Delayed sleep phase syndrome (DSPS). In DSPS, the sleep-wake circadian rhythm is delayed compared to when the individual attempts to sleep. DSPS was first identified by Weitzman, et al. (1981) as a "chronobiological disorder with sleep-onset insomnia". Individuals report difficulty falling asleep at a desired bedtime, but have normal sleep if they attempt to sleep a few hours later. Daily sleep-wake diaries of individuals with DSPS show late sleep onset, few awakenings, early wake-up times when work or social demands are present, and late (midafternoon) wake-up times when there are no such demands on their time. The disorder is associated with daytime sleepiness that is most pronounced in the morning (Thorpy, et al., 1988). Polysomnography shows that, compared to age matched norms, patients with DSPS have longer latencies to stages 2 and 3 and decreased sleep efficiency (Allen, et al., 1989). In addition, DSPS patients have more awakenings and less slow wave sleep in the first part of the night. These findings indicate a reduced depth and quality of sleep in the first part of the night which is consistent with the phase delay.

Delayed sleep phase individuals commonly identify themselves as 'night people' and report being most alert during the late evening and night hours. Many case study reports on the disorder come from adolescence and young adult population (Ferber, 1985). Adults who suffer from DSPS often report childhood onset of the symptoms (Weitzman, et al., 1981). The prevalence of the diagnosis among patients in sleep disorders centers is estimated at 7 percent. The prevalence of the disorder in the general population is unknown, but some researchers estimate the prevalence is higher, particularly with adolescents and young adults (Henschel & Lack, 1987; Thorpy, et al., 1988).

Although patients with delayed sleep phase experience an inability to phase advance their rhythm, they usually have no such difficulty with phase delay. This is the basis for chronotherapy (Czeisler, et al., 1981). In chronotherapy, bedtime is successively delayed by daily increments of 3 hours until a desired bedtime is reached. This strategy is often augmented with appropriately timed light exposure (see below). Although chronotherapy with or without light exposure is effective (Czeisler, et al., 1981), it requires high motivation and, in the case of adolescents, clear

behavioral contracts and monitoring (Dahl, 1992). Efficacy of chronotherapy with adolescents who manifest school refusal or when other motivational factors are present is not very high (Ferber, 1983). In these cases treatment needs to explicitly address intrinsic and environmental factors that reinforce the delayed bedtime behavior. Even when treatment successfully shifts the sleep wake rhythm to a desired time, the risk of relapse is high and the maintenance of a regular sleep-wake schedule is important for relapse prevention.

Advanced sleep phase syndrome (ASPS). Patients with ASPS present with the converse set of complaints from those with DSPS, namely, inability to stay awake until the desired bedtime and inability to remain asleep until the desired wake-up time. Other than a shift in the major sleep episode toward earlier sleep-onset time with respect to 24-hour day, the sleep of individuals with ASPS is normal in quality and duration. Typical sleep-onset times are between 6 p.m. and 8 p.m., and no later than 9 p.m., and wake times are between 1 a.m. and 3 a.m., and no later than 5 a.m. Unlike other sleep maintenance disorders, the early morning awakening occurs after a normal amount of otherwise undisturbed sleep (ASDA, 1997).

As with DSPS, ASPS afflicted individuals come to clinical attention only when the inherent sleep-wake schedule interferes with social activities and/or work schedule. Problems may also occur as a result of attempting to adhere to a conventional sleep schedule. For example, when a patient attempts to remain awake until the desired bed time, the early awakening aspect of the syndrome can lead to chronic insufficient sleep and excessive daytime sleepiness (Richardson & Malin, 1996).

ASPS is much more common in older individuals than in the young and the complaint of waking up too early in the morning may be confused with depression. It is thought that the higher prevalence of ASPS in elderly individuals is due to shortening of the endogenous circadian timing system that accompanies normal aging. However, sleep maintenance insomnia in the elderly may be due to an intrinsic sleep disorder or secondary to a mental, neurologic or other medical disorder (see the sections on intrinsic sleep disorders and sleep disorders associated with neurological disorders). Some types of depression, for example, also appear to exhibit phase advance features.

The early morning awakening of patients with depression is usually accompanied by other sleep and somatic symptoms and altered mood (see the section on depression).

Current approach to treatment of ASPS is bright light exposure in the evening and avoidance of light exposure (e.g. wearing dark, wraparound sunglasses) in the morning. Bright light exposure in the evening and the avoidance of bright light in the morning are thought to help accomplish reentrainment of the sleep-wake cycle into the circadian rhythm (Wagner, 1996; Hauri, 1992; see the section on light treatment).

Irregular sleep-wake pattern. This rare disorder is characterized by a variable and disorganized sleep-wake pattern, suggesting the absence of circadian rhythmicity. Sleep is broken into several short sleep episodes, but the cumulative sleep for a 24-hour period is at normal levels. Polysomnographic studies show no abnormalities in sleep parameters except for the short duration of each episode (Roehrs, Zorick, & Roth, 1994). The absence of a sleep-wake rhythm is confirmed by the absence of a temperature rhythm. This pattern has been found to be common in elderly people with dementia compared to age matched controls (Okawa, Mishima, Hishikawa, Hozumi, Hori, & Takahashi, 1991). Treatment consists of a gradual decrease in the number and duration of daily naps. Increase in activity levels and social interaction is recommended to facilitate the process (Hauri, 1982; Okawa, et al, 1991).

Non-24-hour sleep-wake syndrome. This is a disorder in which individuals are unable to entrain to a 24-hour day and instead maintain 25 to 27 hour sleep-wake cycles. Some individuals with this syndrome tend to progressively phase delay. The disorder is rare in the general population and is assumed to be of higher prevalence among blind people (Miles, et al., 1977). Treatment focuses on entraining the circadian rhythm to a 24-hour day through social interaction, exposure to light, and melatonin. Melatonin has been successful in treating this disorder in blind individuals (Palm, Blennow, & Wetterberg, 1997).

Extrinsic circadian rhythm disorders

Shift work. Because of family and social demands, night shift workers usually attempt to live their days off on a different schedule than their work days. A disrupted sleep-wake schedule

often results in disturbed and shortened sleep, sleepiness on the job, reduced performance levels, and psychological distress due to disruptions in family and social life. Workers on rotating shift schedules have greater difficulty than those on permanent night shifts. The severity of the problem increases with age. Aschoff (1978) and Reinberg, et al. (1978) found that individuals whose temperature rhythm had low amplitude could better adapt to shift work.

Polysomnographic studies of the sleep and sleepiness of night shift workers show short durations of sleep following work nights (5 to 6 hours) and reduced sleep efficiency (Walsh, et al., 1984), reduced amounts of stage 2 and REM sleep (Akerstedt, 1985) and increased sleepiness on the MSLT during waking hours (Akerstedt, et al., 1982).

Many researchers recommend that rotating shift schedules should be designed to be consistent with the natural tendency to phase delay. That is, the direction of rotation should be progressively later and the duration of the shift should be long enough to allow for adaptation (Roehrs, Zorick, & Roth, 1994). European researchers, on the other hand, prefer a very rapidly rotating system of two days on each shift since that allows the circadian rhythm to remain constant (Akerstedt, 1985). A variety of methods for enhancing alertness and performance among shift workers have been suggested (Penn & Bootzin, 1990). The optimal timing of work breaks, social activity during breaks, bright light and other sensory stimulation have the most potential for short-term alerting effects. Stress coping techniques, sleep hygiene information, and family counseling have the most potential for addressing the long-term effects of shift work.

Time-zone change disorders. Dyssomnia associated with rapid time-zone change ("jet lag") is due to a desynchrony between the endogenous sleep-wake rhythm and the light/dark cycle. Symptoms include an inability to sustain sleep and excessive sleepiness. For most people these symptoms subside after a few days, depending on the number of time-zones crossed. Frequent travelers, such as transatlantic airline crews, may experience more persistent difficulties. Westward travel is associated with disturbed sleep at the end of the sleep period, which coincides with habitual wakeup time, and eastward travel is associated with sleep onset insomnia (Roehrs,

Zorick, & Roth, 1994). Due to the natural tendency to phase delay, travel westbound is easier to adjust to than travel eastbound.

Light treatment. Results show that properly timed exposures to bright light (7,000-12,000 lux) for 2 to 3 days can shift the phase of the sleep rhythm (Czeisler, et al., 1989). As a means of comparison, typical indoor room light is less than 500 lux; a few minutes after dawn, sunlight produces about 2500 lux; and at noon, sunlight is in the 100,000 lux range (Terman, 1994). The direction of the shift depends on the timing of the exposure to light. A phase advance is achieved by light exposure in the morning, while a phase delay is achieved by light exposure in the evening (Lewy, et al., 1984). In addition to the proper timing of bright light, it is also important to have periods of darkness during which no bright light is allowed (Czeisler, et al., 1989; Rosenthal, et al., 1990).

Preliminary results indicate that bright light treatment may be effective for a number of circadian rhythm sleep disorders. Bright light treatment during night shift work resulted in increased duration of daytime sleep and improved alertness on the job (Czeisler, et al., 1990). Bright light treatment has also been shown to benefit jet lag sufferers (Daan & Lewy, 1984; Sasaki, et al., 1989), insomnia during the "dark period" in northern Norway (Lingjaerde, et al., 1985), early morning awakening (Lack & Wright, 1993), and delayed sleep phase syndrome (Rosenthal, et al., 1990).

The disruptive effects of time-zone travel on circadian rhythms can also be alleviated through melatonin administration about an hour before bedtime in the new time-zone. Melatonin is a circadian-setting hormone released by the pineal gland and has been shown to induce drowsiness and shorten sleep latency. Thus, timely administration may serve to advance or delay circadian phase. However, research concerning the optimal dose and the effects of long-term use are lacking (Chase & Gidal, 1997; Sack, Hughes, Edgar, & Lewy, 1997).

Intrinsic Sleep Disorders

The intrinsic sleep disorders are sleep disorders due primarily to internal mechanisms including insomnia, narcolepsy, sleep apnea, periodic limb movements, and restless legs.

Insomnia

Insomnia includes difficulty falling asleep, frequent or prolonged awakenings during the night, early-morning awakenings, and the experience of poor quality sleep. Epidemiological surveys indicate that about 15 percent of adults report severe or frequent insomnia and another 15 percent report mild or occasional insomnia (Bixler, et al., 1979; Mellinger, Balter, & Uhlenhuth, 1985). The prevalence of insomnia increases with age. Over 25 percent of those over 65 years of age report having had considerable difficulty in falling or staying asleep during the past 12 months (Mellinger, et al., 1985).

The two most common types of intrinsic insomnia are psychophysiological insomnia and sleep state misperception.

Psychophysiological insomnia. Psychophysiological insomnia refers to sleep disturbances that can be verified by objective measures (such as polysomnography) and that are not associated with either extrinsic determinants such as noise or drugs or with other disorders such as major depression. About 15 percent of patients seen at sleep disorders centers with a complaint of insomnia receive this diagnosis (ASDA, 1997).

The major determinants of psychophysiological insomnia are stress, expectations of disturbed sleep, and poor sleep habits. Other determinants such as circadian rhythm disturbances, changes associated with aging, drug abuse, and misinformation about sleep may contribute to the problem. Learned sleep-preventing associations are often central in psychophysiological insomnia and may contribute to the exacerbation and maintenance of other sleep disturbances, as well.

Insomniacs frequently engage in activities at bedtime that are incompatible with falling asleep. Many insomniacs organize their activities around their bedrooms with television, telephone, books, and food within easy reach. For others, bedtime is the first time during the day available to think about the day's events and to plan and worry about the next day. Under these conditions, bed and bedtime become cues for arousal rather than cues for sleep (Bootzin & Nicassio, 1978).

Another source of arousal for the insomniac is that the bedroom can become a cue for the anxiety and frustration associated with trying to fall asleep. Insomniacs often can sleep any place other than their own bed. They may fall asleep in a chair or on a couch and often have less difficulty sleeping away from home. In contrast, good sleepers often have difficulty in strange surroundings. For them, there are strong cues for sleep associated with their bed and they only have difficulty sleeping when these cues are not available (Bootzin & Nicassio, 1978).

Sleep State Misperception. Sleep state misperception is the most recent label for instances in which the complaint of insomnia is not verified by objective measures. In the past, this disorder has been called pseudoinsomnia, subjective insomnia, and disorder of initiating or maintaining sleep without objective findings. Fewer than 5 percent of patients seen at sleep disorders centers for complaints of insomnia receive this diagnosis (ASDA, 1997).

A number of investigations have indicated that insomniacs of all types overestimate sleep latency and underestimate total sleep and number of nocturnal awakenings compared to polysomnography (e.g., Borkovec & Weerts, 1976; Carskadon, et al., 1976). Those with sleep state misperception are the most extreme on this dimension. It should be emphasized that this diagnosis is not the sleep equivalent of hypochondria. Sleep state misperception often involves perceptual and cognitive dysfunctions that are not detected by polysomnography.

Some patients with this diagnosis have difficulty distinguishing sleep states from wake-sleep transition states (Perlis, et al., 1997) due perhaps to increased access to cognitive rumination during sleep. Other patients are hypervigilant to environmental stimuli during sleep and are able to remember and report on their occurrence (Anch, Saskin, & Moldofsky, 1989; Loewy & Bootzin, 1998).

CAPS and alpha sleep. Two arousal-related electrophysiological patterns have been found in the sleep of insomniacs: Cyclic Alternating Pattern Sequences (CAPS) and alpha sleep. CAPS are a bi-phasic electrical pattern that is found in the microstructure of NREM sleep stages (Terzano, Mancia, Salati, Costani, Decembrino, & Parrino, 1985), consisting of an arousal phase (composed of arousal-related phasic events distinct to each particular NREM sleep stage) that lasts between 2-

and 60-seconds, followed by a return to tonic or baseline activity. CAPS are a normal pattern of NREM sleep. Such arousal and de-arousal patterns occupy about 25% of NREM sleep in young, healthy, adult sleepers. CAPS are significantly more elevated (68%) in the sleep of insomniacs, suggesting a hyperaroused state during sleep. The exact relation of CAPS to the pathophysiology of insomnia is currently unknown, however, treatment of insomnia with hypnotics has been shown to reduce CAPS to a normal level (Terzano & Parrino, 1992).

Alpha rhythm, 8- to 12-hertz, is the dominant electrical pattern found in people who are awake, but relaxed. Many hypervigilant patients with insomnia have alpha and sleep EEG waves that occur simultaneously. This has been called alpha-delta sleep (Hauri & Hawkins, 1973) or, more recently, alpha sleep. During wake, alpha is seen primarily from occipital leads whereas during sleep the alpha rhythm is more frontal and central. Alpha sleep is often experienced as nonrestorative sleep (i.e., not feeling rested after sleeping). Alpha sleep has been found in insomnia-affected patients having fibromyalia, rheumatoid arthritis, post-traumatic stress disorder, chronic pain disorders, depression, chronic fatigue syndrome, AIDS, and alcoholism (Fredrickson & Krueger, 1994; Moldofsky, Scairsbrick, England, & Smythe, 1975; Norman, et al., 1989; Ware, Russell & Campos, 1986; Whelton, Saskin, Salit, & Moldofsky, 1988; for additional information see the section on fibromyalgia).

Treatment of insomnia. The prescription of sedative/hypnotics is the most frequently-used treatment for insomnia. About 4.3% of adults in the U.S. use medically prescribed psychoactive medication to promote sleep (i.e., hypnotics, anxiolytics, and antidepressants; Mellinger, Balter, & Uhlenhuth, 1985). Of the sedative/hypnotics, benzodiazepines are the most frequently prescribed, having almost completely replaced barbiturates (Morin & Kwentus, 1988). Five principles for pharmacotherapy for persistent insomnia have been summarized by Kupfer and Reynolds (1997): use the lowest effective dose; use intermittent dosing to delay tolerance (two to four times weekly); prescribe medication for short-term use; discontinue medication gradually; and be alert for rebound insomnia following discontinuation. The use of sedative/hypnotics to induce sleep is effective for short-term use, with effects that last 2 to 4 weeks. However, there have been no published

randomized clinical trials of hypnotics for longer than 35 days (Kupfer & Reynolds, 1997). Thus, long-term effectiveness is unknown and long-term use of hypnotics has generally been discouraged because of problems of tolerance, side-effects, and dependence (see the section on hypnotic-dependent sleep disorder).

A number of nonpharmacological treatments have been found to be effective for insomnia, In a recent review by the American Academy of Sleep Medicine, the task force report concluded that nonpharmacological therapies produce reliable and durable changes in sleep and that between 70% and 80% of patients improve (Morin, Hauri, Espie, et al., 1999). The nonpharmacological treatments that are most frequently used include stimulus control instructions, sleep restriction, relaxation training, paradoxical intention, and cognitive therapy.

Stimulus control instructions consists of a set of instructions designed to help the insomniac establish a consistent sleep-wake rhythm, strengthen the bed and bedroom as cues for sleep, and weaken them as cues for activities that might interfere with sleep. The following rules constitute the stimulus control instructions (Bootzin, 1972, 1977, Bootzin, Epstein, & Wood, 1991).

1. Lie down intending to go to sleep only when you are sleepy.
2. Do not use your bed for anything except sleep; that is, do not read, watch television, eat, or worry in bed. Sexual activity is the only exception to this rule. On such occasions, the instructions are to be followed afterward when you intend to go to sleep.
3. If you find yourself unable to fall asleep, get up and go into another room. Stay up as long as you wish and then return to the bedroom to sleep. Although we do not want you to watch the clock, we want you to get out of bed if you do not fall asleep immediately. Remember the goal is to associate your bed with falling asleep quickly! If you are in bed more than about 10 minutes without falling asleep and have not gotten up, you are not following this instruction.
4. If you still cannot fall asleep, repeat Step 3. Do this as often as is necessary throughout the night.

5. Set your alarm and get up at the same time every morning irrespective of how much sleep you got during the night. This will help your body acquire a consistent sleep rhythm.
6. Do not nap during the day.

Stimulus control therapy has been found to be effective for both sleep onset and sleep maintenance insomnia. Meta-analyses of the treatment outcome literature for insomnia have found stimulus control to be one of the most effective of the nonpharmacological treatments (Morin, Culbert, & Schwartz, 1994; Murtagh & Greenwood, 1995).

Sleep restriction (Spielman, Saskin, & Thorpy, 1987) is based on the observation that many insomniacs have low sleep efficiency; i.e., the proportion of time they are in bed that they are actually asleep is less than 85 percent. To help consolidate sleep, insomniacs are instructed to limit the time that they are in bed to the number of hours of sleep that they normally obtain. At first, patients experience partial sleep deprivation since they usually underestimate how much sleep they normally get. The sleep deprivation, however, helps to consolidate sleep. Patients are then instructed to follow a gradual schedule of increasing the amount of time spent in bed while maintaining the improved sleep efficiency. Sleep restriction has been effectively used in combination with sleep education and stimulus control instructions for the treatment of sleep maintenance insomnia in older adults (Hoelscher & Edinger, 1988).

A commonly recommended treatment for insomnia is some type of relaxation training. This includes a variety of procedures such as progressive relaxation, autogenic training, transcendental meditation, yoga, hypnosis, and EMG biofeedback. As treatments for insomnia, all of these procedures are based on the same premise; i.e., if people can learn to be relaxed at bedtime, they will fall asleep faster. Because many insomniacs are aroused and anxious during the day, relaxation training may provide a double benefit--first, as a means of helping to induce sleep, and second, as a general coping skill to be used to deal more effectively with the stresses of the day (Bootzin & Nicassio, 1978). The different types of relaxation procedures have all been found to be about equally effective in controlled studies (Bootzin & Rider, 1997).

Progressive relaxation training has been found to be effective in producing sleep onset latency improvement in both sleep state misperception and psychophysiological insomniacs (Borkovec, et al., 1979). Improvement of the sleep state misperception patients was found on daily sleep diaries and on subjective estimates while in the sleep laboratory. Since these patients did not exhibit a problem on polysomnographic measures, no improvement was observed on those measures. Improvement of psychophysiological insomniacs, on the other hand, was found on both sleep diaries and polysomnography.

Cognitive treatments have focused on patients' beliefs and expectations. Insomniacs often subscribe to a number of irrational beliefs about sleep. Examples of these beliefs would be that the individual must get at least 8 hours of sleep to feel refreshed and function well the next day, or the worry that if the individual goes for one or two nights without sleep he or she will have a nervous breakdown, or the belief that the individual should avoid or cancel social, family, and work obligations after a poor night's sleep (Morin, 1993). Treatment involves providing accurate information and having the insomniac identify and rehearse alternative belief statements. These techniques have been effective as part of multicomponent treatments (Morin, et al., 1999; Morin, Stone, McDonald, & Jones, 1994).

A cognitive intervention that has been frequently evaluated is paradoxical intention (PI). Many insomniacs exacerbate their problem by worrying about whether they will be able to fall asleep. To reduce the anticipatory anxiety associated with "trying" to fall asleep, insomniacs are instructed to stay awake as long as possible. Controlled evaluations of PI for sleep onset insomnia have been mixed. The rationale provided by the therapist for the paradoxical instruction may be a crucial component of its effectiveness. In a meta-analysis of the application of PI to a number of different problems, Shoham-Salomon and Rosenthal (1987) found that rationales that emphasize a positive benefit or the positive qualities of the person having the problem are more effective than rationales that are neutral or that emphasize negative aspects of the problem (Shoham-Salomon & Rosenthal, 1987).

Many controlled studies have examined the efficacy and durability of psychological treatments for chronic insomnia. Two separate meta-analyses have been published (Morin, Culbert, & Schwartz, 1994; Murtagh & Greenwood, 1995). Both meta-analyses concluded that psychological treatments have been found to improve the sleep of insomniacs over control conditions, and improvements were maintained at six month follow-ups. Murtagh & Greenwood (1995) concluded that there are few differences between different active treatments although stimulus control instructions had the strongest effects. Morin, Culbert, & Schwartz (1994) concluded that both stimulus control instructions and sleep restriction, as single-component treatments, had the strongest effects.

In recent years the focus has shifted from efficacy studies of single-component treatments to effectiveness studies of multi-component treatments. In one study, primary care nurses within a community general medical clinic were trained to deliver a multi-component treatment consisting of stimulus control instructions, sleep restriction, and cognitive therapy (Espie, Inglis, Tessier, & Harvey, in press). The treatment was more effective than a control condition in improving sleep and 84% of patients who were initially using hypnotics remained drug-free during the follow-up period. Another innovative intervention presented a course of 8 television programs broadcast in the Netherlands. About 200,000 people viewed the course of whom 23,000 ordered course materials. An evaluation of a sample of those participating found that the course produced improvements in sleep latency and total sleep, and decreases in hypnotic drug use (Oosterhuis & Klip, 1997).

Narcolepsy

Narcolepsy is characterized by excessive daytime sleepiness and abnormal manifestations of REM sleep (ASDA, 1997). The REM abnormalities associated with narcolepsy include sleep onset REM periods and dissociated REM processes such as cataplexy, sleep paralysis, and hypnagogic hallucinations.

Narcolepsy has a prevalence of between 5 and 10 per 10,000 individuals (Guilleminault, 1994a). Age at onset can range from childhood to the fifth decade, but peaks in the second decade.

Researchers have documented a strong association between narcolepsy and the human leucocyte antigen HLA-DR2 phenotype lending support to genetic theories of narcolepsy (Honda, Asaka, Tanimura, & Furusho, 1983). However, it has not been a useful diagnostic measure because as many as 25% of nonnarcoleptics also have the HLA-DR2 phenotype. The gene for canine narcolepsy, which is characterized primarily by symptoms of cataplexy (see below), has been found to be due to a recessive gene that affects the hypocretin (orexin) receptor 2 gene (Lin, et al., 1999). Although genetics is definitely involved in the development of narcolepsy, there is also a strong environmental component since only 30% of identical twins are concordant for narcolepsy (Mignot, 1998).

Narcolepsy is classified as a disorder of excessive somnolence. However, narcoleptics do not sleep abnormally long within a 24-hour period. Narcoleptics may sleep 8 hours a night and be awake 16 hours during the day, but they will have repeated naps or lapse into sleep of short duration lasting about 10 to 20 minutes. They awaken feeling refreshed but begin to feel sleepy again within 2 to 3 hours, at which point the pattern repeats itself (ASDA, 1997). These sudden and irresistible sleep attacks, also called excessive daytime sleepiness (EDS), are most common in, but not limited to, sleep- inducing circumstances such as sedentary activities. They may occur in situations where the individual is actively involved in a task such as taking an examination, eating, walking, driving, or talking.

An accurate diagnosis of narcolepsy is dependent on differentiating it from two other medical conditions associated with the symptoms of excessive somnolence, breathing disorders during sleep and central nervous system hypersomnia (Guilleminault, 1994a). The four classic symptoms of narcolepsy include: (a) sleep attacks--characterized by an irresistible urge to sleep, (b) cataplexy--an abrupt and reversible decrease or loss of muscle tone that ranges in severity from mild weakness to complete postural collapse, with no loss of consciousness, elicited by emotion (usually pleasant or exciting emotions, e.g., laughter, pride, anger, and surprise) and ranging from a few seconds to several minutes, (c) hypnagogic hallucinations--frightening and vivid visual or auditory hallucinations that occur at the onset of sleep, and (d) sleep paralysis--muscle paralysis

upon falling asleep or awakening, characterized by inability to move limbs, speak, or breathe deeply, lasting from one to several minutes, and is often a frightening experience. Only 20% to 25% of narcoleptics have all four of the core symptoms, and the latter three typically decrease over time. Sleep disruption and frequent nocturnal awakenings are common, as are reports of memory problems and automatic behavior (ASDA, 1997).

Positive diagnosis of narcolepsy requires either irresistible sleepiness or cataplexy plus sleep onset REM episodes documented by polysomnogram (ASDA, 1997). On the basis of polysomnographic recording, confirmatory diagnosis can be made if the mean MSLT score is below 5, two or more sleep onset REM periods occur during MSLT testing, and REM sleep occurs within 20 minutes of sleep onset during a nighttime recording (Association of Professional Sleep Societies, 1986). Caution must be exercised, however, since individuals without complaints of daytime sleepiness occasionally have two or more sleep onset REM periods (Aldrich, Chervin, & Malow, 1997; Bishop, Rosenthal, Helmus, Roehrs, & Roth, 1996) and some individuals with narcolepsy do not have multiple sleep onset REM periods on the first day of MSLT testing (Choo & Guilleminault, 1998)

Conventional treatment of narcolepsy focuses on treating the separate symptoms. Stimulants (methylphenidate and dextroamphetamine) are often used to treat EDS, and antidepressants (protriptyline and viloxazine) are used for the REM-related symptoms of cataplexy, sleep paralysis, and hypnagogic hallucinations (Guilleminault, et al., 1986; Mitler, et al., 1986). A routine of medication and naps (Roehrs, et al., 1986) can reduce sleep attacks from three per day to one or two per month (Mitler, Nelson, & Hajdukovic, 1987). Support groups (Guilleminault, 1994a) and counseling for the families of narcoleptics (Karacan & Howell, 1988) are useful in helping patients and their families deal with the psychological and social effects of narcolepsy, including loss of self-esteem, depressive reactions, and family discord.

Sleep Apnea

Sleep apnea is a respiratory disorder characterized by repetitive episodes of cessation of airflow lasting at least 10 seconds. Sleep apnea is one of the most common causes of sleep

disturbance. The prevalence is higher in men than in women and increases with age. While an occasional pause in breathing is normal, sleep apnea becomes a health problem when apneas occur frequently and are associated with significant reduction in blood oxygen saturation, cardiac arrhythmia or impaired daytime functioning secondary to frequent arousals and fragmented sleep. In general, more than five apneas per hour of sleep in adults is considered abnormal (Guilleminault & Dement, 1988). Three types of sleep apnea have been defined: (a) *obstructive*--cessation of airflow secondary to upper-airway obstruction; (b) *central*--cessation of airflow secondary to lack of ventilatory effort; (c) *mixed* –cessation of airflow in a pattern suggesting lack of ventilation effort initially, and subsequent upper airway obstruction. While as mentioned, the term *apnea* refers to a complete cessation of airflow, *hypopnea* refers to a partial reduction in airflow, again usually accompanied by an arousal. The hypopneas and apneas cause similar clinical features (e.g., unrefreshed sleep, excessive daytime sleepiness). Patients with obstructive sleep apnea can demonstrate obstructive, central, or mixed apneas, in addition to hypopneas throughout the night. Thus the severity of the disorder is measured by combining all of the above events in a total score, referred to as the respiratory disturbance index (RDI). Many individuals with sleep apnea have obstructive, central, and mixed events in one night with as many as 300 such events per night.

Obstructive sleep apnea (OSA). Of the three types of sleep apnea OSA is the most common. The term *sleep disordered breathing* (SDB) is sometimes used synonymously with OSA. A recent epidemiological study reported that the prevalence of OSA is higher than previously estimated, approximately 4% and 2% in middle-aged men and women, respectively (Young, et al., 1993). Kripke et al. (1997), based on a group of community dwelling adults ages 40-60 years estimated the prevalence of OSA to be even higher, 9.3 % for men and 5.2% for women. Patients with OSA are often overweight. Although OSA is a common disorder in middle-aged adults and appears to increase the risk of or exacerbates already existing cardiovascular diseases, it remains underrecognized and underdiagnosed (Young, et al., 1997; Chan, et al., 1998; Partinen & Guilleminault, 1990). The onset of OSA is usually insidious and if untreated, complications including mortality can ensue (Redline & Stroh; 1998).

During sleep the upper airway musculature relaxes, reducing the caliber of the airway and leading to increased respiratory effort. Snoring, which has been reported in up to 50% of males over age 40, is an indication of partial airway obstruction and is produced by the vibration of pharyngeal tissues on inspiration as the airflow becomes increasingly turbulent in the narrowed orophayngeal space. Further narrowing produces hypopnea or with complete obstruction, apnea. Factors that reduce the diameter of the upper airway and predispose patients to snoring and OSA include obesity (via fat deposition), enlarged tonsillar tissue mass, and craniofacial abnormalities. In addition, excessive upper airway muscle relaxation and narrowing occur with the use of alcohol, or other respiratory depressants (Redline & Stroh, 1998; Bootzin, Quan, Bamford, et al. 1995).

Patients with obstructive sleep apnea usually snore loudly, as reported by their bed partners, and their snoring is irregular and interrupted by pauses. These pauses end with a loud snort as the patient's progressively stronger ventilatory efforts finally produce arousals, contraction of the upper airway muscles, and normal breathing. Arousals can be brief and not recalled by the patient or prolonged with complete awakening. As the patient returns to sleep, the cycle of progressive upper airway narrowing begins again.

In addition to the hallmark symptom, loud snoring, nighttime symptoms of OSA may include restlessness, frequent awakenings, choking, tachycardia, heartburn, enuresis, nocturia, and profuse sweating. Daytime symptoms include waking up feeling unrefreshed with feelings of disorientation or grogginess, sometimes accompanied by a headache. Additionally, some patients may also experience decreased libido and changes in personality (e.g., increased irritability, depression, and aggressiveness) (Guilleminault, 1994b; ASDA, 1994). Daytime sleepiness is common and can range from fatigue to involuntary sleep attacks, which can occur while the patient is driving or in conversation. Definitive diagnosis and determination of appropriate treatment require that the patient undergo a polysomnographic study.

The treatment of OSA depends on the severity of the condition as expressed by the disturbance in nocturnal sleep, cardiac or neurologic complications, and daytime symptoms. The

goals of treatment are to eliminate snoring and upper airway obstruction, maintain nocturnal oxygenation and ventilation, and normalize sleep architecture (Chan et al. 1998). Several treatment modalities are available for OSA including behavioral, medical, and surgical interventions. Behavioral interventions to modify risk factors generally are considered first or are sometimes recommended as an adjunct to more aggressive therapies. In patients with mild to moderate OSA weight loss (Brownman et al. 1984), avoidance of alcohol and other CNS depressants (Issa & Sullivan, 1982; Robinson & Zwillich, 1985), and position therapy (measures designed to keep the patient in the lateral rather than the supine position when asleep) (Cartwright, Lloyd, Lilie, & Kravitz, 1985) can be effective interventions.

Because the pathophysiology of OSA is primarily due to the intermittent collapse of a narrowed airway, mechanical or surgical techniques to enlarge the airway seem to be the most logical treatment approach. Nasal continuous positive airway pressure (CPAP) is by far the treatment of choice for moderate to severe OSA. CPAP is applied by means of an airtight nasal mask connected to a flow generator and acts as a pneumatic internal splint of the upper airway to prevent it from collapsing. Nasal CPAP is highly effective in abolishing apneic events and produces immediate improvement in symptoms, quality of life and cognitive function (Sullivan, Issa, Berthon-Jones & Eves, 1981; Engleman, Martin, Deary & Douglas, 1997). Many patients, however, do not tolerate the CPAP appliance, leading to poor compliance. Kribbs and colleagues (1993) have reported that although the majority of patients claim to use CPAP nightly, only 16 of 35 (46%) in their study met criteria for regular use. And when used, the mean duration of CPAP use was less than 5 hours per night.

Surgical procedures for OSA include tonsillectomy, nasal surgery (e.g., correcting deviated septum, removing nasal polyps), and uvulopalatopharyngoplasty (UPPP). The long-term efficacy of UPPP is highest in patients with mild to moderate disease, but even in this population satisfactory results occur in less than 50% of patients (Conway, Fujita, Zorick et al. 1988). Mandibular advancement devices (MRD) that reposition the mandible, the tongue, and other structures to increase upper airway dimension appear to be effective in the treatment of snoring and

mild OSA. The long-term efficacy of MRD, however, is still unclear (Chan et al. 1998; Chervin & Guilleminault, 1996).

Central sleep apnea. CSA represents a loss of ventilatory drive or rhythmicity. Most CSA episodes occur at sleep onset and are benign. CSA is considered pathological only when the events are sufficiently frequent to disturb sleep or result in hypoxemia or cardiac arrythmias or daytime functioning. The severity of the CSA and the extent of sleep disturbance are partially dependent on underlying pathophysiology. Clinical presentation of patients with CSA differs from patients with OSA in a number of ways, however, there is also considerable overlap. Pure CSA is rare as patient with this condition constitutes fewer than 10% of patients evaluated in sleep laboratories. Compared to patients with OSA, CSA patients less commonly complain of daytime hypersomnolence, and obesity and snoring while sometimes present, are not prominent features. The primary complaints of CSA patients are usually insomnia, and frequent awakenings during the night, sometimes accompanied by a gasp for air and shortness of breath. Daytime symptoms may include morning headache, tiredness, fatigue, sleepiness, difficulty in memory and other cognitive functions, sexual dysfunction, and depression (ASDA, 1997).

CSA occurs secondary to lesions that affect the neural systems involved in ventilation (White, 1994). For example, CSA is a known complication of several neuromuscular diseases (e.g., amyotrophic lateral sclerosis (ALS), motor-sensory neuropathy, myotonic dystrophy). These patients usually demonstrate daytime hypoventilation as manifested by elevated blood carbon dioxide level. At night, at the onset of sleep, loss of the behavioral control of ventilation the so-called "wakefulness" stimulus leads to further hypoventilation and oxygen desaturation. Typically, CSA worsens during REM sleep because these patients lose the use of accessory muscles of respiration which compensate for diaphragm weakness due to the muscle atonia that occurs in REM sleep. Profound hypoxemia can result (Guilleminault & Robinson, 1998).

Because CSA remains a disorder that is not well understood, current available treatments are not entirely satisfactory. Central respiratory stimulants such as medroxyprogesterone and have shown to be effective in central sleep apnea for a short time, but result have been variable with

long-term use (Bootzin, et al. 1995). Tricyclic antidepressant agents, which suppress REM sleep and increase respiratory musculature tone, have been used to treat both CSA and OSA with little success (Guilleminault & Robinson, 1996). Oxygen therapy helps some patients by decreasing the wide swings in blood oxygen content that characterize some forms of CSA and affect central nervous system rhythmiticity. Nighttime ventilatory support, usually administered through appliances similar to CPAP devices, can be effective treatment for patients with CSA secondary to neuromuscular disorders. The boost in ventilation provided compensate for muscle weakness and correct oxygen and carbon dioxide abnormalities, leading to none consolidated sleep.

Periodic Limb Movements and Restless Legs Syndrome

Periodic limb movement (PLM) disorder is characterized by periodic episodes of repetitive and stereotypic limb movements during sleep. Also known as nocturnal myoclonus, periodic movements during sleep, and periodic leg movements, PLMs are described as episodes of rhythmic extensions of the big toe and dorsiflexions of the ankle, sometimes with flexions of the knee and hip.

The most common sleep characteristics associated with PLMs are frequent arousals and complaints of nonrestorative sleep. Patients are often unaware of PLMs and present with complaints of insomnia or excessive daytime sleepiness or seek help as a result of a bed partner's complaints of excessive nighttime movement.

Accurate diagnosis of PLMs is complex. The incidence of PLMs increases with age. It is known to exist concurrently with other disorders of excessive somnolence such as narcolepsy, sleep apnea, or restless legs syndrome (Moore & Gurakar, 1988) and may be associated with medical conditions such as chronic uremia, anemia, chronic lung disease, and fibromyalgia (Montplaisir, et al., 1994). PLMs may be induced or aggravated by the use of tricyclic antidepressants and monoamine oxidase inhibitors, as well as withdrawal from drugs such as anticonvulsants, benzodiazepines, barbiturates, and other hypnotic agents (ASDA, 1997). A polysomnogram with leg EMG is necessary to establish a final diagnosis of PLMs.

Polysomnographic recording of PLMs reveals repetitive episodes of muscle contraction measured by EMG, occurring every 20 to 40 seconds (ASDA, 1997). These episodes usually occur in stages 1 and 2 sleep, decrease in stages 3 and 4, and are usually absent during REM sleep (Montplaisir, et al., 1985). A PLM index (number of PLMs per hour of sleep) greater than 5 is considered pathological.

Restless legs syndrome (RLS) is a disorder characterized by irresistible leg movements usually prior to sleep onset (ASDA, 1997) and often described as a "aching" sensation. The most prominent characteristic of this disorder is the partial or complete relief of the sensation with leg motion and return of the symptom with cessation of movement. Symptoms are often exacerbated soon after getting into bed and tend to cease long enough for the patient to fall asleep, only to reappear later in the night. However, RLS may occur at times during the day after prolonged periods of sitting. The severity of symptoms with RLS may wax and wane throughout a patient's lifetime. Remissions may last for years and symptoms reappear suddenly without warning. Most patients with RLS also show PLMs during sleep. Symptoms are associated with a number of conditions such as the last trimester of pregnancy, caffeine intake, fatigue, exceptionally warm environment, prolonged exposure to cold (Montplaisir, et al., 1994), anemia, and rheumatoid arthritis (ASDA, 1997).

Treatment for PLMs and RLS is pharmacological. The most effective drugs to date are carbidopa/levodopa , benzodiazepines (clonazepam, temazepam, lorazepam, and nitrazepam), and opioids. Carbidopa/levodopa are considered the drugs of choice and have been shown to reduce the quantity of movements and increase the quality of sleep (reference). Benzodiazepines may be considered in milder cases (Mitler, Brownman, Gujavarty, Timms, & Menn, 1984; Moldofsky, Tullis, Quance, & Lue, 1985), however, their use should be considered carefully, especially n the elderly, since they may induce or exacerbate sleep apnea and prevent arousal from apneic episodes (Montplaisir, et al., 1994).