

CURRENT CONCEPTS

OBSTRUCTIVE SLEEP APNEA

PATRICK J. STROLLO, JR., M.D.,
AND ROBERT M. ROGERS, M.D.

OUR understanding of the nature and consequences of upper-airway obstruction in adults during sleep has evolved considerably over the past two decades. Sleep apnea — defined as repeated episodes of obstructive apnea and hypopnea during sleep, together with daytime sleepiness or altered cardiopulmonary function — is common.¹ Epidemiologic studies estimate that the condition affects 2 to 4 percent of middle-aged adults.² Only a small portion of the cases in this group of adults have been diagnosed; this is related to insufficient awareness of sleep apnea among physicians and the public at large.³

DEFINITIONS

The manifestations of upper-airway closure during sleep are described in Table 1. The syndromes of sleep apnea, sleep hypopnea, and upper-airway resistance share two common features, daytime sleepiness and disruption of sleep due to increased ventilatory effort in response to upper-airway closure.^{4,6} Distinctive physiologic characteristics of obstructive apnea, obstructive hypopnea, and upper-airway resistance are shown in Figure 1.

Episodes of obstructive apnea and obstructive hypopnea frequently occur in the same patient. Although obstructive apnea may be associated with greater oxyhemoglobin desaturation, distinguishing apnea from hypopnea has little effect on the approach to treatment. Many laboratories report the combined number of episodes of apnea and hypopnea per hour of sleep as a single apnea-hypopnea index or respiratory-disturbance index.

The upper-airway resistance syndrome is characterized by arousal in response to increased upper-airway resistance without an elevated apnea or hypopnea index. Patients with the upper-airway resistance syndrome are usually heavy snorers.⁶

PATHOGENESIS

Narrowing or closure may occur at one or more sites in an unstable upper airway (i.e., in the velopharynx, oropharynx, or hypopharynx).^{7,9} Upper-airway dysfunction and the specific sites of narrowing or closure are influenced by the underlying neuromuscular tone, up-

per-airway muscle synchrony, and the stage of sleep.¹⁰ These events are generally most prominent during rapid-eye-movement (REM) sleep because of the hypotonia of the upper-airway muscles characteristic of this stage of sleep.

Upper-airway size is determined by soft-tissue and skeletal factors that are also the major determinants of upper-airway patency during sleep.¹¹ In obese patients, increased adipose tissue in the neck may predispose the airway to narrowing. Magnetic resonance imaging has documented fatty infiltration into the pharyngeal tissue of patients with sleep apnea.^{12,13} Patients of normal body weight in whom sleep apnea develops may have tonsillar hypertrophy or craniofacial skeletal abnormalities that also predispose the airway to narrowing or closure during sleep.¹⁴ These craniofacial abnormalities may be evident on a cephalometric radiograph, although not readily apparent on physical examination.¹⁴

Genetic and environmental factors may also adversely affect airway size. Sleep apnea has been identified as common to some families. The increased incidence of sleep apnea in these families is not explained by obesity alone.¹⁵ Genetically determined craniofacial features or abnormalities of ventilatory control may account for this pattern of familial apnea.

If the soft palate is exposed to recurrent vibratory trauma (snoring) and high negative inspiratory pressure, the result can be lengthening of the soft palate due to stretching and thickening caused by edema.¹⁶ It is possible that the changes in the soft palate of patients with sleep apnea may thus be a consequence of breathing against increased upper-airway resistance rather than the cause of that increased resistance.

PATHOPHYSIOLOGIC CONSEQUENCES

Patients with sleep apnea have an increased risk of diurnal hypertension, nocturnal dysrhythmias, pulmonary hypertension, right and left ventricular failure, myocardial infarction, and stroke.¹⁷ Retrospective studies indicate that there is an association of sleep apnea with morbidity and mortality due to cardiovascular and cerebrovascular causes.^{18,19} Recent data indicate that the relation between sleep apnea and diurnal hypertension is independent of obesity, age, and sex.²⁰ The risk of vascular disease appears to be mediated by the complex interaction between the mechanical and chemical effects (hypoxia and hypercapnia) of repetitive upper-airway closure and their effect on the autonomic nervous system.⁸ The repetitive increase in sympathetic tone in patients with sleep apnea may be responsible for the development of diurnal hypertension.²¹ Sleepiness, fatigue, irritability, and personality change have been attributed to nocturnal desaturation and the chronic sleep deprivation caused by sleep fragmentation. Sleep fragmentation may be the most important predictor of daytime sleepiness.²²

Patients with sleep apnea are also at increased risk for motor vehicle accidents. The accident rate for such

From the Division of Pulmonary, Allergy, and Critical Care Medicine, University of Pittsburgh School of Medicine, 440 Scaife Hall, 3550 Terrace St., Pittsburgh, PA 15261, where reprint requests should be addressed to Dr. Strollo.

©1996, Massachusetts Medical Society.

Table 1. Manifestations of Upper-Airway Closure during Sleep.

Distinctive features of syndromes	
Obstructive sleep apnea	Cessation of airflow for ≥ 10 seconds despite continuing ventilatory effort
	5 or more episodes per hour of sleep
	Usually associated with a decrease of $\geq 4\%$ in oxyhemoglobin saturation
Obstructive sleep hypopnea	Decrease of 30–50% in airflow for ≥ 10 seconds
	15 or more episodes per hour of sleep
	May be associated with a decrease of $\geq 4\%$ in oxyhemoglobin saturation
Upper-airway resistance	No significant decrease in airflow (snoring is usual)
	15 or more episodes of arousal per hour of sleep (?)
	No significant decrease in oxyhemoglobin saturation
Features common to all three syndromes	
Arousal associated with increasing ventilatory effort	(as measured with an esophageal balloon)
Excessive daytime sleepiness	

patients has been reported to be seven times that of the general driving population.²³

DIAGNOSIS

Most patients with sleep apnea are objectively sleepy, although daytime sleepiness is underreported because it generally manifests itself over a prolonged period and patients change their lifestyles gradually to compensate for it. Loud snoring, fatigue, or both are frequently the patient's only symptoms. A focused history taking and physical examination of patients who report such symptoms may aid in identifying persons at risk for sleep apnea. Other patient characteristics associated with sleep apnea include male sex; age of more than 40 years; habitual snoring; nocturnal gasping, choking, or resuscitative snoring; observed apnea; and a history of systemic hypertension.^{2,24} Symptoms of daytime somnolence, unrefreshing sleep, morning headaches, cognitive impairment, depression, nocturnal esophageal reflux, and nocturia are commonly reported, but do not distinguish sleep apnea from other, nonpulmonary, sleep disorders.

The presence of certain physical characteristics should heighten the physician's suspicion of upper-airway dysfunction during sleep.²⁵ Retrognathia and discrete upper-airway abnormalities, such as an enlarged soft palate or tonsillar hypertrophy, are clinical clues. An increased body-mass index (the weight in kilograms divided by the square of the height in meters), hypertension, and an increased neck circumference (measured at the cricothyroid membrane) are often characteristic of patients with sleep apnea.²⁴ Increased upper-body obesity, which is reflected by the neck circumference, is a particularly good predictor of sleep apnea.

A sleep study should be strongly considered for two groups of patients: those who habitually snore and report daytime sleepiness, and those who habitually snore

and have observed apnea (regardless of daytime symptoms).

SLEEP STUDIES

A sleep study is performed to confirm the presence of upper-airway closure during sleep and to assess the patient's level of risk. A full night of polysomnography, conducted by a technologist in a sleep laboratory, has traditionally been regarded as the gold standard for diagnosing sleep apnea. The polysomnogram is a comprehensive study used to record many physiologic variables in order to diagnose a wide spectrum of pulmonary and nonpulmonary disorders of sleep.

Portable, unattended monitoring systems that can be used outside the hospital promise a more cost-effective alternative to the standard diagnostic nocturnal polysomnography. Whether abbreviated testing, inside or outside the hospital, can successfully establish a diagnosis of sleep apnea is a subject of controversy.²⁶ Portable systems vary in the manner in which physiologic signals are recorded and scored, as well as in whether cardiopulmonary variables alone, or sleep and cardiopulmonary variables together, may be monitored. One major concern about the use of portable monitors is that airflow, ventilatory effort, and arousal may not be measured at all (or may be measured less precisely than in the laboratory) and that the monitors may therefore miss episodes of hypopnea or arousal due to upper-airway resistance.²⁷

TREATMENT

Therapeutic strategies for patients with sleep apnea may be grouped into three general categories: behavioral, medical, and surgical (Table 2). Treatment decisions should be based on the effect of the sleep disorder on daytime symptoms and cardiopulmonary function rather than on the absolute number of episodes of apnea or hypopnea. The goals of treatment are to establish normal nocturnal oxygenation and ventilation, abolish snoring, and eliminate disruption of sleep due to upper-airway closure.

Behavioral Treatment

All patients with sleep apnea should be counseled about the potential benefits of therapy and the risks of going without treatment. The value of avoiding factors that increase the severity of upper-airway obstruction — such as sleep deprivation; the use of alcohol, sedatives, and hypnotic agents; and increased weight — should be discussed.^{28–32} Alcohol selectively reduces upper-airway muscle tone and increases the frequency of abnormal breathing during sleep.³⁰ Alcohol also prolongs apnea by delaying arousal.²⁹ In obese patients, weight loss can significantly decrease the severity of the apnea.³² In some patients, upper-airway dysfunction is present only during sleep in the supine position; training these patients to sleep exclusively in the lateral recumbent position may be useful,³³ although the long-

Figure 1. Manifestations of Upper-Airway Closure.

Panel A depicts obstructive apnea. Increasing ventilatory effort is seen in the rib cage, the abdomen, and the level of esophageal pressure (measured with an esophageal balloon), despite lack of oronasal airflow. Arousal on the electroencephalogram (EEG) is associated with increasing ventilatory effort, as indicated by the esophageal pressure. Oxyhemoglobin desaturation follows the termination of apnea. Note that during apnea, the movements of the rib cage and the abdomen (Effort) are in opposite directions (arrows) as a result of attempts to breathe against a closed airway. Once the airway opens in response to arousal, rib-cage and abdominal movements become synchronous. Panel B depicts obstructive hypopnea. Decreased airflow is associated with increasing ventilatory effort (reflected by the esophageal pressure) and subsequent arousal on the EEG. Rib-cage and abdominal movements are in opposite directions during hypopnea (arrows), reflecting increasingly difficult breathing against a partially closed airway. Rib-cage and abdominal movements become synchronous after arousal produces airway opening. Oxyhemoglobin desaturation follows the termination of hypopnea. Panel C depicts upper-airway resistance. Asynchronous movements of the rib cage and abdomen and a substantial decrease in airflow are not seen. Arousal on the EEG is associated with increasing ventilatory effort due to increased airway resistance, as reflected by the esophageal pressure. There is no significant oxyhemoglobin desaturation.

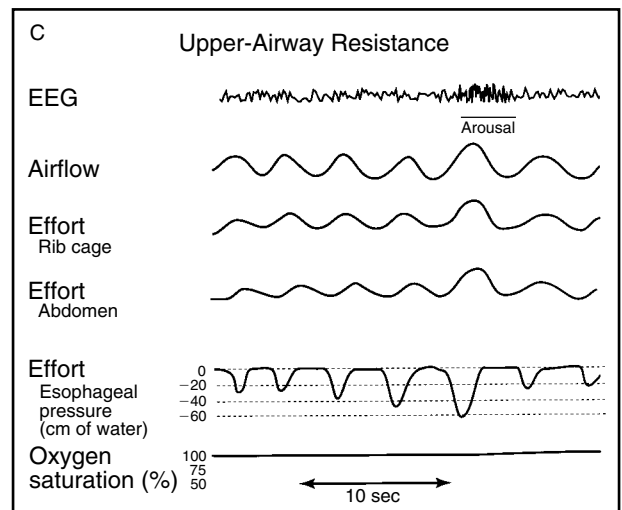
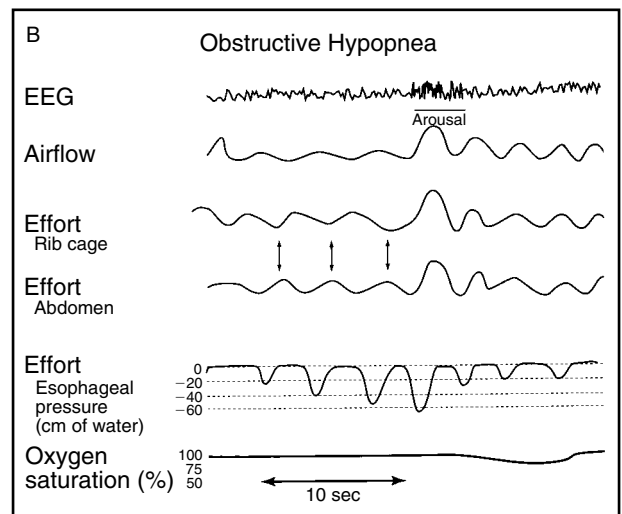
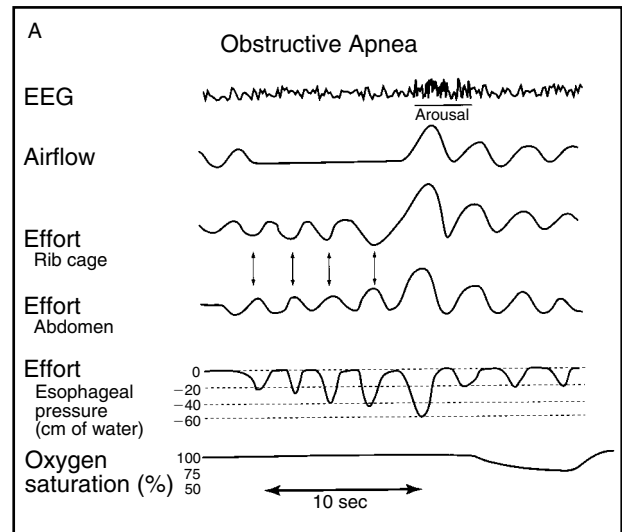
term effectiveness of this intervention is unclear. The diagnostic polysomnogram must be carefully analyzed if positional therapy is to be recommended as the sole treatment. A patient's moving from the supine to the lateral recumbent position may make apnea less apparent or convert it to another form of sleep-disordered breathing, hypopnea, or upper-airway resistance.

Medical Treatment

Positive Airway Pressure

Positive airway pressure, delivered through a mask, is the initial treatment of choice in clinically important sleep apnea. Machines for creating continuous positive airway pressure run on household current, weigh approximately 2 kg (5 lb), and fit easily on a bedside table. The systems cost about \$1,000 each. Continuous positive pressure is applied to the upper airway with a nasal mask, nasal prongs, or a mask that covers both the nose and mouth.^{1,34,35} A pneumatic splint is also provided that prevents narrowing and closure of the upper airway regardless of the site of obstruction.³⁶ The level of positive pressure required to sustain patency of the upper airway during sleep should be determined in the sleep laboratory. To decrease the cost of polysomnography and facilitate treatment, some physicians have attempted both to diagnose the condition and to initiate treatment with positive airway pressure in a single night of observation. With this approach, an adequate determination of the degree of pressure needed for treatment can be achieved approximately 60 percent of the time.³⁷ It is unclear, however, how this approach affects the patient's likelihood of accepting and complying with treatment.

Subjective estimates of patient compliance are high-



er than objectively determined values. Using objective data, Kribbs et al. demonstrated that 46 percent of patients treated with continuous positive airway pressure had acceptable compliance, defined as use of the machine for more than four hours per night for more than 70 percent of the observed nights.³⁸ The degree to which a given patient is compliant appears to be more closely related to the relief of daytime symptoms and the restoration of alertness than to the severity of the apnea-hypopnea index.¹

Patients treated with continuous positive airway pressure delivered nasally have repeatedly demonstrated improvement in neuropsychiatric function and a lessening of daytime sleepiness.^{39,40} Nocturnal desaturation, ventilatory-related arousals, nocturnal dysrhythmias, pulmonary hypertension, and right-sided heart failure have also been effectively treated.¹ Preliminary data suggest that the treatment can also improve control of diurnal hypertension, probably by correcting nocturnal desaturation and lowering nocturnal catecholamine release.⁴¹ These results parallel those observed after tracheostomy, but continuous positive airway pressure does not entail the morbidity and disfigurement associated with that procedure.⁴² Retrospective studies suggest that patients treated with nasally delivered continuous positive airway pressure or tracheostomy have improved survival.¹⁸

Serious complications of therapy with continuous positive airway pressure are rare.¹ Side effects reported by patients usually involve discomfort or irritation related to the nasal mask.¹ Patients may complain of nasal congestion, dryness, or occasional rhinorrhea.¹ Nasal congestion can be treated with antihistamines or topical corticosteroids. Topical saline sprays or humidification will improve nasal dryness. Some patients may complain of increased resistance to exhalation or a sensation of too much pressure in the nose. A system that is fitted with a ramp may solve this problem. The ramp

allows a gradual increase in the positive pressure to the prescribed level over a period of 5 to 45 minutes. There are no published data indicating that use of a ramp improves either acceptance of positive-pressure therapy or compliance with treatment. If a ramp unit is not effective, a machine with bilevel pressure may be. Bilevel systems allow the independent adjustment of positive airway pressure during inspiration and expiration. This usually produces upper-airway patency at lower expiratory pressures than are necessary with continuous positive airway pressure.⁴³ Bilevel systems run on household current and are similar in size and weight to the continuous-pressure systems, but they are more expensive (about \$3,000 each). Patient acceptance of therapy may be better with bilevel systems, but compliance is similar to that associated with continuous-pressure systems.⁴⁴

Certain patients become claustrophobic when using positive airway pressure. Changing from a nasal mask to the less confining nasal prongs may alleviate this problem. If this change is not effective, progressive desensitization to the mask may be helpful.⁴⁵ Optimal treatment with positive airway pressure can also be hampered by air leaks from the mouth that cause a loss of pressure or by nasal congestion that is refractory to medical therapy. In those situations, a mask that covers both the nose and the mouth can be helpful.^{34,35}

Oral Appliances

Several studies have demonstrated that an oral appliance can be a useful alternative to positive airway pressure for some patients with sleep apnea.^{46,47} A wide variety of appliances are available, differing both in construction and in the manner in which they alter the oral cavity. Two of the more common oral appliances are shown in Figure 2. The appliances are worn only during sleep and are generally well tolerated. Not all patients have a clinically meaningful response to oral appliances, which are currently regarded as second-line therapy. Patients with mild sleep apnea who do not tolerate therapy with positive airway pressure are good candidates for a trial of an oral appliance. Close collaboration between the physician and the dental consultant is necessary to ensure optimal patient selection and to avoid any alteration of dental occlusion or temporomandibular-joint discomfort.⁴⁶

Medication

The use of medication to treat sleep apnea has been disappointing. Protriptyline and fluoxetine have been used with varying degrees of success in mild cases but are of little help in more severe cases.⁴⁸ In patients with hypothyroidism, thyroxine replacement may significantly improve upper-airway function during sleep.⁴⁹ Nocturnal oxygen therapy is a possibility for patients who have severe desaturation and are intolerant of or will not accept other, more effective, treatments. Oxygen will decrease the nadir of oxyhemo-

Table 2. Interventions for Sleep Apnea.

Behavioral
Weight loss
Avoidance of alcohol and sedatives
Avoidance of sleep deprivation
Nocturnal positioning
Medical
First-line therapy
Positive pressure through a mask
Second-line therapy
Oral appliance
Other
Fluoxetine or protriptyline
Thyroid hormone (in hypothyroid patients)
Nocturnal oxygen
Surgical
Upper-airway bypass
Tracheostomy
Upper-airway reconstruction
Uvulopalatopharyngoplasty
Genioglossal advancement
Maxillomandibular advancement



A



B

Figure 2. Oral Appliances.

The tongue-retaining device (Panel A) enlarges the airway by keeping the tongue in an anterior position during sleep. The Herbst appliance (Panel B) forces the mandible forward, thereby enlarging the airway. (Photographs provided by Robert R. Rogers, D.M.D.)

globin desaturation but its effect on the duration of apnea varies.⁵⁰

There is no role for benzodiazepine sedative-hypnotic agents in patients with otherwise untreated sleep apnea. These medications will further destabilize the upper airway during sleep, impede arousal, and potentiate airway closure and oxyhemoglobin desaturation.

Surgical Treatment

Tracheostomy

The availability and acceptance of positive-pressure therapy have lessened the need for tracheostomy. There remains a small subgroup of patients with severe apnea who cannot tolerate positive pressure and for whom other interventions are ineffective or unacceptable. A tracheostomy can provide dramatic improvement and be lifesaving, although additional medical and psychological morbidity may be associated with this treatment.^{42,51}

Palatal Surgery

Surgery to modify, rather than bypass, a specific site of upper-airway closure, although less disfiguring than tracheostomy, offers more variable results. The most commonly performed procedure, uvulopalatopharyngoplasty, is curative in less than 50 percent of patients.⁵² Preoperative imaging studies have not adequately predicted surgical success.²⁵ Even when the technical results of surgery are good, obstruction may continue at the site of surgery in the soft palate, or elsewhere in the upper airway.⁵² Laser-assisted uvulopalatopharyngoplasty has recently been introduced as an outpatient treatment for snoring. This procedure is currently not recommended for the treatment of sleep apnea.⁵³

Maxillofacial Surgery

A variety of procedures have been developed to enhance upper-airway patency during sleep in patients with obstruction at or below the base of the tongue. These procedures involve genioglossal advancement, with or without resuspension of the hyoid bone, and may be performed in conjunction with a uvulopalatopharyngoplasty.^{54,55} Such procedures usually require a team of surgeons that includes an otolaryngologist and an oral surgeon. These operations are not uniformly successful, although individual patients have had excellent results.

Patients with sleep apnea who have major craniofacial abnormalities, or who have had an unsuccessful genioglossal advancement, with or without uvulopalatopharyngoplasty, may benefit from a maxillomandibular advancement. These procedures should be reserved for patients with sleep apnea who are either unwilling or unable to be treated with positive airway pressure.

We are indebted to Dr. Mark Sanders, Dr. Wishwa Kapoor, and the faculty of the Division of Pulmonary, Allergy, and Critical Care Med-

icine for their helpful comments, and to Mrs. Alice Lawson for her assistance in preparing the manuscript.

REFERENCES

- Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes. *Am J Respir Crit Care Med* 1994;150:1738-45.
- Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230-5.
- Rosen RC, Rosekind M, Rosevear C, Cole WE, Dement WC. Physician education in sleep and sleep disorders: a national survey of U.S. medical schools. *Sleep* 1993;16:249-54.
- The international classification of sleep disorders: diagnostic and coding manual. Rochester, Minn.: American Sleep Disorders Association, 1990:52-8.
- Gould GA, Whyte KF, Rhind GB, et al. The sleep hypopnea syndrome. *Am Rev Respir Dis* 1988;137:895-8.
- Guilleminault C, Stoohs R, Clerk A, Cetel M, Maistros P. A cause of excessive daytime sleepiness: the upper airway resistance syndrome. *Chest* 1993;104:781-7.
- Hudgel DW. Mechanisms of obstructive sleep apnea. *Chest* 1992;101:541-9.
- Bonsignore MR, Marrone O, Insalaco G, Bonsignore G. The cardiovascular effects of obstructive sleep apnoeas: analysis of pathogenic mechanisms. *Eur Respir J* 1994;7:786-805.
- Shepard JW Jr, Thawley SE. Localization of upper airway collapse during sleep in patients with obstructive sleep apnea. *Am Rev Respir Dis* 1990;141:1350-5.
- Sullivan CE, Issa FG. Obstructive sleep apnea. *Clin Chest Med* 1985;6:633-50.
- Davies RJO, Stradling JR. The relationship between neck circumference, radiographic pharyngeal anatomy, and the obstructive sleep apnoea syndrome. *Eur Respir J* 1990;3:509-14.
- Schwab RJ, Gupta KB, Gefer WB, Metzger LJ, Hoffman EA, Pack AI. Upper airway and soft tissue anatomy in normals and patients with sleep-disordered breathing. *Am J Respir Crit Care Med* (in press).
- Horner RL, Mohiaddin RH, Lowell DG, et al. Sites and sizes of fat deposits around the pharynx in obese patients with obstructive sleep apnoea and weight matched controls. *Eur Respir J* 1989;2:613-22.
- Partinen M, Guilleminault C, Quera-Salva MA, Jamieson A. Obstructive sleep apnea and cephalometric roentgenograms: the role of anatomic upper airway abnormalities in the definition of abnormal breathing during sleep. *Chest* 1988;93:1199-205.
- Mathur R, Douglas NJ. Family studies in patients with the sleep apnea-hypopnea syndrome. *Ann Intern Med* 1995;122:174-8.
- Woodson BT, Garancis JC, Toohill RJ. Histopathologic changes in snoring and obstructive sleep apnea syndrome. *Laryngoscope* 1991;101:1318-22.
- Yamashiro Y, Kryger MH. Why should sleep apnea be diagnosed and treated? *Clin Pulm Med* 1994;1:250-9.
- 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;94:9-14.
- Partinen M, Jamieson A, Guilleminault C. Long-term outcome for obstructive sleep apnea syndrome patients: mortality. *Chest* 1988;94:1200-4.
- Hla KM, Young TB, Bidwell T, Palta M, Skatrud JB, Dempsey J. Sleep apnea and hypertension: a population-based study. *Ann Intern Med* 1994;120:382-8.
- Fletcher EC. The relationship between systemic hypertension and obstructive sleep apnea: facts and theory. *Am J Med* 1995;98:118-28.
- Colt HG, Haas H, Rich GB. Hypoxemia vs sleep fragmentation as a cause of excessive daytime sleepiness in obstructive sleep apnea. *Chest* 1991;100:1542-8.
- Findley LJ, Unverzagt ME, Suratt PM. Automobile accidents involving patients with obstructive sleep apnea. *Am Rev Respir Dis* 1988;138:337-40.
- Flemons WW, Whitelaw WA, Brant R, Remmers JE. Likelihood ratios for a sleep apnea clinical prediction rule. *Am J Respir Crit Care Med* 1994;150:1279-85.
- Shepard JW Jr, Gefer WB, Guilleminault C, et al. Evaluation of the upper airway in patients with obstructive sleep apnea. *Sleep* 1991;14:361-71.
- Stiller RA, Strollo PJ, Sanders MH. Unattended recording in the diagnosis and treatment of sleep-disordered breathing: unproven accuracy, untested assumptions, and unready for routine use. *Chest* 1994;105:1306-9.
- Ferber R, Millman R, Coppola M, et al. Portable recording in the assessment of obstructive sleep apnea: ASDA standards and practice. *Sleep* 1994;17:378-92.
- Neilly JB, Kribbs NB, Maislin G, Pack AI. Effects of selective sleep deprivation on ventilation during recovery sleep in normal humans. *J Appl Physiol* 1992;72:100-9.
- Berry RB, Desa MM, Light RW. Effect of ethanol on the efficacy of nasal continuous positive airway pressure as a treatment for obstructive sleep apnea. *Chest* 1991;99:339-43.
- Bonora M, Shields GI, Knuth SL, Bartlett D Jr, St John WM. Selective depression by ethanol of upper airway respiratory motor activity in cats. *Am Rev Respir Dis* 1984;130:156-61.
- Bonora M, St John WM, Bledsoe TA. Differential elevation by protriptyline and depression by diazepam of upper airway respiratory motor activity. *Am Rev Respir Dis* 1985;131:41-5.
- Smith PL, Gold AR, Meyers DA, Haponik EF, Bleecker ER. Weight loss in mildly to moderately obese patients with obstructive sleep apnea. *Ann Intern Med* 1985;103:850-5.
- Cartwright R, Ristanovic R, Diaz F, Caldarelli D, Adler G. A comparative study of treatments for positional sleep apnea. *Sleep* 1991;14:546-52.
- Prosisre GL, Berry RB. Oral-nasal continuous positive airway pressure as a treatment for obstructive sleep apnea. *Chest* 1994;106:180-6.
- Sanders MH, Kern NB, Stiller RA, Strollo PJ Jr, Martin TJ, Atwood CW Jr. CPAP therapy via oronasal mask for obstructive sleep apnea. *Chest* 1994;106:774-9.
- Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet* 1981;1:862-5.
- Sanders MH, Kern NB, Costantino JP, et al. Adequacy of prescribing positive airway pressure therapy by mask for sleep apnea on the basis of a partial-night trial. *Am Rev Respir Dis* 1993;147:1169-74.
- 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;147:887-95.
- Derderian SS, Bridenbaugh RH, Rajagopal KR. Neuropsychologic symptoms in obstructive sleep apnea improve after treatment with nasal continuous positive airway pressure. *Chest* 1988;94:1023-7.
- Lamphere J, Roehrs T, Wittig R, Zorick F, Conway WA, Roth T. Recovery of alertness after CPAP in apnea. *Chest* 1989;96:1364-7.
- Levinson PD, Millman RP. Causes and consequences of blood pressure alterations in obstructive sleep apnea. *Arch Intern Med* 1991;151:455-62.
- Guilleminault C, Simmons FB, Motta J, et al. Obstructive sleep apnea syndrome and tracheostomy: long-term follow-up experience. *Arch Intern Med* 1981;141:985-8.
- Sanders MH, Kern N. Obstructive sleep apnea treated by independently adjusted inspiratory and expiratory positive airway pressures via nasal mask: physiologic and clinical implications. *Chest* 1990;98:317-24.
- Reeves-Hoche MK, Hudgel DW, Meck R, Wittman R, Ross A, Zwillich CW. Continuous versus bilevel positive airway pressure for obstructive sleep apnea. *Am J Respir Crit Care Med* 1995;151:443-9.
- Edinger JD, Radtke RA. Use of in vivo desensitization to treat a patient's claustrophobic response to nasal CPAP. *Sleep* 1993;16:678-80.
- Clark GT, Arand D, Chung E, Tong D. Effect of anterior mandibular positioning on obstructive sleep apnea. *Am Rev Respir Dis* 1993;147:624-9.
- 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;149:905-9.
- Hanzel DA, Proia NG, Hudgel DW. Response of obstructive sleep apnea to fluoxetine and protriptyline. *Chest* 1991;100:416-21.
- Rajagopal KR, Abbrecht PH, Derderian SS, et al. Obstructive sleep apnea in hypothyroidism. *Ann Intern Med* 1984;101:491-4.
- Fletcher EC, Munafo DA. Role of nocturnal oxygen therapy in obstructive sleep apnea: when should it be used? *Chest* 1990;98:1497-504.
- Conway WA, Victor LD, Magilligan DJ Jr, Fujita S, Zorick FJ, Roth T. Adverse effects of tracheostomy for sleep apnea. *JAMA* 1981;246:347-50.
- Shepard JW Jr, Olsen KD. Uvulopalatopharyngoplasty for treatment of obstructive sleep apnea. *Mayo Clin Proc* 1990;65:1260-7.
- Practice parameters for the use of laser-assisted uvulopalatoplasty. *Sleep* 1994;17:744-8.
- Riley RW, Powell NB, Guilleminault C. Obstructive sleep apnea syndrome: a review of 306 consecutively treated surgical patients. *Otolaryngol Head Neck Surg* 1993;108:117-25.
- Johnson NT, Chinn J. Uvulopalatopharyngoplasty and inferior sagittal mandibular osteotomy with genioglossus advancement for treatment of obstructive sleep apnea. *Chest* 1994;105:278-83.