Normal Sleep

Sleep is more than a respite from consciousness or sensory stimulation. It is a complex and dynamic process. Much of what we now know about the anatomy of sleep is based on lesion studies in animals. The hypothalamus is critical to the organization of sleep. It is involved in a network of brain nuclei that regulate an intrinsic time clock, body temperature, and sleep-wake cycles, while concurrently relying on cues from light as perceived by the eyes and skin. The thalamus is most closely involved in the control of the sleep-wake cycle. Massive bilateral destruction of the thalamus is characteristic of fatal familial insomnia, which results in progressive insomnia and neurologic deterioration leading to death. Both the hypothalamus and thalamus extensively modulate the actions of the brainstem, the primary site of origin for REM sleep. The reticular activating system, raphe nuclei and locus ceruleus, in particular, have key roles in the generation of REM sleep.

The neuropharmacology of sleep is related to the anatomic regulatory centers of sleep. The fact that the raphe nuclei and locus ceruleus are crucial to REM sleep suggests that serotonin and norepinephrine, respectively, play a crucial role in sleep mechanisms. In clinical practice, however, serotonin precursors have conflicting effects on sleep. Drugs which alter the storage, release and re-uptake of serotonin have minimal effects. Acetylcholine may play an important role in REM sleep because of the cholinergic neurons in the brainstem, which regulate REM sleep. The effect of norepinephrine and dopamine on sleep has been extensively studied in patients with Parkinsonism,
but no significant changes have been found. Pharmacologically, we know that stimulants, such as amphetamines, act by increasing brain norepinephrine and dopamine concentrations. The stimulants reduce total sleep and REM sleep times. Hypnotics, such as benzodiazepines, act by enhancing inhibitory GABAergic neurotransmission. Clinically, they promote sleep onset and reduce slow wave and REM sleep.

In normal day-night conditions, the sleep-wake cycle is 24 hours long. With external time cues removed, the sleep-wake cycle lengths to about 25 hours. The intrinsic cycling of bodily functions, such as the sleep-wake cycle and body temperature, is referred to as the circadian rhythm. It is determined by an internal pacemaker, which for the sleep-wake cycle is located in the suprachiasmatic nucleus (SCN) of the hypothalamus. The SCN has connections to the retina, which regulate the light-dark synthesis and release of melatonin by the pineal gland. Individuals blind from birth, who lack the SCN-retinal connection, do not have a 24-hour sleep-wake cycle. In normal individuals, the internal 24-hour clock is stable; however, it can be reset by external cues, particularly light, as in travel across time lines. Body temperature is the most reliable marker of circadian rhythm in humans and the biological rhythm most closely linked with sleepiness. Low body temperature correlates with sleep onset while rising body temperatures correlate with sleep offset. Body temperature reaches a nadir twice a day: a relatively small drop in mid-afternoon and a more drastic fall in the early hours of the morning, coinciding with REM sleep.

Normal sleep consists of several stages. Each stage is associated with certain physical properties and EEG findings. Drowsiness or light sleep is Stage 1. The subject is relaxed. Slow random eye movements and slow pupillary constriction and dilatation are noted. On EEG, background activity is slow compared to wakefulness. As sleep continues, Stage 2 is entered. In this stage, bursts of EEG activity called sleep spindles, vertex sharp waves and K complexes appear. With continued sleep, during which the subject is harder to awaken, stages 3 and 4 are entered. During these stages, collectively referred to as slow wave sleep, the EEG shows high amplitude slow waves. About 90 minutes after the onset of sleep, the subject enters rapid eye movement (REM) sleep. This stage of sleep is associated with vivid dreams that follow a story line and are accompanied by realistic imagery. Dream recall is more frequent in awakenings from REM sleep than from non-REM (NREM) sleep. There is loss of skeletal muscle tone except for brief twitching and rapid eye movements. Autonomic changes also occur, including elevated blood pressure, irregular heart rate, and irregular respirations. Arrhythmias such as ventricular tachycardia, atrial fibrillation, and heart block are more likely to occur during REM sleep. It is suspected that myocardial infarction and strokes that occur during sleep happen during REM sleep because of the associated autonomic changes. Penile erection also occurs during REM sleep. Patients with psychological causes of impotence will have an erection during REM sleep, while patients with organic etiologies do not.

NREM sleep, which consists of stages 1, 2, 3, and 4, usually occupies the first 60–90 minutes of sleep, followed by REM sleep. A night of sleep usually consists of four to six NREM-REM cycles. The duration of slow wave sleep is longest during the first half of the night, while REM sleep becomes more prolonged during the second half of the night. Age-related changes in sleep architecture have been reported. During the neonatal period, most of the day is spent asleep, with half of the sleep time in active sleep, the equivalent of REM sleep. As one ages, the
percentage of total sleep that constitutes REM sleep remains fairly constant at 20–25 percent. During adolescence, there is a peak in the percentage of slow wave sleep after which it declines with aging. Conversely, stage 1 sleep increases with age. Nocturnal sleep efficiency, or the percentage of time in bed spent asleep, is reduced to about 70–80 percent in the elderly, most likely as a result of increased nocturnal awakenings. Total sleep time, which takes into account daytime napping in addition to nocturnal sleep, is fairly constant between young and old. Thus, it is a myth that old people need less sleep.

The functional importance of individual stages of sleep has been investigated with selective sleep deprivation studies. These studies, which eliminate one or more stages of sleep, most commonly REM sleep and, less frequently, slow wave sleep, find that total sleep time, not selective sleep stage deprivation, is the most important predictor of cognitive performance.

**Insomnia**

Patients with sleep problems are common challenges in primary care offices; at least 40 million Americans have sleep disorders. Less than 20 percent of these people report that they have discussed their problems with their physicians. Sleep problems are often missed, although they have been shown to lead to health risks such as accidents and absenteeism, and, in the case of patients who may have obstructive sleep apnea (OSA), potential cardiovascular complications. Diagnosing sleep problems can be made easier with simple tools for sleep evaluation, including the Epworth Sleep Scale (see below) and the American Academy of Sleep Medicine’s self-assessment (see Internet resources below).

With insomnia, finding out whether the patient has trouble falling asleep or staying asleep, or just does not feel rested, can help guide the treatment, or lead to the possibility of diagnosing anxiety or depression. Consider underlying causes: the medical illnesses that may cause pain or sleep disruption; the psychiatric illnesses that may be the source of the problem or co-exist with it; the drugs, caffeine or alcohol that may interfere with sleep. A sleep log kept for two or three weeks is very helpful. It should include the time the patient got into bed, in addition to the time he fell asleep; the timing and duration of naps, meals, and exercise; a description of the sleep environment; and information on what the patient is using to try to get to sleep, since rebound insomnia because of sleep medication use is not uncommon.

Untreated insomnia has significant risks, including increased accidents and psychiatric disorders, but pharmacologic treatment has its risks, too, such as drug dependence and daytime sedation. In primary insomnia especially, the approach that has been shown to work, and keep working, is behavioral. Medications should be used, if behavioral approaches are not successful, for the shortest time possible in the smallest dose possible. Sleep hygiene—avoiding daytime naps, avoiding stimulants close to bedtime, exercising regularly early in the day, having a nighttime routine, using the bed only for sleep or sex, and getting out of bed if unable to fall asleep after a designated time period, such as thirty minutes—is, as the late Dr. Lee points out, common sense advice.

There are also behavioral therapy techniques. Sleep restriction limits the amount of time spent in bed to the amount of time spent asleep; stimulus control has the patient who cannot fall asleep leave the bed, go to another room until he feels sleepy, and then return to bed. These methods take persistence on the
part of the doctor and cooperation on the part of the patient, but do work. They need to be tried because there is no ideal sleep medication. If one is needed, thinking about the timing and duration of the sleep problem helps guide the choice: very short acting if the problem is getting to sleep, longer acting if the problem is early awakening, provided depression or anxiety is not suspected. If insomnia has been present for six months and there is no response to medical, behavioral, or psychiatric treatment, consider a sleep study.

Insomnia has a greater prevalence in the elderly as a result of comorbidities, depression, sleep apnea (which grows more common as women age), and polypharmacy. In a 2003 National Science Foundation (NSF) poll of older adults, the need to go the bathroom was the most common reason for interrupted sleep. Pain, cough, heartburn, and headache were much less prevalent. Medications in the elderly frequently contribute to insomnia. The elderly seem to require the same seven to nine hours of sleep younger adults do, although their sleep architecture changes. Both the 2003 NSF survey and a 2005 Gallup survey found that the better the health of older adults, the more likely they were to sleep well. Poor sleep in the elderly seems to indicate poor overall health.

Children’s sleep problems are a challenge because of changes in their sleep patterns as they grow, especially if they are out of the average range of age for expected changes. Many of their sleep problems, including night terrors, sleepwalking, and enuresis, are the result of central nervous system immaturity and require only supportive and protective measures. Obstructive sleep apnea (OSA) is an exception and is diagnosed much like adult OSA. Children, who for whatever reason are sleep deprived, can become hyperactive, have mood and behavior changes, or develop problems learning. They need a consistent schedule, a relaxing bedtime routine, and a dark bedroom without a TV or computer. Social factors (such as families that share living spaces, or the habit of co-sleeping) may make optimum sleep hygiene difficult to achieve.

In the case of the parasomnias, which are undesirable motor or autonomic activity during sleep, the specific parasomnia may point to the need to treat a medical problem: peripheral neuropathy and iron-deficiency anemia are associated with restless leg syndrome (RLS), for example, and a urinary tract infection or spinal cord disease that may lead to (secondary) enuresis. The parasomnias, apart from RLS and periodic limb movements of sleep, which are treated with levodopa compounds, benzodiazepines or opioids, may not require treatment. In one study, 15 percent of women in the third trimester of pregnancy developed RLS; they were often iron or folate deficient. RLS becomes more prevalent with age, and severity can also increase.

The hypersomnic patient who does not have narcolepsy or neurologic illness needs testing in a sleep lab if obstructive sleep apnea (OSA) is suspected, because treatment depends on the findings of a sleep study. A bed partner, parent or roommate may provide valuable clues, such as apneas or the presence of loud snoring in other positions than supine, to the diagnosis of OSA. Obesity or a thick neck may be tip-offs to OSA.

OSA in the overweight or obese is often helped by weight loss. Appliances or surgery may be helpful in mild to moderate OSA, but continuous positive airway pressure (CPAP) is the usual treatment for moderate or severe OSA.

Finding out about the patient’s expectations and beliefs is always helpful, as is asking if the patient or family members are willing to make the changes you
recommend. Environments and cultural practices need to be explored. Offer follow-up of sleep problems to find out what works and to offer alternatives.

**Excessive Sleepiness**

Excessive daytime somnolence is a more common complaint in sleep clinics than insomnia. The major causes of this symptom are sleep apnea, narcolepsy or neurologic illness such as head injury, post-viral infection, myotonic dystrophy, developmental disorders, Parkinson disease, Alzheimer disease and, occasionally, parasomnias. The diagnosis is determined by history, physical exam, and objective testing for daytime sleepiness, such as the **multiple sleep latency test** (MSLT), which is almost always preceded by an overnight polysomnogram to document adequate sleep. The history is often best obtained or corroborated by a bed partner or family member who can provide witnessed accounts of daytime somnolence and the patient’s nocturnal sleep patterns.

**Obstructive sleep apnea (OSA)** is due to complete or partial obstruction of the upper airway. During sleep, the tone of pharyngeal muscles diminishes. When pharyngeal muscles collapse, resistance to airflow increases and results in elevated negative intrathoracic pressures during inspiration. Complete obstruction of the upper airway results in apnea or cessation of airflow across the nose and mouth, often, but not always, with associated hypoxemia. Partial obstruction causes a **hypopnea**, which is defined as a 50–90 percent reduction in airflow. At the end of an apnea or hypopnea, a person is often aroused. An arousal or brief awakening stimulates pharyngeal muscle tone and normal inspiratory airflow resumes. Severity of hypoxemia is dependent on baseline oxygenation, lung oxygen stores and apnea duration. For example, a markedly obese patient is likely to have severe OSA-associated hypoxemia because elevated abdominal pressures are compressing the thoracic cavity and reducing lung oxygen stores. There are many causes of upper airway obstruction. Tonsillar hypertrophy is a common cause of OSA in children and adolescents. Craniofacial abnormalities such as retrognathia, micrognathia, and deviated nasal septum, increase upper airway obstruction, as does fatty infiltration of pharyngeal soft tissues from weight gain. Macroglossia, which may be associated with hypothyroidism, acromegaly, amyloidosis, and Down syndrome, usually causes obstruction at the base of the tongue, lower down the pharynx. Neuromuscular disorders, such as myotonic dystrophy, often cause abnormal laxity of pharyngeal muscle tone during sleep.

OSA is common in the general population. The Wisconsin Sleep Cohort, a comprehensive epidemiologic study investigating the prevalence of obstructive sleep apnea in middle-aged adults, found that 4 percent of men and 2 percent of women had obstructive sleep apnea syndrome (OSAS), a diagnosis defined by both clinical criteria and a sleep study. However, 24 percent of men and 9 percent of women had OSA as defined by sleep study results alone. Among commercial truck drivers a high prevalence of OSA is suspected.

A thorough history can provide clues to the diagnosis of OSAS. Apneas or hypopneas during sleep are best confirmed by the patient’s family or bed partner. The physiologic effects of apneas and hypopneas are equal. **The most prevalent complaint is fatigue or daytime somnolence, which results from fragmentation of nocturnal sleep by recurrent apnea-associated arousals.** Choking or gasping at the termination of an obstructive apnea is a common observation and can cause self-arousal. The severity of daytime somnolence
can be ascertained by the frequency and duration of naps and the likelihood of falling asleep during activities such as reading, watching television, or driving. Sleep deprivation from OSA often has a paradoxical effect on children, who are more likely to present with hyperactivity. Hypoxemia and sleep fragmentation may result in impairment of memory, attention and concentration, changes in mood and personality, loss of libido, and morning headaches. Snoring is a common, but not requisite, symptom in patients with OSA. The intensity of snoring increases with weight gain and reflects increasing upper airway resistance. Loud snoring in all positions of sleep is more likely to be associated with OSA than snoring in just the supine position. Enuresis and nocturia may occur in patients with OSA as respirations against an obstructed upper airway lead to increased intra-abdominal pressure on the bladder. Restless sleep, described as frequent movements of the limbs and trunk, is common in subjects with frequent apnea-associated arousals. Lastly, a family history of OSA can identify individuals who are at risk for OSA, as risk increases with the number of affected family members.

Several factors increase upper airway resistance and thus exacerbate the frequency and duration of apneas. Hypnotics, sedatives, and alcohol, reduce pharyngeal muscle tone during sleep. Inflammation of the nasopharynx and pharyngeal soft tissues from respiratory allergies increase upper airway resistance. Smoking and high altitudes exacerbate apnea-associated hypoxemia.

The physical examination can be used to identify conditions associated with OSA. **Obesity is reported in two-thirds of patients.** A neck circumference of greater than 17 inches in men and greater than 16 inches in women is associated with increased risk for OSA. As previously mentioned, anatomical abnormalities of the head and neck, such as micrognathia, retrognathia, and macroglossia can cause upper airway narrowing. OSA is more prevalent in men compared to women, at ratios reported between 2:1–10:1, most likely reflecting gender differences in head and neck anatomy. Prevalence increases for both genders with increasing age.

The diagnosis and treatment of OSAS is important in lieu of its potential hematologic and cardiovascular complications. Polycythemia, from chronic hypoxemia, is relatively uncommon in patients with OSA. Hypertension, ischemic heart disease, and cerebrovascular disease occur with higher prevalence in subjects with OSA compared to the general US population; however, the relationship between OSA and these diseases is poorly understood. Pulmonary hypertension is a known complication of chronic, untreated OSA and is strongly associated with severe nocturnal hypoxemia and hypercapnea. Cardiac arrhythmias are common in patients with severe hypoxemia. The type of arrhythmias observed include premature ventricular contractions, sinus arrest, sinus bradycardia, second-degree atrioventricular block, atrial tachycardia, paroxysmal atrial fibrillation, atrial flutter, and unsustained ventricular tachycardia. These cardiac arrhythmias are reversible with treatment for OSA.

The differential diagnosis for OSAS includes disorders associated with loud snoring and daytime somnolence. Primary snoring is characterized by loud snoring only and is not associated with daytime hyper somnolence. Excessive daytime somnolence may be due to behavioral or psychophysiolologic factors, psychiatric disorders, environmental factors, drug dependency from hypnotics or stimulants, central sleep apnea syndrome, parasomnias, disruption in the
timing of the sleep-wake cycle such as shift work sleep disorder, narcolepsy, idiopathic central nervous system hypersomnia, degenerative central nervous system disorders, and hormone-related conditions such as pregnancy and menstruation.

The evaluation of a patient with OSAS must include a sleep study. There are two types of sleep studies: an overnight polysomnogram, performed in a laboratory under the guidance of a certified sleep technician, and an ambulatory sleep study performed in the patient’s own home. Ambulatory studies tend to monitor a limited number of parameters, i.e. respiratory effort, airflow, heart rate and oxygen saturation. Polysomnograms also record electroencephalography to stage sleep and determine total sleep time monitored, electrooculography and electromyography (EMG) of the chin to determine the onset of rapid eye movement (REM) sleep, airflow, chest and abdominal wall motion, EMG of the legs to detect periodic leg movements of sleep, oximetry, and body position (Figure 12-1).

Figure 12-1: Polysomnogram with obstructive apnea. Airflow is absent across the nose while thoracic and abdominal respiratory effort are preserved. Oxygen desaturation is evident on the SaO2 channel. An arousal terminates the apnea, as indicated by an increase in activity on the EEG, chin EMG and left and right tibial EMG channels. Note the paradoxical (or out of phase) movements of the thoracic and abdominal walls prior to the apnea which then corrects, or becomes in phase, after the arousal. Paradoxical thoracic and abdominal wall movements indicate increased upper airway resistance. EOG = electrooculogram, EEG = electroencephalogram, EKG = electrocardiogram, EMG = electromyogram.

The major advantages of a laboratory study are the ability of a sleep technician to intervene when an electrode or monitor is displaced and the reliability and comprehensiveness of the sleep data obtained. The major advantage of an ambulatory study is lower cost. In patients suspected of severe OSAS, an ambulatory monitor can serve as a screening test, although a negative study should be followed up with a polysomnogram. For most patients with OSAS,
A polysomnogram is the preferred study. A sleep study is scored on several parameters, including **sleep efficiency** (total sleep time divided by total time in bed, expressed as a percentage), **sleep latency** (time it takes to fall asleep from the beginning of the study), **percentage of each stage of sleep relative to total sleep time**, **number of apneas**, **range of apnea duration and oxygen desaturation**, **number of arousals**, **number of periodic leg movements**, **REM latency** (time it takes to enter REM sleep from the time of sleep onset), and **associated cardiac arrhythmias**. An apnea is defined as cessation of airflow for at least 10 seconds. **There are three types of apneas: obstructive, central and mixed.**

**Obstructive apneas** imply the absence of airflow in the presence of continued thoracic and abdominal effort (Figure 12-1). **Central apneas** are often due to dysfunction of regulatory respiratory centers in the central nervous system. Airflow is absent and so, too, is thoracic and abdominal effort. Insomnia, rather than daytime somnolence, is more likely to be the presenting symptom. **Mixed apneas** have features of both obstructive and central apneas. They are often due to upper airway obstruction.

The severity of OSA is determined by the apnea-hypopnea index (AHI), or the frequency of apneas and hypopneas per hour of sleep, the frequency of arousals and awakenings, body position during apneas, oxygen desaturation, and type of cardiac arrhythmias. REM sleep and sleep in the supine position are of particular interest as obstructive apneas tend to be longer in duration and oxygen desaturation more severe. In general, mild OSAS may be characterized by an AHI of less than 15, mild oxygen desaturation, no cardiac arrhythmias, and minimal or no daytime fatigue. Moderate OSAS may be characterized by an AHI of 15–30, moderate oxygen desaturation (i.e., 70–85 percent), moderate daytime sleepiness, and sometimes premature ventricular contractions. In severe OSAS, the AHI is usually greater than 40 and associated with oxygen desaturations below 70 percent, cardiac arrhythmias, and severe daytime sleepiness. Polysomnogram results should be congruent with the clinical history. If not, the diagnosis of OSAS must be reconsidered. Occasionally, the polysomnogram may reveal frequent unexplained arousals or crescendo snoring just before an arousal, but no apneas. In such cases, a repeat polysomnogram with esophageal balloon pressure monitoring of intrathoracic pressures may disclose upper airway resistance syndrome. This condition is treated in the same manner as OSAS.

The treatment of OSAS is dependent on its severity, the presumed cause, and the patient’s age. In obese patients with OSA, weight loss or the correction of hormonal abnormalities can improve or eliminate OSA. However, weight loss is an unrealistic goal for most patients. Positional therapy, or conditioning the patient to sleep in the lateral recumbent position, is effective in patients with mild OSA in the supine position. Younger patients and those with craniofacial abnormalities may prefer surgical over medical treatment.

Mild to severe OSAS may be treated with appliances and/or surgical procedures, which maintain patency of the airway. Oral appliances are used in patients with mild OSAS or primary snoring. The basic working principle of oral appliances is that they advance the mandible or pull the base of the tongue...
forward to enlarge the upper airway. Mandibular advancing devices, look like mouth guards and tongue retainers, hold the tongue in a bulb of negative pressure, which fits between the teeth and lips (Figure 12-2). They can be bought over the counter as prefabricated devices or are designed from dental impressions made by a dentist.

CPAP is the treatment of choice for moderate to severe OSAS. It keeps the airway open during sleep by delivering positive air pressure via a nasal mask (Figure 12-3) or nasal pillows which fit snugly in the nostrils. CPAP pressures are titrated to eliminate apneas and snoring in a follow-up polysomnogram to the diagnostic study. In about 80–90 percent of patients, symptoms and cardiac arrhythmias are improved. However, noncompliance with CPAP is a leading cause of persistent symptoms. Skin breakdown over the bridge of the nose or, rarely, an allergic reaction to the silicone in the mask may prevent continued use of the mask. Some patients find the mask uncomfortable or experience claustrophobia. Several variations of CPAP may circumvent this problem: 1) nasal pillows, 2) a bilevel CPAP device (bi-PAP) which delivers lower positive pressure during expiration than inspiration, and 3) a ramp which gradually increases CPAP pressures over a period of time during which the patient is allowed to fall asleep. A humidifier attachment prevents drying of mucosal membranes and nosebleeds. CPAP will be ineffective if the patient is a mouth-breather, in which case a chin strap is used to prevent pressure loss.

Surgery is considered when CPAP cannot be tolerated or fails to treat OSAS adequately. Surgery is designed to reconstruct the upper airway at a particular site or bypass it altogether. Tracheostomy is the last option considered and rarely performed. In most children with OSAS, tonsillectomy and adenoidectomy is effective treatment, but not so in adults. Uvulopalatopharyngoplasty (UPPP) is the most common upper airway surgery performed in adults with primary snoring. It enlarges the retropalatal airway through a tonsillectomy, excision of the uvula and posterior portion of the palate, and excision of tonsillar fossae mucosa if tonsillectomy has already been performed (Figure 12-4).

Complications from a UPPP are rare, but include nasal reflux of liquids, postoperative bleeding, nasopharyngeal stenosis, voice change, vague foreign body sensation and death secondary to airway obstruction. While UPPP may initially improve mild OSAS, its success diminishes with time and is
thus not considered a reliable treatment option for OSAS. Laser-assisted uvulopalatopharyngoplasty (LAUP) is indicated for snoring only. A LAUP involves laser-guided resection of the soft palate and uvula (Figure 12-5), which is less than the amount of tissue resected in a UPPP.

Figure 12-5: On the left, a low-lying soft palate is marked for laser-assisted uvulopalatopharyngoplasty. On the right, postoperative retraction of the soft palate is shown.

This procedure is highly successful for elimination of snoring, but postoperative pain in the area of surgery has caused it to lose favor as a treatment option.

**Genioglossal advancement (GA)** is designed to enlarge the retrolingual airway by pulling the base of the tongue anteriorly (Figure 12-6).

Figure 12-6: In genioglossal advancement, a section of freed mandible with attached genioglossus is positioned anterior to the mandible (upper arrow), thereby moving the base of the tongue anteriorly too. The hyoid is freed from its inferior attachments in the neck for suspension anteriorly, either from the mandible or thyroid cartilage (lower arrow) to further enlarge the airway.

It is often performed after unsuccessful UPPP. The success rate for GA, with or without previous UPPP, is high. **Maxillomandibular advancement (MMA)** is typically performed after failed GA, except in patients with primary facial skeletal deformities in whom MMA is the treatment of choice. It allows for maximal enlargement of the retrolingual airway, as well as enlargement of the retropalatal space. Maxilla and mandible are advanced simultaneously, thereby advancing the base of the tongue more than GA (Figure 12-7). **The response rate to MMA is close to 100 percent.** The major complication is transient anesthesia of the cheek and chin. After all surgical procedures, a follow up polysomnogram is indicated to document the success of treatment. Because of the diminishing efficacy of surgery in some patients, serial polysomnograms may be warranted, particularly if the patient complains of recurrent symptoms.

**Narcolepsy** is a chronic disorder of unknown etiology. It usually begins in the second to third decade of life, rarely before age 5 or after age 50. It affects men and women equally. Narcolepsy is characterized by a tetrad of symptoms: 1) excessive daytime somnolence, 2) sleep paralysis, 3) hypnagogic
hallucinations, and 4) cataplexy. Only 20–25 percent of patients experience the full tetrad of symptoms. The symptoms of narcolepsy reflect the inappropriate intrusion of REM sleep and its properties of atonia and visual hallucinations into wakefulness and other stages of sleep. For example, sleep paralysis occurs when REM-associated atonia intrudes on the transition between wakefulness and sleep. The patient is consciousness, but unable to move his limbs. Hypnagogic hallucinations are vivid, REM-associated dream-like visual hallucinations which occur at sleep onset, while hypnopompic hallucinations occur upon awakening. Sleep paralysis, hypnagogic hallucinations and hypnopompic hallucinations can occur in normal people who have a disruption in their normal sleep pattern, as with sleep deprivation.

Cataplexy is unique to narcolepsy, although about 30 percent of patients with narcolepsy do not experience it. REM-associated atonia intruding into wakefulness causes loss of axial and/or appendicular muscle tone for a few seconds, without loss of consciousness. The longer the episode, the more likely it will lead directly into REM sleep. This phenomenon is often precipitated by extremes of emotion, such as anger, fear, excitement, or, most commonly, laughter. It can occur several times daily or rarely. Cataplexy can endanger a person’s life if it occurs while driving, bathing or swimming.

Restless sleep is a common complaint among patients with narcolepsy, but not a major cause of daytime sleepiness. Sleep apnea and periodic limb movements of sleep occur with higher frequency in patients with narcolepsy compared to the general population, but the treatment of these conditions does not improve daytime sleepiness.

The cause of narcolepsy has yet to be determined. An immunologic cause has been suggested by the high association of certain class II human leukocyte antigens (HLA) in patients with narcolepsy with cataplexy. Greater than 85 percent of narcoleptic patients with cataplexy, of various ethnic backgrounds, share a specific HLA allele, DQB1*0602 (previously known as DQw1), often occurring concomitantly with HLA DR2, in comparison to 12–38 percent of the general population. Other associated HLA antigens have been reported. Nevertheless, class II HLA typing is not a routine diagnostic test as these antigens may be absent in some patients with narcolepsy with cataplexy and present in asymptomatic persons.

The definitive diagnosis of narcolepsy is based on a polysomnogram that reveals no cause of hypersomnia and a multiple sleep latency test (MSLT). The MSLT is a daytime study that consists of a series of four to five nap trials. Severity of daytime sleepiness is based on sleep latency, or time it takes a subject to fall asleep, and presence of sleep-onset REM (SOREM), or REM sleep within 10 minutes of sleep onset. A sleep latency of less than 5 minutes is indicative of a pathologically sleepy state, while a sleep latency of 5–10 minutes is only suggestive of it. The laboratory diagnosis of narcolepsy requires an average sleep latency of less than 10 minutes and SOREM in at least two nap trials. As SOREM can occur with REM-sleep deprivation from sleep apnea or drug and alcohol withdrawal, an overnight polysomnogram prior to the MSLT is done to screen out such causes. A two-week period of alcohol or drug abstinence is required before an MSLT. Compliance can be monitored with a drug screen prior to the study.

The treatment of narcolepsy is often difficult. Excessive daytime sleepiness and cataplexy are particularly difficult to treat. The mainstay of treatment is a
A combination of several planned naps daily and CNS stimulants, such as pemoline, methylphenidate, amphetamine, and modafinil (Provigil®). To avoid medication tolerance, weekly drug vacations for one to two days are recommended. Cataplexy, sleep paralysis and hypnagogic hallucinations are treated with tricyclic antidepressants, namely clomipramine, imipramine, nortriptyline, and protriptyline, and other serotonin reuptake inhibitors such as fluoxetine.

**Circadian Sleep-Wake Rhythm Disorders**

This group of disorders is characterized by a mismatch between the patient’s sleep patterns and the time at which the patient wishes to fall asleep. The most common scenario in which this complaint occurs is with shift work or jet lag. With shift work, rotating shifts are more disruptive to the sleep-wake cycle than fixed evening or night shifts. Patients older than 40 years of age experience greater difficulty in adapting to shift work than younger workers. Jet lag has the same effect on sleep as shift work. Its effect is exacerbated by alcohol and dehydration. In general, east to west travel across several time zones results in sleep disturbances that last about 4–5 days. Travel from west to east can disrupt sleep for up to 10–14 days. Melatonin and benzodiazepines may reduce jet lag in some people, but their use is not recommended because of inadequate data supporting their efficacy. Furthermore, the long-term side effects of melatonin are unknown.

There are three major circadian rhythm sleep disorders: 1) delayed sleep phase syndrome, 2) advanced sleep phase syndrome and 3) non-24 hour sleep-wake syndrome. In **delayed sleep phase syndrome**, patients usually go to sleep about 6–8 hours later than socially acceptable. Once asleep, however, sleep architecture and duration are normal. Patients complain of nocturnal insomnia and daytime sleepiness. Psychopathology is common. Delayed sleep phase syndrome occasionally coincides with the onset of bipolar disorder or schizophrenia. Lifestyle, mood, personality, family problems and school problems may be contributing factors. Sometimes, delayed sleep phase syndrome begins in childhood and persists throughout life. It can be familial. The success of treatment with hypnotics, melatonin, stimulants, and psychotherapy is highly dependent on patient motivation, but is usually disappointing. Chronotherapy, which involves delaying bed time by one hour every day, until the desired bed time is achieved, is usually not successful. Another way to advance the circadian rhythm is to expose the patient to a bright light of greater than 5000 lux in the early morning, between 5 and 8 a.m. The results are highly dependent on patient motivation.

**Advanced sleep phase syndrome** is very rare and is thus questioned as a true entity. It is characterized by early evening sleep onset, i.e., 7 p.m. or 8 p.m., and early morning awakening. Sleep duration and architecture are normal. Attempts to delay the time of sleep onset are usually unsuccessful. The sleep patterns of the elderly most closely match the advanced sleep phase syndrome. The major difference is that the total duration of nocturnal sleep in the elderly is shorter and fragmented. Chronotherapy may be beneficial, as with delayed sleep phase syndrome. For patients with advanced sleep phase syndrome, exposure to bright light between 9 p.m. and 1 a.m. may induce a phase shift in bed time.

The **irregular sleep-wake pattern** or **non-24 hour sleep-wake syndrome** reflects a complete loss of circadian rhythm. There is disorganization and tremendous variability in the sleep-wake schedule. Overall sleep in a 24-hour
period is reduced and fragmented into short sleep periods. The fragmentation of sleep parallels the random fluctuations in body temperature as well as the irregularity of other lifestyle habits such as meals. Typically, patients complain of daytime sleepiness, fatigue, and insomnia. Alzheimer’s dementia may be associated with the irregular sleep-wake pattern, although circadian rhythm of core body temperature is preserved. Behavioral treatment is the mainstay of establishing a normal sleep-wake schedule. A set bedtime is established. The number of naps is restricted. In some Alzheimer patients, bright lights have been used in the early evening with some success in reducing sleep fragmentation and sundowning.

The diagnosis of circadian rhythm disorders is based on history and the examination of detailed sleep diaries. A polysomnogram may be helpful in assessing time at sleep onset, total sleep time, and sleep architecture while the MSLT can be used to determine severity of daytime sleepiness in patients refractory to treatment for the assumed diagnosis.

Parasomnias

Parasomnias collectively refer to undesirable motor or autonomic activity during sleep or upon arousal. They include hypnic jerks, sleep myoclonus, periodic leg movements of sleep, head banging, sleep paralysis, REM sleep behavior disorder, sleepwalking, nightmares, night terrors, bruxism (teeth grinding), and bed-wetting. It is more common in children than adults. They may be associated with: 1) abnormal sleep architecture such as REM behavior disorder, 2) familial predisposition such as sleepwalking or night terrors, 3) transition between sleep stages or a particular stage of sleep, such as head banging and REM behavior disorder, respectively, and 4) multiple factors as in bed wetting. Anxiety, sleep deprivation or changes in sleep habit may exacerbate the frequency or severity of parasomnias in children and adults.

Hypnic jerks or sleep starts are brief jerks of one or more limbs during sleep onset. They are normal. Often, they may be accompanied by a sensation of falling. Exercise, emotional stress or caffeine in the evening are precipitants. No treatment is required.

Sleep myoclonus refers to rhythmic leg jerking, usually involving the tibialis anterior. It is commonly benign, often familial, and increases with age. The diagnosis is based on history provided by the patient’s bed partner and the electromyographic appearance of rhythmic leg movements on polysomnogram. Although the etiology is idiopathic, it has been associated with some medical conditions such as uremia and anemia, neurologic disorders such as sensory neuropathy, narcolepsy, and drug treatment with levodopa for Parkinson’s disease, clomipramine for depression, and amphetamines for narcolepsy. Most patients with sleep myoclonus are asymptomatic. Treatment with clonazepam is recommended only when patients complain of insomnia or daytime somnolence.

Periodic limb movements of sleep (PLS) are characterized by repetitive, stereotyped, and asymmetrical leg movements during sleep. The leg movements are often, but not always, associated with cyclical arousals or awakenings. The patient is usually unaware of the limb movements or fragmentation of sleep. PLS may present as insomnia or, less commonly, as excessive daytime somnolence. Men and women are equally affected. Prevalence increases with age, but is rare
before the age of 30. The etiology is unknown.

PLS frequently occurs in association with restless legs syndrome (RLS). RLS is characterized by an uncomfortable, ill-described sensation involving the calves, which results in an irresistible urge to move the legs. Symptoms are most severe when the legs are at rest. Most patients with RLS have PLS, but the reverse is not true. In patients with RLS, the major identifiable cause is sensory peripheral neuropathy.

The diagnosis of PLS is confirmed by a polysomnogram, which demonstrates a series of periodic bursts of muscle activity over the leg EMG leads. These bursts of muscle activity are often followed by brief arousals or awakenings. Occasionally, PLS is an incidental finding, often associated with no or infrequent arousals. The polysomnogram can also exclude other causes of excessive daytime somnolence associated with frequent nocturnal limb movements, namely sleep apnea and fragmentary myoclonus.

Levodopa, benzodiazepines, and the opioids constitute first-line therapy for PLS and RLS. Long-term treatment with these medications is hindered by tolerance. Pergolide has been shown to be effective alternative therapy, although other antiparkinsonism medications and some antiepileptic medications are only anecdotally reported as promising to date.

**Head banging**, otherwise called rhythmic movement disorder or jactatio capitis nocturna, often involves body rocking. These movements, which are pleasurable to the patient, occur during sleep onset and stages 1 and 2 of sleep. It is usually confined to infancy and early childhood. Predisposing factors are low IQ, immaturity, and maternal neglect. Most children are normal. Trauma is unusual, although subdural hematoma and retinal hemorrhage may occur. Treatment is recommended only if injuries occur. Benzodiazepines reduce, but do not eliminate, this behavior.

**Sleep paralysis** refers to paralysis of skeletal muscles during the transition from wakefulness to sleep or from sleep to wakefulness. The severity of paralysis is variable from patient to patient. Some patients have mild weakness of the limbs, while others cannot open their eyes or speak. It is often described as a terrifying experience. Respiration is unaffected. Sleep paralysis may occur under four different circumstances: 1) an isolated, rare event, 2) familial, in which case it can occur several times nightly and may be associated with excessive daytime sleepiness, 3) as a symptom of narcolepsy, or 4) as result from sleep-onset REM secondary to sleep deprivation or sleep fragmentation.

**REM sleep behavior disorder** is characterized by retention of muscle tone during REM, a finding confirmed by polysomnogram. Under normal circumstances, REM sleep is characterized by loss of muscle tone and paralysis. Patients with REM sleep behavior disorder are able to enact their dreams, which are usually frightening and combative. Self-injury or injury to bed partners is usually the precipitating reason for medical attention. This condition most commonly occurs in elderly men. Most cases are idiopathic although it may occur in diseases that affect anatomical areas responsible for REM sleep, for example dementia, subarachnoid hemorrhage, stroke, brainstem lesions and multiple sclerosis. Treatment is quite satisfactory in most cases with clonazepam 0.5–1.0 mg at bedtime.

**Sleepwalking, night terrors and nightmares** are distinguished by the particular sleep stage in which these behaviors occur. Sleepwalking and night terrors

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occur during slow wave sleep, usually within the first two hours of sleep. They are more common in children and may be familial. Most children are normal, contrary to popular belief, and outgrow these behaviors. Sleep deprivation, anxiety or fever are predisposing factors. Sleepwalking and night terrors are associated with variable degrees of responsiveness. Night terrors are characterized by piercing, inconsolable crying and autonomic hyperactivity, i.e., tachycardia, piloerection, and sweating. If awoken, children are disoriented and cannot recall what has happened. The inability to recall a dream, as well as its occurrence during slow wave sleep is what distinguishes night terrors from nightmares. Most children with nightmares have some recall of content, as it is essentially a terrifying dream during REM sleep.

A regular sleep schedule is usually effective treatment for sleepwalking. When self-injury occurs as a result of sleep walking, diazepam 2–5 mg nightly may be beneficial because it reduces arousals. Tricyclic antidepressants may also help reduce sleep walking although it can also exacerbate it in some patients. Benzodiazepines can be prescribed to treat severe, frequent night terrors.

**Bruxism or teeth grinding** is relatively uncommon. It may result in abnormal wear of teeth or jaw pain. This behavior usually occurs during the early stages of sleep and is often associated with stress. It is also observed in patients with mental retardation or in comatose states. A tooth guard may prevent undue wear of teeth.

**Bed-wetting** occurs in all stages of sleep, including REM sleep. It is often familial and slightly more common in boys than girls. The etiology is believed to be a combination of behavioral and psychiatric problems. If bed-wetting occurs after a period of dryness at night, one should consider diseases of the urinary tract or spinal cord. Behavioral therapy may be effective, with positive reinforcement for dry nights and negative reinforcement with a buzzer that goes off when a pad is soaked. Tricyclic antidepressants, such as imipramine 10–25 mg nightly, may also be beneficial because urinary retention is one of the anticholinergic side effects. Hypnotics, however, may worsen bed-wetting.

**References**


Self-Assessment Questions

1. Night terrors are characterized by:
   A. Occurrence during slow wave sleep
   B. Occurrence during REM sleep
   C. A child’s ability to recall the content of a terrifying dream
   D. Persistence into adulthood
   E. Psychopathology

2. Obstructive sleep apnea is:
   A. More common in men than women
   B. Often associated with snoring
   C. Due to obesity
   D. All of the above
   E. A and B

3. The stage of sleep, which remains relatively constant throughout life, relative to total sleep time, is:
   A. Stage I
   B. Stage II
   C. Stage III
   D. Stage IV
   E. REM sleep

4. Daytime somnolence and insomnia are most likely to be the presenting complaints of:
   A. Delayed sleep phase syndrome
   B. Non-24 hour sleep-wake syndrome
   C. Primary snoring
   D. Sleep walking
   E. Advanced sleep phase syndrome

5. Narcolepsy is characterized by:
   A. Excessive daytime somnolence
   B. Sleep paralysis
   C. Periodic limb movements of sleep
   D. A and B
   E. A, B, and C

6. Sleep deprivation may cause or precipitate all of the following, except:
   A. Sleep paralysis
   B. Hypnagogic hallucinations
   C. Sleepwalking
   D. Periodic limb movements of sleep
   E. Sleep-onset REM
7. Periodic limb movements of sleep most commonly coexists with:
   A. Narcolepsy
   B. Obstructive sleep apnea
   C. Central sleep apnea
   D. Restless leg syndrome
   E. Sensory peripheral neuropathy

ANSWERS

1. A. Night terrors occur during slow wave sleep while nightmares occur during REM sleep.

2. E. Obstructive sleep apnea is more common in men than women and is often, but not always, associated with snoring. Obesity, while commonly associated with obstructive sleep apnea, is not the sole cause.

3. E. The percentage of REM sleep, relative to total sleep time, remains fairly constant after the first year of life.

4. B. In non-24 hour sleep-wake syndrome, sleep is reduced and fragmented. Patients complain of daytime sleepiness, fatigue, and insomnia.

5. D. Narcolepsy is characterized by excessive daytime somnolence, hypnagogic hallucinations, sleep paralysis and cataplexy. Periodic limb movements of sleep are not a symptom of narcolepsy although it occurs with higher frequency in patients with narcolepsy than the general population.

6. D. Sleep paralysis, hypnagogic hallucinations, and sleep-onset REM can occur in normal individuals with a disruption in normal sleep pattern. Sleep deprivation may predispose to sleepwalking.

7. D. Restless leg syndrome and periodic limb movements of sleep often coexist and, together, constitute the fourth most common cause of insomnia. Sensory peripheral neuropathy is the most common identifiable cause of restless leg syndrome.