

**TITLE: Health Related Consequences of Obstructive Sleep Apnea and Response to Therapy**  
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## **Introduction**

In the last thirty years there has been a blossoming body of knowledge regarding the diagnosis and treatment of sleep disorders. The otolaryngologist is frequently involved in the management of these patients. A thorough understanding of sleep disorders and their treatment is key for the practicing otolaryngologist. Specifically, one must be familiar with the health-related consequences of obstructive sleep apnea [OSA] such as neuropsychological sequelae, metabolic derangements, hypertension, heart and vascular disease. The otolaryngologist must also be able to counsel patients on available treatments for OSA and the relative ability of these treatments to impact the health-related consequences of OSA.

## **Definitions**

To understand the specific disorders one must understand some of the definitions. An *apnea* is defined as cessation of airflow for ten seconds which results in an arousal. If the chest wall continues to mechanically move during this time, then it is an *obstructive apnea*. If the chest wall does not attempt to ventilate, then it is presumably due to a neurologic etiology and is termed a *central apnea*. Sometimes there are characteristics of both an obstructive and a central apnea, and this is termed a *mixed apnea*. The number of apneas per hour is termed the *apnea index*.

A *hypopnea* is a less well-defined entity, but usually is considered a diminution in airflow which results in hypoxemia and results in an arousal. The number of hypopneas per hour is termed the *hypopnea index*.

Functionally, there is little difference between apneas and hypopneas, and the sum of these vents per hour is termed the *apnea-hypopnea index* (AHI). This is also referred to as the *respiratory disturbance index* (RDI). Occasionally a lab will also report the *arousal index*, which is the number of arousal per hour. This may be different than the RDI due to limb movement or other causes of arousal.

Generally the *obstructive sleep apnea syndrome* (OSAS) is considered to be an RDI > 5. Also described is the *obstructive sleep hypopnea syndrome* (OSHS) which is a hypopnea index of greater than 15, but as mentioned there is little clinical utility in differentiating this from OSAS. Severity of OSAS is also stratified by the RDI, with mild being considered 5-20, moderate 20-40, moderate-severe 40-60, and severe > 60.

As the field of sleep medicine progressed there arose an awareness of certain patients who report excessive daytime sleepiness but do not have OSAS (e.g. RDI < 5). By esophageal manometry some of these patients have been shown to have increased negative thoracic pressure during inspiration. Thus, their increased work of breathing is thought to be responsible for their symptoms. This syndrome has been termed the *upper airway resistance syndrome* (UARS). Together with OSAS these are jointly referred to as *sleep-disordered breathing* (SDB). Those patients who snore but have an RDI < 5 and who do not have increased intrathoracic pressure upon inspiration simply have *primary snoring*. One hypothesis is that these disorders represent a spectrum of disease with primary snoring being the mildest, followed by UARS, and finally OSAS as the full manifestation of the disease.

## Pathophysiology

Although incompletely understood, the pathophysiology of OSAS relates to airway collapse. This may occur at various levels, including the palate, the base of tongue, and the hypopharynx. Nasal obstruction appears to facilitate or exacerbate the syndrome although it does not appear to be primarily responsible. Unfavorable anatomy appears to be the most important cause. This can be due to a narrow palate, an elongated uvula, redundant tissue at the base of tongue, micro/retrognathia, a retrodisplaced hyoid, and so on. Adenotonsillar hypertrophy may be a cause as well, particularly in the pediatric population. Experimental evidence shows that in the pharynx the collapse occurs predominantly from the lateral walls, not merely from anteroposterior collapse as might seem likely in patients with elongated palates. This also may explain the way in which obesity increases the prevalence of OSAS, as the lateral pharyngeal fat pads may narrow the airway in the lateral dimension.

Although unfavorable anatomy is important etiologically, there also appears to be a physiologic defect in the pharyngeal dilators. There is also experimental evidence that longitudinal tension appears to be inversely related to airway collapse. Additionally, extrinsic factors such as sedating medications may exacerbate the physiologic defects.

## Rationale for treating OSAS

Untreated, OSAS has a rather impressive list of deleterious consequences:

### I. Neuropsychological Sequelae:

- a. Sleepiness/tendency to fall asleep. Patients with severe OSA often have mean sleep onset latencies in the pathological range of 5 minutes or less, some 2 standard deviations below normal mean values of 12. Improvements in both subjective and objective tests of sleepiness are seen with CPAP therapy for OSA. These improvements are moderate to large.

- b. b.Attention. There is a sizable effect of OSA on the ability to sustain attention over time, particularly on the quality of the performance rather than simple reaction time. In terms of **attention**-based cognitive outcomes, there is a modest improvement of functioning with CPAP.
- c. Cognitive function. Moderate to severe OSA negatively impacts memory and executive performance—although presence and degree of deficit in these categories is controversial
- d. Quality of life. Studies indicate that patients with OSA have significantly impaired QOL and social functioning and a high prevalence of minor psychiatric morbidity. The large impairments in sleepiness and energy related QOL scores show substantial improvement with CPAP—those with the most severe OSA reap the most benefit.

## II. **Metabolic Effects—Insulin Resistance**

### a. **Meslier et al 2003**

- 595 male patients referred for polysomnography underwent a 2 hour oral glucose tolerance test.
- 494 pts had OSAS (AHI > 10)
- Fasting and postload blood glucose increased with severity of sleep apnea
- Insulin sensitivity decreased with increasing severity of sleep apnea
- BMI, age and AHI are all have an independent effect on blood glucose and insulin sensitivity

### • **Ip et al 2002**

- 185 pts with OSAS (AHI>5)
- Insulin resistance increased with age obesity (main determinant)
- Independent determinants of OSA were AHI and min O2 sat

### • **Punjabi et al 2003 [Review]**

- Habitual snoring is associated with abnormal fasting glucose and insulin values independent of age and BMI
- Prospective data from two separate studies indicate that habitual snoring is associated with more than a 2-fold risk of developing DM type II over a ten year period independent of BMI and other confounders
- Several studies have suggested that the minimum oxygen saturation and AHI are predictive of glucose intolerance and insulin resistance independent of BMI, age and waist to hip ratio

### • **Babu et al 2005**

- 25 pts with DM type II, obesity (mean BMI 42.7), and OSA (mean AHI 56) were evaluated before and after a 90 day trial of CPAP

- There were significant reductions in postprandial glucose values
- Concluded that OSA is pathophysiologically related to impaired glucose homeostasis and that CPAP is an important therapy for pts with DM type II and OSA
- **Harsch et al 2003**
- Forty patients with AHI>20 were evaluated for insulin sensitivity before, 2 d after and 3 mos after treatment with CPAP. Insulin sensitivity significantly increased after two days and remained stable after three months of treatment.
- Patients with BMI < 30 had a much greater improvement in insulin sensitivity.

### III. Hypertension

- Wisconsin Sleep Cohort Study.** Demonstrated an increased risk for development of hypertension in patients with OSA over a 4 to 8 year follow up period. The severity of OSA increased risk for development of hypertension independent of baseline blood pressure status, age, gender, BMI, alcohol and cigarette use.
- Sleep Heart Health Study.** There is an elevated risk for hypertension found in subjects with sleep disordered breathing after adjusting for demographics, BMI, alcohol consumption and smoking. Association between SDB and HTN was seen regardless of age, gender, ethnicity, BMI.
- Mechanism:** Individual episodes of sleep apnea cause acute surges in HR and BP at apnea termination driven by hypoxia. Epidemiologic evidence and physiologic studies in humans and animals support the idea that chronic exposure to repeated apneas may lead to a sustained diurnal HTN via increased sympathetic tone and activation of the renin-angiotensin system.
- d. Treatment of OSAS does appear to lower blood pressure although the literature is inconsistent.

### IV. Cardiovascular effects

- **Marin** et al published results of 10 year observational study of 377 primary snorers, 403 pt with untreated mild to moderate OSA, 235 pts with severe OSA who refused treatment, 372 pts with OSA treated with CPAP, 264 healthy pts. The endpoints [myocardial infarction, stroke, or acute coronary insufficiency requiring invasive management, death of myocardial infarction or stroke] were 3 times as high in pts with untreated severe apnea as in the healthy control individuals.

- **Milleron** et al prospectively monitored 54 patients with both CAD ( $\geq 70\%$  coronary artery stenosis) and OSA (AHI  $\geq 15$ ), 25 of whom were treated with CPAP or upper airway surgery and 29 who declined treatment for OSA, for a median of  $86.5 \pm 39$  months. The endpoint (cardiovascular death, acute coronary syndrome, hospitalization for heart failure, or need for coronary revascularization) was reached in only 24% of the treated patients compared with 58% of those who declined OSA treatment.

## **Conclusion**

Sleep medicine is an exciting, relatively new field that has emerged. The otolaryngologist has become a key figure in the diagnosis and management of sleep disorders due to his or her familiarity with the airway and the ability to intervene surgically. An understanding of the medical and surgical issues involved is necessary for the otolaryngologist to deal with this field which is rapidly evolving.

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