JOURNAL OF INSURANCE MEDICINE

J Insur Med 2003;35:36–50

REVIEW ARTICLE

Sleep Apnea: A Review for Life Insurance Medical Directors and Underwriters

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Object.—Obstructive sleep apnea (OSA) is a commonly encountered impairment in both clinical and insurance medicine. Surprisingly, relatively few data exist regarding the mortality or morbidity of sleep apnea. This paper reviews the mortality and morbidity implications of this disorder.

Methods.—Literature review using Medline.

Results and Conclusions.—Much of the morbidity and mortality attributed to obstructive sleep apnea may be due, in part, to the presence of co-morbid conditions (obesity, hypertension, cardiovascular and cerebrovascular disease). An assessment of additional risk attributable specifically to OSA requires review of polysomnographic results, including the respiratory disturbance index (RDI), minimum arterial oxygen desaturation, minimum and maximum heart rates, and sleep architecture. Integral to this risk assessment is also the presence and severity of the consequences of OSA, chiefly the severity of disability due to daytime hypersomnolence as well as the other co-morbidities (control of hypertension, weight gain or loss). It is this author's opinion that adequately treated OSA may carry little, if any, mortality risk.

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Key words: Sleep apnea, obstructive sleep apnea, sleep studies, polysomnography, mortality, morbidity.

Few clinical entities have proven so troublesome to underwrite as sleep disorders of breathing and, in particular, obstructive sleep apnea (OSA). The frequency with which underwriters encounter this problem and the potential for premature morbidity and mortality has led the Board of Insurance Medicine to define OSA as 1 of the 5 specific entities in pulmonary disease with which board-certified medical directors are expected to have special knowledge. This paper will review the medical literature of sleep apnea, with particular reference to those aspects of the disease that may prove useful in underwriting applicants who are either at risk of having, or who have been diagnosed with, this disorder.

DIFINITIONS AND PATHOPHYSIOLOGY

A common misconception is that the clinical syndrome of obstructive sleep apnea was first described by the English writer, Charles Dickens, in his description of ''Joe, the fat boy,'' in his novel *The Posthumous Papers of the Pickwick Club.* Osler, and later Burwell, are credited for naming this syndrome ''The Pickwickian Syndrome.'' We now know that Dickens' character Joe more aptly describes the obesity-hypoventilation syndrome, a disease entity, which almost invariably includes OSA as one of its components. But obstructive sleep apnea and the obesity-hypoventilation syndrome should not be confused, as the latter entity carries a much worse mortal-

ity than the former. Obesity-hypoventilation syndrome is characterized by extreme obesity and alveolar hypoventilation occurring while awake. Given sufficient motivation, these patients can voluntarily hyperventilate to a eucapnic state, but immediately revert back to high levels of P_aCO_2 and hypoxia once the voluntary hyperventilation ceases. Half of these patients are polycythemic, and the disorder has a very high mortality.[1] Thus, ''Pickwickian Syndrome'' refers to obesity-hypoventilation syndrome, and not obstructive sleep apnea.

Credit for discovering the sleep apnea portion of the obesity-hypoventilation syndrome and defining it as a separate entity goes to Gastaut and coworkers. They not only described all 3 types of sleep apnea but were also the first to postulate that the sleepiness associated with this syndrome was due to repeated arousals associated with the resumption of breathing that terminated the apneic/hypopneic events.[2]

Sleep apnea refers to >10 seconds of no air movement. In central sleep apnea, no effort to breathe is made, whereas in OSA there is ventilatory effort but no airflow because of upper airway closure. In mixed apnea there is typically no initial effort followed by effort without airflow due to obstruction. Sleep hypopneas are defined by some decrease in airflow signal in conjunction with an arbitrary reduction in oxygen saturation measured by pulse oximetry. Hypopneas may be central and/or obstructive in nature, but this distinction is not made in ordinary polysomnography testing.[3]

Dividing the total number of apneas and hypopneas by the total sleep time defines the apnea/hypopnea index (AHI), also frequently referred to as the respiratory disturbance index (RDI) or disordered breathing event index. Older literature referred to just the apnea index (AI), but subsequent studies have shown that hypopneas and apneas often have the same physiologic consequence. Therefore, most studies add both apneas and hypopneas into the apnea/hypopnea index, or AHI (or RDI).

It should be noted that an RDI of 10 does not necessarily mean that the studied subject is having 10 apneas/hypopneas per hour. More commonly, the events may occur in groupings related to body position (supine vs. lying on the side or prone) or stage of sleep. Rapid eye movement (REM) sleep, for instance, is often characterized by a general atonia of the peripheral musculature. Not surprisingly, obstructive events are, therefore, often much worse during REM sleep, as opposed to other stages of sleep. Studies that don't include REM sleep (such as ''half and half'' polysomnograms, where the first 3 hours of sleep document the presence or absence of OSAs. The remainder of the night's study is for CPAP titration. Most of a subject's REM sleep will be missed in these studies, and will, therefore, possibly underestimate the severity of RDI disturbance.) will commonly underestimate the severity of obstructive/hypopneic apneas. Hypopneas and apneas are terminated by arousal, a transient (3–14 second) partial or complete return to awake physiology.

The pathophysiology of obstructive sleep apnea is, simply put, the abnormal narrowing and/or closure of the pharynx during sleep. An abnormal pharynx can be kept open in wakefulness by appropriate compensatory increase in dilator muscle activity, but during sleep this compensation fails and the airway collapses.[4] Partial collapse results in snoring, hypopneas, and in some cases prolonged obstructive hypoventilation. Complete closure results in apnea.

Arousal from sleep to wakefulness is required for the return of sufficient pharyngeal dilator muscle activity to open the pharynx and reestablish adequate airflow. With arousal and the relief of obstruction, there is often observed a ventilatory ''overshoot,'' with the resulting rise in P_aO_2 and fall in P_aCO_2 setting the stage for the next apnea.[5] Sleep fragmentation from repeated arousal is thought to be the primary cause of the hypersomnolence.

The actual point of obstruction is most often in the nasopharynx, although it may occur anywhere in the pharynx. The sympa-

thetic response to the apneic and hypopneic episodes are thought to account for many of the long-term cardiovascular consequences of sleep apnea.

An important but as yet unanswered question is whether there is really a central apnea syndrome in the same sense that there is an OSA. Patients with central sleep apnea are certainly a more heterogeneous group than those with OSA. They are broadly classified into 2 categories based upon their level of respiratory drive. Decreased respiratory drive is seen with patients with waking hypercapnea from any cause (eg, idiopathic or neuromuscular disease). This type of central sleep apnea is relatively rare and might best be classified by the underlying respiratory system abnormality. The Pickwickian Syndrome belongs to this category. Increased respiratory drive is seen in the majority of individuals with central sleep apnea. These patients may have repetitive or periodic apneas or hypopneas but otherwise have an unusually high respiratory drive resulting in hypocapnea, both during wakefulness and when asleep. Causation may be idiopathic (presumably from some abnormality at the midbrain respiratory center) or secondary to other causes for an increased drive to breathe, including heart failure, hypoxia of high altitude, pain and anxiety.

Patients have been observed in whom frequent arousals from sleep are associated with subtle airflow limitation due to significantly increased airway resistance. When such arousals appear to have the same consequences on sleep architecture or oxygen desaturations, these persons are said to have upper airway resistance syndrome. Esophageal manometry and more quantitative flow measurements than the usual oral-nasal thermistors reveal increasing efforts leading to arousal, but unaccompanied by increasing airflow. These patients almost always also have crescendo snoring proceeding the arousal.[6] Some non-snorers also have the physiologic and clinical manifestations of upper airway resistance syndrome, so the lack of a snoring history does not preclude this diagnosis. The consequences for daytime sleepiness due to upper airway resistance syndrome appear to be approximately the same as for OSA syndrome.

REVIEW OF SLEEP PHYSIOLOGY AND SLEEP TESTING[7]

Virtually all sleep researchers and clinicians utilize a standard manual prepared by a committee chaired by Drs. Rechtshaften and Kales and first published in 1968.[8] All sleep is analyzed in 20 to 30 second epochs, with each epoch being assigned a stage of sleep. The Rechtshaften and Kales system (commonly referred to as the R&K system) subdivides all sleep into REM and non-REM sleep, and then further subdivides non-REM sleep into 4 non-REM stages.

REM sleep is characterized by 3 main features. The first is a low voltage, fast frequency EEG pattern, which in many ways resembles an active, awake EEG pattern. For this reason it is often called paradoxical sleep. The second characteristic is an atonic electromyogram (EMG), consistent with inactivity of voluntary muscles except the extraocular muscles and small muscles of the extremities. When paralysis is incomplete during REM sleep, both humans and other animals appear to be acting out their dreams, which may be dangerous. This disorder is called REM behavior disorder (RBD).[9] The third characteristic is the presence of rapid eye movements. Usually patients will report dreaming if awakened during REM sleep.

Actually, all 3 of these characteristics may not be present simultaneously. REM sleep actually consists of 2 different states, based on the occurrence of rapid eye movements in phasic bursts (phasic REM sleep) interspaced between periods of atonic REM sleep. REM sleep is a predominantly parasympathetic (vagal) state, but during phasic REM sleep there are sudden bursts of sympathetic nervous system activity associated with rapid eye movements. These bursts of sympathetic activity may be associated with sudden increases in arterial blood pressure, cardiac or

cerebral ischemia, cardiac arrhythmias, sudden changes in heart and respiratory rates, and short central apneas and/or hypopneas.[10,11] It has been theorized that cardiovascular and cerebrovascular ischemic events that occur more frequently in the early morning hours may be related to REM sleep (and phasic REM sleep in particular).

Long periods of sinus arrest and asystole lasting up to 9 seconds have been reported in 4 apparently healthy young adults, all occurring during phasic REM sleep. Two of these 4 subjects had infrequent syncope while ambulatory at night, and all 4 had vague chest symptoms during the day. All 4 subjects had electrophysiologic studies done with no evidence of structural heart disease.[12]

The actual function of REM sleep is unknown, although there is speculation that it is important for memory consolidation. The essentialness of REM sleep, however, is suggested by studies where rats totally deprived of REM sleep die after several weeks.[13]

Narcolepsy is thought to be a disorder of REM sleep.

The atonia of REM sleep may exacerbate sleep apnea. REM sleep may be suppressed by alcohol, monoamine oxidase (MAO) inhibitors, tricyclic antidepressants (TCA), stimulants, and some, but not all, hypnotic and sedative medicines. Drugs with predominant anticholinergic effects may also delay or suppress REM sleep.

Non-REM sleep consists of 4 stages of sleep, which are defined primarily by EEG frequency and amplitude. Stage 1 sleep is a transition from wakefulness to sleep, and is characterized by fast EEG frequencies in the theta range (4 to 7 Hz). Subjects awakened from stage 1 sleep typically do not perceive that they were actually asleep. Stage 1 sleep accounts for 2% to 4% of total sleep time in young adults. Increased percentages of stage 1 sleep suggests sleep fragmentation due to a sleep disorder.

Stage 2 sleep is sometimes called intermediate sleep. It typically accounts for 40% to 50% of total sleep time and is characterized by a slowing of EEG frequency and increase in amplitude. There are 2 distinct EEG features of stage 2 sleep. First are sleep spindles that are transient ''spindle''-shaped EEG spikes with a frequency of 12–14 Hz and lasting at least 0.5 seconds, most prominent at the vertex of the scalp. Second are k-complexes, a high amplitude negative wave followed by a negative wave, and usually associated with arousal. Benzodiazepines often increase stage 2 sleep, at the expense of stages 3 and 4 sleep.

Stages 3 and 4 are frequently referred to as deep or slow-wave sleep, accounting for 20% of total sleep time in young adults. These stages are characterized by transition of the EEG to high amplitude delta waves (1.5 to 3 Hz), and are thought to provide ''restorative sleep,'' or restoration of alertness and energy. The arousal threshold is highest in stage 3 and 4 sleep.

Sleep stages occur in cycles lasting 90 to 120 minutes each, with normal individuals having 4 to 5 cycles during a normal night's sleep. During the first half of the night, individuals typically pass from wakefulness into stages 1, 2, 3 and 4, in that order. Stages 3 and then 2 typically reappear, after which REM sleep occurs for the first time. During the second half of the night, stage 2 and REM sleep commonly alternate.

Both the quantity and quality of sleep change with age, with a decline in stages 3 and 4 and an increase in stage 1. This correlates with both increased number of arousals and amount of wakefulness seen in later years.[14]

Polysomnography is a multi-channel recording of sleep and breathing and is the diagnostic test of preference for the diagnosis of OSA and other common causes of sleep disruption, such as periodic limb movements of sleep (PLMS). Polysomnography typically monitors sleep stages, respiratory effort, airflow, oxygen saturation (S_aO_2), an electrocardiogram (ECG), body position, and movements.

Multiple sleep latency testing (MSLT) is a test where individuals are placed in a quiet, darkened room 4 or 5 times in a day and in-

structed to fall asleep as quickly as possible. EEG, eye movements, and muscle tone are measured. The time from wakefulness to sleep onset is termed ''sleep latency.'' A mean sleep latency of 5 minutes or less is indicative of severe daytime sleepiness; a mean sleep latency of 15 minutes or more is considered normal. The abnormal appearance of REM sleep in 2 or more sessions is consistent with a diagnosis of narcolepsy.[15]

A variation of the MSLT, called the maintenance of wakefulness test (MWT), was developed to be a more practical test of whether a person's sleepiness is likely to impair ability to drive or work. Instead of being instructed to fall asleep as quickly as possible (in a darkened and quiet room), subjects are instructed to stay awake.[16]

Another tool in evaluating sleep problems is the commonly used Epworth Sleepiness Scale. It describes situations (passenger in a car, sitting quietly after lunch) and assigns points for likelihood of the subject to become very sleepy or fall asleep in these settings. A score of ≥12 is generally considered abnormal.[17]

Table 1. Symptoms of Obstructive Sleep Apnea (OSA)

- Excessive daytime sleepiness
- Nocturnal snoring
- ''Restless sleep'' (awakenings with gasping or choking)
- Non-refreshing sleep
- Morning dry mouth or sore throat
- Personality change and/or intellectual impairment
- Decreased libido and/or impotence
- Morning headaches and/or confusion.

Table 2. Signs of Obstructive Sleep Apnea (OSA)

- Obesity (present in 60% to 80% of patients)
- Hypertension (present in 50% of patients)
- Loud intermittent snoring (''resuscitative snort'')
- Irregular respirations during sleep
- Large neck (shirt collar size >17½)
- Upper airway abnormalities
  - Nasal polyps or obstruction
  - ''Crowded'' throat—a low-hanging soft palate, large uvula, enlarged tonsils/adenoids, possibly retrognathia or micrognathia

Thin females with high arched hard palate, slim neck, low body mass index have been described in upper airway resistance syndrome, with dramatic responses to nasal continuous airway pressure (CPAP) therapy.

SLEEP PATHOLOGY

Snoring is such a common occurrence that it has not usually been considered pathologic. Sleep apnea is considered pathologic and is defined in most polysomnography laboratories as no air movement for 10 or more seconds and 4% or more oxygen desaturation. Sleep hypopnea is similarly defined as reduced air movement for 10 or more seconds and 2% or more oxygen desaturation. In terms of physiological consequence, apneas and hypopneas are considered co-equals.

An apneic episode is considered ''central'' when there is no measured chest or diaphragmatic effort recorded. ''Obstructive'' apnea is characterized by a crescendo of both chest and diaphragmatic effort until arousal occurs and airflow commences. Upper airway resistance syndrome (UARS) is diagnosed when an arousal occurs without measurable apnea or hypopnea (with the arousal being caused by progressively increasing upper airway resistances).

The significance of sleep apnea/hypopnea without any symptomatic or physiologic consequence is unknown. When sleep apnea/hypopnea occurs with symptoms (usually daytime hypersomnolence), then sleep apnea syndrome is defined. Commonly, patients with sleep apnea syndrome are referred to as having OSA even when actual testing may reveal hypopneas or UARS causing many of the arousals.

In a large cross-sectional population of males in Northern Italy, every night snoring was reported in 17%. More than 10% of these every-night snorers had more than 10 oxygen desaturations per hour, and nearly 5% had greater than 20 oxygen desaturations per hour.[18] The prevalence of sleep apnea in em-

Table 3. Important Parameters Derived From Polysomnographic Studies

- Total sleep time: light sleep (stages 1+2) + deep sleep (stages 3+4) + REM
- Sleep Efficiency: total sleep time/time in bed
- Sleep Architecture: (see text for description of normal sleep architecture)
- Arousal Index: total number of arousals/total sleep time (TST)
- RDI: total number apneas and hypopneas/total sleep time (TST)
- Minimum S_aO_2 desaturation recorded
- Percentage of time $S_aO_2 < 85\%$
- Minimum and maximum heart rates recorded
- Periodic Limb Movement Index
- Significant cardiac arrhythmias occurring during sleep

ployed middle-aged (30 to 60 years old) adults comes from a random sample of 602 subjects studied in the Wisconsin Sleep Cohort Study. Two percent of women and 4% of men met the minimal diagnostic criteria for sleep-apnea syndrome (an apnea/hypopnea score of 5 or more and hypersomnolence). In this study, 24% of men and 9% of women had apnea/hypopnea scores greater than 5 but without hypersomnolence and, therefore, did not fulfill criteria for the syndrome. Obesity and habitual snorers were strongly associated with sleep-disordered breathing. Habitual snorers, both men and women, tended to have a higher prevalence of apnea/hypopnea scores of 15 or higher.[19]

MORBIDITY AND MORTALITY ATTRIBUTED TO SLEEP APNEA

The health consequences of OSA are controversial. A 1997 meta-analysis suggested that there is little evidence to establish an unequivocal cause-and-effect relationship between sleep apnea and cardiovascular disease. These authors suggested the link between sleep apnea and daytime sleepiness and road traffic accidents is stronger but still inconclusive.[20]

That having been said, the overwhelming majority of clinicians and researchers in the field of sleep medicine are convinced that OSA does cause adverse physiologic and pathologic consequences, even if the actual proof is lacking. The best documented cause of increased mortality due to OSA is the relationship of OSA's daytime sleepiness and a 2- to 7-fold increased risk of having a motor vehicular accident. Although the 2 most recognized causes of motor vehicular accidents are speeding and alcohol,[21] the most common medical disorder causing excessive daytime sleepiness is sleep apnea.[22,23] Sleep-related motor vehicular accidents comprise 15% to 20% of all automobile accidents.[24,25] Numerous articles have been written in testament to this association.[26–32]

Although various hemodynamic changes occur in association with sleep apnea (including post-apneic systolic blood pressures as high as 300 mm Hg in patients who may be normotensive by day),[33] a causal relationship between these observations and cardiovascular morbidity and mortality remains unproven. For instance, early clinical series of patients with OSA reported a high prevalence of systemic hypertension. However, many of these early series failed to account for comorbid conditions, most commonly obesity, that may also cause or be associated with elevated blood pressures.

The most compelling evidence that OSA causes elevated blood pressure comes from the Wisconsin Sleep Cohort Study, a prospective population study of apparently healthy state workers. In study subjects with more than 5 apneic/hypopneic events per hour and daytime sleepiness (ie, fulfilling criteria for sleep apnea syndrome), significantly higher blood pressures were found than snoring subjects without sleep apnea syndrome or in non-snorers without apnea. The incidence in blood pressure found in those workers with defined sleep apnea syndrome was present during both wakefulness and sleep, and the effect of OSA on blood pressure during wakefulness was evident even when investigators controlled for weight and gender.[34] This relationship between sleep apnea and hypertension has been confirmed by a number of large population studies.[35–37]

As an example, in the Sleep Heart Health Study, the RDI and percentage of sleep time with oxygen saturation below 90% were each linearly related to both systolic and diastolic blood pressures independent of body mass index (BMI). However, the body habitus measurement did contribute to the linear regression model. For the severest degrees of sleep apnea (RDI >30 or >12% of sleep time with S_aO_2 <90%), the mean odds ratio for hypertension adjusted for BMI, neck circumference, waist-to-hip ratio, alcohol and smoking was 1.37 to 1.45.[38] Despite the evidence provided by these well-conducted studies, other studies have failed to confirm the association between sleep apnea and hypertension. A community-based study in Newcastle, Australia, (441 subjects ages 34 to 69, recruited from random sampling) found the odds ratio for hypertension was 3.8 when individuals with sleep apnea were compared with non-snoring, non-apneic subjects. But after adjusting for age, gender, BMI, current alcohol consumption, and smoking, the odds ratio fell to 1.5 and the confidence limits included 1.0 (ie, no statistically significant increase in risk).[39]

Many clinicians feel that OSA is a frequent cause of difficult-to-control hypertension. Several studies have examined blood pressure readings in OSA patients (both hypertensive and normotensive) before and immediately after initiation of therapy for OSA. Such studies have shown that acute therapy of OSA, either with tracheotomy or nasal continuous positive airway pressure (nasal CPAP), results in a significant decrease in systemic blood pressures.[40,41] In 1 report, for example, long-term therapy with nasal CPAP in 12 patients led to a reduction in the RDI index from 58 to 2 and a fall in mean blood pressure readings from 147/82 to 126/69. These changes occurred without a decrease in body weight.[42]

More recently, Logan et al studied 41 patients (24 men and 17 women) with drug-resistant hypertension.[43] Their mean age was 57 years, and their mean BMI was 34 kg/m^2. Each had blood pressure of 140/90 or higher despite taking 3 or more anti-hypertensive medications (mean, 3.6) at maximally recommended doses. Eighty-three percent of patients had an apnea-hypopnea index >10/hour, with the mean apnea-hypopnea index 32.2 events per hour for men vs. 14 events per hour for women. Other studies have shown a linear relationship between the apnea-hypopnea index and blood pressure, even controlling for BMI, the most important confounding variable.[44–47] Further, CPAP has been shown to reduce blood pressure compared to placebo (in the absence of specific anti-hypertensive treatment) in several well-designed trials.[48–53]

Pulmonary hypertension and right heart failure have also been attributed by some to OSA. Although the nocturnal desaturation seen in many patients with OSA would seem to be an obvious explanation for the pulmonary hypertension and right-sided heart failure, at least 1 report that looked at this hypothesis found that all OSA patients with features of cor pulmonale also had daytime hypoxia.[54] Other researchers feel that mild pulmonary hypertension is not at all uncommon in OSA and that it can cause pulmonary vascular remodeling. One report attempted to isolate the effect of OSA on pulmonary hypertension by selecting only patients without coexisting lung disease or daytime hypoxia. Eleven of 27 subjects (41%) had pulmonary hypertension, but the magnitude of the effect was small (mean pulmonary artery pressure was <26 mm Hg in all patients) suggesting that OSA was not a common cause of significant pulmonary hypertension.[55] Similarly, in the Sleep Heart Health Study, when subjects with markedly elevated RDI (mean = 42 episodes/hour) were compared echocardiographically to those with a low RDI (mean = 5), the only difference noted was a small but statistically significant increase in right ventricular thickness (0.78 cm vs 0.68 cm).[56] Thus, OSA should not be sought as a cause of sustained, severe pulmonary hypertension in the absence of co-morbid conditions producing daytime hypoxia.

Both myocardial infarction and cerebrovascular disease have been felt to occur with in-

creased incidence in OSA. Several epidemiologic studies using snoring as a surrogate marker for OSA suggested a relationship between OSA and cardiovascular disease. For instance, 1 study found that male snorers had an elevated odds ratio for angina pectoris (OR = 2.0, $p < 0.01$), even after adjustment for age, BMI, and the presence of hypertension. Female snorers did not share this increased risk.[57]

Another study reported crude odds ratios of 3.5 for coronary artery disease and 3.7 for occlusive vascular disease. However, after adjusting for age, sex, BMI, smoking and current alcohol consumption, these ratios fell to 1.4 and 1.5, respectively. Confidence intervals for these odds ratios included 1.0 (ie, they were not statistically significant).[39] A third study examined the incidence of OSA in patients hospitalized for acute myocardial infarction, and compared the incidence to a normal population. The highest quartile for RDI had an odds ratio of 23 for myocardial infarction, even after adjustment for coronary artery disease risk factors.[58] This study has been criticized, however, for the potential bi-directional nature of the relationship of myocardial infarction to OSA. Since myocardial infarction, particularly if complicated by heart failure, may contribute to the development of sleep apnea by increasing the tendency for periodic breathing.[59]

The rhythm disturbances associated with OSA include extreme bradycardia and ventricular asystole lasting longer than 10 seconds.[60–63] Therapy with nasal CPAP abolishes all episodes of ventricular asystole and bradyarrhythmias in most patients.[63,64] An intriguing example of the possible bi-directional nature of the relationship between OSA and cardiac arrhythmias was seen in a study of 15 patients with OSA and permanent pacemakers placed previously for symptomatic bradycardia. It was found that atrial overdrive pacing at a rate of 15 beats per minute faster than the patient's nocturnal heart rate resulted in improvements in the RDI (9 vs. 3, $p < 0.001$).[65]

TREATMENT OF SLEEP APNEA SYNDROME

A study undoubtedly familiar to most life insurance medical directors is that of He et al. In this study, the probability of cumulative survival over 8 years in 385 men with OSA was 96% for patients with an RDI <20, compared to only 63% for those with an RDI >20.[66] This difference in mortality related to RDI was particularly true in the patients less than 50 years of age in whom mortality from other causes is not common. This study would also appear to validate the benefit of treating OSA, as there were no deaths in patients treated with tracheotomy or nasal CPAP (but not UPPP) regardless of their RDI.

Another study of male OSA patients (average RDI = 39) who were effectively treated confirmed significant reduction in heath care utilization compared with pretreatment utilization.[67] A related study revealed average yearly medical costs for undiagnosed OSA patients (mean RDI = 37) were approximately double those of age- and sex-matched controls without OSA. These costs appear to be linearly related to the severity of OSA.[68] Such findings have led some clinical and research experts in the field of sleep to recommend treatment for all patients with an RDI >20.[69]

Weight loss can be demonstrated to result in clinical improvement in persons with OSA. In one study of 15 hypersomnolent patients with moderately severe OSA, weight loss from a mean of 106.2 to 96.9 kg was associated with a mean fall in RDI from 55 to 29, as well as a decrease in oxygen desaturation and an improvement in daytime hypersomnolence.[70] Another study was done in 15 morbidly obese patients with OSA who underwent gastric bypass surgery, who lost from 27 to 100 kg of weight, and who were then followed for 1 to 12 years. A reduction in average RDI was seen (from 96 to 11), as well as improved oxygenation (from pre-operative mean minimal saturation of 59% to mean minimal saturation of 85%). Eight of the 15 patients had tracheotomies, and all 8 tolerat-

ed decannulation and closure of the tracheal stoma.[71]

Unfortunately, achieving weight loss in OSA patients is difficult, especially so if they are untreated or less than ideally compliant with therapy (usually nasal CPAP). Furthermore, apnea may recur in spite of maintained weight loss.[72–74]

Nasal CPAP, which prevents apnea by maintaining adequate upper airway patency, is currently the treatment of choice for OSA.[75,76] Unfortunately, approximately 20% to 40% of patients will not use CPAP at all, and of those who do use it, many may not be strictly compliant.[77–81] Kribbs et al gave patients CPAP machines with a microprocessor that monitored actual pressure at the mask for every minute of each 24-hour day for an average of 106 days per patient.[82] The patients were unaware of the presence of the microprocessor monitor. Patients attempted to use CPAP 66% of the time, and the mean duration of use was 4.88 hours. Although the majority (60%) of patients claimed to use the CPAP every night, only 46% met criteria for regular use (defined as use of CPAP for at least 4 hours/night on 70% of the days monitored). The 1 bright spot of this study relevant to the life insurance industry is that both frequency and duration of CPAP use in the first month reliably predicted use in the third month ($p = 0.0001$).

A similar study, also done with a covert monitor built into the CPAP machine, revealed roughly similar results. The RDI of this study group was 58, their mean BMI was 42, and all complained of daytime sleepiness. Almost 20% of the study group discontinued therapy within 3 months or less. The actual mean nightly hours of use was 4.7, representing 68% of the stated total sleep time. The RDI did not correlate with compliance, and subjective initial complaints of daytime sleepiness correlated with compliance only during the first visit ($p = 0.05$). No predictors for compliance were found.[83]

More encouraging is a Canadian study of 296 patients with apnea-hypopnea indexes of 20 or greater. Eighty-one percent of this group were men, the mean age was 41, and the mean BMI was 35 kg/m^2. Compliance data was obtained from a monitoring chip in the CPAP machine. The patients received daily telephone contact for the first week, and follow-up visits at 2 and 4 weeks and 3 and 6 months. The CPAP usage averaged 6 hours/day, and 86% of subjects used their device at least 4.5 hours/day. The Epworth Sleepiness Scale decreased by 44% within the first 2 weeks and continued to fall over the subsequent visits to 6 months. On multivariate analysis, women used CPAP more frequently, as did older patients and those with lower Epworth Sleepiness Scale scores.[84]

Surgical therapy for OSA has included fairly drastic measures, such as mandibular reconstructions and geniohyoid advancement, but most commonly consisted of uvulopalatopharyngoplasty (UPPP), a procedure much favored by otolaryngologists over the last decade. However, the outcomes for this latter procedure have been less than successful and are difficult to predict.[85] A less invasive modification of UPPP has been radiofrequency tissue ablation (RFA) of the proximal tongue base, uvula or soft palate. Evidence suggests that these procedures provide only marginal benefit at best,[86,87] and may cause serious complications at worst.[88,89] Another modification of UPPP is laser-assisted uvulopalatoplasty (LAUP). Finkelstein et al found in their series of patients that follow-up polysomnography showed an objective success rate of 31%, but another 31% of patients had deterioration in their respiratory disturbance index.[90] Pharyngeal dryness was a common adverse effect, occurring in 54% of patients. Their conclusions were that ''LAUP offers good subjective results at short-term follow-up, yet much of the improvement is lost after 1 year.'' Objective assessments suggest that the original apnea may grow worse after the procedure, most likely, because of velopharyngeal narrowing and laser-induced palatal fibrosis.

There are an increasing number of devices that are worn orally at night and that attempt to either hold the mandible forward, or hold

the tongue forward, or both, to prevent nocturnal obstruction at the posterior pharyngeal wall.[91–93] In 1 crossover study comparing such a device to nasal CPAP, the nasal CPAP treatment attained much lower RDIs (reducing RDI to a mean of 2.2) than did the oral device (reducing RDI to a mean of 13.6). Treatment success was defined as reduction of RDI to ≤10 and relief of symptoms. By these criteria, CPAP yielded a 70% success rate compared to 55% with the oral device. However, there was greater patient satisfaction with the oral device than the CPAP ($p = 0.01$), but there were no reported differences in side effects or compliance.[94]

Both static and dynamic airway imaging using both rapid spiral CT and MRI has revealed a possible explanation for the failure of surgery and oral appliances to work better than they do. The relevant anatomy includes the retropalatal region, defined as being from the level of the hard palate to the distal margin of the soft palate, and the retroglossal region from the distal margin of the soft palate to the base of the epiglottis.[95] Upper airway caliber is significantly less in patients with sleep apnea compared with normal subjects. In both patients with OSA and without, airway narrowing is greatest in the retropalatal region. The upper airway in patients with OSA has its major axis oriented in an anterior-posterior dimension (lateral narrowing). Whereas in those without OSA, the major axis is oriented in a horizontal dimension.[96,97]

Lateral narrowing of the upper airway in OSA is explained by larger lateral pharyngeal walls. The lateral pharyngeal walls, and not the soft palate, tongue, or parapharyngeal fat pads, appear to be the important anatomic factor causing airway narrowing in OSA. This is despite the fact that the total volume of parapharyngeal fat is greater in patients with OSA, and despite OSA patients having larger soft palate and tongues than normal.[98]

Airway dimensional changes are greater in the lateral than in the anterior-posterior direction during respiration. This emphasizes the importance of the lateral pharyngeal walls in mediating upper airway changes, especially at the end of expiration, where airway caliber decreases significantly.[98]

The airway is narrowest in the retropalatal region during both wakefulness and sleep. The minimum airway area decreases by approximately 30% during sleep in both patients with OSA and without. The lateral pharyngeal walls thicken during sleep as the airway decreases in size, again suggesting that the lateral pharyngeal walls may be important in the causation of sleep apnea.[98] Airway cross-sectional area and volume increase significantly with CPAP, with the increase in airway area occurring in both the retropalatal and retroglossal regions. Airway dimensional changes in CPAP are greater in the lateral than in the anterior-posterior dimensions. In fact, CPAP predominantly affects structures lateral to the airway (ie, the lateral pharyngeal wall and parapharyngeal fat pads) rather than the tongue and soft palate. There is an inverse relationship between pharyngeal wall thickness and the level of CPAP.[99,100]

Thus, surgery aimed at ''tightening'' the soft palate and removing the uvula (UPPP), or scarring the soft palate (RFA) would not seem to be attacking the site of obstruction (the lateral pharyngeal walls), at least as evidenced by radiographic studies.[101]

SLEEP APNEA IN THE ELDERLY

Sleep problems are so common in the elderly that it may be difficult to separate a disease process like OSA from those symptoms associated with normal aging.[102] In general, the elderly complain more of difficulty maintaining sleep than in initiating sleep. This is because their sleep latency is generally normal, but their sleep efficiency (ratio of time asleep to time in bed) falls with age, due to increasing tendency to nocturnal awakenings, some of which may be prolonged.

The elderly are also prey to the many disease processes that interrupt sleep. In males, worsening urinary outlet obstruction due to prostatism requires increasingly frequent awakenings throughout the night to urinate. Other conditions causing pain (osteoarthritis,

neuropathies) will also seriously interrupt normal sleep. Finally, many of the elderly, once freed from the schedules of employment and child-rearing, practice poor sleep habits that include daytime naps and possibly increased evening alcohol consumption.

At least 1 study suggests that parameters reflecting severity of sleep apnea are not different in the elderly compared with younger apnea patients.[103] There is general agreement that the occurrence of sleep apnea increases with age. In 1 study of healthy, non-obese elderly subjects, sleep apnea was found in 2.9% at age 60, 33% at age 70, and 40% at age 80. Significant oxygen desaturations (below 85%) were seen in 37% of these normal 80-year-olds.[104]

There is also evidence that sleep apnea in the elderly does affect mortality. In 1 study of 196 patients with mean age 66, mortality was increased by a factor of 2.7 in those subjects with an RDI >10.[105]

CONCLUSIONS ABOUT UNDERWRITING SLEEP APNEA

Although the medical (and life insurance) community is awaiting the results of a large NIH-sponsored multi-institutional prospective study that will hopefully quantify the morbidity and mortality risk of OSA apart from its co-morbid conditions, some reasonable estimates at risk may be made from available data.

Certainly, underwriters should underwrite the co-morbid conditions (obesity, hypertension, cardiovascular and cerebrovascular disease) as is usually done. An assessment of additional risk attributable specifically to OSA requires the underwriter to examine the polysomnographic results (RDI, minimum S_aO_2 desaturation, minimum and maximum heart rates, severity of disruption of normal sleep architecture) and not simply accept a medical interpreter's assessment as to the severity of abnormality present. Integral to this risk assessment is also the presence and severity of the consequences of OSA, chiefly the severity of disability due to daytime hypersomnolence, as well as the other co-morbidities (control of hypertension, weight gain or loss).

It is this author's opinion that adequately treated OSA may carry little if any mortality risk. Unfortunately, it is the rare exception, rather than the rule, to find evidence in the medical record of polysomnographic correction of the defect, or verification that the applicant is being compliant with the prescribed treatment. Such information must necessarily come more from inference (decreases in weight and/or blood pressure, stated improvements in quality of sleep or decrease in daytime sleepiness) than from direct evidence.

Comparing 2 applicants with a history suggesting hypersomnolence, does the first applicant with an RDI of 40 but no obesity, no hypertension, and no S_aO_2-desaturation have a worse mortality than the second with an RDI of only 10 but who is hypertensive, has a BMI of 40 kg/m^2, and desaturates to 80%?

For the present, there is probably considerable art as well as science in correctly assessing mortality risk from sleep apnea.

REFERENCES

1. Miller A, Granda M. In-hospital mortality in the Pickwickian Syndrome. *Am J Med.* 1974;56:144.
2. Gastaut H, Tessarini CA, Duron B. Polygraphic study of the episodic diurnal and nocturnal (hypnic and respiratory) manifestations of the Pickwick Syndrome. *Brain Res.* 1965;2:167.
3. Westbrook PR. An overview of sleep apnea: Definitions. *UpToDate.* (Pulmonology and Critical Care, Sleep disorders) 2002;10(2). Available at: uptodate.com.
4. Mezzanotte WS, Tangel DJ, White DP. Waking genioglossal EMG in sleep apnea patients versus normal controls (a neuromuscular compensatory mechanism). *J Clin Invest.* 1992;89:1571.
5. Westbrook PR. An overview of obstructive sleep apnea: Epidemiology, pathophysiology, clinical presentation, and treatment. *UpToDate.* (Pulmonology and Critical Care, Sleep disorders) 2002; 10(2). Available at: uptodate.com.
6. Shepard J, Kaplan J, Parish J, et al. Snoring and sleep disordered breathing. In: Shepard JW, ed. *Atlas of Sleep Medicine.* Mt Kisco, Futura; 1991:81.
7. Pressman MR. Stages and architecture of normal

sleep. *UpToDate.* (Pulmonology and Critical Care, Sleep disorders) 2002, 10(2). Available at: uptodate.com.
8. Rechtshaften A, Kales A, eds. A manual of standardized terminology and scoring system for sleep stages of human subjects. NIH Publication. Washington, DC: US Government Printing Office; No. 204, l968.
9. Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: A new category of parasomnia. *Sleep.* 1986;9:293.
10. Somers VK, Dyken ME, Mark AC, Abboud FM. Sympathetic nerve activity during sleep in normal subjects. *N Engl J Med.* 1993;328:328.
11. Hornyak M, Cejnar M, Elam M, et al. Sympathetic nerve activity during sleep in man. *Brain.* 1991;114:1281.
12. Guillimenault C, Pool P, Motta J, Gillis AM. Sinus arrest during REM sleep in young adults. *N Engl J Med.* 1984;311:1006.
13. Rechtshaften A, Bergman BM, Everson CA, et al. Sleep deprivation in the rat. X integration and discussion of the findings. *Sleep.* 1989;12:68.
14. Hirshkowitz M, Moore CA, Hamilton CR, et al. Polysomnography of adults and elderly: Sleep architecture, respirations and leg movements. *J Clin Neurophysiol.* 1992;9:56.
15. Carskadon MA, Dement WC, Mitler MW, et al. Guidelines for the multiple sleep latency test (MSLT): A standard measure of sleepiness. *Sleep.* 1986;9:519.
16. Mitler NM, Gujavarty KS, Brownman CP. Maintenance of wakefulness test: A polysomnographic technique for evaluating treatment efficacy in patients with excessive somnolence. *Electroenceph Clin Neurophysiol.* 1982:53:658.
17. Johns MW. A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. *Sleep.* 1991;14:40.
18. Ferini-Strambi L, Zucconi M, Polazzi S, et al. Snoring and nocturnal oxygen desaturations in an Italian middle-aged population. Epidemiologic study with an ambulatory device. *Chest.* 1994: 105:1759.
19. Young T, Palta M, Dempsy J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med.* 1993:328:1230.
20. Wright J, Johns R, Watl I, et al. Health effects of obstructive sleep apnoea and the effectiveness of continuous positive pressure: A systematic review of the research evidence. *BMJ.* 1997:314:851.
21. Moldoff WM. Annotation, physician's duty to inform patient of nature and hazards of disease or treatment. 79 A.L.R.2d 1028, 1961 (Supp. 1990).
22. Arbus L, Tiberge M, Serres A, Rouge D. Drowsiness and traffic accidents: Importance of diagnosis. *Neurophysiologie Clinique.* 1991;21:39.
23. National Commission on Sleep Disorders Research report. Vol 1. Executive summary and executive report. Bethesda, MD: National Institutes of Health; 1993.
24. Horne J, Reyner L. Sleep-related vehicle accidents. *BMJ.* 1995;310:565.
25. Massa JF, Rubio M, Findley LJ. Habitually sleepy drivers have a high frequency of automobile crashed associated with respiratory disorders during sleep. *Am J Respir Crit Care Med.* 2000;162: 1407.
26. Findley L, Unverzadt M, Surrat P. Automobile accidents in patients with obstructive sleep apnea. *Am Rev Respir Dis.* 1988;138:337.
27. George C, Nickerson P, Hanly P, et al. Sleep apnoea patients have more automobile accidents. *Lancet.* 1987;2:447.
28. Alpert M, Ancoli-Israel S, Kripke D, et al. Sleep-disordered breathing and car accidents in the elderly. *Sleep Research.* 1992;21:167.
29. Stoohs R, Guilleminault C, Itoi A, Dement W. Traffic accidents in commercial long-haul drivers: The influence of sleep-disordered breathing and obesity. *Sleep.* 1994;17:619.
30. Findley L, Weiss J, Jabour ER. Serious automobile crashes caused by undetected sleep apnea. *Arch Intern Med.* 1991;151:1451.
31. Noda A, Yagi T, Yokota M, et al. Daytime sleepiness and automobile accidents in patients with obstructive sleep apnea syndrome. *Psychiatry Clin Neurosci.* 1998;52:221.
32. Horstmann S, Hess CW, Bassetti C, et al. Sleepiness-related accidents in sleep apnea patients. *Sleep.* 2000;23:383.
33. Podszus T, Mayer J, Penzel T, et al. Nocturnal hemodynamics in patients with sleep apnea. *Eur J Resp Disease Suppl.* 1986;146:435.
34. Hla KM, Young TB, Birdwell T, et al. Sleep apnea and hypertension: a population based study. *Ann Intern Med.* 1994;120:382.
35. Lauie P, Herer P, Hoffstein V. Obstructive sleep apnea syndrome as a risk factor for hypertension: Population study. *BMJ.* 2000;320:479.
36. Young TB, Poppard P, Palta M, et al. Population-based study of sleep-disordered breathing as a risk factor for hypertension. *Arch Intern Med.* 1997;157:1746.
37. Grote L, Ploch T, Heitmann J. Sleep-disordered breathing is an independent risk factor for systemic hypertension. *Am J Respir Crit Care Med.* 1999;160:1875.
38. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. *JAMA.* 2000;283:1829.

39. Olson LG, King MT, Hensley MJ, Saunders NA. A community study of snoring and sleep-disordered breathing: Health outcomes. *Am J Respir Crit Care Med.* 1995;152:717.
40. Guilleminault HC, Simmons FB, Motta J, et al. Obstructive sleep apnea syndrome and tracheostomy: Long term follow-up experience. *Arch Intern Med.* 1981;141:985.
41. Pepprell JC, Ramdassingh-Dow S, Crosthwaite N, et al. Ambulatory blood pressure after therapeutic and subtheraputic continuous positive airway pressure for obstructive sleep apnea: A randomized parallel trial. *Lancet.* 2002;359:204.
42. Mayer J, Becker H, Brandenburg U, Penrel T, Peter JH, vonWichert P. Blood pressure and sleep apnea: results of long term continuous positive airway pressure therapy. *Cardiology.* 1991;79:84.
43. Logan Ag, Perlikowski SM, Mente A, et al. High Prevalence of Unrecognized Sleep Apneoea in Drug-Resistant Hypertension. *J Hypertens.* 2001; 19:2271–2277.
44. Lavie P, Herer P, Hoffstein V. Obstructive sleep apnea syndrome as a risk factor for hypertension: Population study. *BMJ.* 2000;320:479–482.
45. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *JAMA.* 2000;283:1829–1836.
46. Grote L, Ploch T, Heitmann J, et al. Sleep-related breathing disorder is an independent risk factor for systemic hypertension. *Am J Respir Crit Care Med.* 1999;160:1875–1882.
47. Peppard PE, Young T, Palta M, et al. Prospective study of the association between sleep-disordered breathing and hypertension. *J Engl J Med.* 2000; 342:1378–1384.
48. Dimsdale JE, Loredo JS, Profant J. Effect of continuous positive airway pressure on blood pressure: A placebo trial. *Hypertension.* 2000;35:144–147.
49. Akashiba T, Minemure H, Yamamoto H, et al. Nasal continuous positive airway pressure changes blood pressure ''non-dippers'' to ''dippers'' in patients with obstructive sleep apnea. *Sleep.* 1999; 22:849–853.
50. Faccenda JF, Mackay TW, Boon N, et al. Randomized placebo-controlled trial of continuous positive airway pressure on blood pressure in the sleep-apnea-hypopnea syndrome. *Am J Respir Crit Care Med.* 2001;163:344–348.
51. Jenkinson C, Davies RJ, Mullins R, et al. Comparison of therapeutic and sub-therapeutic nasal continuous positive airway pressure for obstructive sleep apnea: A randomized prospective parallel trial. *Lancet.* 1999;353:2100–2105.
52. Suzuki M, Otsuka K, Guilleminault C. Long-term nasal continuous positive airway pressure can normalize hypertension in obstructive sleep apnea patients. *Sleep.* 1993;16:545–549.
53. Pepperell JCT, Ramdassingh-Dow S, Crosthwaite N, et al. Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: A randomized parallel trial. *Lancet.* 359: 204–214.
54. Bradley TD, Rutherford R, Grossman RF, et al. Role of daytime hypoxemia in the pathogenesis of right heart failure in the obstructive sleep apnea syndrome. *Am Rev Respir Dis.* 1985;131:835.
55. Sajkov D, Cowie RJ, Thornton AT, Espinoza HA, McEroy RD. Pulmonary hypertension and hypoxemia in obstructive sleep apnea syndrome. *Am J Respir Crit Care Med.* 1994:149:416.
56. Guidry UC, Mendes LA, Evans JC, et al. Echocardiographic features of the right heart in sleep-disordered breathing: the Framingham Heart Study. *Am J Respir Crit Care Med.* 2001;164:933.
57. Koskenvuo M, Kaprio J, Partinen M, Langinvainio H, Sarna S, Heikkila K. Snoring as a risk factor for hypertension and angina pectoris. *Lancet.* 1985;1:893.
58. Hung J, Whitford EG, Parsons RW, Hillman DR. Association of sleep apnea with myocardial infarction in men. *Lancet.* 1990;336:261.
59. Weiss JW. Cardiovascular and cerebrovascular effects of sleep apnea. *UpToDate.* (Pulmonology and Critical Care, Sleep disorders) 2002;10(2). Available at: uptodate.com.
60. Tilkian AG, Guilleminault C, Schroeder JS, Lehrman KL, Simmons FB, Dement WC. Sleep-induced apnea syndrome. Prevalence of cardiac arrhythmias and their reversal after tracheostomy. *Am J Med.* 1977;63:348.
61. Miller WP. Cardiac arrhythmias and conduction disturbances in the sleep apnea syndrome. Prevalence and significance. *Am J Med.* 1982;73:317.
62. Zwillich C, Devlis T, White D, Douglas N. Bradycardia during sleep apnea. Characteristics and mechanisms. *J Clin Invest.* 1982;69:1286.
63. Grimm W, Hoffman J, Menz V, et al. Electrophysiologic evaluation of sinus node function and atrioventricular conduction in patients with prolonged ventricular asystole during obstructive sleep apnea. *Am J Cardiol.* 1996;77:1301.
64. Becker H, Brandenburg V, Conradt R, et al. Influence of NCPAP therapy on bradycardiac arrhythmias in sleep apnea. *Pneumologie.* 1993;47 (Suppl 4):706.
65. Garrigue S, Bordier P, Jais P, et al. Benefit of atrial pacing in sleep apnea syndrome. *N Engl J Med.* 2002;346:404.
66. He J, Kryger MH, Zorick FJ, Conway W, Roth T. Mortality and apnea index in obstructive sleep

apnea. Experience in 385 male patients. *Chest.* 1988;94:9.
67. Bahamman A, Delaive K, Ronald J, Manfreda J, Roos L, Kryger MH. Health care utilization in males with obstructive sleep apnea syndrome two years after diagnosis and treatment. *Sleep.* 1999;22:740.
68. Kapur V, Blough DK, Sandbloom RE, et al. The medical costs of undiagnosed sleep apnea. *Sleep.* 1999;22:749.
69. Kryger MH. Overview of the management of sleep apnea. *UpToDate.* (Pulmonology and Critical Care, Sleep disorders). 2002;10(2). Available at: uptodate.com.
70. Smith PL, Gold AR, Meyers DA, Haponik EF, Bleeker ER. Weight loss in mildly to moderately obese patients with obstructive sleep apnea. *Ann Intern Med.* 1985;103:850.
71. Scheuller M, Weider D. Bariatric surgery for treatment of sleep apnea syndrome in 15 morbidly obese patients: long term results. *Otolaryngol Head Neck Surg.* 2001;125:299.
72. Pillar G, Peled R, Lavie P. Recurrence of sleep apnea without concomitant weight increases 7.5 years after weight reduction surgery. *Chest.* 1994; 106:1702.
73. Bray GA. Barriers to the treatment of obesity. *Ann Intern Med.* 1991;115:152.
74. Kajaste S, Telakiui T, Pihl S, Partinen M. Effects of a weight reduction program on sleep apnea: a two year follow-up. *Sleep Res.* 1991;20A:332.
75. Kryger MH. Management of obstructive sleep apnea-hypopnea syndrome: Overview. In: Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine.* 3rd ed. Philadelphia, Pa: Saunders; 2000:940–954.
76. Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes. American Thoracic Society. Official statement adopted March 1994. *Am J Respir Crit Care Med.* 1994;150:1738.
77. Waldhorn RE, Herrick TW, Nguyen MC, O'Donnel AE, Sodero J, Potolicchio SJ. Long-term compliance with nasal continuous positive airway pressure therapy of obstructive sleep apnea. *Chest.* 1990;97:33.
78. Rolfe I, Olson LG, Saunders NA. Long-term acceptance of continuous positive airway pressure in obstructive sleep apnea. *Am Rev Respir Dis.* 1991;144:1130.
79. Hoffstein V, Viner S, Mateika S, Conway J. Treatment of obstructive sleep apnea with nasal CPAP. Patients compliance, perception of benefit, and side effects. *Am Rev Respir Dis.* 1992;145:841.
80. Kreiger J, Kurtz D. Objective measurement of compliance with nasal CPAP treatment for obstructive sleep apnoea syndrome. *Eur Resp J.* 1988; 1:436.
81. Meuria JC, Dore P, Paquereau J, et al. Predictive factors of long-term compliance with nasal continuous positive pressure treatment in sleep apnea syndrome. *Chest.* 1994;105:429.
82. Kribbs NB, Pack AI, Kline LR, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. *Am Rev Respir Dis.* 1993;147:887.
83. Reeves-Hoche MK, Meck R, Zwillich CW. Nasal CPAP: An objective evaluation of patient compliance. *Am Rev Respir Crit Care Med.* 1994;149:149–154.
84. Sin DD, Mayers I, Man GCW, et al. Long-term compliance rates to continuous positive airway pressure in obstructive sleep apnea: A population-based study. *Chest.* 2002;121:430–435.
85. Keenan SP, Burt H, Ryan CF, Fleetham JA. Long-term survival of patients with obstructive sleep apnea treated by uvuloplatopharyngoplasty or nasal CPAP. *Chest.* 1994;105:155.
86. Brown DJ, Kerr P, Kryger MH. Radiofrequency tissue reduction of the palate in patients with moderate sleep-disordered breathing. *J Otolaryngol.* 2001;30:193.
87. Woodson BT, Nelson L, Mickelson S, Huntley T. A multi-institutional study of radiofrequency volumetric reduction in OSAS. *Otolaryngol Head Neck Surg.* 2001;125:303.
88. Pazos G, Mair EA. Complications of radiofrequency ablation in the treatment of sleep-disordered ablation in the treatment of sleep-disordered breathing. *Otolaryngol Head Neck Surg.* 2001;125:462.
89. Terris DJ, Chen V. Occult mucosal injuries with radiofrequency ablation of the palate. *Otolaryngol Head Neck Surg.* 2001;125:468.
90. Finkelstein Y, Stein G, Ophir D, et al. Laser-assisted uvulopalatoplasty for the management of obstructive sleep apnea: myths and facts. *Arch Otolaryngol Head Neck Surg.* 2002;128:429–434.
91. Eveloff SE, Rosenberg CL, Carlisle CC, Millman RP. Efficacy of a herbst mandibular advancement device in obstructive sleep apnea. *Am J Respir Crit Care Med.* 1994;149:905.
92. O'Sullivan RA, Hillman DR, Mateljan R, Pantin C, Finucane KE. Mandibular advancement splint: an appliance to treat snoring and obstructive sleep apnea. *Am J Respir Crit Care Med.* 1995;151: 194.
93. Lowe AA. Dental appliance for the treatment of snoring and obstructive sleep apnea. In: Kyrger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine.* Philadelphia, Pa: Saunders; 1994:722.
94. Furguson KA, Ono T, Lowe AA, al-Majed S, Love

LL, Fleetham JA. A short-term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnea. *Thorax.* 1997;52:362.
95. Hudgel DW. The role of upper airway anatomy and physiology in obstructive sleep apnea. *Clin Chest Med.* 1992;13:383.
96. Schwab RJ, Gefter WB, Hoffman EA, et al. Dynamic upper airway imaging during respiration in normal subjects and patients with sleep disordered breathing. *Am Rev Respir Dis.* 1993;148: 1385.
97. Schwab RJ, Gefter WB, Pack AI, Hoffman EA. Dynamic imaging of the upper airway during respiration in normal subjects. *J Appl Physiol.* 1993; 74:1504.
98. Schwab RJ, Gupta KB, Gefter WB, et al. Upper airway soft tissue anatomy in normals and patients with sleep disordered breathing. Significance of the lateral pharyngeal walls. *Am J Respir Crit Care Med.* 1995;152:1673.
99. Ryan CF, Lowe AA, Li D, Fleetham JA. Magnetic resonance imaging of the upper airway in obstructive sleep apnea before and after chronic nasal continuous positive airway pressure. *Am Rev Respir Dis.* 1991;144:939.
100. Schwab RJ, Pack AI, Gupta KB, et al. Upper airway soft tissue structural changes induced by CPAP in normal subjects. *Am J Respir Crit Care Med.* 1996;154:106.
101. Schwab RJ. Radiographic imaging in the diagnostic evaluation of sleep apnea. *UpToDate.* (Pulmonology and Critical Care, Sleep disorders) 2002;10(2). Available at: uptodate.com.
102. Feinsilver S, Hertz G. Sleep in the elderly patient. *Clin Chest Med.* 1993;14:405.
103. Levy P, Pepin JL, Malauzat D, Emerian JP, Leger JM. Is sleep apnea syndrome in the elderly a specific entity? *Sleep.* 1996;19(3 Suppl):S29–S38.
104. Hach C, Reynolds CF III, Monk TH, et al. Comparison of sleep-disordered breathing among health elderly in the seventh, eighth, and ninth decades of life. *Sleep.* 1990;13:502.
105. Bliwise DL, Bliwise NG, Partinen M, Pursley AM, Dement WC. Sleep apnea and mortality in an aged cohort. *Am J Public Health.* 1998;78:5.