

consider the duration of action. Benzodiazepines carry a risk of addiction and abuse, especially in patients with a history of alcohol or sedative abuse. Like alcohol, some sleep-promoting medications can worsen sleep apnea. Sedatives can also produce complex behaviors during sleep, such as sleep walking and sleep eating, although this seems more likely at higher doses.

### RESTLESS LEGS SYNDROME

Patients with restless legs syndrome (RLS) report an irresistible urge to move the legs. Many patients report a creepy-crawly or unpleasant deep ache within the thighs or calves, and those with more severe RLS may have discomfort in the arms as well. For most patients with RLS, these dysesthesias and restlessness are much worse in the evening and first half of the night. The symptoms appear with inactivity and can make sitting still in an airplane or when watching a movie a miserable experience. The sensations are temporarily relieved by movement, stretching, or massage. This nocturnal discomfort usually interferes with sleep, and patients may report daytime sleepiness as a consequence. RLS is very common, affecting 5–10% of adults and is more common in women and older adults.

A variety of factors can cause RLS. Iron deficiency is the most common treatable cause, and iron replacement should be considered if the ferritin level is less than 50 ng/mL. RLS can also occur with peripheral neuropathies and uremia and can be worsened by pregnancy, caffeine, alcohol, antidepressants, lithium, neuroleptics, and antihistamines. Genetic factors contribute to RLS, and polymorphisms in a variety of genes (*BTBD9*, *MEIS1*, *MAP2K5/LBXCOR*, and *PTPRD*) have been linked to RLS, although as yet, the mechanism through which they cause RLS remains unknown. Roughly one-third of patients (particularly those with an early age of onset) have multiple affected family members.

RLS is treated by addressing the underlying cause such as iron deficiency if present. Otherwise, treatment is symptomatic, and dopamine agonists are used most frequently. Agonists of dopamine  $D_{2/3}$  receptors such as pramipexole (0.25–0.5 mg q7PM) or ropinirole (0.5–4 mg q7PM) are considered first-line agents. Augmentation is a worsening of RLS such that symptoms begin earlier in the day and can spread to other body regions, and it can occur in about 25% of patients taking dopamine agonists. Other possible side effects of dopamine agonists include nausea, morning sedation, and increases in rewarding behavior such as gambling and sex. Opioids, benzodiazepines, pregabalin, and gabapentin may also be of therapeutic value. Most patients with restless legs also experience periodic limb movement disorder, although the reverse is not the case.

### PERIODIC LIMB MOVEMENT DISORDER

Periodic limb movement disorder (PLMD) involves rhythmic twitches of the legs that disrupt sleep. The movements resemble a triple flexion reflex with extensions of the great toe and dorsiflexion of the foot for 0.5 to 5.0 s, which recur every 20–40 s during NREM sleep, in episodes lasting from minutes to hours. PLMD is diagnosed by a polysomnogram that includes recordings of the anterior tibialis and sometimes other muscles. The EEG shows that the movements of PLMD frequently cause brief arousals that disrupt sleep and can cause insomnia and daytime sleepiness. PLMD can be caused by the same factors that cause RLS (see above), and the frequency of leg movements improves with the same medications as used for RLS, including dopamine agonists. Recent genetic studies identified polymorphisms associated with RLS/PLMD, suggesting that they may have a common pathophysiology.

### PARASOMNIAS

Parasomnias are abnormal behaviors or experiences that arise from or occur during sleep. A variety of parasomnias can occur during NREM sleep, from brief confusional arousals to sleepwalking and night terrors. The presenting complaint is usually related to the behavior itself, but the parasomnias can disturb sleep continuity or lead to mild impairments in daytime alertness. Two main parasomnias occur in REM sleep: REM sleep behavior disorder (RBD) and nightmares.

**Sleepwalking (Somnambulism)** Patients affected by this disorder carry out automatic motor activities that range from simple to complex. Individuals may walk, urinate inappropriately, eat, exit the house, or drive a car with minimal awareness. Full arousal may be difficult, and occasional individuals may respond to attempted awakening with agitation or violence. Sleepwalking arises from NREM stage N3 sleep, usually in the first few hours of the night, and the EEG usually shows the slow cortical activity of deep NREM sleep even when the patient is moving about. Sleepwalking is most common in children and adolescents, when these sleep stages are most robust. About 15% of children have occasional sleepwalking, and it persists in about 1% of adults. Episodes are usually isolated but may be recurrent in 1–6% of patients. The cause is unknown, although it has a familial basis in roughly one-third of cases. Sleepwalking can be worsened by insufficient sleep, which subsequently causes an increase in deep NREM sleep; alcohol; and stress. These should be addressed if present. Small studies have shown some efficacy of antidepressants and benzodiazepines; relaxation techniques and hypnosis can also be helpful. Patients and their families should improve home safety (e.g., replace glass doors, remove low tables to avoid tripping) to minimize the chance of injury if sleepwalking occurs.

**Sleep Terrors** This disorder occurs primarily in young children during the first few hours of sleep during NREM stage N3 sleep. The child often sits up during sleep and screams, exhibiting autonomic arousal with sweating, tachycardia, large pupils, and hyperventilation. The individual may be difficult to arouse and rarely recalls the episode on awakening in the morning. Treatment usually consists of reassuring the parents that the condition is self-limited and benign, and like sleepwalking, it may improve by avoiding insufficient sleep.

**Sleep Bruxism** Bruxism is an involuntary, forceful grinding of teeth during sleep that affects 10–20% of the population. The patient is usually unaware of the problem. The typical age of onset is 17–20 years, and spontaneous remission usually occurs by age 40. Sex distribution appears to be equal. In many cases, the diagnosis is made during dental examination, damage is minor, and no treatment is indicated. In more severe cases, treatment with a tooth guard is necessary to prevent tooth injury. Stress management or, in some cases, biofeedback can be useful when bruxism is a manifestation of psychological stress. There are anecdotal reports of benefit with benzodiazepines.

**Sleep Enuresis** Bedwetting, like sleepwalking and night terrors, is another parasomnia that occurs during sleep in the young. Before age 5 or 6 years, nocturnal enuresis should be considered a normal feature of development. The condition usually improves spontaneously by puberty, has a prevalence in late adolescence of 1–3%, and is rare in adulthood. Treatment consists of bladder training exercises and behavioral therapy. Symptomatic pharmacotherapy is usually accomplished in adults with desmopressin (0.2 mg qhs), oxybutynin chloride (5 mg qhs), or imipramine (10–25 mg qhs). Important causes of nocturnal enuresis in patients who were previously continent for 6–12 months include urinary tract infections or malformations, cauda equina lesions, emotional disturbances, epilepsy, sleep apnea, and certain medications.

**REM Sleep Behavior Disorder (RBD)** RBD ([Video 38-2](#)) is distinct from other parasomnias in that it occurs during REM sleep. The patient or the bed partner usually reports agitated or violent behavior during sleep, and upon awakening, the patient can often report a dream that accompanied the movements. During normal REM sleep, nearly all skeletal muscles are paralyzed, but in patients with RBD, the polysomnogram often shows limb movements during REM sleep, lasting for seconds to minutes. The movements can be dramatic, and it is not uncommon for the patient or the bed partner to be injured.

RBD primarily afflicts older men, and most either have or will develop a neurodegenerative disorder. In longitudinal studies of RBD, half of the patients developed a synucleinopathy such as Parkinson's disease ([Chap. 449](#)) or dementia with Lewy bodies ([Chap. 448](#)), or occasionally multiple system atrophy ([Chap. 454](#)), within 12 years, and over 80% developed a synucleinopathy by 20 years. RBD can occur