Annu. Rev. Med. 1999. 50:387–400

SLEEP AND ITS DISORDERS

A. N. Vgontzas, MD and A. Kales, MD

Department of Psychiatry, Penn State University, College of Medicine, Hershey, Pennsylvania 17033; e-mail: axv3@psu.edu

KEY WORDS: insomnia, sleepwalking, night terrors, nightmares, narcolepsy, sleep apnea

ABSTRACT

Sleep disorders are very prevalent in the general population and are associated with significant medical, psychological, and social disturbances. Insomnia is the most common. When chronic, it usually reflects psychological/behavioral disturbances. Most insomniacs can be evaluated in an office setting, and a multidimensional approach is recommended, including sleep hygiene measures, psychotherapy, and medication. The parasomnias, including sleepwalking, night terrors, and nightmares, have benign implications in childhood but often reflect psychopathology or significant stress in adolescents and adults and organicity in the elderly. Excessive daytime sleepiness is typically the most frequent complaint and often reflects organic dysfunction. Narcolepsy and idiopathic hypersomnia are chronic brain disorders with an onset at a young age, whereas sleep apnea is more common in middle age and is associated with obesity and cardiovascular problems. Therapeutic naps, medications, and supportive therapy are recommended for narcolepsy and hypersomnia; continuous positive airway pressure, weight loss, surgery, and oral devices are the common treatments for sleep apnea.

NORMAL SLEEP

Humans spend at least one third of their lives asleep, yet there is little understanding of why we need sleep and what mechanisms underlie its capacities for physical and mental restoration. However, there has been a significant increase of empirical knowledge that is useful in the evaluation and management of most sleep complaints and their underlying disorders.

The interaction of circadian effects, i.e. the usual time to go to sleep and the amount of prior wakefulness (homeostatic response), determines the onset and amount of sleep (1). Natural sleep-wake rhythms cycle at about 25 h rather

0066-4219/99/0201-0387$08.00

than coinciding with the solar 24-h schedule (2). As a result, many persons depend on external cues to keep their diurnal cycle "on time." The normal diurnal clock resists natural changes in its pattern by more than about 1 h per day, which explains the sleep difficulties that usually accompany adaptation to new time zones or switches in work shifts.

Individuals differ considerably in their natural sleep patterns. Most adults in nontropical areas are comfortable with 6.5 to 8 h daily, taken in a single period. Children and adolescents sleep more than adults, and young adults sleep more than older ones. Normal sleep consists of four to six behaviorally and electroencephalographically (EEG) defined cycles, including periods during which the brain is active (associated with rapid eye movements, called REM sleep), preceded by four progressively deeper, quieter sleep stages graded 1 to 4 on the basis of increasingly slow EEG patterns (3). Deep sleep (stages 3 and 4) gradually lessens with age and usually disappears in the elderly.

SLEEP DISORDERS

Sleep disorders are very prevalent in the general population and are associated with significant medical, psychological, and social disturbances (4, 5). Insomnia, the most common sleep disorder, most often reflects psychological disturbances. Excessive daytime sleepiness is the predominant complaint of most patients evaluated in sleep disorders clinics and often reflects organic dysfunction. Narcolepsy, hypersomnia, and sleep apnea are the most common disorders associated with excessive daytime sleepiness. Narcolepsy and hypersomnia are chronic brain disorders with an onset at a young age; sleep apnea occurs predominantly in middle-aged men and (to a lesser degree) women and is associated with obesity and cardiovascular problems. The parasomnias, including sleepwalking, night terrors, and nightmares, have benign implications in childhood but often reflect psychopathology or significant stress in adolescents and adults and organicity in the elderly.

Sleep complaints are common at all ages and range widely in their nature and biologic importance. It is the task of the physician and the sleep specialist to distinguish trivial from serious problems and to appraise their medical importance. Accordingly, the first step in evaluation is a thorough history (Table 1).

Insomnia

Insomnia is the most common sleep complaint, affecting as many as one fifth of all patients who consult general physicians (6, 7). It occurs more frequently with age and in women. Short-term insomnia often results from stressful life events or the recent onset of medical disorders. Chronic, severe insomnia, by contrast, often becomes a central complaint and a distinct disorder itself. It ap-

Table 1 Guidelines for taking a sleep history

Define the specific sleep problem
Assess the onset and clinical course of the condition
Evaluate 24-h sleep/wakefulness patterns
Question the bed partner
Determine the presence of other sleep disorders
Obtain a family history of sleep disorders
Evaluate the personal and societal impact of the sleep disorder

pears that chronic insomnia not only subjectively but also pathophysiologically can become a separate disorder from the underlying cause, usually of a psychological nature.

CLINICAL FEATURES Most patients with chronic insomnia report difficulty in falling asleep. This complaint may exist alone or in combination with difficulty in staying asleep or early final awakening (6, 7). In contrast to normal sleepers, insomniacs feel worse in the morning than late at night and arise feeling sleepy, groggy, physically and mentally fatigued, anxious, and irritable. Characteristically, these symptoms persist during the day and contribute to feelings of fatigue and depression. As bedtime approaches, insomniac patients become more tense, anxious, and worried about health, death, work, and personal problems. Many such persons show autonomic hyperactivity before or during sleep, evidenced by increased heart rate, muscle tension, increased body temperature, and peripheral vasoconstriction (8).

ETIOLOGY Acute or short-term insomnia can be associated with a variety of situational problems (work-related, interpersonal, or financial difficulties) or with medical problems, including pain, cardiopulmonary and gastrointestinal disorders, thyrotoxicosis, or the febrile prodromes to influenza. Various drugs, such as caffeine, nicotine, alcohol, steroids, amphetamines, stimulating antidepressants, central adrenergic blockers, and bronchodilators, can impair both falling asleep and staying asleep.

Notwithstanding the above possible causes, psychological distress is the most common cause of chronic insomnia (6, 7). Some degree of psychopathology is present in almost all chronic insomniacs, even in those diagnosed with "primary insomnia" (9). Most insomniacs are diagnosed with minor psychiatric disorders, such as dysthymic or anxiety disorders, or even subsyndromal states, e.g. compulsive personality traits (9, 10). Patients with longstanding sleep difficulties show less than adequate coping mechanisms for stressful life events. Many display specific personality patterns characterized by chronic anxiety, rumination, depression, inhibition of emotions, and an inability to discharge anger outwardly (11). They generally handle external stress and con-

flicts by internalizing their emotions, generating a combination of emotional arousal and physiological activation. This mental and physiological hyperarousal leads to difficulty in initiating sleep, whether at the beginning of the sleep period or when returning to sleep following awakenings. Fear of sleeplessness further intensifies the emotional arousal. All of these factors, through behavioral conditioning, lead to a vicious circle that perpetuates insomnia.

DIAGNOSIS Evaluation of transient or situational insomnia focuses on identifying stressful factors and providing reassurance about those that interfere with restful sleep. The short-term use of a sedative hypnotic may be indicated. The evaluation of chronic insomnia should include a complete history that assesses various sleep, drug, medical, and emotional factors (Table 1) (12). It is important to assess sleep/wakefulness patterns on a 24-h basis, particularly in the elderly. The high prevalence of insomnia affecting this age group results in their ingesting the highest proportion of all the sedatives prescribed in the United States.

In taking the general medical and drug history, the physician should identify conditions and medications known to be associated with disturbed sleep. Although sleep apnea and nocturnal myoclonus only rarely cause the primary complaint of insomnia, symptoms of these disorders necessitate a detailed history, including obtaining information from the bed partner. Most importantly, underlying emotional factors contributing to chronic sleep difficulty must be identified.

MANAGEMENT Most sleep specialists advocate a multidimensional approach, including general measures for improving sleep hygiene and lifestyle; supportive, insight-oriented, or behavioral psychotherapeutic techniques; and hypnotic or antidepressant medication (6).

Measures for improving sleep hygiene and lifestyle include regularizing the patient's daily activities schedule, emphasizing that the bedroom should be used for rest and sleep rather than conflict and worry, and improving the sleep environment by minimizing noise and disruptions. Also, regular exercise, not close to bedtime, has been shown to increase early-night slow-wave sleep in normal sleepers. In the elderly, special instructions include education regarding age's effects on sleep patterns; discouraging multiple naps (but, if taken, including nap sleep in the 24-h total for sleep time); and suggesting daytime activities, hobbies, and special interests.

In counseling the insomniac, it is helpful to explain how anxiety participates in the vicious circle that exacerbates and maintains the condition. Patients can be taught to reduce stress and anxiety by managing emotions more effectively through pertinent stress management techniques (Table 2) (6, 7). Patients with severe, chronic insomnia may also benefit from psychotherapy that focuses on "here and now."

Table 2 General measures in treating insomnia

Recommendation	Implementation
Sleep-hygiene measures	Minimize use of caffeine, cigarettes, stimulants, and other medications
	Recognize that alcohol may cause fragmentation of sleep
	Maintain a regular sleep schedule
	Exercise regularly and not close to bedtime
	Avoid napping, particularly after 2:00 p.m.
Stress-management measures	Recognize association between stressful events and sleeplessness
	Ventilate conflicts and anger to avoid internalization
	Address daily worries a few hours before bedtime
	Be tolerant of occasional sleeplessness
	Avoid rumination over sleep difficulty
	Try relaxation techniques

Benzodiazepine hypnotics are widely used in the pharmacologic treatment of insomnia, primarily because of their greater margin of safety and degree of effectiveness. The choice of a specific benzodiazepine hypnotic is based on its side-effect profile and the therapeutic needs of the patient. Benzodiazepines with a long half-life, primarily associated with daytime sedation, produce few side effects in terms of withdrawal difficulties and drug dependence. Because of the long duration of their action, they can be used intermittently to reduce tolerance and dependency. In the elderly, smaller doses of benzodiazepines with an intermediate half-life are more appropriate. Benzodiazepines with a short half-life are more likely to cause rapid development of tolerance, withdrawal difficulties including rebound insomnia (13), and daytime hyperexcitability phenomena, and their use is rather discouraged.

The use of antidepressants as "hypnotics" in insomniacs without a diagnosis of major depression appears to have expanded recently because insomnia is often a chronic, nonremitting disorder, and benzodiazepines are not recommended for long-term use. The sedative qualities of the old tricyclics, as well as of the newer antidepressants (e.g. trazodone, nefazodone), reduce the physiological and mental hyperarousal of the insomniac at night. In contrast, stimulant antidepressants, such as fluoxetine, may have sleep-disturbing effects when given at bedtime (14). Neuroleptics with sedative effects are preferred for psychotic patients who have insomnia. Finally, melatonin does not appear to be beneficial in the large majority of chronic insomniacs.

Parasomnias: Sleepwalking, Night Terrors, and Nightmares

The parasomnias are common. About 15% of children, for example, have had at least one sleepwalking episode, and 1–3% report night terrors (7). Night-

mares are a current problem for approximately 5% of the general population and a past problem for another 5%.

CLINICAL FEATURES Sleepwalking (somnambulism) occurs in episodes lasting several minutes (7). During this period, patients generally have blank expressions, behave as if indifferent to the environment, and exhibit low levels of awareness and reactivity, manifested by clumsiness and purposeless activity. They rarely recall the events upon awakening. Night terror episodes have the additional and often dramatic characteristics of extreme vocalization and movement, excessive autonomic discharges, and panic. Sleepwalking and night terrors appear to fall along a pathophysiologic continuum and share many clinical and physiologic similarities.

Nightmares are usually associated with fears of attack, falling, or death, and in many patients the nightly themes recur (7). Nightmares occur during REM sleep. They may occur at any time during the night but are more likely during the later part, when REM-sleep periods increase in length. Patients typically report considerable sleep disruption and have vivid recall of the dream content—characteristics that clearly differentiate nightmares from the more dramatic but forgotten night terrors. Recently, a REM-sleep behavior disorder has been described that is associated with dream-enacting behavior, often resulting in violent acts or injuries (15).

ETIOLOGY Genetic, developmental, organic, and psychological factors have been proposed as causes of parasomnias (7). There is an increased familial incidence, and maturational components are implicit in the common pattern of onset in childhood and termination by late adolescence. Febrile episodes and brain tumors occasionally have been implicated, particularly in the elderly, but are rare causes. Somnambulism-like episodes also have been pharmacologically induced by lithium, high doses of neuroleptic drugs, and triazolam. Furthermore, withdrawal of certain drug treatments, resulting in an increase in REM sleep (REM rebound), may be associated with a temporary increase in the intensity of dreaming and the possible occurrence of nightmares. REM behavior disorder is more prevalent in advanced age and is often associated with neurological disorders. However, most cases are considered idiopathic (15).

Psychological abnormalities seldom accompany early childhood parasomnias. When the disorders begin in late childhood or adolescence or resurface in adulthood, they usually are associated with psychological disturbances and tend to worsen under stress.

DIAGNOSIS Sleepwalking or night-terror–like activity that begins in middle or old age should prompt the physician to rule out brain tumor, stroke, or other cerebral disorders, including sedative intoxication (7). Night terrors should be differentiated from temporal lobe epilepsy, although the latter rarely expresses

itself during sleep. Most "sleepwalking" in elderly persons reflects episodes of confusion and nocturnal wandering rather than a parasomnia.

A careful drug history is important in the evaluation of persons who have nightmares. This is because administration or withdrawal of certain drugs, including alcohol, induces marked changes in the frequency, intensity, and disturbing content of dreaming. Many patients are unaware of such connections.

Adult patients with chronic parasomnias commonly show some degree of psychopathology warranting psychiatric consultation (7). Some adult patients with a history of childhood parasomnias may have their disorder resurface, particularly under stressful conditions and when adequate coping mechanisms are lacking. It is important to differentiate night terrors, and particularly sleepwalking, from hysterical dissociative phenomena such as amnesia, fugue states, and multiple personalities. Most patients experiencing the latter conditions demonstrate complex and purposeful behaviors and describe episodes lasting up to several hours as opposed to the minutes-long duration of sleepwalking. Lastly, when there is secondary gain, malingering as a cause of sleepwalking-type behavior should be considered.

Sleep laboratory recordings, including audiovisual monitoring, are not routinely recommended in evaluating parasomnias except when nocturnal epilepsy is strongly suspected or when monitoring is needed to differentiate parasomnias from dissociative phenomena. Also, sleep-laboratory documentation of sleep-related violent behavior may be useful, particularly in cases involving litigation.

MANAGEMENT The most important consideration in managing episodic sleepwalking or night terrors is protection from injury (7). Episodes should not be interrupted, since intervention often confuses and frightens the patient even more.

Minimizing children's exposure to potentially traumatic experiences, such as terrifying movies and television programs or frightening bedtime stories, can help reduce the frequency of nightmares. Parents should be counseled and reassured that affected children usually outgrow the conditions by late adolescence, if not sooner.

Drugs that suppress stage 3 and stage 4 sleep, such as diazepam and flurazepam, may be prescribed as adjuncts to psychotherapy for adults who experience night terrors or sleepwalking. Psychotropic medication is not recommended in children except in severe cases. Clonazepam appears to be useful in REM behavior disorder (15). Depression, especially in men with nightmares, deserves special attention because these persons may be at higher risk for suicide. Overtly psychotic behavior associated with nightmares is best treated with neuroleptic drugs.

Table 3 Differentiation among disorders of excessive sleep

Characteristics	Narcolepsy	Idiopathic Hypersomnia	Psychogenic Hypersomnia	Obstructive Sleep Apnea
Sleepiness	Paroxysmal	Constant	Variable	Increases with severity
Sleep Attacks	Relatively brief and irresistible	Prolonged and rather resistible	Usually not present	Increases with severity
Cataplexy	Usually	Absent	Absent	Absent
Nocturnal sleep	May be disrupted	Prolonged and deep	Disrupted	Fragmented
Usual onset	20s	20s	Variable	40–55
Heredity factor[a]	+++	++	?	++
Psychopathology	Secondary or independent	Secondary or independent	Primary	Secondary
Loud snoring/ breath cessation	Occasional	Occasional	Occasional	Usual
Obesity	Sometimes	Sometimes	Sometimes	Usual and severe
Hypertension	Infrequent	Mild hypotension	Increased compared with healthy controls	Frequent
Sex distribution	Equal	Equal	Slightly more females	Men:women (4:1)

[a]+++, strong; ++, moderate; ?, unknown

Disorders of Excessive Daytime Sleepiness

Excessive daytime sleepiness is a significant problem in about 5% of the general population (4) and is the chief complaint of the majority of patients in sleep disorders clinics (16). Sleep apnea, narcolepsy, idiopathic hypersomnia, and psychogenic hypersomnia are the four most common diagnoses among sleep-disorders clinic patients presenting with excessive daytime sleepiness (Table 3) (16). In the general population, frequent sources of daytime fatigue are sleep apnea, obesity, sleep deprivation, and adverse drug reactions.

NARCOLEPSY Narcolepsy is a serious clinical problem that usually begins before age 25 and persists throughout life. The estimated incidence is about one person per thousand population, with men and women equally affected.

Clinical Features Narcolepsy is characterized by excessive daytime sleepiness and irresistible sleep attacks that usually occur in conjunction with one or more of the three auxiliary symptoms: cataplexy, sleep paralysis, and hypnagogic hallucinations (17–19). The sleep attacks may last from a few seconds to half an hour and may be precipitated by sedentary, monotonous activity of any kind, including driving, sitting in lectures, or even eating meals. Excessive

daytime sleepiness and sleep attacks are the first manifestations of this disorder, with the auxiliary symptoms appearing several years later.

About three fourths of narcolepsy patients have cataplexy, a brief and sudden loss of muscle control without loss of consciousness (17–19). The severity of cataplectic attacks ranges from light knee buckling or drooping of the jaw to complete collapse. Episodes are precipitated by strong emotions such as fear, surprise, laughter, or anger.

Sleep paralysis and hypnagogic hallucinations are short (a minute or less) episodes that occur during the transition between wakefulness and sleep (17–19). Sleep paralysis consists of a transient experience of being unable to move any muscle (breathing persists). Hypnagogic hallucinations are vivid hallucinations (usually visual or auditory) perceived particularly while drifting into sleep. These two symptoms are quite prevalent in the general population and thus are of limited diagnostic value for narcolepsy. About half of narcoleptic patients complain of disturbed nocturnal sleep, which appears to be primarily a direct effect of the disorder.

Etiology Family studies showing a 10–50% incidence of affected first-degree relatives and a high incidence of HLA concordance (almost 100% of patients with narcolepsy and cataplexy) imply a strong genetic predisposition (20). The pattern must be multifactorial, however, since monozygotic twins have a high rate of discordance. It has been proposed that the combination of genetic factors and stress, including emotional stress, is what leads to the manifestation of narcolepsy. The sleep attacks and other auxiliary symptoms appear to be closely related to aberrations in the neurophysiologic mechanisms of REM sleep, since REM sleep comes early (within 5–10 min after sleep onset) in a large proportion of narcoleptic sleep patterns, in contrast to normal sleep patterns, in which the first REM period occurs after about 70–90 min of nonrapid-eye-movement (NREM) sleep.

Psychopathology is frequently present in narcoleptics but appears to be a secondary reaction to the disorder.

Diagnosis Narcolepsy must be differentiated from other organic disorders of excessive daytime sleepiness, e.g. sleep apnea and idiopathic hypersomnia (17–19). Infrequently, it should be differentiated from hysteria (rarely expressed as brief, episodic hypersomnia) and seizures (characterized by automatisms but not brief sleep states). A history of cataplexy, which is considered a pathognomonic symptom of narcolepsy, makes the diagnosis certain (12). In questionable instances, especially in the absence of clear-cut cataplexy, multiple daytime nap recordings may detect sleep-onset REM periods (SOREMs) and/or extremely short sleep latencies in narcoleptics. An average sleep latency of less than 5 min and at least two sleep-onset REM periods in

five 20-min opportunities to sleep between 10:00 AM and 6:00 PM increase the diagnostic certainty (21).

Management One must advise patients gently but honestly that this is a frequently misunderstood chronic disorder. All concerned must learn that narcolepsy is a physical illness and not under voluntary control (17–19). Patients should be warned about the potential dangers of driving or other activities requiring full alertness and muscle control. Physicians should check with their local department of motor vehicles regarding the legal responsibility for reporting narcolepsy.

Therapeutic naps enhance daytime alertness and reduce the need for high doses of stimulants. Pharmacotherapy involves separate treatments for the sleep attacks and cataplexy (22). Methylphenidate is the preferred drug for treating sleep attacks because of its prompt onset of action and relatively few side effects. Other potential agents include amphetamines, mazindol, selegiline, and modafinil. Modafinil, recently introduced in the United States, is reported to be as effective as the classical stimulants with the advantage of decreased potential for dependence and abuse.

Tricyclic antidepressants, including imipramine and clomipramine, can be helpful in preventing cataplexy (18, 19). Anticholinergic phenomena, impotence, and increased sleepiness are frequent side effects of these medications. Gamma-hydroxybutyrate (GHB) has been found effective in controlling cataplexy; more recently, serotonin-uptake inhibitors such as fluvoxamine and fluoxetine have proven to be effective anticataplectic medications. The combination of stimulants and nonsedating antidepressants, e.g. serotonin-uptake inhibitors, can have a syngeristic effect for both sleep attacks and auxiliary symptoms.

IDIOPATHIC (PRIMARY) HYPERSOMNIA Hypersomnia is a disorder of excessive diurnal and nocturnal sleep. Its prevalence in the general population is not known. However, based on clinical samples, the ratio of idiopathic hypersomnia to narcolepsy ranges from 1/1 to about 1/5, a variation reflecting difficulties in defining the disorder.

Clinical Features The age at onset varies from the first to the fifth decade with a peak in the second decade (17). Idiopathic central nervous system (CNS) hypersomnia is characterized by virtually constant somnolence, lengthy but nonrefreshing naps, prolonged night sleep, major difficulty with morning awakening, and sometimes sleep drunkenness. It is possible that with the increase of sleep-inducing changes in the work and daily living environments, i.e. automation and less physical activity, even relatively mild cases and those with a later age of onset come to the clinician's attention nowadays. The condition tends to be chronic over the life span.

Etiology As "idiopathic" denotes, the cause of this type of hypersomnia is not clear. Nonetheless, several studies have shown a familial incidence. Studies of HLA antigens in hypersomnia have demonstrated that it is associated with HLA-DR5 (23). The neurochemical basis of hypersomnia appears to involve increased dopamine turnover and/or subtle hypocortisolism and inferred deficiency of central corticotropin releasing hormone (CRH).

Diagnosis The differential diagnosis must consider narcolepsy without cataplexy. In such cases, daytime sleep episodes are usually both irresistible and refreshing, and a mean sleep latency of 5 min or less along with at least two SOREM episodes are documented on multiple daytime naps.

Psychogenic hypersomnia may be difficult to differentiate from idiopathic CNS hypersomnia. Complaints of prolonged night sleep and daytime somnolence may be similar. However, in subjects with a psychogenic hypersomnia, hypersomnolence is variable, psychopathology is primary, and an association between hypersomnolence and psychiatric symptoms is more apparent. Also, sleep-laboratory testing in patients with psychogenic hypersomnia, compared with healthy controls, indicates increased nighttime sleep latency and wakefulness after sleep onset, as well as increased sleep latencies during daytime testing.

Management Hypersomnia can be disabling and is not always well controlled by stimulant medication or therapeutic naps. Nonetheless, the mainstay of treatment is stimulant medication at about the same dose levels as in narcolepsy. In most cases the stimulant medication should be taken immediately on awakening, especially when sleep drunkenness is present.

SLEEP APNEA This disorder affects men more than women and is often associated with obesity and hypertension (19, 24, 25). The prevalence of sleep apnea is about 4% in the general male population and tends to increase with age (26). However, the clinical significance (severity) of the disorder decreases with age. The spectrum of disordered breathing in sleep extends from simple loud snoring to severe apnea with hundreds of apneic events and a significant drop of oxygen saturation.

The clinical diagnosis of sleep apnea syndrome includes quantification of the number of apneic events, the degree of associated oxygen desaturation, and the patient's total clinical picture. Apneas are characterized as central (i.e. neurogenic), obstructive (peripheral), or mixed. In central apnea, which is rare in a clinical setting, breathing efforts cease or become minimal. In obstructive apnea, the most common form of sleep apnea, respiratory efforts persist and even become unusually prominent but are rendered ineffective by upper airway blockage. The obstructive nature of the apneic events does not preclude

the potential importance of brain mechanisms in the pathophysiology of this disorder.

Clinical Features Patients with obstructive sleep apnea characteristically provide a history of excessive daytime sleepiness, sleep attacks, and repetitive nocturnal breath cessations followed by brief arousals (probably related to choking or hypercapnia); breathing resumes accompanied by loud snorting and gasping sounds (12, 19, 24, 25). The disorder in men usually has its onset before the age of 40 and peaks at 55.

In most cases, the patient's bed partner or roommate observes episodes of breath cessation followed by snorting and gasping. Some patients become self-aware of nighttime choking experiences. Excessive body movements during sleep, diaphoresis, early morning headaches, secondary enuresis, and sexual impotence may occur.

Most patients with symptomatic obstructive sleep apnea have at least moderate systemic hypertension and obesity. The hypoxia and carbon dioxide retention, as well as the sleep fragmentation associated with the nocturnal apneic events, eventually can induce systemic hypertension, dysregulation of glucose metabolism, weight gain, and persistent cardiac dysrhythmias as well as cognitive impairment, psychological distress, and psychosocial disruption. Less frequently, sleep apnea is associated with polycythemia, pulmonary hypertension, cardiomegaly, and right-sided heart failure.

Etiology The etiology of sleep apnea is unknown. Obesity appears to be a strong risk factor for sleep apnea, and the roles of familial predisposition and of a menopausal lessening of the respiratory-stimulating effects of progestational hormones are increasingly recognized. Clinical inspection usually detects no anatomic abnormalities of the upper airway but smaller pharyngeal areas have been demonstrated in some cases. In children, however, tonsillar/adenoid enlargement is a frequent cause of sleep disordered breathing. Alcohol ingestion, sedatives, and sleep deprivation can increase the number and severity of sleep-apneic events. Finally, from a biochemical standpoint, the pro-inflammatory cytokines tumor necrosis factor a (TNFa) and interleukin-6 (IL-6) have been suggested in the pathogenesis of sleep apnea and excessive daytime sleepiness (27).

Diagnosis Thorough assessment of suspected sleep apnea begins with a complete sleep history (see Table 1). When a patient reports excessive daytime sleepiness, sleep attacks, or unusual snorting or gasping during sleep, families or roommates should be questioned about severe snoring or interrupted breathing (12, 17). A complete medical history and a physical examination should follow, as well as measurements of hematocrit, thyroid function, and electrocardiography. A family history of loud snoring or excessive daytime sleepi-

ness may be present. The patient's psychosocial and vocational functioning should be assessed. Ultimately, the clinician depends on a sleep-laboratory evaluation with recording of respiration and oximetry to confirm the diagnosis and its severity.

Management The decision to treat is based on an integration of clinical and laboratory findings. The presence of daytime fatigue or sleepiness, cardiovascular problems (e.g. hypertension), an apnea/hypopnea index of more than 20, and/or hemoglobin oxygen desaturation of more than 10% usually necessitate a therapeutic intervention (19). However, even simple snoring warrants treatment when associated with sleep fragmentation and daytime sleepiness (26, 28). A more aggressive approach is recommended for the young symptomatic patient (less than 55 years) than for the asymptomatic elderly, even with a high apnea/hypopnea index (26). Weight loss and the use of continuous positive airway pressure (CPAP) appear to be the most effective and frequently recommended modalities. However, many patients are not able to lose weight, and compliance problems with CPAP use are increasingly recognized. Dental appliances or surgery [uvulopalatopharyngoplasty (UPP)] are alternative options if weight loss or CPAP fails. However, the patient should be informed about the relatively high failure rate of these treatments, particularly in those with severe apnea and morbid obesity. Symptomatic central sleep apnea may be treated with CPAP or medication, such as acetazolamide or fluoxetine.

Steps should be taken to improve underlying medical illnesses or complications such as congestive heart failure, chronic reversible respiratory disorders, and metabolic abnormalities that could impair upper airway functioning. Drugs that depress the central ventilatory drive, such as sedative/hypnotics, barbiturates, narcotics, sedating analgesics, and alcohol, should be avoided. Finally, the physician should advise the patient, his family, and, if appropriate, his employer that the excessive daytime sleepiness and associated symptoms are beyond volitional control and are likely to improve.

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