years ago and a cholecystectomy performed 15 years ago.

KEY CLINICAL QUESTIONS

1. At what point should this patient be considered for a work-up for obstructive sleep apnea (OSA)?
2. How does sleep apnea differ from other sleep syndromes?
3. What are the main causes of OSA and why are some patients more predisposed to sleep apnea?
4. Are there any long-term sequellae associated with chronic OSA?
5. What are the appropriate diagnostic procedures and treatments for OSA?
LEARNING OBJECTIVES

1. Identify the main signs and symptoms of OSA.
2. Understand the pathophysiology behind OSA.
3. Create a differential diagnosis for a patient with suspected OSA.
4. Utilize appropriate diagnostic interventions for patients with signs or symptoms suggestive of OSA.
5. Become familiar with currently available treatment options for patients with OSA.

EPIDEMIOLOGY

Sleep apnea is defined as a cessation of breathing during sleep. Sleep apnea can be caused centrally from the brain, by anatomical obstruction, or have a mixed pattern. OSA, which is characterized by interruptions in breathing caused by intermittent complete or partial obstruction of the airway is the most common form of sleep apnea and is the focus of this chapter. Patients with OSA must have at least 10 apneic (cessation of breath for >10 seconds) or hypopneic (reduction of airflow and thus oxygenation) episodes per sleep hour. This causes sleep interruptions that lead to symptoms of excessive daytime sleepiness (EDS), and is associated with many chronic conditions.

The identification of individuals with OSA depends on a number of selection criteria, which can differ among clinicians. Varying opinions on what constitutes OSA and one’s own experience in recognizing classic signs and symptoms of sleep apnea lead to inconsistent reporting (1). In evaluating the prevalence of sleep apnea, it is useful to consider the results of four large prevalence studies, all of which used similar methods in gathering and analyzing data. For those adults with an average body mass index of 25 to 28 kg/m², it is suspected that 1 in 5 white adults suffer from mild sleep apnea, and 1 in 15 suffer from moderate disease (2–6). It is estimated that sleep apnea syndrome affects nearly 5% of adults in Western countries (6). Three factors generally accepted as important to the development of sleep apnea include baseline obesity, older age, and the presence of snoring (6).

Data from the Wisconsin Sleep Cohort study indicates that individuals with mild sleep apnea will progress to moderate or severe disease with a sixfold risk if a 10% weight gain occurs (7). Obesity as a factor for the development of sleep apnea is especially significant in circumstances in which the airway narrowing is perhaps in part because of excess soft tissue in the oropharynx (8). Some studies that show a correlation between neck circumference and prevalence of sleep apnea only support this theory. Some literature suggest men have a higher prevalence of sleep apnea than women, often citing hormonal causes as an explanation for the varying prevalence (1). Furthermore, postmenopausal women are
more frequently affected with sleep apnea than premenopausal women (6). It is suspected that hormone replacement therapy may alleviate this difference in prevalence among women (9).

The correlation between age and the prevalence of sleep apnea is vague. Several studies show an increase in prevalence with increasing age, whereas others show a limited correlation after age 65. Overall, the literature demonstrates conflicting reports on age as a factor in the development of sleep apnea (1). Although data is limited on the prevalence of sleep apnea in non-white populations, great variability does not exist among different ethnicities (10–13).

EDS is the most common presenting symptom among patients with sleep apnea (1). Precise quantification of sleepiness is difficult given the variable descriptions provided by patients. In assessing patients for sleep apnea, the challenge for the clinician exists in determining when further evaluation is necessary. Given the high correlation between motor vehicle accidents and patients with sleep apnea, it can be argued that such quantification should be less important than the presence or absence of daytime sleepiness (14,15).

The causal relationship between EDS and sleep apnea results from the fragmentation of the affected patient’s sleep. Such fragmentation is associated with central nervous system arousal during each apneic episode (1). Arousal from sleep is further evidenced by such objective measures as transient blood pressure or heart rate elevations. Despite the alterations in vital signs during sleep, patients with sleep apnea do not typically demonstrate any change on the electroencephalogram (16).

The complexity of recognizing sleep apnea is further evidenced by reports of patients diagnosed with sleep apnea but who did not present with EDS. It is therefore important for the clinician to consider as many factors, subjective and objective, in evaluating a patient who may have sleep apnea. For example, the correlation between snoring and sleep apnea is significant despite the subjective nature of snoring. It is important to note that additional factors, such as snoring, may have their own independent correlations with EDS (17).

**PATHOPHYSIOLOGY**

The classic pattern of sleep is inclusive of rapid eye movement (REM) sleep, one of several stages during the normal sleep cycle. During REM sleep, elevations in heart rate and blood pressure are commonly seen, whereas non-REM sleep is typified by decreased sympathetic outflow and lower heart rate and blood pressure. This continual modulation during the sleep stages is disturbed in patients with OSA, which results in a loss of homeostasis (18).

Craniofacial abnormalities are partly to blame in terms of the anatomical differences in patients with sleep apnea. Specifically, these include macroglos-
sia, retrognathia, and acromegaly (19). Despite the seemingly clear linkage of these abnormalities to the pathophysiology of OSA, only a small percentage of sleep apnea patients are characterized as having these craniofacial abnormalities. Therefore, it is likely that other factors are largely responsible for causing sleep apnea in most affected patients (1). Specifically, atonia of the pharyngeal dilator muscles and the presence of excess nonadipose soft tissue in the pharyngeal space are most likely the major contributing factors for disease in patients with sleep apnea (1). In affected patients, high levels of electromyographic activity are seen during wakeful hours with significantly less activity seen during sleeping hours. This suggests a compensatory mechanism in affected patients during wakeful hours that is absent when the patient falls asleep. It is specifically the loss of this compensatory mechanism that results in brief periods of apnea (20,21).

The accumulation of apneic episodes results in a temporary state of hypercapnia and hypoxemia. The body’s response to the abnormal acid–base balance is provided by a series of chemoreceptors, the most significant of which are located in the carotid bodies (located in the internal carotid arteries) (1). The response of the carotid bodies is primarily determined by the serum oxygen tension (22). By contrast, serum carbon dioxide tension is primarily monitored by the brainstem central chemoreceptors (23). The healthy individual will experience a blunted response by these receptors during sleep as compared with wakefulness (quantification of the gas tensions seen during sleep in the normal patient are on the order of an increase of partial pressure of carbon dioxide by 2 to 6 mmHg and a decrease in oxygen saturation of up to 2%) (24). Thus, the effect in a patient with sleep apnea is all the more critical and results in an inadequately compensated acid–base balance irregularity.

There are several medical conditions that are comorbid with OSA, and causative associations are currently under investigation. Cardiovascular disease is common in patients with OSA (1). Hypertension has been documented in patients with OSA, and may be a consequence of the disease (25). There have also been associations with OSA and arrhythmias, myocardial infarctions, and stroke. Cardiomyopathy can be caused by OSA, and reverses with successful treatment. Patients with both chronic obstructive pulmonary disease and OSA are predisposed to severe nighttime oxygen desaturations, and this may lead to persistent pulmonary hypertension and right-sided heart failure. Finally, psychosocial problems can affect patients with OSA. Affected patients often have depression, irritability, and impaired concentration (1).

**DIAGNOSIS**

Confirming the diagnosis of OSA generally requires a sleep study. However, clinical history is extremely important. Patients with symptoms or who are at risk of having sleep apnea (Table 1) should first be asked whether or not they snore.
Clinicians should further define if this occurs frequently, if the snoring is loud, and if it is affected by sleeping position (lying on back or side). Because patients are not aware of their own snoring in most cases, it is important to query their sleeping partners. Additionally, clinicians should ask about EDS. Finally, if there is a sleeping partner, the clinician should inquire whether or not the partner observes any apneic episodes during the night. If any of these questions are positive, further work-up with an objective test should be considered.

In order to make a diagnosis of sleep apnea, a clinician may decide to request one or more objective tests. The gold standard for diagnosing sleep apnea is in-laboratory polysomnography. Another method frequently used to diagnose sleep apnea is nocturnal pulse oximetry. A third method employed by clinicians is morphometric examinations of the head and neck. Although such examination is often more cost-effective and does not require valuable bed space in sleep laboratories, the imprecise, operator-dependent nature of this test makes it unreliable as the sole mechanism in determining sleep apnea. Furthermore, nocturnal pulse oximetry is also a less specific test, whereby a negative result will still require polysomnography to confirm the negative result. Despite the high expense and scarcity of bed space in the sleep lab, high clinical suspicion should always result in appropriate diagnostic testing to avoid the long-term negative consequences on the health of a patient with sleep apnea (1).

### Table 1

**Symptoms and Signs of Patients at Risk for Sleep Apnea**

**Symptoms**

- Chronic, loud snoring
- Gasping or choking episodes during sleep
- Excessive daytime sleepiness (especially drowsy driving)
- Automobile or work-related accidents as a result of fatigue
- Personality changes or cognitive difficulties related to fatigue

**Signs**

- Obesity, especially nuchal obesity (neck size ≥17 inches in males, ≥16 inches in females)
- Systemic hypertension
- Nasopharyngeal narrowing
- Pulmonary hypertension
- Cor pulmonale (rarely)

From ref. 12.
In-laboratory polysomnography or sleep study measures the number and severity of apneas (cessations of airflow) and/or hypopneas (reductions in airflow) that cause sleep disruption. These are measured in events per hour and are referred to as the apnea–hypopnea index or respiratory disturbance index. Apneas or hypopneas that last at least 10 seconds are considered clinically significant. Most apneas or hypopneas last between 20 and 30 seconds and can sometime last more than 1 minute. Episodes usually resolve when the patient is slightly aroused, although the patient is usually not aware of this. Apnea–hypopnea or respiratory disturbance indexes higher than 20 are considered a sign of significant disease warranting treatment. However, patients with fewer than five events per hour may also benefit from treatment if they have significant symptoms or comorbid conditions. In addition, some patients can have several hundred episodes per night.

**TREATMENT OPTIONS**

The goal of treatment of OSA is to eliminate apnea and hypopnea, reduce snoring and arousal, and ultimately improve sleep and eliminate symptoms and conditions attributed to sleep disturbance, as well as reduce risk of adverse events such as involvement in motor vehicle collisions. The various treatments available for reducing the degree of sleep apnea are limited to a few options (Table 2).

The first option is weight loss, because a high degree of clinical improvement is seen with a 10% reduction in body weight (26). The literature demonstrates that the correlation between amount of weight lost and the degree of sleep apnea is inversely related to one another. However, it should be noted that such reductions in weight do not result in a complete cure of the sleep apnea but rather only improvements in the severity of disease (6).

The most studied treatment, continuous positive airway pressure (CPAP), is widely considered to be the most effective therapy for the treatment of sleep apnea (1). There is significant evidence that CPAP improves upper airway flow and reduces the daytime symptoms in patients. Other studies have demonstrated that CPAP improves mood and functional status, and can decrease the incidence of motor vehicle collisions. This form of treatment often compensates for the pathophysiological consequences of sleep-disordered breathing discussed earlier. Some studies suggest that daytime symptoms are an important determining factor in the effectiveness of CPAP, and the absence of such symptoms may be less of an indication for CPAP therapy. Although CPAP is still an effective option, it has been show to have minimal effect on improving sleep apnea-induced change in blood pressure in those patients who do not show daytime symptoms (27).

The CPAP unit is a machine containing a fan that delivers pressurized air to the patient’s nostrils and thus acts as a pneumatic splint that keeps the airway
open. CPAP does not correct the disorder, and must be used by the patient each evening. CPAP machine pressure settings are best determined in the sleep lab during a sleep study. Once the diagnosis is confirmed, a trial of CPAP is usually observed while the patient is sleeping in the lab. During this study, adjustments are made to the CPAP pressure setting, and reductions of apnea and hypopnea are documented. Once therapy is initiated, patients should be re-evaluated periodically because pressure requirements can change over time.

Despite the high efficacy of CPAP, its universal use in the treatment of sleep apnea is inhibited by patient intolerance or refusal secondary to discomfort caused by the CPAP apparatus. The most common complaint made by patients after initiating CPAP treatment is excessive nasal congestion. In-line heated humidification and the use of moisturizing creams or corticosteroids have been shown in some patients to make therapy tolerable (1).

Surgical treatment options for OSA are not as widely used because of a lack of data supporting this treatment modality as being highly effective. One

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Treatment of Sleep Apnea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Modification of behavioral factors</strong></td>
<td></td>
</tr>
<tr>
<td>• Weight loss (including exercise regime)</td>
<td></td>
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<tr>
<td>• Avoidance of alcohol and sedatives before sleep</td>
<td></td>
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<tr>
<td>• Avoidance of supine sleep position</td>
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<tr>
<td><strong>Nasal CPAP</strong></td>
<td></td>
</tr>
<tr>
<td>• Noninvasive</td>
<td></td>
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<tr>
<td>• Very effective</td>
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<tr>
<td>• Patient adherence variable</td>
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<tr>
<td><strong>Oral/dental devices</strong></td>
<td></td>
</tr>
<tr>
<td>• May be useful in mild to moderate cases</td>
<td></td>
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<tr>
<td>• Not uniformly effective</td>
<td></td>
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<tr>
<td><strong>Surgical procedures (UPPP, nasal surgery, tonsillectomy, LAUP, maxillofacial surgery, tracheostomy)</strong></td>
<td></td>
</tr>
<tr>
<td>• Invasive</td>
<td></td>
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<tr>
<td>• Not uniformly effective</td>
<td></td>
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<tr>
<td>• May carry risk</td>
<td></td>
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<tr>
<td>• Repeat sleep study is necessary after each procedure</td>
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CPAP, continuous positive airway pressure; UPPP, uvulopalatopharyngoplasty; LAUP, laser-assisted uvulopalatoplasty.
example of a commonly performed procedure is uvulopalatopharyngoplasty, a procedure that only shows improvement in a small portion of patients (28). This finding suggests that several anatomical features contribute to sleep apnea. Objective data from imaging studies and airway pressure measurements indicate that the two areas most susceptible to collapse are the spaces behind the soft palate and tongue base (29,30). Notably, despite initial perceived improvements postsurgically, there is concern for permanent improvement in the patient with sleep apnea. As a result, it is recommended that polysomnography be repeated within 4 to 6 months after the surgical procedure (1).

Finally, mandibular devices can be used as an alternative to the previous treatment options. As discussed previously, retrognathia is one of the contributing factors in the development of sleep apnea. Therefore, mandibular devices function to reduce retroglossal airway collapse by inducing mandibular protrusion in those patients needing such anatomical adjustment. Such devices are most useful in patients with mild disease or nonapneic snoring, and improvement in daytime symptoms has been noted with the consistent use of mandibular devices (31,32).

REFERENCES