Paparella: Volume I: Basic Sciences and Related Principles

Section 9: Otolaryngologic Manifestations of Systemic Diseases and Pain

Chapter 44: Sleep Disorders

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Otolaryngologists and sleep disorders scientists are becoming increasingly aware that each of their disciplines is making a significant contribution to the other, most specifically in the diagnosis and treatment of sleep apnea. This chapter attempts to provide the otolaryngologists with a brief history of sleep disorder medicine, an outline of the research and diagnostic procedures used in sleep disorder clinics, a discussion of some findings with regard to normal sleep stages and patterns, the physiology of sleep, and the neurologic basis of sleep (especially as they relate to the work of otolaryngologists), and a discussion of specific symptoms of and treatments for sleep apnea.

The History of Sleep Disorder Medicine

Although the contributions of scientists and clinicians over the last 30 years have increased out understanding of sleep physiology and pathology, it has been the recognition that sleep apnea is a life-threatening condition affecting a large number of people that has stimulated the proliferation of sleep disorder centers around the country. The expanded research activities associated with these centers have accelerated the development of new surgical, behavioral, and pharmacologic treatments for a wide range of sleep-related disorders. One result of the increased research and consequent successful treatment is that sleep disorder medicine has become a discipline of its own, with an accrediting body (Association of Sleep Disorders Centers) and a national board examination.

The variety of clinicians with a special interest in sleep during the early days of sleep research - psychiatrists, psychologists, and physiologists - has increased to include pulmonologists, otolaryngologists, cardiologists, and neurologists. All have contributed to our knowledge of narcolepsy, insomnia, enuresis, sleep apnea and other sleep disorders, the biochemistry and pharmacology of sleep and, most recently, the relationship between chronobiology and sleep.

The discovery of sleep apnea, then, has caused an increase in research activity, which has expanded the possibility for treating other types of sleep disorders. Another factor that has contributed to the expansion of the field of sleep disorder medicine was the discovery that, at any one time, one-third of the population suffers from sleep-related complaints, such as classic insomnia, enuresis, periodic leg movements, nightmares, narcolepsy, and sleep apnea. Nevertheless, despite our own experience that getting a good night's sleep makes a difference in the level of functioning the next day and, despite the expanding body of knowledge regarding

sleep, we still continue to take sleep for granted both in our daily lives and, until recently, in the practice of medicine.

Sleep Disorders and Otolaryngology

Otolaryngologists are becoming increasingly involved in sleep disorder medicine as major consultants to sleep disorder centers and, less frequently, as clinicians involved in directing the evaluation and treatment of patients with sleep disorders. More specifically, otolaryngologists have made major contributions in the area of sleep apnea management, because it is sleep apnea that brings the otolaryngologist and sleep disorder scientists more closely together.

As a result, surgical treatments for obstructive sleep apnea have increased in complexity, from the original tracheostomy to uvulopalatopharyngoplasty (UPPP), mandibular advancement, and tongue reduction. Otolaryngologists and sleep disorder specialists have, in addition, become increasingly involved in identifying diagnostic procedures that can lead to the appropriate treatment for sleep apnea.

The otolaryngologists can also be involved in the treatment of snoring and apnea in stroke patients, because obstructive sleep apnea triples the risk of stroke. Finally, the cooperation of the otolaryngologist and the sleep disorder specialist in maintaining a patient's nasal and oral airway may ultimately be understood as critical to ensuring the full restorative contribution of sleep.

Characteristics of Normal Sleep

Polysomnographic Analysis and Sleep Monitoring

Sleep disorders centers follow a relatively standard procedure for all-night polysomnographic analysis. The use of the polysomnogram allows for a distinction of specific sleep stages. Subjects have electrodes pasted and taped to various parts of their scalp, abdomen and, sometimes, legs to determine sleep stages, respiratory activity, electrocardiac activity, heart rate, and muscle tone.

Because electroencephalogram (EEG) patterns can vary according to electrode placement and derivation, a standard array has been developed using the International 10-20 system of electrode placement. To determine sleep stages at least eight electrodes are used. Two central scalp electrodes (C-3 and C-4) record the EEG; two electrodes, placed above and below the outer canthi, record eye movements; electrodes placed below the chin on the submental muscles record the electromyogram (EMG). In addition, there are generally two reference electrodes on the earlobes or mastoid processes.

For the assessment of respiration, sensors are attached to determine air flow and respiratory effort. The flow of air can be measured by CO_2 sensors, thermistors, or thermocouples. Respiratory effort can be determined by a bellows-type respiratory transducer or by EMG monitoring of intercostal muscle activity.

Occasionally it is necessary to obtain a patient's complete clinical EEG during sleep when screening for nocturnal seizure activity. Standard placements are made for recording the electrocardiogram (ECG). To determine the possibility of nocturnal myoclonus, surface electrodes are placed over the anterior tibialis muscles of the legs.

All-night polysomnography requires that technicians be present to monitor the subjects throughout the night. Computerized scoring systems have been developed to analyze the recordings. They have a scoring accuracy and reliability closely approaching traditional hand-scoring reliability and a consistency, scope, and speed that are superior to those of manual analysis. The polysomnographic recordings are interpreted according to standardized, internationally accepted criteria defining specific sleep stages.

In addition to the regular, all-night evaluation of sleep patterns, it is sometimes important to conduct daytime nap studies. Patients' daytime sleep activity is monitored using a multiple sleep latency test, which consists of five opportunities for short naps every 2 hours. This test evaluates levels of daytime sleepiness and provides an objective, quantifiable means of assessing the impact of disrupted sleep on daytime alertness. The multiple sleep latency test also allows for the assessment of the specific abnormalities in sleep architecture that are characteristic of narcolepsy.

Normal Sleep Stages and Patterns

The research in sleep disorder centers has produced voluminous documentation of normal and abnormal sleep patterns and their corollary physiologic activity.

Stages of Sleep

REM and NREM Sleep

Once the polysomnograph has been generated, the initial analysis is made of the distinction between rapid eye movement (REM) and nonrapid eye movement (NREM) sleep. This distinction was first made by Aserinsky and Kleitman, who observed that bursts of rapid eye movements appear periodically during sleep. Other corollary physiologic activities defined clearly by polysomnography have led to the clinical distinction between REM and NREM sleep.

REM sleep alternates with NREM sleep at intervals ranging from approximately 50 minutes in full-term infants to 70 to 90 minutes in adults. REM sleep generally occupies approximately 20 per cent of the sleep period, with the remaining 80 per cent consisting of wakefulness and NREM sleep.

On the basis of predominant EEG frequencies and the appearance of specific brain wave patterns, NREM sleep has been somewhat arbitrarily divided into stages I through IV. Stage I involves theta waves and has mainly 3- to 7-cycles/second (cps) activity. Stage II has 12- to 14-cps sleep spindles and involves K complexes. Stages III and IV, commonly known as delta sleep,

involve delta waves; 0.5- to 2-cps brain activity, and 75-microV amplitude activity. When a 30-second epoch of the EEG tracing shows 20 to 50 per cent delta waves, the record is scored as stage III. If the epoch has more than 50 per cent delta waves, it is scored as stage IV. In most laboratories, stages III and IV are scored as delta sleep, without noting this distinction.

REM sleep, on the other hand, produces an EEG pattern that resembles stage I sleep, with relatively rapid 3- to 7-cps brain waves and a relatively lower voltage. REM sleep is also characterized by a sudden drop in skeletal muscle tone, usually recorded by submental EMG. In addition there is increased involuntary muscle activity, and dreaming apparently occurs only during REM sleep. Thus, despite the superficial similarity to stage I of NREM sleep, REM sleep represents a distinctly different state than NREM sleep or wakefulness. Therefore, to most investigators, REM sleep is completely separate from non-REM sleep.

The Sleep Cycle

The sleep cycle is usually preceded by a period of relaxed wakefulness that is characterized by the presence of alpha wave activity of 8 to 12 cps. Sleep onset begins with the appearance of a few signs of stage I sleep, followed contiguously by stage II and then delta sleep. Sleep tends to be deeper in each succeeding sleep stage (using auditory awakening thresholds as criteria). After 70 to 90 minutes of NREM sleep there is a return to stage II, followed by the first REM period. The length of this first REM period is usually brief, lasting only 5 to 10 minutes.

The cycle repeats itself throughout the night at 70- to 90-minute intervals, with REM sleep occupying succeedingly greater percentages of each sleep cycle. In addition, delta sleep may disappear by the second or third cycle so that, in the last part of the night, sleep frequently alternates between REM and stage II sleep. Sleep also tends to lighten across the night, so that the stage II sleep early in the night is often deeper than in the latter portion of the night.

The Sleep Cycle and Aging

The ability to sleep and the quality of sleep change with age but, contrary to popular belief, the need for sleep does not. The sleep of an elderly person is commonly disrupted by hundreds of arousals, often leading to complaints of poor sleep quality or to an increase in complaints of insomnia. The percentage of delta sleep decreases steadily from childhood to old age, but the percentage of REM sleep tends to remain approximately the same throughout life.

One important effect of growth and development on sleep patterns occurs early in life. REM sleep occupies approximately 50 per cent of the total sleep time of neonates, and then decreases to 25 to 30 per cent in childhood and to 20 per cent throughout the rest of life.

The Physiology of Sleep

The physiology of sleep differs in many ways from the physiology of wakefulness. Physiologic activity waxes and wanes during sleep, with REM sleep showing the greatest level

of activity. Changes during sleep in respiration, heart rate, brain activity, and hormonal activity have been well documented.

Respiratory Changes

Distinctly different patterns of respiration characterize NREM and REM sleep. In NREM sleep, respiration decreases in both rate and minute ventilation but, in REM sleep, it is more rapid and irregular. In addition, during REM sleep there is loss of muscle tone in certain respiratory muscles. Although the diaphragm maintains tone, intercostal muscles and certain upper airway muscles become atonic, complicating respiratory efforts. This has important clinical implications for obese patients and for other patients with obstructive lung pathologies; their decreased rib cage excursion can lessen their total respiratory volume. Other studies have revealed that mucociliary clearance is reduced during sleep, so that noxious stimuli or stimulation of the larynx usually does not produce coughing as they would during wakefulness, but they can produce a reflex apnea. Swallowing and esophageal motility decrease during sleep, so patients with gastroesophageal reflux can experience esophagitis. Also, hypoxic and hypercapnic ventilatory responses are altered during sleep.

Cardiovascular Changes

Cardiovascular physiology also undergoes changes during sleep. Blood pressure is generally lower during sleep than wakefulness, with the lowest levels occurring during delta sleep. Heart rate also slows during sleep, with its most regular rate occurring during NREM sleep; similarly, cardiac output decreases during sleep. In REM sleep, however, there are increased changes in heart rate and blood pressure. More specifically, the sleep-related variability of the blood pressure of hypertensive patients shows wider than normal changes. Pulmonary pressure tends to increase dramatically during the sleep of snorers. Some cardiac dysrhythmias diminish or disappear during sleep, whereas others, particularly premature ventricular contractions, tend to increase during REM sleep.

Brain Changes

Researchers have reported changes of blood flow, pressure waves, and temperature in the brain during sleep. Cerebral blood flow increases from 60 to 170 per cent during sleep, with peaks occurring in REM sleep. These changes are not uniform, however, because both increases and decreases in the blood flow in different parts of the brain have been reported during NREM sleep. In addition, large intracranial pressure waves occur in REM sleep, but not in NREM sleep. In one study in monkeys, there were increases during REM sleep to 170 mm of pressure above NREM levels. Although most people have a pressure reserve, it is possible for these pressure waves to cause a decrease in nerve function in patients with little reserve. Brain temperature has also been reported to increase in REM sleep and decrease in NREM sleep, suggesting differences in brain metabolic activities.

Gastric Activity and Temperature Changes

Some studies have shown an increase in the secretion rate of gastric acid during sleep, with peaks occurring during REM sleep, particularly in patients with duodenal ulcer disease.

Temperature regulation also seems to be affected by sleep. Temperature regulation has a circadian rhythm, but body temperature generally falls during the night. The lowest body temperature tends to occur in the early morning hours. Of great interest is the discovery that thermal regulation and perspiration are absent in REM sleep.

Endocrine Changes

Endocrine function is altered during sleep, with the most notable changes occurring in growth hormone levels. Peaks in growth hormone levels have been reported in NREM sleep, specifically during delta sleep. These peaks are sensitive to changes in the time of sleep onset, so that going to sleep at a different time causes the growth hormone surges to move with the timing of sleep. More specifically, prolactin levels tend to increase approximately 90 minutes after sleep onset, reaching their maximum during the early morning hours. Conversely, the thyroid-stimulating hormone (TSH) level tends to peak in the evening and then decrease during sleep. TSH changes occur in relation to circadian rhythms, however, and are not regulated by sleep processes.

The Neurologic Basis of Sleep

A model of the neurologic activity occurring during sleep has been developed from a series of elaborate studies of brain stem-transected animals. Early studies by Bremer and by Moruzzi and Magoun led to the proposal of the existence of the reticular activating system for initiating arousal and maintaining wakefulness, introspection, and attentiveness. Based on this system for monitoring wakefulness, Hess suggested the presence of a similarly active sleep-inducing center and identified a number of sites that seem to modulate sleep. Closely monitored activity in such areas as the basal forebrain, the dorsal raphe nucleus, and the solitary tract in the medulla oblongata support this hypothesis. Data from other studies, however, suggest that the suprachiasmic nucleus might be the regulator of the body's circadian rhythms and therefore be involved in sleep-wake cycling.

Further biochemical studies by Jouvet, Hobson and colleagues, and others have resulted in a model in which the interactions of serotonin, catecholamines, and acetylcholine modulate the REM:NREM wake balance. Biochemical sleep mechanisms may also involve an intriguing intermediary that builds up during wakefulness or sleep deprivation and causes sleepiness - a hypnotoxin. Thus, the most recent model for the neurologic basis of sleep is that there is no *locus* for the control of sleep, as there is for the control of wakefulness. Sleep is controlled by biochemical processes.

Based on this assumption, researchers have sought and isolated a number of sleep-promoting factors in the brains of sleep-deprived animals. A body of evidence is accumulating to suggest that one of these factors is a delta sleep-inducing peptide. It accumulates during sleep deprivation and can cause sleep when injected into the ventricles of other animals. More recent studies have suggested leukotriene-I as a sleep-inducing factor; it tends too accumulate during the sleeplessness of illness and causes sleepiness when injected into awake animals.

These findings suggest a role for the immune system in the initiation of sleep - specifically, that sleepiness occurring with fever generates a need for energy-conserving sleep. Such sleep allows a more focused use of energy in fighting microbial invaders. Further evidence for the involvement of the immune system in controlling sleep is suggested by the finding of the HLA-DR2 antigen in over 95 per cent of all narcoleptic patients. This compares to a 25 per cent incidence of HLA-DR2 in the non-narcoleptic population.

All these data are intriguing and support our intuitive sense that sleep deprivation can "lower resistance". Sleep is obviously more than just "rest", and a more precise understanding of its role in maintaining wellness is now emerging.

Patient Evaluation

A well-conducted interview is the first requisite for determining whether to refer a patient to a sleep disorder center.

Interviewing Patients with Sleep-Related Disorders

Obtaining a sleep history for patients who present with sleep-related complaints is critical and often involves questioning the bed partner as well as the patient. The initial interview should determine the extent to which the patient has reasonable sleep habits - sleep of appropriate length and quality is critical to proper daytime functioning and feelings of well-being.

More specifically, good sleep habits require the following: (1) regular times for going to sleep and awakening; (2) a regimen of regular exercise (carried out early in the day to contribute to the depth of sleep); (3) attention to the sleep environment by, among other things, minimizing noises and maintaining a comfortable temperature level; (4) avoiding alcohol and the use of potential stimulating drugs in the evening; and (5) establishing an appropriate presleep ritual as a means of relaxing prior to sleep.

In patients with complaints of insomnia, the physician must evaluate the potential medical causes, including pain, renal dysfunction, nocturnal cardiovascular symptoms, asthma, and gastroesophageal reflux. The physician should also question the bed partner regarding signs of nocturnal twitching or kicking, which can be suggestive of myoclonus or seizure. It is important to determine whether the sleep difficulty occurs under all conditions - for example, on weekends, during vacations, in hotels - as it does in the home environment. The interviewer should also carefully question the patient to evaluate signs of anxiety or depression. It is important to

document by polysomnography the sleep pattern of insomniac patients to confirm the number of arousals, sleep onset time, sleep latency, and total sleep time.

On the other hand, patients with excessive sleepiness or hypersomnia might have poor sleep habits and should also be evaluated for possible medical causes of their condition (eg endocrine dysfunction, Kleine-Levin syndrome, hypersomnia associated with the menstrual cycle). The abuse of alcohol or hypnotic compounds can also contribute to hypersomnia and to insomnia. Patients with excessive daytime sleepiness should be questioned regarding the presence of auxiliary signs of narcolepsy. Questioning the bed partner of the hypersomniac patient can elicit whether symptoms of sleep apnea (eg snoring, gasping, and snorting) exist. One should also investigate the possibility of nonrestorative sleep for these patients, which is characterized by the presence of alpha-delta sleep patterns in the EEG.

Polysomnography

Polysomnography can confirm patient complaints of poor sleep and provides the most objective, reproducible means of determining whether sleep-related abnormalities are contributing to the etiology of the patient's symptoms.

Cost Effectiveness

The cost of sleep laboratory evaluation makes the decision to refer a patient for polysomnography one that requires considerable thought and judgment. The critical consideration in the referral should be whether the information obtained can make a difference in the diagnosis or management of the patient's condition. The duration and severity of their complaints rank high in the decision to refer patients to a sleep disorder center. Patients with persistent complaints extending over a period of months or whose symptoms occur a number of times each week require considerable time and effort for proper diagnosis of symptoms. They may reasonably be considered for polysomnographic evaluation. More specifically, patients with suspected sleep apnea and daytime sleepiness can pose risks to themselves and to others, and they should be considered for immediate diagnosis and treatment. All-night polysomnography with multiple sleep latency testing can immediately diagnose the problem and shorten the time necessary for its resolution.

From a purely cost-effective point of view, the use of the sleep laboratory to evaluate all patients with depression or insomnia is not practical. Even though studies have suggested that up to 20 per cent of insomniac patients have sleep apnea or nocturnal myoclonus underlying their symptoms, carefully taken and scrupulously examined histories result in the selective use of the sleep laboratory to evaluate such patients.

The Polysomnographic Examination

Clinical polysomnographers believe that it is necessary to record a patient's sleep parameters to permit an understanding of the patient's sleep architecture, the identification of

specific sleep-related abnormalities, and their relation to specific sleep stages and time of night. In addition, the patient should be monitored throughout the night, because some abnormalities might be sleep stage-specific or vary in severity as a function of sleep stage. For example, the duration and severity of apnea and cardiac arrhythmias can change as a function of sleep stage or time of night, with the most frequent and severe events occurring in the later portion of the night, when REM sleep predominates. For most patients, a single night in the laboratory can be sufficient to document myoclonus or apnea. For others, however, such as the insomniac patient who might require a period of adaptation, a series of nights might be necessary. Patients who are evaluated for sexual dysfunction often require two to three consecutive nights in the laboratory for careful distinction to be made between organic and psychogenic sexual dysfunction.

Sleep Apnea

Because most otolaryngologists deal specifically with sleep apnea, it is important that the procedures for its diagnosis be presented in some detail.

Diagnostic Measures

Studying sleep apnea requires monitoring air flow at the nose and mouth and measuring respiratory effort. Both are necessary to differentiate among obstructive, central, and mixed apnea. Obstructive apnea is described physiologically as the cessation of air flow at the nose and mouth, but with concomitant inspiratory efforts. Central apnea is defined as the cessation of both air flow and respiratory effort, with the subsequent simultaneous resumption of both inspiratory effort and air flow. Mixed apnea has components of both central and obstructive apnea, with the central component occurring first and followed by the patient's inspiratory efforts, which are obstructed.

The most effective and reliable means of differentiating between central and obstructive apnea involves an esophageal balloon to measure transpleural pressure and a monitor to detect expired carbon dioxide at the nose and mouth. Most laboratories use thermistors, thermocouples, or CO_2 monitors effectively to detect air flow and various noninvasive measures (eg impedance pneumography, inductance plethysmography) to measure respiratory effort. Most laboratories also monitor the patient visually to provide information on effects of the sleep position on the severity of apnea.

Some laboratories regularly use multiple sleep latency testing (MSLT) in patients complaining of daytime sleepiness. This evaluation is important because of the medicolegal implications of the effects of sleep apnea on daytime levels of alertness - MSLT helps to determine the degree of daytime sleepiness and the level of risk associated with the patient's complaint of hypersomnolence accurately and concisely. In addition, results of MSLT can help in making recommendations for post-treatment follow-up, especially in regard to the resolution of daytime somnolence and the patient's risk in driving or operating dangerous equipment. The mean sleep onset latency in normal persons is between 10 and 15 minutes for the four- to five-nap opportunity, but narcoleptics generally exhibit a mean sleep onset latency of 5 minutes or

less, a period also commonly seen in patients experiencing obstructive sleep apnea.

In addition to determining whether apnea is central obstructive or mixed, sleep disorder specialists describe apnea in terms of the frequency of events, using either the apnea index (number of apnea events per hour), apnea-hypopnea index (number of apneas and hypopneas per hour), or the disordered breathing index. These are merely different ways of measuring the same phenomenon. Apneas are also described in terms of their mean duration and the degree of oxygen desaturation they cause.

Anatomy and Physiology of Apnea

Three major factors are now recognized as critical in determining whether the airway collapses or remains open during sleep: (1) the muscle activity of the dilators of the pharyngeal airway; (2) the negative pressure generated during inspiration, which opposes the activity of the dilators; and (3) the structural anatomy of the airway.

Muscle Activity

Understanding apnea requires a review of respiration during sleep. Detailed reviews of basic respiration during sleep have been presented by Sullivan and Issa and by Phillipson. As indicated earlier in this chapter, the respiration rate tends to be lower during NREM sleep but shows significant variability during REM sleep. In addition to the lowering of respiration rate during REM sleep there is a loss of muscle tone, which can have a major impact on respiration. For example, Tusiewicz and associates have reported that, during NREM sleep, approximately 44 per cent of the tidal volume is accounted for on the basis of thoracic respiration, whereas during REM sleep this drops to 19%. The difference is apparently related to the muscle inhibition of the intercostal muscles that occurs during REM sleep. This change in rib cage mechanics can also lead to decreased lung volume and greater susceptibility to hypoxemia, especially in obese patients.

Examining the activity of other muscle groups, Sauerland and Harper observed that genioglossal muscle activity decreases during NREM sleep and decreases further in tone during REM sleep. In contrast to this general decrease in activity, genioglossal muscle activity is momentarily increased during the inspiratory phase of respiration, which prevents the tongue from prolapsing against the posterior pharynx. Similarly the laryngeal muscles also show changes in overall tone, during both REM and NREM sleep. Sauerland and Huerston further demonstrated the presence of decreased activity of the medial pterygoid and tensor palatini muscles during sleep. All these changes are important in maintaining the patency of the airway. Such changes in tone during sleep may contribute to the susceptibility of airway occlusion.

Negative Pressure and Snoring

The dynamics of obstructive sleep apnea is often described to patients and students in terms of traditional concepts of physics, the Venturi effect and the Bernoulli principle. The

Venturi effect describes the acceleration of air flow as a current of air enters a narrowed passageway, such as the increase in the wind velocity between buildings or the increase in the rate of flow of water from a garden hose as one places the thumb over the nozzle. Using these examples, highly technical concepts can be illustrated for patients who present with various airway obstructions, such as deviated septum, hypertrophied turbinates, enlarged tonsils, high-arched palate, enlarged tongue, and retrognathia, which leads to a narrowing at the back of the airway.

The Bernoulli principle states that a partial vacuum or negative pressure exists at the outer edges of a current of flowing air or water. The faster the air flow, the greater the partial vacuum or negative pressure. In the human airway, as air is moved through a narrow orifice, negative pressure is created. Thus, when the negative pressure or suction is greater than the tension provided by the muscle dilators of the airway, the airway collapses. During wakefulness, the muscle tone of the dilators maintains the patency of the airway. As the muscle tone diminishes during sleep, however, the negative pressure can often exceed the ability of the muscle dilators to maintain the patency of airway, with resultant collapse.

More specifically, the fast-moving column of air, the velocity of which has been increased by the obstructions in the airway, meets resistance and can induce vibrations at various points along the upper airway within the resonating tissues lining the oral pharynx, producing a snoring sound. This phenomenon is similar to the vibration that occurs when a saxophone reed vibrates or a flag flutters in the breeze. The faucial pillars in the oropharynx are the structures that are prone to resonate. The loudness is determined by the force of the air being drawn in and the resistance met; the pitch and tone of the snoring are determined by the thickness and consistency of the tissues that are vibrating.

Snoring therefore represents obstructed breathing, in which an individual breathes against resistance in a narrow airway. Thirty-one per cent of males and 19 per cent of females are habitual snorers, with 60 per cent of men and 40 per cent of women between the ages of 60 and 65 snoring regularly. Depressant compounds such as alcohol make snoring worse, and increase the frequency and duration of apneic episodes.

Structural Considerations

The snorer's soft palate can undergo secondary structural changes and become elongated and redundant, leading to an increase in snoring. A characteristic finding in some patients are redundant vertical folds in the tissues of the posterior pharynx, making it look more like the interior of an intestine than an airway. One-third of adult snorers also have tonsils large enough to contribute to the airway problem. Bulky pharyngeal tissues are notable in obese persons. Retrognathia or a receding chin line can result in a tongue that is too large for the space available for it to occupy. Suratt and colleagues and Haponik and associates have shown that the dilator effect of the pharyngeal muscles and the protrusive effect of the genioglossus muscles are inadequate during sleep. Therefore, during sleep, the tongue tends to fall backward into the airway, resulting in vibration against the soft palate, uvula, and pharyngeal tissues.

Physiology of Sleep Apnea

A number of physiologic consequences are associated with apneas - cessation of air flow, hypoxia, and hypercarbia. In addition to episodes of oxygen desaturation, other cardiovascular effects are common. Nocturnal cardiac arrhythmias secondary to oxygen desaturation can occur. Bradycardia is the most common arrhythmia during the hypoxic phase, alternating with tachycardia during the phase of normal respiration.

In addition, premature ventricular contractions, premature atrial contractions, ventricular tachycardia, sinus pauses, and sinus arrests have been reported to accompany apneic events. Arrhythmias often worsen later in the night because apneas and desaturations lengthen as the night progresses, especially during REM sleep. These arrhythmias are generally absent when the patient is awake and would remain undetected unless the patient is monitored in a sleep disorder center or with a Holter monitor. Oxygen desaturation can cause pulmonary vasoconstriction leading to pulmonary hypertension, and ultimately to sustained hypertension and cor pulmonale. Patients with severe obstructive sleep apnea often show right heart enlargement and heart failure, which is thought to be secondary to the severe nocturnal hypoxia that has been occurring regularly over a prolonged period. Oxygen desaturation can also cause secondary polycythemia.

Symptoms of Sleep Apnea

Up to 5.000.000 patients suffer from sleep apnea syndrome, and it is therefore important to note that all patients with central sleep apnea do not present with the same symptoms. Patients with sleep apnea often present with various clinical features, including excessive daytime sleepiness, that are thought to be related to the degree of hypoxia experienced by the apneic patient. They complain of excessive daytime fatigue, believed to be related to the degree of sleep fragmentation they experience. They experience an increase in pulmonary and systemic arterial pressures in response to nocturnal oxygen desaturation, and so it is not surprising that 80 per cent of sleep apnea patients are hypertensive, and that sleep apnea patients constitute 30 per cent of the overall hypertensive population.

Some patients with sleep apnea, especially the obstructive type, have a long history of noisy, intermittent snoring, which has been called "heroic snoring", punctuated by gasping and snorting noises. Obesity is a major disorder associated with obstructive sleep apnea, and approximately 70 per cent of these patients are 15 per cent over their ideal body weight. In some, hypothyroidism is an important etiologic factor. For many patients, excessive daytime sleepiness and inappropriate sleep episodes are the major clinical symptoms; in some cases, these are the only clinical symptoms. The daytime sleepiness is usually more evident when patients are sitting still; patients indicate that they have little difficulty when they are active. Situations such as reading, watching television, and driving a car tend to unmask the daytime sleepiness. Sleepiness is not satiated by brief naps or by extending the nighttime sleep period. A number of these patients complain of a deterioration in memory and judgment associated with morning sleep drunkennes. They also have difficulty maintaining alertness and express difficulty in concentrating.

Sleep apnea can also have an impact on memory, morning irritability, sexual dysfunction, nighttime heartburn, and nausea, and can even cause vomiting during the night. In addition, patients can awaken with complaints of headache and sleep drunkenness. Occasionally, episodes of nocturnal enuresis can occur, especially in patients whose apnea is quite severe. Sleep apnea can occur during infancy and can be chronic or acute, such as in patients with tonsillitis. Daytime symptoms of sleep apnea vary in children in that they tend not to complain of daytime sleepiness, but instead show hyperactive types of behavior, deficiencies in attention span, and decreased levels of school performance.

Treatment of Apnea

A number of different treatments for snoring and sleep apnea have been advocated, each with varying degrees of success. No one type is effective for all patients. Such treatments include the use of mechanical devices, weight loss, pharmacotherapy, and surgery.

Mechanical Devices

Various approaches have been suggested for the treatment of snoring. An old remedy for snoring is the "snore ball", in which a tennis ball is put into an old sock that is pinned to the back of the snorer's pajama top, often between the shoulder blades, to discourage back sleeping. In the American Revolution this technique was reported to have been used by Colonial soldiers. Snore balls are often effective for individuals whose snoring is limited to the supine position. They can also be helpful in preventing vibrations that might lead to the snorer's palate and ultimately to the worsening of snoring, and the consequent development of obstructive sleep apnea. Of course, the aging process itself can lead to loosening of tissue so, even using the snore ball, snoring tends to increase. The ultimate failure of the snore ball can be demonstrated by the fact that over 300 antisnoring devices have been patented in the United States during this century, including electronic gadgetry, prosthetic devices that immobilize the tongue and jaw, and body harnesses attached to immovable objects to keep snorers from rolling over on their back.

A tongue-retaining device has been developed that consists of a mouthpiece into which the tongue is voluntarily inserted and held throughout the night. The advancement of the tongue ostensibly widens the air space, resulting in less snoring and apnea. Unfortunately, the device is difficult to wear, and compliance might be a problem.

A dental appliance known as the equalizer has been tested. Worn much like an orthodontic retainer, it has two tubes extending anteriorly out of the airway. Their function is to balance intraoral and extraoral pressures, thereby preventing the collapse of the airway associated with negative inspiratory pressure. The device is reportedly effective for those with mild to moderate apnea, but it is not indicated for those with severe obstructive sleep apnea. In addition, a patent nasal airway is essential to wearing the equalizer, because the jaws are clipped together. A number of other dental appliances have been developed and have been assigned various claims of efficacy for treating snoring and apnea.

Weight Loss

Another suggested treatment is weight loss, because obesity clearly worsens the severity of obstructive sleep apnea. Unfortunately, voluntary loss of large amounts of weight is difficult for many patients, and maintaining such a weight loss is a significant problem. Patients seem to be most successful with weight loss when they are carefully supervised in structured programs. Surgically induced weight loss - including intestinal bypass, gastric stapling and, most recently, the use of the gastric bubble - has also been reported to resolve the sleep apnea syndrome.

Drug Therapy

Pharmacotherapy has been suggested as a treatment for those with mild sleep apnea. Most commonly prescribed is protriptyline (Vivactyl), a tricyclic antidepressant. It has been described as reducing the severity of obstructive sleep apnea by inhibiting upper airway muscle activity. Tricyclic antidepressants are effective REM suppressants, but their effectiveness in relieving sleep apnea might be secondary to their REM suppressant effects. There is some evidence, nevertheless, that Vivactyl might actually reduce snoring episodes as well and have some effect on pharyngeal muscle tone. In addition, the compound has a general alerting effect, which could provide some subjective improvement in sleepiness without reducing the frequency of apneic episodes.

Medroxyprogesterone, a synthetic oral preparation, has also been proposed as a possible treatment for central sleep apnea. The rationale for its use is based on the marked difference in the incidence of apnea in females compared to males with the known respiration-stimulating properties of this compound. Even though it has limited effectiveness for those with central sleep apnea, it has no demonstrable effectiveness in patients with obstructive sleep apnea.

Similarly, theophylline or aminophylline compounds, used effectively in children with apnea or periodic breathing, are occasionally useful in patients with central apnea, but again have not been shown to be effective for those with obstructive sleep apnea.

Acetazolamide, a carbonic anhydrase inhibitor, has also been shown to be helpful in the treatment of central sleep apnea. The original data have not been easily reproduced, however, and the possibility needs to be examined that the environment of the original study (conducted at a high altitude) might have played a role in the effectiveness of acetazolamide in the treatment of central sleep apnea.

Nasal Constant Positive Airway Pressure

Recently, the most effective nonsurgical treatment for obstructive sleep apnea has been the use of nasal constant positive airway pressure, or nasal C-PAP. A number of studies have reported almost 100 per cent success in ameliorating obstructive sleep apnea with the use of the C-PAP appliance. In addition, some studies of central apnea have also suggested a positive response to this treatment approach. The C-PAP unit provides a splinting action to maintain the

patency of the airway, and directly reduces the negative oropharyngeal pressure generated during inspiration. The technique is simple, safe, and inexpensive, and readily portable. At least one-third of all patients are noncompliant, however, or find that the discomfort of wearing the nasal mask prevents them from effectively using nasal C-PAP as a treatment alternative.

Surgical Management

Much controversy surrounds the surgical management of the patient with obstructive sleep apnea. Should all patients first undergo a trial of conservative therapy or should all the severely affected patients, with obvious anatomic deformity, be recommended for surgery? In addition, if surgery is contemplated, what type of surgery should be performed to optimize the success of the procedure?

Many surgical procedures are available for the treatment of sleep apnea, and details regarding techniques are available in the voluminous literature on this topic.

Tonsillectomy and Adenoidectomy. Tonsillectomy and adenoidectomy have proved to be markedly effective in curing children with obstructive sleep apnea. Less commonly, similar results have been obtained in adults. Unfortunately, not all children achieve a dramatic result, probably because of a tendency to airway collapse. Those in this subgroup, who prove refractory to adenotonsillectomy, might require tracheostomy to obtain relief.

Nasal Surgery. There is little doubt that nasal obstruction, caused either by a deviated septum or by mucosal abnormalities, can exacerbate sleep apnea or even be the cause of mild sleep apnea. Correction of a deviated septum, turbinectomy, or the removal of nasal polyps might, in fact, relieve snoring or mild apnea and be the only treatment necessary.

On the other hand, a patient with severe sleep apnea necessitating a uvulopharyngopalatoplasty (UPPP; see below) could be further improved by nasal surgery performed simultaneously or at a later date. Thus, many surgeons recommend that the nasal surgery be routinely performed together with a UPP, and claim improved results. Whether these results are always indicated depends on the nasal findings and experience of the surgeon.

Uvulopharyngopalatoplasty. The UPPP burst on the medical scene in the United States in the early 1980s, and was rapidly heralded as the newfound cure for obstructive sleep apnea and severe snoring. Although initial enthusiastic reports claimed a high percentage of cures, a more realistic cure rate of about 50 to 60 per cent was subsequently reported. The major dilemma is the inability to determine which patient will, in fact, obtain a satisfactory result from the surgery, with various criteria, including preoperative weight, objective evidence of anatomic obstruction, collapse of the airway, and fiberoptic laryngeal and nasopharyngeal examination (Müller maneuver), all being touted as important prognostic factors. Cephalometry and somnofluoroscopy have also been suggested as techniques to aid in this determination.

The objective of UPPP is to increase the space in the pharynx and to decrease the chance of collapse of the airway during sleep. The aim of procedure is actually somewhat naive, because the disorder, as already stated, is multifactorial in its pathogenesis.

The technique consists of trimming the soft tissue of the soft palate, but not the underlying muscle, which could lead to velopharyngeal incompetence. The tonsils are removed and the anterior and posterior pillars are sutured together. If there is any redundant tissue on the posterior pharyngeal wall, it is also removed. This technique has been modified and remodified over the years, with surgeons having their own little tricks to improve the success rate. Whether these modifications truly make any difference remains to be seen, because the obvious criterion for improving the results is improved selection of patients for the operation. The question of whether all UPPP operations should be combined with nasal surgery is debatable. Occasionally, a temporary tracheostomy might also be included.

Tracheostomy. Tracheostomy can be performed as the permanent solution for sleep apnea or can be temporary, together with UPPP, to protect the airway in the immediate postoperative period.

A permanent tracheostomy is usually required when the patient is morbidly obese with severe sleep apnea or has severe associated cardiopulmonary dysfunction. If these criteria exist, it is better to forgo UPPP or other conservative surgical procedures and proceed to the more definitive tracheostomy.

Numerous techniques have been described for performing permanent tracheostomy in sleep apnea patients. They usually consist of local skin flaps sewn to the walls of the trachea to minimize the amount of granulation tissue and to make maintenance easier. Defatting techniques, including local liposuction, have been recommended for very obese patients.

Other Procedures. A number of other, less well established techniques have been attempted in dealing with this complex problem, and varying degrees of success have been reported. They include surgical reduction of the base of the tongue and expansion hyoidoplasty designed to prevent posterior collapse of the base of the tongue. Mandible advancement procedures have been used in the patients with obvious congenital micrognathia and also with malocclusion caused by a retrognathic mandible.

Further Considerations

The discovery of sleep apnea is relatively recent, and the amount of information regarding apnea and the associated snoring has exploded on the scientific community over the last 15 years. As such, with every new discovery, especially one that involves new treatment opportunities, there are controversies about when patients should be treated and which treatments are most appropriate. For some, snoring is seen as a progressive disease, with the result being apnea and its potential for the creation and exacerbation of other medical conditions; for others, it is simply a nuisance. Some researchers have attempted to establish guidelines for specific diagnosis and

treatment based on an apnea-hypopnea index and on levels of oxygen desaturation. An apnea-hypopnea index of 5 or greater is considered by some to be of clinical significance, whereas others focus on the degree of oxygen desaturation. Not all patients, however, show significant O_2 desaturation, but most present with complaints of fatigue and sleepiness. I believe that each situation should be viewed on an individual basis, and that the impact of the apnea in terms of daytime function and interaction with other medical conditions (eg hypertension, risk of stroke) be incorporated into the decision-making process.

In the area of sleep disorder medicine, as in every developing field, there are still more questions than answers, but we have come a long way. The discovery of obstructive sleep apnea has had a major impact on otolaryngology, and has created important liaisons with those in other areas of medicine and surgery. Further research will undoubtedly reveal appropriate surgical procedures for the correction of obstructive sleep apnea, so that presurgical evaluations can elicit the procedure necessary to correct the condition. Surgical correction, however, will probably remain as one alternative for managing this condition. Because of the growing awareness that obstructive sleep apnea can contribute to a wide variety of disorders, otolaryngologists will increasingly interact with thoracic surgeons, pulmonologists, endocrinologists, pediatricians, psychiatrists, and gerontologists. Sleep apnea is the ultimate cause of a number of conditions treated by these specialists, and, as each of these specialists begins to regard snoring as the potential warning noise, the role of the otolaryngologist in contributing to the management of his or her patients will become increasingly important.