Obstructive sleep apnea

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For many years clinicians viewed sleep with detached interest. Perhaps sleep was regarded as a secure harbor in which the weary patient could seek refuge, later emerging refreshed to confront the trials of the next day's voyage. This assumption was facilitated because physicians had not been able to examine the harbor, which now has been shown to change rapidly, at times becoming turbulent and exerting demands of its own.

A night of sleep consists of repeated cycling between rapid eye movement (REM) and non-REM sleep. Mechanisms governing vital body functions are surprisingly different in these states, such that we are forced to shift physiologic gears frequently each night.[1] Some individuals have serious problems in one or both sleep states despite seemingly good health during wakefulness.

Another serious misconception has prevailed from the time of Burwell's description of the Pickwickian syndrome.[2] Sleep-induced ventilatory failure often has been thought of as a relatively uncommon problem, associated for the most part with morbid obesity. Therapeutic efforts frequently have concentrated on altered pulmonary mechanics, ventilation-perfusion mismatch, impaired ventilatory drive, and the various cardiovascular and thromboembolic complications of this readily diagnosed entity.

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In contrast, the past decade has revealed that sleep apnea is not rare, and that only a minority of those afflicted are morbidly obese. Finally, upper airway obstruction during sleep has emerged as the greatest single factor in most cases of sleep-induced ventilatory failure.

Definitions

An episode of sleep apnea denotes cessation of airflow at the mouth and nose for 10 seconds or more.[3] Such episodes can occur in normal persons, particularly during the onset of sleep, during REM bursts, and following body movements. They become pathologic when they are frequent (>35 episodes per night), evident in both REM and non-REM sleep, or caused by upper airway obstruction.

Most patients with abnormal sleep apneas have the latter problem, occasionally with an initial, central failure of ventilatory effort preceding the onset of ineffective, increasingly vigorous attempts to overcome obstruction (mixed or complex apneas). Purely central, pathologic sleep apneas are unusual except in premature and newborn infants.[4] Repetitive, partial upper airway occlusion (obstructive hypoventilation) characterizes the sleep of some patients who may experience hypoxemia as intense as hypoxemia in individuals with complete airway closure. Hypoventilation without elements of upper airway obstruction or discrete apneas do occur, but less frequently than sleep apnea with upper airway obstruction.

The Pickwickian syndrome classically describes subjects with waking cyanosis, waking carbon dioxide retention, right ventricular failure, hypersomnolence, and extreme obesity. Many Pickwickian patients have obstructive sleep apnea, even if adipose tissue has not narrowed their airways. Ondine's curse refers to central nervous system failure of automatic ventilation both during wakefulness and sleep, such that the patient must be "reminded to breathe."[5] When idiopathic, it sometimes has been called primary alveolar hypoventilation. Cheyne-Stokes respiration also can persist during wakefulness; it is characterized by crescendo-decrescendo respiratory clusters and intervening central apneas.[6] More than half such cases that we have evaluated have varying amounts of superimposed upper airway obstruction during the repeated crescendo increases in ventilatory effort.[7]

Pathophysiology

Upper airway obstruction therefore emerges as highly prevalent among patients with sleep-associated ventilatory failure. It also is particularly devastating because it tends to provoke profound hypoxemia, generally to a greater degree than that resulting from purely central apnea.[8] The resulting blood gas aberrations seem to precipitate secondary worsening of ventilatory drive in some instances, conceivably by mechanisms such as hypoxic suppression of hypoxic responsiveness. Hence, to focus only upon therapeutic efforts to enhance ventilatory drive would be analogous to tinkering with the carburetor of an automobile with a clogged fuel line.

The sequelae of the intense hypoxemia, acidosis, and frantic struggling resulting from obstructive sleep apnea are varied and include increased catecholamine release, pulmonary vasoconstriction, pulmonary hypertension, and right ventricular failure.[8] Congestive heart failure, systemic hypertension, and sudden death in sleep are known to occur.[9] Fatalities may reflect the propensity of these patients to cardiac dys-

rhythmias.[10] The early to midportions of apneic periods are often accompanied by intense vagotonia manifested by sinus bradycardia, atrioventricular block, and prolonged asystoles. Increasing respiratory efforts then are associated with tachycardia, at times in conjunction with extrasystoles, ventricular couplets, and runs of ventricular tachycardia. The resulting 10-second or longer "tachy-brady" cycles offer strong presumptive evidence on ambulatory cardiac monitoring for a diagnosis of sleep apnea. Noninvasive indices of cardiac dysfunction and 24-hour urinary catecholamine levels provide useful information regarding severity of apnea and hypoxemia in the absence of other disease processes that could produce similar findings.[11] Glucose intolerance also can occur, perhaps in part as a result of stress and increased catecholamine release.

Somnolence, sleep attacks, and drowsiness-induced periods of automatic behavior appear to result de novo from obstructive sleep apnea in those individuals whose symptoms resolve after upper airway obstruction is eliminated.[3] Other patients with primary, preexisting narcolepsy or hypersomnolence unfortunately appear at greater risk of developing sleep apnea than the general population. The result is an atypical, progressive worsening of what otherwise would be a relatively static degree of impaired wakefulness from the time of early adulthood. Other symptoms include postdormital sleep drunkenness, headaches, and arousal difficulty. The latter phenomenon sometimes is associated with enuresis and adult-onset somnambulism; it also can prevent awakenings during apneas, such that many patients remain unaware of their breathing difficulties during sleep.

The patient with sleep apnea does not feel well, is forgetful and irritable, and becomes frustrated by his declining performance. His chronic sleepiness may lead to breakdown of marital, social, family, and occupational relationships. Yet, he may remain unaware of his sleep attacks and may not realize that his problems have resulted from drowsiness. Finally, a few patients are not excessively sleepy.

Specific manifestations of the upper airway obstruction per se include a distinctive, irregular pattern of snoring, in which pauses are terminated by inspiratory choking gasps. Spouses often are forced to sleep elsewhere, even in the absence of such characteristically loud snoring; the patient's struggling against respiratory obstruction can precipitate abrupt flinging of the arms and sudden sitting up or standing up in sleep. Some spouses suffer bruises and blackened eyes as a result. Postdormital throat pain, another complication of repeated airway closure, infrequently can be accompanied by swelling of the uvula.[12]

Why does the upper airway close during sleep? Expert otolaryngologic assessment of each patient is mandatory to avoid missing a correctable anatomic cause. Unfortunately, however, the yield is low, except in childhood when tonsil-loadenoidal hypertrophy is observed more frequently.[13] A few adults have micrognathia,[14] macroglossia, vocal cord paresis,[15] a congenitally malformed or hypotrophied glottis, hypopharyngeal masses or lymphomas involving Waldeyer's ring.[16] The majority have anatomically normal airways that they simply fail to coordinate properly during sleep.

The site of onset of occlusion may vary. Although a case of repetitive closure of the true vocal cords has been described,[17] other evidence would suggest that most patients experience su-

praglottic obstruction. Lateral cineradiographs have implicated apposition of the free edge of the soft palate against the posterior pharyngeal wall.[18] And electromyographic studies have indicated hypotonia in the muscles of the hypopharynx favoring passive collapse.[19] Other endoscopic investigations have been interpreted as showing active constriction of the hypopharynx.[20] The role of the tongue has been debated; genioglossus electromyographic activity has been reported to be diminished,[21] but endoscopy has not always confirmed involvement of the base of the tongue in pharyngeal closure.[20] It seems possible that the tongue instead might prolapse against the palate, thus sealing the oral airway.

In any event, a single mechanism may not apply to all cases. Also, the origins of the incoordination might lie elsewhere within the nervous system, but they remain to be defined.

Diagnosis

Sleep apnea is a syndrome, not a disease. It can occur at all ages. Severe degrees are most often noted in men older than 40 years, particularly when their habitus is similar to that of an ex-football player: stocky; often mildly to moderately obese; short, thick neck. Extreme obesity in such cases simply makes a bad situation worse by virtue of superimposed restrictive pulmonary dysfunction and other attendant complications.

Sleep apnea of hemodynamic consequence seldom develops in women unless they are obese; in our experience they usually have been postmenopausal.

Most patients have an unusually brisk gag reflex. Signs of otolaryngologic deformities, small ecchymoses or petechiae on the soft palate or uvula, and secondary cardiovascular sequelae should be looked for. A surprising number had signs of mitral valve prolapse, which appear particularly common in narcoleptics.[11]

Although most of our patients have family histories of sleep apnea or other disorders of impaired wakefulness, others have underlying structural disorders of the nervous system, e.g., carotid body chemodectoma, acoustic neuroma with brainstem compression, cervical cord injury, such that thorough neurologic assessment becomes essential. Myotonic dystrophy[22] and Down's syndrome[23] have been associated with sleep-induced ventilatory failure. Finally, sleep apnea can be mimicked by apneic seizures, especially in infancy. Unusual neuroendocrine abnormalities have characterized most of our patients with positive family histories,[24] whereas many patients with normal neuroendocrine function to date have had other underlying disorders in conjunction with negative family histories.

The importance of an interview with anyone who has observed the patient asleep cannot be overemphasized. Denial of illness or symptoms is common. A few awaken during periods of apnea, but many of these individuals are unaware of any choking sensation at such times. They instead may describe a sensation of smothering or chest discomfort that might suggest left ventricular failure or nocturnal angina, were it not for the immediate relief that they describe following a few deep breaths.[12] Some patients provide an additional diagnostic clue by stating that they feel they must make several forceful attempts to breathe before "anything happens," even when they cannot recall any sensation of blockage in the throat. Still other patients awaken with nonspecific anxiety; a few complain of repeated

arousals without distress, placing them at considerable risk of being treated with hypnotics.

The definitive laboratory study for diagnostic confirmation of sleep apnea is polysomnography, which involves polygraphic monitoring of sleep stages, air exchange, ventilatory effort, electrocardiogram, and arterial oxygen saturation.[12] Other parameters can be evaluated as well: movement of extremities, additional electroencephalographic monitoring, body temperature, nocturnal penile tumescence, and other physiologic correlates of sleep. Empiric treatment based solely on a history of loud snoring appears inadvisable. A few patients assessed in our laboratory have had characteristically noisy, irregular snoring with gasping sounds with minimal airway occlusion or arterial oxygen desaturation.

Treatment

A detailed review of treatment is beyond the scope of this discussion. Tracheostomy[25] is essential for most extremely severe symptoms in patients with a predominant element of upper airway obstruction, e.g., more than 300 episodes per night, unless correctable aggravating factors can be identified. Our center has utilized pharmacologic treatment, protriptyline, for a number of patients with less severe symptoms, but this patient population is unduly sensitive to the drug's arrhythmogenic properties. Extreme caution, frequently repeated polysomnograms, and 24-hour ambulatory cardiac monitoring are mandatory when the latter approach is attempted.[26] When tracheostomy appears warranted, it should be performed without delay. Inappropriate trials of other therapeutic measures with less likelihood of success simply leave the severely afflicted patient at risk of sudden death. Weight loss in the patient with repeated, serious episodes of upper airway obstruction may be virtually impossible to achieve, and it may not assure adequate reduction in the severity of sleep apnea.

Finally, the nature of the illness must be thoroughly understood before treatment is attempted. An obese, somnolent, cyanotic man with right heart failure would not benefit from tracheostomy if upper airway obstruction did not play an important role in sleep-induced ventilatory failure. Similarly, stimulation of ventilatory drive often achieved with medroxyprogesterone acetate will have minimal impact in patients whose basic problem is repetitive upper airway obstruction during sleep.[27]

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