

CHAPTER 23.

Sleep Disorders

A significant number of people suffer with problems sleeping at night or difficulty staying awake during the day (excessive daytime sleepiness). Ten percent of general population reports excessive daytime sleepiness (EDS). This disorder has been implicated in several major industrial accidents (Three Mile Island, Exxon Valdez, Chernobyl, Bhopal) and is major factor in motor vehicle accidents. An estimated 15% of the general population has serious sleep disorders, and 35% have transient but frequently recurrent sleep difficulties. Sleep disorders can have serious medical, social, occupational, and personal ramifications. The problem of sleep disorders has been systematically studied in specialized sleep laboratories. This research, which includes carefully monitored all-night electroencephalographic (EEG) recordings (polysomnography), has led to increase in knowledge of normal and abnormal sleep patterns. In the sleep laboratory EEG electrodes and physiologic sensors are used (electrodes over the outer canthi of the eyes to record eye movements, electrodes over the chin to measure mentalis muscle tone, sensors to measure respiratory rate and air flow, and an electrocardiogram monitor). The polysomnogram (PSG) allows careful minute-to-minute analysis of sleep-wake pattern, respiratory function, and muscle activity. Sleep patterns are defined on the basis of behavioral and physiological parameters (EEG, electro-oculogram, EMG, respiratory and cardiac factors).

PHYSIOLOGY OF SLEEP

Sleep is normal periodic interruption of consciousness that is necessary for restoration of mental and other body functions. Biological functions of sleep include – brain tissue restoration, energy conservation, memory consolidation. Sleep onset occurs when there is decrease in activity in reticular activating system (largely from decrease in environmental stimulation). As drowsiness occurs, certain ascending sleep-inducing neurons are activated, and these maintain sleep. Sleep is not a single event; it is divided into five stages:

Stage I. This represents transition between full wakefulness and sleep. During this stage, reactivity to external stimuli is reduced. Patients feel awake, but memory and thinking are impaired. EEG shows low amplitude, slower voltage pattern than in awake state. Muscle tone is slightly reduced. This stage lasts 1 to 7 minutes.

Stage II. This is first definite sleep stage (light sleep). Muscle tone is reduced compared with stage I, and eye movements are absent. EEG shows low-amplitude, mixed-frequency pattern with predominant pattern being 4 to 8 cps (theta wave) activity. Sleep spindles (bursts of 12 to 14 cps rhythmical activity) and K-complexes (high-voltage, mixed slow and sharp waves) are seen. The onset of stage II is usually within 7 to 30 minutes.

Stages III and IV. These stages represent deep sleep and are usually entered within 30 to 40 minutes. Muscle tone is reduced, and eye movements are absent. EEG shows high-amplitude slow (delta) waves, which are less than 4 cps.

Stage V. This is characterized by marked reduction in muscle tone (hypotonus), although facial and occasional limb twitching can occur. The initial REM sleep episode occurs 60 to 90 minutes after sleep onset. REM sleep accounts for 20 to 25% of sleep time. Rapid eye movements (REM) are most characteristic. EEG is similar to stage I with low-amplitude, mixed-frequency pattern. Active dreaming takes place during REM sleep and is more emotionally

charged, complex and bizarre as contrasted with non-REM dreams which are more realistic. During REM sleep the following physiological changes occur: (1) autonomic function cycles irregularly as result of changes in balance between sympathetic and parasympathetic tone; blood pressure, heart rate, and cardiac output increase; (2) respiratory activity changes (it can become irregular, and increase or decrease in frequency); (3) thermoregulation is impaired; (4) cerebral blood flow and brain metabolism increase (at times even exceeding waking levels); and (5) penile erection occurs. REM sleep can be classified into two stages – tonic and phasic. In phasic REM, there is rapid eye movements in all directions with wide phasic fluctuations in blood pressure and cardiac rate and irregular respiration pattern. In the tonic phase, there is reduced muscle tone (atonia) and reduced deep tendon reflexes. During non-REM and phasic REM sleep, there is increase in parasympathetic activity; whereas during tonic REM sleep, sympathetic activity becomes unstable which may cause marked blood pressure and heart rate increases.

Stages I, II, III, and IV collectively are called non-rapid eye movement (NREM) sleep. During these stages, EEG slows and amplitude of waves progressively increase. The production of growth hormone is most active early in night when slow-wave sleep predominates. During REM sleep, EEG shows increased rhythm and reduced waveform amplitude. During NREM sleep, general trend is for reduced body function, and during REM sleep, there is increased body function with exception of muscle tone (hypotonia).

Through normal night's sleep, a person's sleep fluctuates between the various stages. Stages III and IV are more frequent early in the night, and REM sleep is more common later in night and toward morning. Several short nocturnal awakenings per night are normal. The general pattern of sleep changes throughout life. Infants spend 50% of night in REM sleep, but by age 20, this drops to 20% and stays at this level throughout life. In general, sleep lightens with age, total sleep time decreases, nocturnal awakenings increase, and stage IV deep sleep decreases substantially with aging.

Other than the normal change in sleep patterns with age, it is important to realize that each person has rather specific sleep need before he or she feels refreshed and can perform efficiently. In some persons (short sleepers) this may be only 3 or 4 hours, whereas in others (long sleepers) 10, 12, or even more hours a day are required. Also, some people's biologic clocks are set so that they function better at night and prefer to sleep when it is light; the reverse is also true. Based upon sleep habit, two types of individuals are defined: 1) evening people ("owls") have difficulty awakening early and are tired and fatigued in the morning but are energetic later in the day. They sleep late and wake up late; 2) morning people ("larks") awaken early and function best in the morning, but must go to sleep early and fade out by the evening. There are physiological differences in the thermoregulatory patterns of these two types of individuals.

The neural substrate of the sleep-wake cycle is complex. Wakefulness is maintained via ascending reticular activating system (ARAS) and thalamic projection system as they stimulate the cortex. If ARAS activity is high, sleep is not possible. If ARAS activity is reduced, transition to sleep state is possible. NREM sleep requires reduced ARAS activity and involvement of serotonergic system of pontine raphe nuclei. For REM sleep to occur there must be interaction between adrenergic (norepinephrine) nucleus ceruleus and cholinergic pontine gigantocellular tegmental field. Insomnia can be induced by lesions of serotonergic cells of raphe nuclei and by inhibition of serotonin synthesis and reversed by administration of substances that enhance serotonin synthesis. Sleep-enhancing neurons are located in preoptic

anterior hypothalamus, whereas waking-enhancing neurons are located in posterior hypothalamus.

SLEEP HISTORY

History taking in patients with sleep disturbance is quite specialized and requires detailed inquiry. Medical illness, psychiatric difficulties, and environmental factors can contribute to sleep disturbances and must be carefully reviewed both with the patient and, if possible with patients bed partners.

Specific Complaint

Most patients complain of either insomnia (difficulty with onset or maintenance of sleep) or excessive daytime sleepiness. The physician should carefully outline- the complaint.

- *Duration.* A sleep disturbance of short duration can mean recent emotional or medical problems, whereas long-term problem usually indicates a constitutional sleep disorder.
- *Age at onset.*
- Is the complaint daily or intermittent?

For a complete profile of 24-hour sleep-wake pattern, see Box 23-1.

LABORATORY EVALUATION

The laboratory evaluation is based on the following:

- General medical evaluation: diabetes, thyroid, blood sugar, and other endocrine conditions
- Psychiatric evaluation
- Polysomnography
- HLA typing for HLA-DR2 and DQw6 in suspected patients with excessive daytime sleepiness (narcoleptics).

CLINICAL SLEEP DISORDER SYNDROMES

Box 23-2 lists the clinical syndromes.

Two terms should be defined: (1) dyssomnias are disturbances in the amount, quality, or timing of sleep (difficulty initiating and maintaining proper sleep or wakefulness) and (2) parasomnias are disturbances relating to abnormal events occurring during sleep, such as sleepwalking, night terrors, and nightmares.

- I. Disorders in initiating or maintaining sleep (insomnia)
 - A. Psychophysiologic: These are disorders of somatized tension and learned sleep.
 1. Transient and situational. The person who is currently undergoing an acute emotional upset will experience (a) difficulty falling asleep, (b) multiple nocturnal arousals, (c) early morning awakening, and (d) subsequent daytime fatigue (not sleepiness). The condition is usually short-lived and resolves as the crisis passes. Treatment should be emotional support and possibly mild tranquilization or sedation at night with a benzodiazepine. These situations are more frequent in highly emotional people. On occasion acute or subacute insomnia is the initial symptom of more serious psychiatric illness or a physical illness such as a metabolic encephalopathy, early cardiac or pulmonary failure, and so on.

2. Persistent. If symptoms continue for more than three weeks after crisis resolution, either the disorders discussed below or the possibility that the patient has conditioned himself or herself to the insomnia should be considered.

B. Psychiatric disorders

1. These include personality disorders such as obsessive, hypochondriacal, or neurotic personality in which anxiety is prominent.
2. Affective disorders. Depression and mania are common affective disorders.
 - a. Depression. The patient easily falls asleep but has frequent arousals and early morning awakening.
 - b. Mania. These patients have trouble falling asleep (sleep-onset insomnia) and sleep only a short time.
3. Schizophrenia. With psychotic decompensation there is severe sleep-onset insomnia as well as difficulty maintaining sleep.

For the emotionally based insomnias it is useful to review the sleeping environment carefully and help the patient establish a regular time of retiring; set proper temperature for the room; decrease noise and light; perform light exercise in the evening; have a warm drink at bedtime (noncaffeinated and nonalcoholic); and possibly intermittently use a benzodiazepine receptor agonists medication (clonazepam, flurazepam, temazepam, lorazepam, triazolam, zolpidem, zaleplon), sedating antidepressants (amitriptyline, doxapin, trazadone) or choral hydrate. In chronic cases relaxation therapy or biofeedback training can be helpful.

C. Insomnia associated with drugs or alcohol (hypnotic-dependent sleep disorder)

1. Tolerance. Depressant drugs (e.g., barbiturates) produce tolerance very shortly and usually lose their effectiveness as a nighttime hypnotic within 2 weeks. Increased dosages are ineffective, and sleep actually becomes less satisfactory than before starting the drug. Long nocturnal awakenings occur, and sleep-onset time lengthens.
2. Withdrawal. On withdrawal of sleeping medication there is a distinct withdrawal insomnia unless the dosage is tapered slowly over several nights. Also, because some drugs suppress REM sleep, patients can experience REM rebound with increased dreaming and nightmares.
3. Sustained use of central nervous system stimulants. Coffee, cola and other soft drinks, tea, chocolate, nicotine, and the caffeine found in many analgesic preparations can all be culpable.
4. Other Drugs. Corticosteroids, (Beta-adrenergic, birth control pills, theophylline, phenytoin, antidepressant medication, and tranquilizers can cause insomnia.
5. Alcohol. This substance acts like other central nervous system depressants in decreasing total sleep, producing persistent interruptions, and acutely suppressing REM sleep. Sleep-onset time is usually shortened in the occasional drinker and lengthened in the alcoholic.

D. Sleep-induced respiratory impairment

1. Sleep apnea syndrome. This syndrome constitutes 5% to 10% of all insomnia cases. The basic problem is that breathing literally stops during sleep. This apnea causes partial or full arousal, and the patient begins to breathe again. Sleep is repeatedly interrupted during the night, in some patients more than 100 times. There are two principal mechanisms: central apnea, in which respiratory centers in CNS fail to function, and obstructive apnea, in which pharynx relaxes and obstructs free flow of air. In central apnea, patient usually does not complain of difficulty getting to sleep

- but has major problem maintaining sleep. There can be some daytime sleepiness, but this is not the principal complaint. The obstructive apnea patient has considerable daytime sleepiness but may be unaware of sleepiness. A combined form of central and obstructive sleep apnea has physiologic and clinical features of both. The most accurate way to document and diagnose sleep apnea is to have the patient studied in a sleep laboratory. Treatment for central apnea has not been very successful, but fortunately, central apnea is less common than obstructive apnea.
2. Alveolar hypoventilation not caused by primary pulmonary disease occurs when there is insufficient air exchange at night but no apnea. Causes include obesity with compression of chest cavity and CNS damage from polio, tumor, encephalitis, or high spinal cord lesions, amyotrophic lateral sclerosis (ALS), myasthenia gravis, or myotonic dystrophy. In addition, another syndrome presumed caused by hypoexcitability of brain stem respiratory center is called "central hypoventilation". Multiple awakenings can occur, and patients may complain of insomnia. Hypnotics and alcohol should not be used to ensure sleep because these can worsen hypoventilation.
- E. Sleep-related spontaneous movement disorders
1. Nocturnal myoclonus. Ten percent of middle-aged and older insomniacs are found to exhibit an unusual episodic movement disorder in which patient experiences frequent (every 20 to 40 seconds, sustained 0.5 to 10 seconds) contractions of anterior tibial muscles and hip flexors. These jerks interrupt sleep patterns and may awaken the patient. The symptoms are usually far more distressing to the bed partner than to the patient. There is sometimes a family history of sleep disorder. Treatment with clonazepam or temazepam has been successful.
 2. Restless-legs syndrome. This is a syndrome in which patients feel deep aching sensation in legs that drives person to move legs. Patients with painful neuropathies (e.g., diabetes, uremia) or radiculopathy from nerve root impingement can experience similar problems. Serum and CSF ferritin levels may be reduced and some patients are have iron-deficient anemia. RLS may be associated with pregnancy, chronic renal failure, iron deficiency anemia, rheumatoid arthritis and antidepressant drug utilization. Diagnosis can be established by PSF. Dopaminergic medication are most effective in controlling RLS and periodic leg movements of sleep. Opioids are second line therapy and have potential for abuse. Treatment is most successful with mild to moderate leg exercise in the evening and utilization of medications at bedtime (Box 23-3).
- F. Medical and environmental. As a cause for insomnia, medical and environmental factors have been noted. Medical and neurologic diseases may interrupt sleep and must be considered. Environmental factors such as noise, heat, light, or a bed partner with nocturnal myoclonus may also be incriminated in some cases.
- G. Abnormal sleep architecture. In some patients a diagnosis can be made only by use of all-night EEG recordings. Some patients display various patterns such as inability to sustain stage IV or REM patterns and alpha (waking) intrusions into sleep. These abnormalities render the patient unable to sustain uninterrupted, restorative night's sleep.
- H. Short sleeper. This refers to the person who requires only 3 to 4 hours of sleep a night.
- I. No objective insomnia (sleep state misperception). There are always patients who complain of insomnia who in fact sleep quite soundly. Reassurance of this fact is sometimes but not always successful in answering the complaint. The issue can be solved by normal

architecture of sleep study.

II. Disorders of Excessive Somnolence

This is the second major syndrome of the sleep disorders. Patients complain of inappropriate and excessive sleepiness, decreased mental and physical performance during the day, unavoidable napping, increased total sleep time, and difficulty achieving full arousal on awakening. This diagnosis should be restricted to patients who have actual sleep attacks or who fall sleep or are drowsy when sedentary and should not be applied to persons who complain of fatigue after inadequate sleep. These disorders cause considerable emotional stress for the patient, and the constant sleepiness interferes with work, socializing, and family relationships.

- A. Psychophysiologic. As in insomnia, emotional factors play a major role in producing daytime fatigue and sleepiness. This may be acute, for example, in depression where patient feels drained and may withdraw to the bed during a crisis.
- B. Psychiatric disorders. Particularly in bipolar depression, patients tend to sleep long hours, take naps, and awake unrefreshed despite adequate sleep.
- C. Drugs and alcohol. Tolerance to or withdrawal from stimulant drugs may produce daytime sleepiness. Constant overuse of depressants will do the same.
- D. Sleep-induced respiratory impairment
 1. Sleep apnea (primarily obstructive). This is a potentially fatal disorder in which soft tissues of throat collapse during sleep onset and actually cause partial or complete upper airway obstruction. The patient attempts to breathe but cannot. Respiratory efforts increase, and finally the effort partially arouses the patient, and he or she emits a loud choking snort. Significant anoxia may occur during this time to produce a generalized seizure. Obstructive episodes may be repeated hundreds of times each night. Patients awaken in the morning mentally fuzzy, unrefreshed, and often with headaches. They complain of excessive sleepiness during the day and may actually have microsleeps in which they literally fall asleep on their feet for few seconds. Automatic behavior may be seen during this time (e.g., fumbling with clothes, staring around, and mumbling). PSG is the definitive study to establish diagnosis of sleep related breathing disorders. Severity is established by degree of oxygen desaturation and apnea-hypopnea index (number of abnormal respiratory events per hour). Because of strain on heart and increased intrathoracic pressure, many patients become hypertensive and develop pulmonary hypertension, cardiac arrhythmias, and cardiac failure. There is increased incidence of hypertension, coronary artery disease and stroke in these patients. Risk factors for this disorder include gender (more common in men), obesity, middle age, abnormalities of upper airway. The initial treatment includes having the patient avoid the following: alcoholic drinks, sedatives, narcotics, diuretics that induce metabolic alkalosis, beta-adrenergic medications (this drug may decrease the ventilatory response to oxygen), and corticosteroids (which may increase body weight and fat deposition). Because the majority of these patients are obese, weight reduction should be undertaken; however, it is not possible to predict those patients who will improve with weight loss. Unfortunately, sleepy overweight individuals have trouble losing weight because they are unable to be very active and do not burn calories very effectively during their frequent naps. Careful assessment by an otolaryngologist is essential; if tonsils are enlarged, tonsillectomy may be indicated; if there is deviated nasal septum or turbinates, corrective surgery is considered; and if there is oropharyngeal obstruction due to soft palate or uvula

- enlargement, uvulo-palatopharyngoplasty is considered. The jaw is assessed for abnormalities (retrognathia or micrognathia) that may warrant mandibular surgery to enhance air movement. The use of continuous positive airway pressure (CPAP) with a mask in which a compressor delivers air at positive pressure to the upper respiratory tract may help correct snoring or obstructive respiratory depression. If these are not effective, elective tracheostomy is the most effective surgical treatment for obstructive apnea.
2. Alveolar hypoventilation. Interruption of sleep in these patients will also lead to daytime sleepiness. This condition can also be treated with CPAP
- E. Nocturnal myoclonus and restless legs. If sleep is sufficiently disturbed, these patients will complain of daytime sleepiness.
- F. Narcolepsy. This is most celebrated of sleep disorders. Narcolepsy syndrome in which attacks of excessive daytime sleepiness are the primary symptom. These can occur while driving, standing, or working but are particularly prone to occur when person is relaxed. The patient often drops into REM sleep in less than 10 minutes. The second symptom in narcolepsy syndrome—cataplexy—is also common and may be partial, such as jaw dropping or weak feeling in knees. Cataplexy is defined as pathologic loss of muscle tone that develops as response to intense affective emotional stimulus (e.g., crying, laughing). Vivid, often frightening hallucinations in drowsy period (hypnagogic hallucinations) and sleep paralysis (total muscular flaccidity) on awakening in morning are final two features of the narcolepsy syndrome. Some patients develop complex automatic behavior such that, during narcoleptic attacks in which consciousness is impaired and for which they have no memory, they may carry out automatic behavior (writing, speaking, and washing). In cases with automatic behavior, EEG may be considered to exclude partial complex seizures. Neurological causes of excessive daytime sleepiness include hypothalamic lesions-tumors, trauma, inflammatory or degenerative conditions. Only a small number of patients have all four of the classic symptoms. Narcolepsy has a familial tendency. Onset is usually during teenage years, and persists throughout life. The peptide hypocretin is produced in lateral hypothalamus and projects diffusely throughout brain and deficiency of hypocretin receptor may cause narcolepsy. Patients with narcolepsy and cataplexy has loss of hypocretin neurons in lateral hypothalamus and CSF levels of this peptide are low or absent. Hypocretin increases wakefulness and inhibits REM sleep by acting on locus ceruleus and dorsal raphe nucleus

The diagnosis of narcolepsy can often be made on the history alone, particularly if cataplexy is present, but supportive evidence from EEG is helpful. The multiple sleep latency test is useful diagnostic procedure that can be performed in EEG laboratory; however, this should be done after a full polysomnogram, which will rule out other sleep disorders. The patient is brought to the EEG laboratory every 2 hours during the day. The patient has 20 minutes to fall asleep. If this occurs, he or she is allowed to sleep 15 minutes. If patient enters REM sleep during two of these periods in absence of other possible explanations, diagnosis of narcolepsy can be made. The narcoleptic usually enters sleep in 3 to 5 minutes. If sleep onset is greater than 10 minutes, pathologic sleepiness is unlikely. Although the narcoleptic exhibits a short sleep-onset time, the patient does not have very sound sleep. Nocturnal myoclonus and other sleep problems are routinely present in narcoleptics and may interrupt their sleep. There are normal persons with short sleep onset latency (less than 5 minutes); they are differentiated from

narcoleptic by otherwise normal sleep and paucity of other symptoms.

HLA typing can be helpful in assisting in the diagnosis of narcolepsy; most whites are HLA-DR2 positive (29% of normals are also positive). In blacks, 66% have HLA-DR2 present and high percentage HLA-DQw6. EEG is warranted to exclude seizure discharges. Narcolepsy is rarely associated with structural brain disease.

Treatment for daytime sleepiness in the narcoleptic is most effective with stimulant medication. Methylphenidate (Ritalin) is usually tried first. Dextro-amphetamine (Adderal). Pemoline (Cylert) or Modafinil (Provigil) are also effective. Modafinil may affect CNS dopamine levels but is better tolerated than other stimulants. Frequent side effects of stimulant medication include irritability, nervousness, tremor, palpitation, anorexia, weight loss. Rarely tachycardia and hypertension occur. The starting dose of Ritalin is usually 5 mg in the morning and at noon, but considerably higher doses are often needed. Most patients benefit from taking medication on demand (e.g., when about to drive or take a test). Cataplexy is best controlled with imipramine (Tofranil) 25 mg three times a day, or clomipramine (Anafranil), 25 to 75 mg h.s. In addition, selective serotonin reuptake inhibitors (Prozac, Paxil, and Zoloft) and sodium oxybate may be used. The effectiveness of controlling cataplexy may be due to their ability to inhibit norepinephrine reuptake. Sodium oxybate is a hypnotic that can consolidate sleep but has potential for abuse. Short naps (20 minutes) spaced throughout the day may also help to prevent the sleep attacks.

- G. Idiopathic hypersomnolence (hypersomnia). This condition is characterized by recurrent sleepiness and irresistible sleep and at times sleep attacks. These patients do not fall asleep while talking or standing but do have sleep episodes. Daytime automatic behavior is common; however lengthy nonrefreshing naps are taken and long, sound nighttime sleep is the rule. Morning arousal is often very difficult, and periods of sleep drunkenness (staggering around with automatic behavior) may last up to 2 hours after arising. Rarely hypersomnia is secondary to a pathologic process involving posterior hypothalamus (encephalitis, head injury, brain hemorrhage). The amphetamines, which are helpful in treating narcolepsy, are far less effective in idiopathic hypersomnolence. Cyproheptadine (Periactin), methysergide (Sansert), and other drugs that suppress serotonin are more effective.
- H. Medical, toxic, and environmental factors. As discussed previously, these factors will also cause sleepiness during the day.
- I. Periodic syndromes. These are uncommon yet unique syndromes of periodic hypersomnolence that seem almost akin to hibernation. The most common is the Klein-Levin syndrome. A condition most common in young (10 to 20 years) males, this syndrome is characterized by periods (hours to days) of sleepiness, increased appetite, abnormal emotional states (dysphoria, aggressive behavior), decreased libido, and irritability. Between attacks, patients show normal sleep-wake cycles. The syndrome is occasionally seen in females when it is related to menstrual cycles. Etiology is unknown, but some type of episodic hypothalamic or diencephalic disturbance is postulated. The disorder is usually self-limited and remits by adulthood.
- J. Fatal familial insomnia. This is rapidly progressive prion disease characterized by insomnia and impaired autonomic regulation. There is impaired sleep-wake cycle with impaired autonomic and endocrine regulation. PSG shows absent sleep pattern including lack of REM pattern. The patient becomes comatose and the disease is fatal.

III. Disorders of sleep-wake schedule (circadian rhythm sleep disorders)

These are situations in which the normal circadian rhythm is disturbed:

- A. Jet lag. This is usually a minor problem for most persons, but individuals who must make frequent long trips over many time zones (worse going west to east) experience considerable difficulty resetting their biologic clocks.
- B. Shift work. A common problem for service personnel (i.e. nurses, pilots, ship captains, bus/truck drivers, police, some industrial workers, and busy physician house officers). Both work and sleeping efficiency are decreased under these circumstances. There is no satisfactory medical solution; occasionally mild sleeping pill used a day or two after a change may help to ensure sleep onset. Some persons tolerate this better than others do, but it is not easy for anyone. Bright light therapy is becoming more commonly used in shift work. If severe problem exists, patient simply must change jobs or find some way that shift schedules can be changed gradually to accommodate the time change.
- C. Non-24-hour circadian rhythm. These persons have 25-hour biologic clocks. They drift in and out of phase with the rest of the world in 24-day cycles.

IV. Parasomnias

- A. Sleepwalking (somnambulism). This is a problem most often seen in children ages 6 to 12. The nocturnal walk is usually in early part of night and may be quite elaborate including opening doors, stepping over furniture, and opening windows. Speech, when present, is mumbled. Occasionally, the child awakens during the peregrination but usually do not. It is important to differentiate sleepwalking from partial complex seizures and psychiatric disorders (hysteria, fugue states). The psychiatric disorders are not always distinguishable from pure somnambulism. Seizures are rarely only reported at night; EEG is helpful in excluding this condition. The problem is usually self-limited, and first treatment is aimed at protecting patient from hurting himself or herself (lock windows, etc.). The problem may recur in 20s or 30s when person is under unusual emotional stress. Some adolescents or young adults develop somnambulism de novo, which is usually associated with emotional stress. Benzodiazepines may be used in severe cases.
- B. Sleep or night terrors. This is a rather frightening although usually benign condition seen in children between the ages of 4 and 15. These children scream or cry out, sit up in bed, and exhibit look of panic or terror. Some may sleepwalk as well. An autonomic (sympathetic) reaction occurs, with dilated pupils, diaphoresis, tachycardia, and tachypnea. The patients usually have little or no memory for the event, cannot be consoled directly after the event, and do not report vivid dreams. Night terrors may be differentiated from nightmares. The latter are frightening dreams in which there is usually no anxiety or heightened sympathomimetic discharge and patient has excellent recall of dream content. Nightmares occur during REM sleep, whereas night terrors occur during initial hours of sleep as part of slow-wave (stage III or IV) sleep. The condition has been known to come on in 20s or 30s and become chronic. Such patients have high incidence of chronic anxiety. Temporal lobe seizures and hypnagogic hallucinations of narcolepsy syndrome must be considered in the differential diagnosis. Treatment with benzodiazepine at night is helpful in some patients.
- C. REM behavior disorder. This was first described in humans in 1987. It is common in patients with degenerative neurological disease—dementia/CVA/SAH/Parkinson's

disease—but is also seen in healthy young patients. Incomplete maintenance of REM atonia may affect arms, legs, and face and permit dream enactment resulting in severe injury to patient or bed partner. This disorder can be clinically indistinguishable from sleepwalking, nocturnal seizure, and psychiatric states. Treat with Clonazepam or other benzodiazepine.

V. Enuresis.

In primary enuresis, child has not been able to control nocturnal urination to remain dry for a period of 1 month. This is not a rare problem; in fact 3% of children remain enuretic by age 12 (1% to 2% by age 18). There is the occasional adult who has never obtained nocturnal continence and continues to be plagued by enuresis. This disorder most commonly occurs in boys. There is usually positive family history of bed-wetting, and urologic studies demonstrate a small functional bladder capacity. In secondary enuresis, the child has controlled nocturnal urination for months to years before the episodes of bed-wetting recur. In evaluating patients with primary enuresis, a careful developmental history should be obtained. Psychological factors including the parent's attitude toward the bedwetting and toilet training and specific life stresses at the time bed-wetting developed must be considered. Urologic evaluation should be carried out to exclude genitourinary abnormalities. In older patients with secondary enuresis, a nocturnal seizure should be considered as the possible mechanism for enuresis. Sleep studies should be performed to exclude nocturnal seizures, obstructive apnea, night terrors, and sleepwalking as being associated with enuresis. Enuresis may occur in any sleep stage but is most common in non-REM sleep and occurs early in the night. Imipramine has been used to reduce the frequency of bedwetting; however, behavioral modification and enuresis alarms (conditioning technique in which the child awakens to a bell that is triggered by urine on the sheet) are also effective.

SUMMARY

Problems getting to sleep and problems staying awake are occasionally experienced by all of us; there are, however, some patients whose sleep problems constitute a major controlling aspect in their lives—these are pathologic sleep disorders. Through the use of special all-night sleep recordings and knowledge of the various sleep syndromes, the physician can usually classify the type of sleep disorder. The cause of these conditions is not understood, but we now recognize the syndromes clinically and can outline a treatment regimen for the specific disorder.

Sleep and Epilepsy

Seizures may be triggered by sleep. During non-REM sleep, diffuse cortical synchronization occurs, whereas during REM sleep there is inhibition of thalamocortical synchronization. Non-REM sleep may activate seizures in hyperexcitable cortex in patients already susceptible to seizures and during REM sleep; there is reduction in epileptic discharges. Sleep deprivation may trigger epileptic discharges to result in clinical seizures. Some patients have seizures, which only occur at night (nocturnal seizures). These may be confused with motor or behavioral parasomnias and PSG is critical to establishing the correct diagnosis of seizures or parasomnias.

Sleep and Headache

Sleep disturbances in obstructive sleep apnea may cause headaches (hypnic). Cluster headaches occur in REM sleep. Hypnic headache occurs in patients older than 60, occurs at

same time each night and responds to lithium or indomethacin. These may be difficult to differentiate from cluster.

Sleep and Cerebrovascular Disease

Sleep apnea predisposes patients to stroke. Snoring and sleep apnea are stroke risk factors. Stroke may predispose patients to sleep disorders, as there may be palatal and tongue disturbances leading to snoring.

Suggested Readings

Diagnosis and Classification

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BOX 23-1 Complete Profile of 24-Hour Sleep-Wake Pattern

1. *Presleep routine.* Exercise, coffee, food, alcohol, or mental strain before retiring will often prolong sleep onset. What is the role of daily or weekend naps? The importance of the bed partner to sleep pattern and possibly any recent change in routine or bed partner should be stressed.
2. *Sleep onset time.* How long after getting in bed does patient fall asleep?
3. *Character of sleep.* It is usually necessary to question the bed partner as well if there is one.
 - a. Number of nocturnal awakenings
 - b. Restlessness or jerking of legs
 - c. Snoring and its character—are there very loud snorts?
 - d. Presence of apnea or breath holding spells—are they terminated with respiratory effort and snorting?
 - e. Sleepwalking, nightmares, or terrors—is there self-injury or injury to bed partner during any of these?
 - f. Time and ease of awakening in the morning
 - g. Total length of sleep
 - h. Is sleep refreshing?
 - i. Any morning symptoms (e.g., headache, confusion, hallucinations, wet bed, or total transient paralysis)?
4. *Character of waking period*
 - a. Refreshed
 - b. Tired during the day
 - c. Sleep attacks (uncontrollable attacks of actual sleep when sitting, driving, or in any situation with decreased environmental stimulation)
 - d. Naps
 - e. Cataplexy (sudden loss of muscle tone with or without falling when experiencing sudden strong emotion, such as fear, anger, or amusement). This can affect hands, masseters, and eyelids as well as antigravity muscles—consciousness is usually preserved unless the attack is prolonged if the patient enters directly into REM sleep.
 - f. Does the patient use substances (e.g., caffeine, amphetamines) to maintain wakefulness?

BOX 23-1 Cont'd.

Life Routine and Environmental Factors

1. Does the patient have a very irregular routine, such as doing shift work or excessive traveling?
2. Is the bedroom too hot (above 75° decreases sleep efficiency)?
3. Is environmental noise or light excessive?
4. Is there a new job, house, baby, or other factor influencing sleep pattern?

Emotional Situation

1. Recent or long-term emotional problems, especially depression or anxiety
2. Marital difficulty
3. Death of family member or friend
4. Sexual problems producing anxiety about going to bed
5. History of abuse, a very common problem in sleep disorders patients

Medical History

1. Medications (especially the use of sleeping pills or psychotropic drugs),
2. Alcohol use. Alcohol makes falling asleep easier, but causes frequent nocturnal awakenings as alcohol is metabolized,
3. Drug abuse or withdrawal. This markedly disrupts sleep patterns.
4. Medical illness (e.g., heart failure or chronic pulmonary disease can cause nocturnal dyspnea and disturbed sleep; thyroid disease and hypoglycemia are also known to disrupt sleep).

Family History

1. A family history of sleep disorder—particularly narcolepsy, restless legs, sleepwalking, night terrors, and hypersomnolence—is obtained in some cases.
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BOX 23-2 Clinical Syndromes of Sleep Disorders

1. Dyssomnias
 - a. Intrinsic sleep disorders (e.g., psychophysiological insomnia, narcolepsy, sleep apnea, restless legs syndrome)
 - b. Extrinsic sleep disorders (e.g., environmental insomnia, insufficient sleep disorder, alcohol-dependent sleep disorder)
 - c. Circadian rhythm sleep disorders (e.g., jet lag [time zone change], shift work sleep disorder, delayed sleep phase syndrome)
2. Parasomnias
 - a. Arousal disorders (e.g., sleepwalking, sleep terrors)
 - b. Sleep-wake transition disorders (e.g., sleep-talking)
 - c. Parasomnias with REM sleep (e.g., nightmares, sleep paralysis)
 - d. Other parasomnias (e.g., bruxism, enuresis, sudden infant death, snoring)
3. Sleep disorders associated with medical/psychiatric disorders
 - a. Mental disorders (e.g., psychosis, mood disorders, anxiety, panic, or alcoholism)
 - b. Neurological disorders (e.g., dementia, parkinsonism, sleep-related epilepsy)
 - c. Medical disorders (e.g., chronic obstructive pulmonary disease, asthma, gastric-reflux, fibromyalgia)
4. Proposed sleep disorders (e.g., short/long sleeper, menstrual/pregnancy-associated sleep disorder, hypnagogic hallucinations)

BOX 23-3

Medications for the Treatment of Restless Legs Syndrome

Clonazepam 0.5 to 2 mg

Temazepam 30 mg with or without codeine 30 mg

Sinemet 25/100 to 50/200 CR

Carbamazepine 200 mg

Other benzodiazepines such as diazepam (5 mgm)

Bromocriptine 2.5 mg

Mirapex (begin with .125 mgm)