are often repetitive in nature or reflect epileptogenic features such as the content of diurnal auras (e.g., unmotivated dread), phosphenes, or ictal imagery. Disorders of arousal, especially confusional arousals, may also be present.

Breathing-related sleep disorders. Breathing-related sleep disorders can lead to awakenings with autonomic arousal, but these are not usually accompanied by recall of nightmares.

Panic disorder. Attacks arising during sleep can produce abrupt awakenings with autonomic arousal and fearfulness, but nightmares are typically not reported and symptoms are similar to panic attacks arising during wakefulness.

Sleep-related dissociative disorders. Individuals may recall actual physical or emotional trauma as a "dream" during electroencephalography-documented awakenings.

Medication or substance use. Numerous substances/medications can precipitate nightmares, including dopaminergics; beta-adrenergic antagonists and other antihypertensives; amphetamine, cocaine, and other stimulants; antidepressants; smoking cessation aids; and melatonin. Withdrawal of REM sleep–suppressant medications (e.g., antidepressants) and alcohol can produce REM sleep rebound accompanied by nightmares. If nightmares are sufficiently severe to warrant independent clinical attention, a diagnosis of substance/medication-induced sleep disorder should be considered.

Comorbidity

Nightmares may be comorbid with several medical conditions, including coronary heart disease, cancer, parkinsonism, and pain, and can accompany medical treatments, such as hemodialysis, or withdrawal from medications or substances of abuse. Nightmares frequently are comorbid with other mental disorders, including PTSD; insomnia disorder; schizophrenia; psychosis; mood, anxiety, adjustment, and personality disorders; and grief during bereavement. A concurrent nightmare disorder diagnosis should only be considered when independent clinical attention is warranted (i.e., Criteria A–C are met). Otherwise, no separate diagnosis is necessary. These conditions should be listed under the appropriate comorbid category specifier. However, nightmare disorder may be diagnosed as a separate disorder in individuals with PTSD if the nightmares are temporally unrelated to PTSD (i.e., preceding other PTSD symptoms or persisting after other PTSD symptoms have resolved).

Nightmares are normally characteristic of REM sleep behavior disorder, PTSD, and acute stress disorder, but nightmare disorder may be independently coded if nightmares preceded the condition and their frequency or severity necessitates independent clinical attention. The latter may be determined by asking whether nightmares were a problem before onset of the other disorder and whether they continued after other symptoms had remitted.

Relationship to International Classification of Sleep Disorders

The *International Classification of Sleep Disorders,* 2nd Edition (ICSD-2), presents similar diagnostic criteria for nightmare disorder.

Rapid Eye Movement Sleep Behavior Disorder

Diagnostic Criteria **327.42 (G47.52)**

A. Repeated episodes of arousal during sleep associated with vocalization and/or complex motor behaviors.

B. These behaviors arise during rapid eye movement (REM) sleep and therefore usually occur more than 90 minutes after sleep onset, are more frequent during the later portions of the sleep period, and uncommonly occur during daytime naps.

C. Upon awakening from these episodes, the individual is completely awake, alert, and not confused or disoriented.
D. Either of the following:
   1. REM sleep without atonia on polysomnographic recording.
   2. A history suggestive of REM sleep behavior disorder and an established synucleinopathy diagnosis (e.g., Parkinson's disease, multiple system atrophy).
E. The behaviors cause clinically significant distress or impairment in social, occupational, or other important areas of functioning (which may include injury to self or the bed partner).
F. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.
G. Coexisting mental and medical disorders do not explain the episodes.

Diagnostic Features

The essential feature of rapid eye movement (REM) sleep behavior disorder is repeated episodes of arousal, often associated with vocalizations and/or complex motor behaviors arising from REM sleep (Criterion A). These behaviors often reflect motor responses to the content of action-filled or violent dreams of being attacked or trying to escape from a threatening situation, which may be termed *dream enacting behaviors.* The vocalizations are often loud, emotion-filled, and profane. These behaviors may be very bothersome to the individual and the bed partner and may result in significant injury (e.g., falling, jumping, or flying out of bed; running, punching, thrusting, hitting, or kicking). Upon awakening, the individual is immediately awake, alert, and oriented (Criterion C) and is often able to recall dream mentation, which closely correlates with the observed behavior. The eyes typically remain closed during these events. The diagnosis of REM sleep behavior disorder requires clinically significant distress or impairment (Criterion E); this determination will depend on a number of factors, including the frequency of events, the potential for violence or injurious behaviors, embarrassment, and distress in other household members.

Associated Features Supporting Diagnosis

Severity determination is best made based on the nature or consequence of the behavior rather than simply on frequency. Although the behaviors are typically prominent and violent, lesser behaviors may also occur.

Prevalence

The prevalence of REM sleep behavior disorder is approximately 0.38%–0.5% in the general population. Prevalence in patients with psychiatric disorders may be greater, possibly related to medications prescribed for the psychiatric disorder.

Development and Course

The onset of REM sleep behavior disorder may be gradual or rapid, and the course is usually progressive. REM sleep behavior disorder associated with neurodegenerative disorders may improve as the underlying neurodegenerative disorder progresses. Because of the very high association with the later appearance of an underlying neurodegenerative disorder, most notably one of the synucleinopathies (Parkinson's disease, multiple system atrophy, or major or mild neurocognitive disorder with Lewy bodies), the neurological status of individuals with REM sleep behavior disorder should be closely monitored.

REM sleep behavior disorder overwhelmingly affects males older than 50 years, but increasingly this disorder is being identified in females and in younger individuals. Symp-

toms in young individuals, particularly young females, should raise the possibility of narcolepsy or medication-induced REM sleep behavior disorder.

Risk and Prognostic Factors

Genetic and physiological. Many widely prescribed medications, including tricyclic antidepressants, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and beta-blockers, may result in polysomnographic evidence of REM sleep without atonia and in frank REM sleep behavior disorder. It is not known whether the medications per se result in REM sleep behavior disorder or they unmask an underlying predisposition.

Diagnostic Markers

Associated laboratory findings from polysomnography indicate increased tonic and/or phasic electromyographic activity during REM sleep that is normally associated with muscle atonia. The increased muscle activity variably affects different muscle groups, mandating more extensive electromyographic monitoring than is employed in conventional sleep studies. For this reason, it is suggested that electromyographic monitoring include the submentalis, bilateral extensor digitorum, and bilateral anterior tibialis muscle groups. Continuous video monitoring is mandatory. Other polysomnographic findings may include very frequent periodic and aperiodic extremity electromyography activity during non-REM (NREM) sleep. This polysomnography observation, termed *REM sleep without atonia,* is present in virtually all cases of REM sleep behavior disorder but may also be an asymptomatic polysomnographic finding. Clinical dream-enacting behaviors coupled with the polysomnographic finding of REM without atonia is necessary for the diagnosis of REM sleep behavior disorder. REM sleep without atonia without a clinical history of dream-enacting behaviors is simply an asymptomatic polysomnographic observation. It is not known whether isolated REM sleep without atonia is a precursor to REM sleep behavior disorder.

Functional Consequences of Rapid Eye Movement Sleep Behavior Disorder

REM sleep behavior disorder may occur in isolated occasions in otherwise unaffected individuals. Embarrassment concerning the episodes can impair social relationships. Individuals may avoid situations in which others might become aware of the disturbance, visiting friends overnight, or sleeping with bed partners. Social isolation or occupational difficulties can result. Uncommonly, REM sleep behavior disorder may result in serious injury to the victim or to the bed partner.

Differential Diagnosis

Other parasomnias. Confusional arousals, sleepwalking, and sleep terrors can easily be confused with REM sleep behavior disorder. In general, these disorders occur in younger individuals. Unlike REM sleep behavior disorder, they arise from deep NREM sleep and therefore tend to occur in the early portion of the sleep period. Awakening from a confusional arousal is associated with confusion, disorientation, and incomplete recall of dream mentation accompanying the behavior. Polysomnographic monitoring in the disorders of arousal reveals normal REM atonia.

Nocturnal seizures. Nocturnal seizures may perfectly mimic REM sleep behavior disorder, but the behaviors are generally more stereotyped. Polysomnographic monitoring employing a full electroencephalographic seizure montage may differentiate the two. REM sleep without atonia is not present on polysomnographic monitoring.

Obstructive sleep apnea. Obstructive sleep apnea may result in behaviors indistinguishable from REM sleep behavior disorder. Polysomnographic monitoring is necessary to differentiate between the two. In this case, the symptoms resolve following effective treatment of the obstructive sleep apnea, and REM sleep without atonia is not present on polysomnography monitoring.

Other specified dissociative disorder (sleep-related psychogenic dissociative disorder). Unlike virtually all other parasomnias, which arise precipitously from NREM or REM sleep, psychogenic dissociative behaviors arise from a period of well-defined wakefulness during the sleep period. Unlike REM sleep behavior disorder, this condition is more prevalent in young females.

Malingering. Many cases of malingering in which the individual reports problematic sleep movements perfectly mimic the clinical features of REM sleep behavior disorder, and polysomnographic documentation is mandatory.

Comorbidity

REM sleep behavior disorder is present concurrently in approximately 30% of patients with narcolepsy. When it occurs in narcolepsy, the demographics reflect the younger age range of narcolepsy, with equal frequency in males and females. Based on findings from individuals presenting to sleep clinics, most individuals (>50%) with initially "idiopathic" REM sleep behavior disorder will eventually develop a neurodegenerative disease—most notably, one of the synucleinopathies (Parkinson's disease, multiple system atrophy, or major or mild neurocognitive disorder with Lewy bodies). REM sleep behavior disorder often predates any other sign of these disorders by many years (often more than a decade).

Relationship to International Classification of Sleep Disorders

REM sleep behavior disorder is virtually identical to REM sleep behavior disorder in the *International Classification of Sleep Disorders,* 2nd Edition (ICSD-2).

Restless Legs Syndrome

Diagnostic Criteria **333.94 (G25.81)**

A. An urge to move the legs, usually accompanied by or in response to uncomfortable and unpleasant sensations in the legs, characterized by all of the following:
   1. The urge to move the legs begins or worsens during periods of rest or inactivity.
   2. The urge to move the legs is partially or totally relieved by movement.
   3. The urge to move the legs is worse in the evening or at night than during the day, or occurs only in the evening or at night.

B. The symptoms in Criterion A occur at least three times per week and have persisted for at least 3 months.

C. The symptoms in Criterion A are accompanied by significant distress or impairment in social, occupational, educational, academic, behavioral, or other important areas of functioning.

D. The symptoms in Criterion A are not attributable to another mental disorder or medical condition (e.g., arthritis, leg edema, peripheral ischemia, leg cramps) and are not better explained by a behavioral condition (e.g., positional discomfort, habitual foot tapping).

E. The symptoms are not attributable to the physiological effects of a drug of abuse or medication (e.g., akathisia).

Diagnostic Features

Restless legs syndrome (RLS) is a sensorimotor, neurological sleep disorder characterized by a desire to move the legs or arms, usually associated with uncomfortable sensations typically described as creeping, crawling, tingling, burning, or itching (Criterion A). The diagnosis of RLS is based primarily on patient self-report and history. Symptoms are worse when the individual is at rest, and frequent movements of the legs occur in an effort to relieve the uncomfortable sensations. Symptoms are worse in the evening or night, and in some individuals they occur only in the evening or night. Evening worsening occurs independently of any differences in activity. It is important to differentiate RLS from other conditions such as positional discomfort and leg cramps (Criterion D).

The symptoms of RLS can delay sleep onset and awaken the individual from sleep and are associated with significant sleep fragmentation. The relief obtained from moving the legs may no longer be apparent in severe cases. RLS is associated with daytime sleepiness and is frequently accompanied by significant clinical distress or functional impairment.

Associated Features Supporting Diagnosis

Periodic leg movements in sleep (PLMS) can serve as corroborating evidence for RLS, with up to 90% of individuals diagnosed with RLS demonstrating PLMS when recordings are taken over multiple nights. Periodic leg movements during wakefulness are supportive of an RLS diagnosis. Reports of difficulty initiating and maintaining sleep and of excessive daytime sleepiness may also support the diagnosis of RLS. Additional supportive features include a family history of RLS among first-degree relatives and a reduction in symptoms, at least initially, with dopaminergic treatment.

Prevalence

Prevalence rates of RLS vary widely when broad criteria are utilized but range from 2% to 7.2% when more defined criteria are employed. When frequency of symptoms is at least three times per week with moderate or severe distress, the prevalence rate is 1.6%; when frequency of symptoms is a minimum of one time per week, the prevalence rate is 4.5%. Females are 1.5–2 times more likely than males to have RLS. RLS also increases with age. The prevalence of RLS may be lower in Asian populations.

Development and Course

The onset of RLS typically occurs in the second or third decade. Approximately 40% of individuals diagnosed with RLS during adulthood report having experienced symptoms before age 20 years, and 20% report having experienced symptoms before age 10 years. Prevalence rates of RLS increase steadily with age until about age 60 years, with symptoms remaining stable or decreasing slightly in older age groups. Compared with nonfamilial cases, familial RLS usually has a younger age at onset and a slower progressive course. The clinical course of RLS differs by age at onset. When onset occurs before age 45, there is often a slow progression of symptoms. In late-onset RLS, rapid progression is typical, and aggravating factors are common. Symptoms of RLS appear similar across the lifespan, remaining stable or decreasing slightly in older age groups.

Diagnosis of RLS in children can be difficult because of the self-report component. While Criterion A for adults assumes that the description of "urge to move" is by the patient, pediatric diagnosis requires a description in the child's own words rather than by a parent or caretaker. Typically children age 6 years or older are able to provide detailed, adequate descriptors of RLS. However, children rarely use or understand the word "urge," reporting instead that their legs "have to" or "got to" move. Also, potentially related to prolonged periods of sitting during class, two-thirds of children and adolescents report daytime leg sensations. Thus, for diagnostic Criterion A3, it is important to compare equal

duration of sitting or lying down in the day to sitting or lying down in the evening or night. Nocturnal worsening tends to persist even in the context of pediatric RLS. As with RLS in adults, there is a significant negative impact on sleep, mood, cognition, and function. Impairment in children and adolescents is manifested more often in behavioral and educational domains.

Risk and Prognostic Factors

Genetic and physiological. Predisposing factors include female gender, advancing age, genetic risk variants, and family history of RLS. Precipitating factors are often time-limited, such as iron deficiency, with most individuals resuming normal sleep patterns after the initial triggering event has disappeared. Genetic risk variants also play a role in RLS secondary to such disorders as uremia, suggesting that individuals with a genetic susceptibility develop RLS in the presence of further risk factors. RLS has a strong familial component.

There are defined pathophysiological pathways subserving RLS. Genome-wide association studies have found that RLS is significantly associated with common genetic variants in intronic or intergenic regions in *MEIS1*, *BTBD9*, and *MAP2K5* on chromosomes 2p, 6p, and 15q, respectively. The association of these three variants with RLS has been independently replicated. *BTBD9* confers a very large (80%) excessive risk when even a single allele is present. Because of the high frequency of this variant in individuals of European descent, the population attributable risk (PAR) approximates 50%. At-risk alleles associated with *MEIS1* and *BTBD9* are less common in individuals of African or Asian descent, perhaps suggesting lower risk for RLS in these populations.

Pathophysiological mechanisms in RLS also include disturbances in the central dopaminergic system and disturbances in iron metabolism. The endogenous opiate system may also be involved. Treatment effects of dopaminergic drugs (primarily D_2 and D_3 nonergot agonists) provide further support that RLS is grounded in dysfunctional central dopaminergic pathways. While the effective treatment of RLS has also been shown to significantly reduce depressive symptoms, serotonergic antidepressants can induce or aggravate RLS in some individuals.

Gender-Related Diagnostic Issues

Although RLS is more prevalent in females than in males, there are no diagnostic differences according to gender. However, the prevalence of RLS during pregnancy is two to three times greater than in the general population. RLS associated with pregnancy peaks during the third trimester and improves or resolves in most cases soon after delivery. The gender difference in prevalence of RLS is explained at least in part by parity, with nulliparous females being at the same risk of RLS as age-matched males.

Diagnostic Markers

Polysomnography demonstrates significant abnormalities in RLS, commonly increased latency to sleep, and higher arousal index. Polysomnography with a preceding immobilization test may provide an indicator of the motor sign of RLS, periodic limb movements, under standard conditions of sleep and during quiet resting, both of which can provoke RLS symptoms.

Functional Consequences of Restless Legs Syndrome

Forms of RLS severe enough to significantly impair functioning or associated with mental disorders, including depression and anxiety, occur in approximately 2%–3% of the population.

Although the impact of milder symptoms is less well characterized, individuals with RLS complain of disruption in at least one activity of daily living, with up to 50% reporting