Substance/medication-induced sleep disorder, insomnia type. Substance/medication-induced sleep disorder, insomnia type, is distinguished from insomnia disorder by the fact that a substance (i.e., a drug of abuse, a medication, or exposure to a toxin) is judged to be etiologically related to the insomnia (see "Substance/Medication-Induced Sleep Disorder" later in this chapter). For example, insomnia occurring only in the context of heavy coffee consumption would be diagnosed as caffeine-induced sleep disorder, insomnia type, with onset during intoxication.

Comorbidity

Insomnia is a common comorbidity of many medical conditions, including diabetes, coronary heart disease, chronic obstructive pulmonary disease, arthritis, fibromyalgia, and other chronic pain conditions. The risk relationship appears to be bidirectional: insomnia increases the risk of medical conditions, and medical problems increase the risk of insomnia. The direction of the relationship is not always clear and may change over time; for this reason, comorbid insomnia is the preferred terminology in the presence of coexisting insomnia with another medical condition (or mental disorder).

Individuals with insomnia disorder frequently have a comorbid mental disorder, particularly bipolar, depressive, and anxiety disorders. Persistent insomnia represents a risk factor or an early symptom of subsequent bipolar, depressive, anxiety, and substance use disorders. Individuals with insomnia may misuse medications or alcohol to help with nighttime sleep, anxiolytics to combat tension or anxiety, and caffeine or other stimulants to combat excessive fatigue. In addition to worsening the insomnia, this type of substance use may in some cases progress to a substance use disorder.

Relationship to International Classification of Sleep Disorders

There are several distinct insomnia phenotypes relating to the perceived source of the insomnia that are recognized by the *International Classification of Sleep Disorders,* 2nd Edition (ICSD-2). These include *psychophysiological insomnia, idiopathic insomnia, sleep-state misperception,* and *inadequate sleep hygiene.* Despite their clinical appeal and heuristic value, there is limited evidence to support these distinct phenotypes.

Hypersomnolence Disorder

Diagnostic Criteria **307.44 (F51.11)**

A. Self-reported excessive sleepiness (hypersomnolence) despite a main sleep period lasting at least 7 hours, with at least one of the following symptoms:
   1. Recurrent periods of sleep or lapses into sleep within the same day.
   2. A prolonged main sleep episode of more than 9 hours per day that is nonrestorative (i.e., unrefreshing).
   3. Difficulty being fully awake after abrupt awakening.

B. The hypersomnolence occurs at least three times per week, for at least 3 months.

C. The hypersomnolence is accompanied by significant distress or impairment in cognitive, social, occupational, or other important areas of functioning.

D. The hypersomnolence is not better explained by and does not occur exclusively during the course of another sleep disorder (e.g., narcolepsy, breathing-related sleep disorder, circadian rhythm sleep-wake disorder, or a parasomnia).

E. The hypersomnolence is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication).

F. Coexisting mental and medical disorders do not adequately explain the predominant complaint of hypersomnolence.

Specify if:

With mental disorder, including substance use disorders

With medical condition

With another sleep disorder

Coding note: The code 307.44 (F51.11) applies to all three specifiers. Code also the relevant associated mental disorder, medical condition, or other sleep disorder immediately after the code for hypersomnolence disorder in order to indicate the association.

Specify if:

Acute: Duration of less than 1 month.

Subacute: Duration of 1–3 months.

Persistent: Duration of more than 3 months.

Specify current severity:

Specify severity based on degree of difficulty maintaining daytime alertness as manifested by the occurrence of multiple attacks of irresistible sleepiness within any given day occurring, for example, while sedentary, driving, visiting with friends, or working.

Mild: Difficulty maintaining daytime alertness 1–2 days/week.

Moderate: Difficulty maintaining daytime alertness 3–4 days/week.

Severe: Difficulty maintaining daytime alertness 5–7 days/week.

Diagnostic Features

Hypersomnolence is a broad diagnostic term and includes symptoms of excessive quantity of sleep (e.g., extended nocturnal sleep or involuntary daytime sleep), deteriorated quality of wakefulness (i.e., sleep propensity during wakefulness as shown by difficulty awakening or inability to remain awake when required), and sleep inertia (i.e., a period of impaired performance and reduced vigilance following awakening from the regular sleep episode or from a nap) (Criterion A). Individuals with this disorder fall asleep quickly and have a good sleep efficiency (>90%). They may have difficulty waking up in the morning, sometimes appearing confused, combative, or ataxic. This prolonged impairment of alertness at the sleep-wake transition is often referred to as *sleep inertia* (i.e., sleep drunkenness). It can also occur upon awakening from a daytime nap. During that period, the individual appears awake, but there is a decline in motor dexterity, behavior may be very inappropriate, and memory deficits, disorientation in time and space, and feelings of grogginess may occur. This period may last some minutes to hours.

The persistent need for sleep can lead to automatic behavior (usually of a very routine, low-complexity type) that the individual carries out with little or no subsequent recall. For example, individuals may find themselves having driven several miles from where they thought they were, unaware of the "automatic" driving they did in the preceding minutes. For some individuals with hypersomnolence disorder, the major sleep episode (for most individuals, nocturnal sleep) has a duration of 9 hours or more. However, the sleep is often nonrestorative and is followed by difficulty awakening in the morning. For other individuals with hypersomnolence disorder, the major sleep episode is of normal nocturnal sleep duration (6–9 hours). In these cases, the excessive sleepiness is characterized by several unintentional daytime naps. These daytime naps tend to be relatively long (often lasting 1 hour or more), are experienced as nonrestorative (i.e., unrefreshing), and do not lead to improved alertness. Individuals with hypersomnolence have daytime naps nearly everyday regardless of the nocturnal sleep duration. Subjective sleep quality may or may not be reported as good. Individuals typically feel sleepiness developing over a period of time, rather than

experiencing a sudden sleep "attack." Unintentional sleep episodes typically occur in low-stimulation and low-activity situations (e.g., while attending lectures, reading, watching television, or driving long distances), but in more severe cases they can manifest in high-attention situations such as at work, in meetings, or at social gatherings.

Associated Features Supporting Diagnosis

Nonrestorative sleep, automatic behavior, difficulties awakening in the morning, and sleep inertia, although common in hypersomnolence disorder, may also be seen in a variety of conditions, including narcolepsy. Approximately 80% of individuals with hypersomnolence report that their sleep is nonrestorative, and as many have difficulties awakening in the morning. Sleep inertia, though less common (i.e., observed in 36%–50% of individuals with hypersomnolence disorder), is highly specific to hypersomnolence. Short naps (i.e., duration of less than 30 minutes) are often unrefreshing. Individuals with hypersomnolence often appear sleepy and may even fall asleep in the clinician's waiting area.

A subset of individuals with hypersomnolence disorder have a family history of hypersomnolence and also have symptoms of autonomic nervous system dysfunction, including recurrent vascular-type headaches, reactivity of the peripheral vascular system (Raynaud's phenomenon), and fainting.

Prevalence

Approximately 5%–10% of individuals who consult in sleep disorders clinics with complaints of daytime sleepiness are diagnosed as having hypersomnolence disorder. It is estimated that about 1% of the European and U.S. general population has episodes of sleep inertia. Hypersomnolence occurs with relatively equal frequency in males and females.

Development and Course

Hypersomnolence disorder has a persistent course, with a progressive evolution in the severity of symptoms. In most extreme cases, sleep episodes can last up to 20 hours. However, the average nighttime sleep duration is around 9½ hours. While many individuals with hypersomnolence are able to reduce their sleep time during working days, weekend and holiday sleep is greatly increased (by up to 3 hours). Awakenings are very difficult and accompanied by sleep inertia episodes in nearly 40% of cases. Hypersomnolence fully manifests in most cases in late adolescence or early adulthood, with a mean age at onset of 17–24 years. Individuals with hypersomnolence disorder are diagnosed, on average, 10–15 years after the appearance of the first symptoms. Pediatric cases are rare.

Hypersomnolence has a progressive onset, with symptoms beginning between ages 15 and 25 years, with a gradual progression over weeks to months. For most individuals, the course is then persistent and stable, unless treatment is initiated. The development of other sleep disorders (e.g., breathing-related sleep disorder) may worsen the degree of sleepiness. Although hyperactivity may be one of the presenting signs of daytime sleepiness in children, voluntary napping increases with age. This normal phenomenon is distinct from hypersomnolence.

Risk and Prognostic Factors

Environmental. Hypersomnolence can be increased temporarily by psychological stress and alcohol use, but they have not been documented as environmental precipitating factors. Viral infections have been reported to have preceded or accompanied hypersomnolence in about 10% of cases. Viral infections, such as HIV pneumonia, infectious mononucleosis, and Guillain-Barré syndrome, can also evolve into hypersomnolence within

months after the infection. Hypersomnolence can also appear within 6–18 months following a head trauma.

Genetic and physiological. Hypersomnolence may be familial, with an autosomal-dominant mode of inheritance.

Diagnostic Markers

Nocturnal polysomnography demonstrates a normal to prolonged sleep duration, short sleep latency, and normal to increased sleep continuity. The distribution of rapid eye movement (REM) sleep is also normal. Sleep efficiency is mostly greater than 90%. Some individuals with hypersomnolence disorder have increased amounts of slow-wave sleep. The multiple sleep latency test documents sleep tendency, typically indicated by mean sleep latency values of less than 8 minutes. In hypersomnolence disorder, the mean sleep latency is typically less than 10 minutes and frequently 8 minutes or less. Sleep-onset REM periods (SOREMPs; i.e., the occurrence of REM sleep within 20 minutes of sleep onset) may be present but occur less than two times in four to five nap opportunities.

Functional Consequences of Hypersomnolence Disorder

The low level of alertness that occurs while an individual fights the need for sleep can lead to reduced efficiency, diminished concentration, and poor memory during daytime activities. Hypersomnolence can lead to significant distress and dysfunction in work and social relationships. Prolonged nocturnal sleep and difficulty awakening can result in difficulty in meeting morning obligations, such as arriving at work on time. Unintentional daytime sleep episodes can be embarrassing and even dangerous, if, for instance, the individual is driving or operating machinery when the episode occurs.

Differential Diagnosis

Normative variation in sleep. "Normal" sleep duration varies considerably in the general population. "Long sleepers" (i.e., individuals who require a greater than average amount of sleep) do not have excessive sleepiness, sleep inertia, or automatic behavior when they obtain their required amount of nocturnal sleep. Sleep is reported to be refreshing. If social or occupational demands lead to shorter nocturnal sleep, daytime symptoms may appear. In hypersomnolence disorder, by contrast, symptoms of excessive sleepiness occur regardless of nocturnal sleep duration. An inadequate amount of nocturnal sleep, or *behaviorally induced insufficient sleep syndrome,* can produce symptoms of daytime sleepiness very similar to those of hypersomnolence. An average sleep duration of fewer than 7 hours per night strongly suggests inadequate nocturnal sleep, and an average of more than 9–10 hours of sleep per 24-hour period suggests hypersomnolence. Individuals with inadequate nocturnal sleep typically "catch up" with longer sleep durations on days when they are free from social or occupational demands or on vacations. Unlike hypersomnolence, insufficient nocturnal sleep is unlikely to persist unabated for decades. A diagnosis of hypersomnolence disorder should not be made if there is a question regarding the adequacy of nocturnal sleep duration. A diagnostic and therapeutic trial of sleep extension for 10–14 days can often clarify the diagnosis.

Poor sleep quality and fatigue. Hypersomnolence disorder should be distinguished from excessive sleepiness related to insufficient sleep quantity or quality and fatigue (i.e., tiredness not necessarily relieved by increased sleep and unrelated to sleep quantity or quality). Excessive sleepiness and fatigue are difficult to differentiate and may overlap considerably.

Breathing-related sleep disorders. Individuals with hypersomnolence and breathing-related sleep disorders may have similar patterns of excessive sleepiness. Breathing-

related sleep disorders are suggested by a history of loud snoring, pauses in breathing during sleep, brain injury, or cardiovascular disease and by the presence of obesity, oropharyngeal anatomical abnormalities, hypertension, or heart failure on physical examination. Polysomnographic studies can confirm the presence of apneic events in breathing-related sleep disorder (and their absence in hypersomnolence disorder).

Circadian rhythm sleep-wake disorders. Circadian rhythm sleep-wake disorders are often characterized by daytime sleepiness. A history of an abnormal sleep-wake schedule (with shifted or irregular hours) is present in individuals with a circadian rhythm sleep-wake disorder.

Parasomnias. Parasomnias rarely produce the prolonged, undisturbed nocturnal sleep or daytime sleepiness characteristic of hypersomnolence disorder.

Other mental disorders. Hypersomnolence disorder must be distinguished from mental disorders that include hypersomnolence as an essential or associated feature. In particular, complaints of daytime sleepiness may occur in a major depressive episode, with atypical features, and in the depressed phase of bipolar disorder. Assessment for other mental disorders is essential before a diagnosis of hypersomnolence disorder is considered. A diagnosis of hypersomnolence disorder can be made in the presence of another current or past mental disorder.

Comorbidity

Hypersomnolence can be associated with depressive disorders, bipolar disorders (during a depressive episode), and major depressive disorder, with seasonal pattern. Many individuals with hypersomnolence disorder have symptoms of depression that may meet criteria for a depressive disorder. This presentation may be related to the psychosocial consequences of persistent increased sleep need. Individuals with hypersomnolence disorder are also at risk for substance-related disorders, particularly related to self-medication with stimulants. This general lack of specificity may contribute to very heterogeneous profiles among individuals whose symptoms meet the same diagnostic criteria for hypersomnolence disorder. Neurodegenerative conditions, such as Alzheimer's disease, Parkinson's disease, and multiple system atrophy, may also be associated with hypersomnolence.

Relationship to International Classification of Sleep Disorders

The *International Classification of Sleep Disorders,* 2nd Edition (ICSD-2), differentiates nine subtypes of "hypersomnias of central origin," including recurrent hypersomnia (Kleine-Levin syndrome).

Narcolepsy

Diagnostic Criteria

A. Recurrent periods of an irrepressible need to sleep, lapsing into sleep, or napping occurring within the same day. These must have been occurring at least three times per week over the past 3 months.

B. The presence of at least one of the following:

   1. Episodes of cataplexy, defined as either (a) or (b), occurring at least a few times per month:

      a. In individuals with long-standing disease, brief (seconds to minutes) episodes of sudden bilateral loss of muscle tone with maintained consciousness that are precipitated by laughter or joking.

b. In children or in individuals within 6 months of onset, spontaneous grimaces or jaw-opening episodes with tongue thrusting or a global hypotonia, without any obvious emotional triggers.

2. Hypocretin deficiency, as measured using cerebrospinal fluid (CSF) hypocretin-1 immunoreactivity values (less than or equal to one-third of values obtained in healthy subjects tested using the same assay, or less than or equal to 110 pg/mL). Low CSF levels of hypocretin-1 must not be observed in the context of acute brain injury, inflammation, or infection.
3. Nocturnal sleep polysomnography showing rapid eye movement (REM) sleep latency less than or equal to 15 minutes, or a multiple sleep latency test showing a mean sleep latency less than or equal to 8 minutes and two or more sleep-onset REM periods.

Specify whether:

347.00 (G47.419) Narcolepsy without cataplexy but with hypocretin deficiency: Criterion B requirements of low CSF hypocretin-1 levels and positive polysomnography/multiple sleep latency test are met, but no cataplexy is present (Criterion B1 not met).

347.01 (G47.411) Narcolepsy with cataplexy but without hypocretin deficiency: In this rare subtype (less than 5% of narcolepsy cases), Criterion B requirements of cataplexy and positive polysomnography/multiple sleep latency test are met, but CSF hypocretin-1 levels are normal (Criterion B2 not met).

347.00 (G47.419) Autosomal dominant cerebellar ataxia, deafness, and narcolepsy: This subtype is caused by exon 21 DNA (cytosine-5)-methyltransferase-1 mutations and is characterized by late-onset (age 30–40 years) narcolepsy (with low or intermediate CSF hypocretin-1 levels), deafness, cerebellar ataxia, and eventually dementia.

347.00 (G47.419) Autosomal dominant narcolepsy, obesity, and type 2 diabetes: Narcolepsy, obesity, and type 2 diabetes and low CSF hypocretin-1 levels have been described in rare cases and are associated with a mutation in the myelin oligodendrocyte glycoprotein gene.

347.10 (G47.429) Narcolepsy secondary to another medical condition: This subtype is for narcolepsy that develops secondary to medical conditions that cause infectious (e.g., Whipple's disease, sarcoidosis), traumatic, or tumoral destruction of hypocretin neurons.

Coding note (for ICD-9-CM code 347.10 only): Code first the underlying medical condition (e.g., 040.2 Whipple's disease; 347.10 narcolepsy secondary to Whipple's disease).

Specify current severity:

Mild: Infrequent cataplexy (less than once per week), need for naps only once or twice per day, and less disturbed nocturnal sleep.

Moderate: Cataplexy once daily or every few days, disturbed nocturnal sleep, and need for multiple naps daily.

Severe: Drug-resistant cataplexy with multiple attacks daily, nearly constant sleepiness, and disturbed nocturnal sleep (i.e., movements, insomnia, and vivid dreaming).

Subtypes

In narcolepsy without cataplexy but with hypocretin deficiency, unclear "cataplexy-like" symptoms may be reported (e.g., the symptoms are not triggered by emotions and are unusually long lasting). In extremely rare cases, cerebrospinal fluid (CSF) levels of hypocretin-1 are low, and polysomnographic/multiple sleep latency test (MSLT) results are negative: repeating the test is advised before establishing the subtype diagnosis. In narco-

lepsy with cataplexy but without hypocretin deficiency, test results for human leukocyte antigen (HLA) DQB1*06:02 may be negative. Seizures, falls of other origin, and conversion disorder (functional neurological symptom disorder) should be excluded. In narcolepsy secondary to infectious (e.g., Whipple's disease, sarcoidosis), traumatic, or tumoral destruction of hypocretin neurons, test results for HLA DQB1*06:02 may be positive and may result from the insult triggering the autoimmune process. In other cases, the destruction of hypocretin neurons may be secondary to trauma or hypothalamic surgery. Head trauma or infections of the central nervous system can, however, produce transitory decreases in CSF hypocretin-1 levels without hypocretin cell loss, complicating the diagnosis.

Diagnostic Features

The essential features of sleepiness in narcolepsy are recurrent daytime naps or lapses into sleep. Sleepiness typically occurs daily but must occur at a minimum three times a week for at least 3 months (Criterion A). Narcolepsy generally produces cataplexy, which most commonly presents as brief episodes (seconds to minutes) of sudden, bilateral loss of muscle tone precipitated by emotions, typically laughing and joking. Muscles affected may include those of the neck, jaw, arms, legs, or whole body, resulting in head bobbing, jaw dropping, or complete falls. Individuals are awake and aware during cataplexy. To meet Criterion B1(a), cataplexy must be triggered by laughter or joking and must occur at least a few times per month when the condition is untreated or in the past.

Cataplexy should not be confused with "weakness" occurring in the context of athletic activities (physiological) or exclusively after unusual emotional triggers such as stress or anxiety (suggesting possible psychopathology). Episodes lasting hours or days, or those not triggered by emotions, are unlikely to be cataplexy, nor is rolling on the floor while laughing hysterically.

In children close to onset, genuine cataplexy can be atypical, affecting primarily the face, causing grimaces or jaw opening with tongue thrusting ("cataplectic faces"). Alternatively, cataplexy may present as low-grade continuous hypotonia, yielding a wobbling walk. In these cases, Criterion B1(b) can be met in children or in individuals within 6 months of a rapid onset.

Narcolepsy-cataplexy nearly always results from the loss of hypothalamic hypocretin (orexin)–producing cells, causing hypocretin deficiency (less than or equal to one-third of control values, or 110 pg/mL in most laboratories). Cell loss is likely autoimmune, and approximately 99% of affected individuals carry HLA-DQB1*06:02 (vs. 12%–38% of control subjects). Thus, checking for the presence of DQB1*06:02 prior to a lumbar puncture for evaluation of CSF hypocretin-1 immunoreactivity may be useful. Rarely, low CSF levels of hypocretin-1 occur without cataplexy, notably in youths who may develop cataplexy later. CSF hypocretin-1 measurement represents the gold standard, excepting associated severe conditions (neurological, inflammatory, infectious, trauma) that can interfere with the assay.

A nocturnal polysomnographic sleep study followed by an MSLT can also be used to confirm the diagnosis (Criterion B3). These tests must be performed after the individual has stopped all psychotropic medications, following 2 weeks of adequate sleep time (as documented with sleep diaries, actigraphy). Short rapid eye movement (REM) latency (sleep-onset REM period, REM latency less than or equal to 15 minutes) during polysomnography is sufficient to confirm the diagnosis and meets Criterion B3. Alternatively, the MSLT result must be positive, showing a mean sleep latency of less than or equal to 8 minutes and two or more sleep-onset REM periods in four to five naps.

Associated Features Supporting Diagnosis

When sleepiness is severe, automatic behaviors may occur, with the individual continuing his or her activities in a semi-automatic, hazelike fashion without memory or consciousness. Approximately 20%–60% of individuals experience vivid hypnagogic hallucinations

before or upon falling asleep or hypnopompic hallucinations just after awakening. These hallucinations are distinct from the less vivid, nonhallucinatory dreamlike mentation at sleep onset that occurs in normal sleepers. Nightmares and vivid dreaming are also frequent in narcolepsy, as is REM sleep behavior disorder. Approximately 20%–60% of individuals experience sleep paralysis upon falling asleep or awakening, leaving them awake but unable to move or speak. However, many normal sleepers also report sleep paralysis, especially with stress or sleep deprivation. Nocturnal eating may occur. Obesity is common. Nocturnal sleep disruption with frequent long or short awakenings is common and can be disabling.

Individuals may appear sleepy or fall asleep in the waiting area or during clinical examination. During cataplexy, individuals may slump in a chair and have slurred speech or drooping eyelids. If the clinician has time to check reflexes during cataplexy (most attacks are less than 10 seconds), reflexes are abolished—an important finding distinguishing genuine cataplexy from conversion disorder.

Prevalence

Narcolepsy-cataplexy affects 0.02%–0.04% of the general population in most countries. Narcolepsy affects both genders, with possibly a slight male preponderance.

Development and Course

Onset is typically in children and adolescents/young adults but rarely in older adults. Two peaks of onset are suggested, at ages 15–25 years and ages 30–35 years. Onset can be abrupt or progressive (over years). Severity is highest when onset is abrupt in children, and then decreases with age or with treatment, so that symptoms such as cataplexy can occasionally disappear. Abrupt onset in young, prepubescent children can be associated with obesity and premature puberty, a phenotype more frequently observed since 2009. In adolescents, onset is more difficult to pinpoint. Onset in adults is often unclear, with some individuals reporting having had excessive sleepiness since birth. Once the disorder has manifested, the course is persistent and lifelong.

In 90% of cases, the first symptom to manifest is sleepiness or increased sleep, followed by cataplexy (within 1 year in 50% of cases, within 3 years in 85%). Sleepiness, hypnagogic hallucinations, vivid dreaming, and REM sleep behavior disorder (excessive movements during REM sleep) are early symptoms. Excessive sleep rapidly progresses to an inability to stay awake during the day, and to maintain good sleep at night, without a clear increase in total 24-hour sleep needs. In the first months, cataplexy may be atypical, especially in children. Sleep paralysis usually develops around puberty in children with prepubertal onset. Exacerbations of symptoms suggest lack of compliance with medications or development of a concurrent sleep disorder, notably sleep apnea.

Young children and adolescents with narcolepsy often develop aggression or behavioral problems secondary to sleepiness and/or nighttime sleep disruption. Workload and social pressure increase through high school and college, reducing available sleep time at night. Pregnancy does not seem to modify symptoms consistently. After retirement, individuals typically have more opportunity for napping, reducing the need for stimulants. Maintaining a regular schedule benefits individuals at all ages.

Risk and Prognostic Factors

Temperamental. Parasomnias, such as sleepwalking, bruxism, REM sleep behavior disorder, and enuresis, may be more common in individuals who develop narcolepsy. Individuals commonly report that they need more sleep than other family members.

Environmental. Group A streptococcal throat infection, influenza (notably pandemic H1N1 2009), or other winter infections are likely triggers of the autoimmune process, pro-

ducing narcolepsy a few months later. Head trauma and abrupt changes in sleep-wake patterns (e.g., job changes, stress) may be additional triggers.

Genetic and physiological. Monozygotic twins are 25%–32% concordant for narcolepsy. The prevalence of narcolepsy is 1%–2% in first-degree relatives (a 10- to 40-fold increase overall). Narcolepsy is strongly associated with DQB1*06:02 (99% vs. 12%–38% in control subjects of various ethnic groups; 25% in the general U.S. population). DQB1*03:01 increases, while DQB1*05:01, DQB1*06:01, and DQB1*06:03 reduce risk in the presence of DQB1*06:02, but the effect is small. Polymorphisms within the T-cell receptor alpha gene and other immune modulating genes also modulate risk slightly.

Culture-Related Diagnostic Issues

Narcolepsy has been described in all ethnic groups and in many cultures. Among African Americans, more cases present without cataplexy or with atypical cataplexy, complicating diagnosis, especially in the presence of obesity and obstructive sleep apnea.

Diagnostic Markers

Functional imaging suggests impaired hypothalamic responses to humorous stimuli. Nocturnal polysomnography followed by an MSLT is used to confirm the diagnosis of narcolepsy, especially when the disorder is first being diagnosed and before treatment has begun, and if hypocretin deficiency has not been documented biochemically. The polysomnography/MSLT should be performed after the individual is no longer taking any psychotropic drugs and after regular sleep-wake patterns, without shift work or sleep deprivation, have been documented.

A sleep-onset REM period during the polysomnography (REM sleep latency less than or equal to 15 minutes) is highly specific (approximately 1% positive in control subjects) but moderately sensitive (approximately 50%). A positive MSLT result displays an average sleep latency of less than or equal to 8 minutes, and sleep-onset REM periods in two or more naps on a four- or five-nap test. The MSLT result is positive in 90%–95% of individuals with narcolepsy versus 2%–4% of control subjects or individuals with other sleep disorders. Additional polysomnographic findings often include frequent arousals, decreased sleep efficiency, and increased stage 1 sleep. Periodic limb movements (found in about 40% of individuals with narcolepsy) and sleep apnea are often noted.

Hypocretin deficiency is demonstrated by measuring CSF hypocretin-1 immunoreactivity. The test is particularly useful in individuals with suspected conversion disorder and those without typical cataplexy, or in treatment-refractory cases. The diagnostic value of the test is not affected by medications, sleep deprivation, or circadian time, but the findings are uninterpretable when the individual is severely ill with a concurrent infection or head trauma or is comatose. CSF cytology, protein, and glucose are within normal range even when sampled within weeks of rapid onset. CSF hypocretin-1 in these incipient cases is typically already very diminished or undetectable.

Functional Consequences of Narcolepsy

Driving and working are impaired, and individuals with narcolepsy should avoid jobs that place themselves (e.g., working with machinery) or others (e.g., bus driver, pilot) in danger. Once the narcolepsy is controlled with therapy, patients can usually drive, although rarely long distances alone. Untreated individuals are also at risk for social isolation and accidental injury to themselves or others. Social relations may suffer as these individuals strive to avert cataplexy by exerting control over emotions.

Differential Diagnosis

Other hypersomnias. Hypersomnolence and narcolepsy are similar with respect to the degree of daytime sleepiness, age at onset, and stable course over time but can be distin-

guished based on distinctive clinical and laboratory features. Individuals with hypersomnolence typically have longer and less disrupted nocturnal sleep, greater difficulty awakening, more persistent daytime sleepiness (as opposed to more discrete "sleep attacks" in narcolepsy), longer and less refreshing daytime sleep episodes, and little or no dreaming during daytime naps. By contrast, individuals with narcolepsy have cataplexy and recurrent intrusions of elements of REM sleep into the transition between sleep and wakefulness (e.g., sleep-related hallucinations and sleep paralysis). The MSLT typically demonstrates shorter sleep latencies (i.e., greater physiological sleepiness) as well as the presence of multiple sleep-onset REM periods in individuals with narcolepsy.

Sleep deprivation and insufficient nocturnal sleep. Sleep deprivation and insufficient nocturnal sleep are common in adolescents and shift workers. In adolescents, difficulties falling asleep at night are common, causing sleep deprivation. The MSLT result may be positive if conducted while the individual is sleep deprived or while his or her sleep is phase delayed.

Sleep apnea syndromes. Sleep apneas are especially likely in the presence of obesity. Because obstructive sleep apnea is more frequent than narcolepsy, cataplexy may be overlooked (or absent), and the individual is assumed to have obstructive sleep apnea unresponsive to usual therapies.

Major depressive disorder. Narcolepsy or hypersomnia may be associated or confused with depression. Cataplexy is not present in depression. The MSLT results are most often normal, and there is dissociation between subjective and objective sleepiness, as measured by the mean sleep latency during the MSLT.

Conversion disorder (functional neurological symptom disorder). Atypical features, such as long-lasting cataplexy or unusual triggers, may be present in conversion disorder (functional neurological symptom disorder). Individuals may report sleeping and dreaming, yet the MSLT does not show the characteristic sleep-onset REM period. Full-blown, long-lasting pseudocataplexy may occur during consultation, allowing the examining physician enough time to verify reflexes, which remain intact.

Attention-deficit/hyperactivity disorder or other behavioral problems. In children and adolescents, sleepiness can cause behavioral problems, including aggressiveness and inattention, leading to a misdiagnosis of attention-deficit/hyperactivity disorder.

Seizures. In young children, cataplexy can be misdiagnosed as seizures. Seizures are not commonly triggered by emotions, and when they are, the trigger is not usually laughing or joking. During a seizure, individuals are more likely to hurt themselves when falling. Seizures characterized by isolated atonia are rarely seen in isolation of other seizures, and they also have signatures on the electroencephalogram.

Chorea and movement disorders. In young children, cataplexy can be misdiagnosed as chorea or pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, especially in the context of a strep throat infection and high antistreptolysin O antibody levels. Some children may have an overlapping movement disorder close to onset of the cataplexy.

Schizophrenia. In the presence of florid and vivid hypnagogic hallucinations, individuals may think these experiences are real—a feature that suggests schizophrenia. Similarly, with stimulant treatment, persecutory delusions may develop. If cataplexy is present, the clinician should first assume that these symptoms are secondary to narcolepsy before considering a co-occurring diagnosis of schizophrenia.

Comorbidity

Narcolepsy can co-occur with bipolar, depressive, and anxiety disorders, and in rare cases with schizophrenia. Narcolepsy is also associated with increased body mass index or obe-

sity, especially when the narcolepsy is untreated. Rapid weight gain is common in young children with a sudden disease onset. Comorbid sleep apnea should be considered if there is a sudden aggravation of preexisting narcolepsy.

Relationship to International Classification of Sleep Disorders

The *International Classification of Sleep Disorders,* 2nd Edition (ICSD-2), differentiates five subtypes of narcolepsy.

Breathing-Related Sleep Disorders

The breathing-related sleep disorders category encompasses three relatively distinct disorders: obstructive sleep apnea hypopnea, central sleep apnea, and sleep-related hypoventilation.

Obstructive Sleep Apnea Hypopnea

Diagnostic Criteria **327.23 (G47.33)**

A. Either (1) or (2):

1. Evidence by polysomnography of at least five obstructive apneas or hypopneas per hour of sleep and either of the following sleep symptoms:
   a. Nocturnal breathing disturbances: snoring, snorting/gasping, or breathing pauses during sleep.
   b. Daytime sleepiness, fatigue, or unrefreshing sleep despite sufficient opportunities to sleep that is not better explained by another mental disorder (including a sleep disorder) and is not attributable to another medical condition.
2. Evidence by polysomnography of 15 or more obstructive apneas and/or hypopneas per hour of sleep regardless of accompanying symptoms.

Specify current severity:

Mild: Apnea hypopnea index is less than 15.
Moderate: Apnea hypopnea index is 15–30.
Severe: Apnea hypopnea index is greater than 30.

Specifiers

Disease severity is measured by a count of the number of apneas plus hypopneas per hour of sleep (apnea hypopnea index) using polysomnography or other overnight monitoring. Overall severity is also informed by levels of nocturnal desaturation and sleep fragmentation (measured by brain cortical arousal frequency and sleep stages) and degree of associated symptoms and daytime impairment. However, the exact number and thresholds may vary according to the specific measurement techniques used, and these numbers may change over time. Regardless of the apnea hypopnea index (count) per se, the disorder is considered to be more severe when apneas and hypopneas are accompanied by significant oxygen hemoglobin desaturation (e.g., when more than 10% of the sleep time is spent at desaturation levels of less than 90%) or when sleep is severely fragmented as shown by an

elevated arousal index (arousal index greater than 30) or reduced stages in deep sleep (e.g., percentage stage N3 [slow-wave sleep] less than 5%).

Diagnostic Features

Obstructive sleep apnea hypopnea is the most common breathing-related sleep disorder. It is characterized by repeated episodes of upper (pharyngeal) airway obstruction (apneas and hypopneas) during sleep. *Apnea* refers to the total absence of airflow, and *hypopnea* refers to a reduction in airflow. Each apnea or hypopnea represents a reduction in breathing of at least 10 seconds in duration in adults or two missed breaths in children and is typically associated with drops in oxygen saturation of 3% or greater and/or an electroencephalographic arousal. Both sleep-related (nocturnal) and wake-time symptoms are common. The cardinal symptoms of obstructive sleep apnea hypopnea are snoring and daytime sleepiness.

Obstructive sleep apnea hypopnea in adults is diagnosed on the basis of polysomnographic findings and symptoms. The diagnosis is based on symptoms of 1) nocturnal breathing disturbances (i.e., snoring, snorting/gasping, breathing pauses during sleep), or 2) daytime sleepiness, fatigue, or unrefreshing sleep despite sufficient opportunities to sleep that are not better explained by another mental disorder and not attributable to another medical condition, along with 3) evidence by polysomnography of five or more obstructive apneas or hypopneas per hour of sleep (Criterion A1). Diagnosis can be made in the absence of these symptoms if there is evidence by polysomnography of 15 or more obstructive apneas and/or hypopneas per hour of sleep (Criterion A2).

Specific attention to disturbed sleep occurring in association with snoring or breathing pauses and physical findings that increase risk of obstructive sleep apnea hypopnea (e.g., central obesity, crowded pharyngeal airway, elevated blood pressure) is needed to reduce the chance of misdiagnosing this treatable condition.

Associated Features Supporting Diagnosis

Because of the frequency of nocturnal awakenings that occur with obstructive sleep apnea hypopnea, individuals may report symptoms of insomnia. Other common, though nonspecific, symptoms of obstructive sleep apnea hypopnea are heartburn, nocturia, morning headaches, dry mouth, erectile dysfunction, and reduced libido. Rarely, individuals may complain of difficulty breathing while lying supine or sleeping. Hypertension may occur in more than 60% of individuals with obstructive sleep apnea hypopnea.

Prevalence

Obstructive sleep apnea hypopnea is a very common disorder, affecting at least 1%–2% of children, 2%–15% of middle-age adults, and more than 20% of older individuals. In the general community, prevalence rates of undiagnosed obstructive sleep apnea hypopnea may be very high in elderly individuals. Since the disorder is strongly associated with obesity, increases in obesity rates are likely to be accompanied by an increased prevalence of this disorder. Prevalence may be particularly high among males, older adults, and certain racial/ethnic groups. In adults, the male-to-female ratio of obstructive sleep apnea hypopnea ranges from 2:1 to 4:1. Gender differences decline in older age, possibly because of an increased prevalence in females after menopause. There is no gender difference among prepubertal children.

Development and Course

The age distribution of obstructive sleep apnea hypopnea likely follows a **J**-shaped distribution. There is a peak in children ages 3–8 years when the nasopharynx may be compromised by a relatively large mass of tonsillar tissue compared with the size of the upper

airway. With growth of the airway and regression of lymphoid tissue during later childhood, there is reduction in prevalence. Then, as obesity prevalence increases in midlife and females enter menopause, obstructive sleep apnea hypopnea again increases. The course in older age is unclear; the disorder may level off after age 65 years, but in other individuals, prevalence may increase with aging. Because there is some age dependency of the occurrence of apneas and hypopneas, polysomnographic results must be interpreted in light of other clinical data. In particular, significant clinical symptoms of insomnia or hypersomnia should be investigated regardless of the individual's age.

Obstructive sleep apnea hypopnea usually has an insidious onset, gradual progression, and persistent course. Typically the loud snoring has been present for many years, often since childhood, but an increase in its severity may lead the individual to seek evaluation. Weight gain may precipitate an increase in symptoms. Although obstructive sleep apnea hypopnea can occur at any age, it most commonly manifests among individuals ages 40–60 years. Over 4–5 years, the average apnea hypopnea index increases in adults and older individuals by approximately two apneas/hypopneas per hour. The apnea hypopnea index is increased and incident obstructive sleep apnea hypopnea is greater among individuals who are older, who are male, or who have a higher baseline body mass index (BMI) or increase their BMI over time. Spontaneous resolution of obstructive sleep apnea hypopnea has been reported with weight loss, particularly after bariatric surgery. In children, seasonal variation in obstructive sleep apnea hypopnea has been observed, as has improvement with overall growth.

In young children, the signs and symptoms of obstructive sleep apnea hypopnea may be more subtle than in adults, making diagnosis more difficult to establish. Polysomnography is useful in confirming diagnosis. Evidence of fragmentation of sleep on the polysomnogram may not be as apparent as in studies of older individuals, possibly because of the high homeostatic drive in young individuals. Symptoms such as snoring are usually parent-reported and thus have reduced sensitivity. Agitated arousals and unusual sleep postures, such as sleeping on the hands and knees, may occur. Nocturnal enuresis also may occur and should raise the suspicion of obstructive sleep apnea hypopnea if it recurs in a child who was previously dry at night. Children may also manifest excessive daytime sleepiness, although this is not as common or pronounced as in adults. Daytime mouth breathing, difficulty in swallowing, and poor speech articulation are also common features in children. Children younger than 5 years more often present with nighttime symptoms, such as observed apneas or labored breathing, than with behavioral symptoms (i.e., the nighttime symptoms are more noticeable and more often bring the child to clinical attention). In children older than 5 years, daytime symptoms such as sleepiness and behavioral problems (e.g., impulsivity and hyperactivity), attention-deficit/hyperactivity disorder, learning difficulties, and morning headaches are more often the focus of concern. Children with obstructive sleep apnea hypopnea also may present with failure to thrive and developmental delays. In young children, obesity is a less common risk factor, while delayed growth and "failure to thrive" may be present.

Risk and Prognostic Factors

Genetic and physiological. The major risk factors for obstructive sleep apnea hypopnea are obesity and male gender. Others include maxillary-mandibular retrognathia or micrognathia, positive family history of sleep apnea, genetic syndromes that reduce upper airway patency (e.g., Down's syndrome, Treacher Collin's syndrome), adenotonsillar hypertrophy (especially in young children), menopause (in females), and various endocrine syndromes (e.g., acromegaly). Compared with premenopausal females, males are at increased risk for obstructive sleep apnea hypopnea, possibly reflecting the influences of sex hormones on ventilatory control and body fat distribution, as well as because of gender differences in airway structure. Medications for mental disorders and medical conditions that tend to induce somnolence may worsen the course of apnea symptoms if these medications are not managed carefully.

Obstructive sleep apnea hypopnea has a strong genetic basis, as evidenced by the significant familial aggregation of the apnea hypopnea index. The prevalence of obstructive sleep apnea hypopnea is approximately twice as high among the first-degree relatives of probands with obstructive sleep apnea hypopnea as compared with members of control families. One-third of the variance in the apnea hypopnea index is explained by shared familial factors. Although genetic markers with diagnostic or prognostic value are not yet available for use, eliciting a family history of obstructive sleep apnea hypopnea should increase the clinical suspicion for the disorder.

Culture-Related Diagnostic Issues

There is a potential for sleepiness and fatigue to be reported differently across cultures. In some groups, snoring may be considered a sign of health and thus may not trigger concerns. Individuals of Asian ancestry may be at increased risk for obstructive sleep apnea hypopnea despite relatively low BMI, possibly reflecting the influence of craniofacial risk factors that narrow the nasopharynx.

Gender-Related Issues

Females may more commonly report fatigue rather than sleepiness and may underreport snoring.

Diagnostic Markers

Polysomnography provides quantitative data on frequency of sleep-related respiratory disturbances and associated changes in oxygen saturation and sleep continuity. Polysomnographic findings in children differ from those in adults in that children demonstrate labored breathing, partial obstructive hypoventilation with cyclical desaturations, hypercapnia and paradoxical movements. Apnea hypopnea index levels as low as 2 are used to define thresholds of abnormality in children.

Arterial blood gas measurements while the individual is awake are usually normal, but some individuals can have waking hypoxemia or hypercapnia. This pattern should alert the clinician to the possibility of coexisting lung disease or hypoventilation. Imaging procedures may reveal narrowing of the upper airway. Cardiac testing may show evidence of impaired ventricular function. Individuals with severe nocturnal oxygen desaturation may also have elevated hemoglobin or hematocrit values. Validated sleep measures (e.g., multiple sleep latency test [MSLT], maintenance of wakefulness test) may identify sleepiness.

Functional Consequences of Obstructive Sleep Apnea Hypopnea

More than 50% of individuals with moderate to severe obstructive sleep apnea hypopnea report symptoms of daytime sleepiness. A twofold increased risk of occupational accidents has been reported in association with symptoms of snoring and sleepiness. Motor vehicle crashes also have been reported to be as much as sevenfold higher among individuals with elevated apnea hypopnea index values. Clinicians should be cognizant of state government requirements for reporting this disorder, especially in relationship to commercial drivers. Reduced scores on measures of health-related quality of life are common in individuals with obstructive sleep apnea hypopnea, with the largest decrements observed in the physical and vitality subscales.

Differential Diagnosis

Primary snoring and other sleep disorders. Individuals with obstructive sleep apnea hypopnea must be differentiated from individuals with primary snoring (i.e., otherwise

asymptomatic individuals who snore and do not have abnormalities on overnight polysomnography). Individuals with obstructive sleep apnea hypopnea may additionally report nocturnal gasping and choking. The presence of sleepiness or other daytime symptoms not explained by other etiologies suggests the diagnosis of obstructive sleep apnea hypopnea, but this differentiation requires polysomnography. Definitive differential diagnosis between hypersomnia, central sleep apnea, sleep-related hypoventilation, and obstructive sleep apnea hypopnea also requires polysomnographic studies.

Obstructive sleep apnea hypopnea must be differentiated from other causes of sleepiness, such as narcolepsy, hypersomnia, and circadian rhythm sleep disorders. Obstructive sleep apnea hypopnea can be differentiated from narcolepsy by the absence of cataplexy, sleep-related hallucinations, and sleep paralysis and by the presence of loud snoring, gasping during sleep, or observed apneas in sleep. Daytime sleep episodes in narcolepsy are characteristically shorter, more refreshing, and more often associated with dreaming. Obstructive sleep apnea hypopnea shows characteristic apneas and hypopneas and oxygen desaturation during nocturnal polysomnographic studies. Narcolepsy results in multiple sleep-onset rapid eye movement (REM) periods during the MSLT. Narcolepsy, like obstructive sleep apnea hypopnea, may be associated with obesity, and some individuals have concurrent narcolepsy and obstructive sleep apnea hypopnea. A diagnosis of narcolepsy does not exclude the diagnosis of obstructive sleep apnea hypopnea, as the two conditions may co-occur.

Insomnia disorder. For individuals complaining of difficulty initiating or maintaining sleep or early-morning awakenings, insomnia disorder can be differentiated from obstructive sleep apnea hypopnea by the absence of snoring and the absence of the history, signs, and symptoms characteristic of the latter disorder. However, insomnia and obstructive sleep apnea hypopnea may coexist, and if so, both disorders may need to be addressed concurrently to improve sleep.

Panic attacks. Nocturnal panic attacks may include symptoms of gasping or choking during sleep that may be difficult to distinguish clinically from obstructive sleep apnea hypopnea. However, the lower frequency of episodes, intense autonomic arousal, and lack of excessive sleepiness differentiate nocturnal panic attacks from obstructive sleep apnea hypopnea. Polysomnography in individuals with nocturnal panic attacks does not reveal the typical pattern of apneas or oxygen desaturation characteristic of obstructive sleep apnea hypopnea. Individuals with obstructive sleep apnea hypopnea do not provide a history of daytime panic attacks.

Attention-deficit/hyperactivity disorder. Attention-deficit/hyperactivity disorder in children may include symptoms of inattention, academic impairment, hyperactivity, and internalizing behaviors, all of which may also be symptoms of childhood obstructive sleep apnea hypopnea. The presence of other symptoms and signs of childhood obstructive sleep apnea hypopnea (e.g., labored breathing or snoring during sleep and adenotonsillar hypertrophy) would suggest the presence of obstructive sleep apnea hypopnea. Obstructive sleep apnea hypopnea and attention-deficit/hyperactivity disorder may commonly co-occur, and there may be causal links between them; therefore, risk factors such as enlarged tonsils, obesity, or a family history of sleep apnea may help alert the clinician to their co-occurrence.

Substance/medication-induced insomnia or hypersomnia. Substance use and substance withdrawal (including medications) can produce insomnia or hypersomnia. A careful history is usually sufficient to identify the relevant substance/medication, and follow-up shows improvement of the sleep disturbance after discontinuation of the substance/medication. In other cases, the use of a substance/medication (e.g., alcohol, barbiturates, benzodiazepines, tobacco) has been shown to exacerbate obstructive sleep apnea hypopnea. An individual with symptoms and signs consistent with obstructive sleep apnea hypop-

nea should receive that diagnosis, even in the presence of concurrent substance use that is exacerbating the condition.

Comorbidity

Systemic hypertension, coronary artery disease, heart failure, stroke, diabetes, and increased mortality are consistently associated with obstructive sleep apnea hypopnea. Risk estimates vary from 30% to as much as 300% for moderate to severe obstructive sleep apnea hypopnea. Evidence of pulmonary hypertension and right heart failure (e.g., cor pulmonale, ankle edema, hepatic congestion) are rare in obstructive sleep apnea hypopnea and when present indicate either very severe disease or associated hypoventilation or cardiopulmonary comorbidities. Obstructive sleep apnea hypopnea also may occur with increased frequency in association with a number of medical or neurological conditions (e.g., cerebrovascular disease, Parkinson's disease). Physical findings reflect the co-occurrence of these conditions.

As many as one-third of individuals referred for evaluation of obstructive sleep apnea hypopnea report symptoms of depression, with as many of 10% having depression scores consistent with moderate to severe depression. Severity of obstructive sleep apnea hypopnea, as measured by the apnea hypopnea index, has been found to be correlated with severity of symptoms of depression. This association may be stronger in males than in females.

Relationship to International Classification of Sleep Disorders

The *International Classification of Sleep Disorders,* 2nd Edition (ICSD-2), differentiates 11 subtypes of "sleep-related breathing disorders," including primary central sleep apnea, obstructive sleep apnea, and sleep-related hypoventilation.

Central Sleep Apnea

Diagnostic Criteria

A. Evidence by polysomnography of five or more central apneas per hour of sleep.
B. The disorder is not better explained by another current sleep disorder.

Specify whether:

327.21 (G47.31) Idiopathic central sleep apnea: Characterized by repeated episodes of apneas and hypopneas during sleep caused by variability in respiratory effort but without evidence of airway obstruction.

786.04 (R06.3) Cheyne-Stokes breathing: A pattern of periodic crescendo-decrescendo variation in tidal volume that results in central apneas and hypopneas at a frequency of at least five events per hour, accompanied by frequent arousal.

780.57 (G47.37) Central sleep apnea comorbid with opioid use: The pathogenesis of this subtype is attributed to the effects of opioids on the respiratory rhythm generators in the medulla as well as the differential effects on hypoxic versus hypercapnic respiratory drive.

Coding note (for 780.57 [G47.37] code only): When an opioid use disorder is present, first code the opioid use disorder: 305.50 (F11.10) mild opioid use disorder or 304.00 (F11.20) moderate or severe opioid use disorder; then code 780.57 (G47.37) central sleep apnea comorbid with opioid use. When an opioid use disorder is not present (e.g., after a one-time heavy use of the substance), code only 780.57 (G47.37) central sleep apnea comorbid with opioid use.

Note: See the section "Diagnostic Features" in text.

Specify current severity:

Severity of central sleep apnea is graded according to the frequency of the breathing disturbances as well as the extent of associated oxygen desaturation and sleep fragmentation that occur as a consequence of repetitive respiratory disturbances.

Subtypes

Idiopathic central sleep apnea and Cheyne-Stokes breathing are characterized by increased gain of the ventilatory control system, also referred to as *high loop gain,* which leads to instability in ventilation and $PaCO_2$ levels. This instability is termed *periodic breathing* and can be recognized by hyperventilation alternating with hypoventilation. Individuals with these disorders typically have pCO_2 levels while awake that are slightly hypocapneic or normocapneic. Central sleep apnea may also manifest during initiation of treatment of obstructive sleep apnea hypopnea or may occur in association with obstructive sleep apnea hypopnea syndrome (termed *complex sleep apnea*). The occurrence of central sleep apnea in association with obstructive sleep apnea is also considered to be due to high loop gain. In contrast, the pathogenesis of central sleep apnea comorbid with opioid use has been attributed to the effects of opioids on the respiratory rhythm generators in the medulla as well as to its differential effects on hypoxic versus hypercapneic respiratory drive. These individuals may have elevated pCO_2 levels while awake. Individuals receiving chronic methadone maintenance therapy have been noted to have increased somnolence and depression, although the role of breathing disorders associated with opioid medication in causing these problems has not been studied.

Specifiers

An increase in the central apnea index (i.e., number of central apneas per hour of sleep) reflects an increase in severity of central sleep apnea. Sleep continuity and quality may be markedly impaired with reductions in restorative stages of non–rapid eye movement (REM) sleep (i.e., decreased slow-wave sleep [stage N3]). In individuals with severe Cheyne-Stokes breathing, the pattern can also be observed during resting wakefulness, a finding that is thought to be a poor prognostic marker for mortality.

Diagnostic Features

Central sleep apnea disorders are characterized by repeated episodes of apneas and hypopneas during sleep caused by variability in respiratory effort. These are disorders of ventilatory control in which respiratory events occur in a periodic or intermittent pattern. *Idiopathic central sleep apnea* is characterized by sleepiness, insomnia, and awakenings due to dyspnea in association with five or more central apneas per hour of sleep. Central sleep apnea occurring in individuals with heart failure, stroke, or renal failure typically have a breathing pattern called *Cheyne-Stokes breathing,* which is characterized by a pattern of periodic crescendo-decrescendo variation in tidal volume that results in central apneas and hypopneas occurring at a frequency of at least five events per hour that are accompanied by frequent arousals. Central and obstructive sleep apneas may coexist; the ratio of central to obstructive apneas/hypopneas may be used to identify which condition is predominant.

Alterations in neuromuscular control of breathing can occur in association with medications or substances used in individuals with mental health conditions, which can cause or exacerbate impairments of respiratory rhythm and ventilation. Individuals taking these medications have a sleep-related breathing disorder that could contribute to sleep disturbances and symptoms such as sleepiness, confusion, and depression. Specifically, *chronic*

use of long-acting opioid medications is often associated with impairment of respiratory control leading to central sleep apnea.

Associated Features Supporting Diagnosis

Individuals with central sleep apnea hypopneas can manifest with sleepiness or insomnia. There can be complaints of sleep fragmentation, including awakening with dyspnea. Some individuals are asymptomatic. Obstructive sleep apnea hypopnea can coexist with Cheyne-Stokes breathing, and thus snoring and abruptly terminating apneas may be observed during sleep.

Prevalence

The prevalence of idiopathic central sleep apnea is unknown but thought to be rare. The prevalence of Cheyne-Stokes breathing is high in individuals with depressed cardiac ventricular ejection fraction. In individuals with an ejection fraction of less than 45%, the prevalence has been reported to be 20% or higher. The male-to-female ratio for prevalence is even more highly skewed toward males than for obstructive sleep apnea hypopnea. Prevalence increases with age, and most patients are older than 60 years. Cheyne-Stokes breathing occurs in approximately 20% of individuals with acute stroke. Central sleep apnea comorbid with opioid use occurs in approximately 30% of individuals taking chronic opioids for nonmalignant pain and similarly in individuals receiving methadone maintenance therapy.

Development and Course

The onset of Cheyne-Stokes breathing appears tied to the development of heart failure. The Cheyne-Stokes breathing pattern is associated with oscillations in heart rate, blood pressure and oxygen desaturation, and elevated sympathetic nervous system activity that can promote progression of heart failure. The clinical significance of Cheyne-Stokes breathing in the setting of stroke is not known, but Cheyne-Stokes breathing may be a transient finding that resolves with time after acute stroke. Central sleep apnea comorbid with opioid use has been documented with chronic use (i.e., several months).

Risk and Prognostic Factors

Genetic and physiological. Cheyne-Stokes breathing is frequently present in individuals with heart failure. The coexistence of atrial fibrillation further increases risk, as do older age and male gender. Cheyne-Stokes breathing is also seen in association with acute stroke and possibly renal failure. The underlying ventilatory instability in the setting of heart failure has been attributed to increased ventilatory chemosensitivity and hyperventilation due to pulmonary vascular congestion and circulatory delay. Central sleep apnea is seen in individuals taking long-acting opioids.

Diagnostic Markers

Physical findings seen in individuals with a Cheyne-Stokes breathing pattern relate to its risk factors. Findings consistent with heart failure, such as jugular venous distension, S_3 heart sound, lung crackles, and lower extremity edema, may be present. Polysomnography is used to characterize the breathing characteristics of each breathing-related sleep disorder subtype. Central sleep apneas are recorded when periods of breathing cessation for longer than 10 seconds occur. Cheyne-Stokes breathing is characterized by a pattern of periodic crescendo-decrescendo variation in tidal volume that results in central apneas and hypopneas occurring at a frequency of at least five events per hour that are accompanied by frequent arousals. The cycle length of Cheyne-Stokes breathing (or time from end of one central apnea to the end of the next apnea) is about 60 seconds.

Functional Consequences of Central Sleep Apnea

Idiopathic central sleep apnea has been reported to cause symptoms of disrupted sleep, including insomnia and sleepiness. Cheyne-Stokes breathing with comorbid heart failure has been associated with excessive sleepiness, fatigue, and insomnia, although many individuals may be asymptomatic. Coexistence of heart failure and Cheyne-Stokes breathing may be associated with increased cardiac arrhythmias and increased mortality or cardiac transplantation. Individuals with central sleep apnea comorbid with opioid use may present with symptoms of sleepiness or insomnia.

Differential Diagnosis

Idiopathic central sleep apnea must be distinguished from other breathing-related sleep disorders, other sleep disorders, and medical conditions and mental disorders that cause sleep fragmentation, sleepiness, and fatigue. This is achieved using polysomnography.

Other breathing-related sleep disorders and sleep disorders. Central sleep apnea can be distinguished from obstructive sleep apnea hypopnea by the presence of at least five central apneas per hour of sleep. These conditions may co-occur, but central sleep apnea is considered to predominate when the ratio of central to obstructive respiratory events exceeds 50%.

Cheyne-Stokes breathing can be distinguished from other mental disorders, including other sleep disorders, and other medical conditions that cause sleep fragmentation, sleepiness, and fatigue based on the presence of a predisposing condition (e.g., heart failure or stroke) and signs and polysomnographic evidence of the characteristic breathing pattern. Polysomnographic respiratory findings can help distinguish Cheyne-Stokes breathing from insomnia due to other medical conditions. High-altitude periodic breathing has a pattern that resembles Cheyne-Stokes breathing but has a shorter cycle time, occurs only at high altitude, and is not associated with heart failure.

Central sleep apnea comorbid with opioid use can be differentiated from other types of breathing-related sleep disorders based on the use of long-acting opioid medications in conjunction with polysomnographic evidence of central apneas and periodic or ataxic breathing. It can be distinguished from insomnia due to drug or substance use based on polysomnographic evidence of central sleep apnea.

Comorbidity

Central sleep apnea disorders are frequently present in users of long-acting opioids, such as methadone. Individuals taking these medications have a sleep-related breathing disorder that could contribute to sleep disturbances and symptoms such as sleepiness, confusion, and depression. While the individual is asleep, breathing patterns such as central apneas, periodic apneas, and ataxic breathing may be observed. Obstructive sleep apnea hypopnea may coexist with central sleep apnea, and features consistent with this condition can also be present (see "Obstructive Sleep Apnea Hypopnea" earlier in this chapter). Cheyne-Stokes breathing is more commonly observed in association with conditions that include heart failure, stroke, and renal failure and is seen more frequently in individuals with atrial fibrillation. Individuals with Cheyne-Stokes breathing are more likely to be older, to be male, and to have lower weight than individuals with obstructive sleep apnea hypopnea.

Sleep-Related Hypoventilation

Diagnostic Criteria

A. Polysomnograpy demonstrates episodes of decreased respiration associated with elevated CO_2 levels. (**Note:** In the absence of objective measurement of CO_2, persistent low levels of hemoglobin oxygen saturation unassociated with apneic/hypopneic events may indicate hypoventilation.)

B. The disturbance is not better explained by another current sleep disorder.

Specify whether:

327.24 (G47.34) Idiopathic hypoventilation: This subtype is not attributable to any readily identified condition.

327.25 (G47.35) Congenital central alveolar hypoventilation: This subtype is a rare congenital disorder in which the individual typically presents in the perinatal period with shallow breathing, or cyanosis and apnea during sleep.

327.26 (G47.36) Comorbid sleep-related hypoventilation: This subtype occurs as a consequence of a medical condition, such as a pulmonary disorder (e.g., interstitial lung disease, chronic obstructive pulmonary disease) or a neuromuscular or chest wall disorder (e.g., muscular dystrophies, postpolio syndrome, cervical spinal cord injury, kyphoscoliosis), or medications (e.g., benzodiazepines, opiates). It also occurs with obesity (obesity hypoventilation disorder), where it reflects a combination of increased work of breathing due to reduced chest wall compliance and ventilation-perfusion mismatch and variably reduced ventilatory drive. Such individuals usually are characterized by body mass index of greater than 30 and hypercapnia during wakefulness (with a pCO_2 of greater than 45), without other evidence of hypoventilation.

Specify current severity:

Severity is graded according to the degree of hypoxemia and hypercarbia present during sleep and evidence of end organ impairment due to these abnormalities (e.g., right-sided heart failure). The presence of blood gas abnormalities during wakefulness is an indicator of greater severity.

Subtypes

Regarding obesity hypoventilation disorder, the prevalence of obesity hypoventilation in the general population is not known but is thought to be increasing in association with the increased prevalence of obesity and extreme obesity.

Diagnostic Features

Sleep-related hypoventilation can occur independently or, more frequently, comorbid with medical or neurological disorders, medication use, or substance use disorder. Although symptoms are not mandatory to make this diagnosis, individuals often report excessive daytime sleepiness, frequent arousals and awakenings during sleep, morning headaches, and insomnia complaints.

Associated Features Supporting Diagnosis

Individuals with sleep-related hypoventilation can present with sleep-related complaints of insomnia or sleepiness. Episodes of orthopnea can occur in individuals with diaphragm weakness. Headaches upon awakening may be present. During sleep, episodes of shallow breathing may be observed, and obstructive sleep apnea hypopnea or central sleep apnea may coexist. Consequences of ventilatory insufficiency, including pulmonary hypertension, cor pulmonale (right heart failure), polycythemia, and neurocognitive dysfunction,

can be present. With progression of ventilatory insufficiency, blood gas abnormalities extend into wakefulness. Features of the medical condition causing sleep-related hypoventilation can also be present. Episodes of hypoventilation may be associated with frequent arousals or bradytachycardia. Individuals may complain of excessive sleepiness and insomnia or morning headaches or may present with findings of neurocognitive dysfunction or depression. Hypoventilation may not be present during wakefulness.

Prevalence

Idiopathic sleep-related hypoventilation in adults is very uncommon. The prevalence of congenital central alveolar hypoventilation is unknown, but the disorder is rare. Comorbid sleep-related hypoventilation (i.e., hypoventilation comorbid with other conditions, such as chronic obstructive pulmonary disease [COPD], neuromuscular disorders, or obesity) is more common.

Development and Course

Idiopathic sleep-related hypoventilation is thought to be a slowly progressive disorder of respiratory impairment. When this disorder occurs comorbidly with other disorders (e.g., COPD, neuromuscular disorders, obesity), disease severity reflects the severity of the underlying condition, and the disorder progresses as the condition worsens. Complications such as pulmonary hypertension, cor pulmonale, cardiac dysrhythmias, polycythemia, neurocognitive dysfunction, and worsening respiratory failure can develop with increasing severity of blood gas abnormalities.

Congenital central alveolar hypoventilation usually manifests at birth with shallow, erratic, or absent breathing. This disorder can also manifest during infancy, childhood, and adulthood because of variable penetrance of the *PHOX2B* mutation. Children with congenital central alveolar hypoventilation are more likely to have disorders of the autonomic nervous system, Hirschsprung's disease, neural crest tumors, and characteristic box-shaped face (i.e., the face is short relative to its width).

Risk and Prognostic Factors

Environmental. Ventilatory drive can be reduced in individuals using central nervous system depressants, including benzodiazepines, opiates, and alcohol.

Genetic and physiological. Idiopathic sleep-related hypoventilation is associated with reduced ventilatory drive due to a blunted chemoresponsiveness to CO_2 (reduced respiratory drive; i.e., "won't breathe"), reflecting underlying neurological deficits in centers governing the control of ventilation. More commonly, sleep-related hypoventilation is comorbid with another medical condition, such as a pulmonary disorder, a neuromuscular or chest wall disorder, or hypothyroidism, or with use of medications (e.g., benzodiazepines, opiates). In these conditions, the hypoventilation may be a consequence of increased work of breathing and/or impairment of respiratory muscle function (i.e., "can't breathe") or reduced respiratory drive (i.e., "won't breathe").

Neuromuscular disorders influence breathing through impairment of respiratory motor innervation or respiratory muscle function. They include conditions such as amyotrophic lateral sclerosis, spinal cord injury, diaphragmatic paralysis, myasthenia gravis, Lambert-Eaton syndrome, toxic or metabolic myopathies, postpolio syndrome, and Charcot-Marie-Tooth syndrome.

Congenital central alveolar hypoventilation is a genetic disorder attributable to mutations of *PHOX2B,* a gene that is crucial for the development of the embryonic autonomic nervous system and neural crest derivatives. Children with congenital central alveolar hypoventilation show blunted ventilatory responses to hypercapnia, especially in non–rapid eye movement sleep.

Gender-Related Diagnostic Issues

Gender distributions for sleep-related hypoventilation occurring in association with comorbid conditions reflect the gender distributions of the comorbid conditions. For example, COPD is more frequently present in males and with increasing age.

Diagnostic Markers

Sleep-related hypoventilation is diagnosed using polysomnography showing sleep-related hypoxemia and hypercapnia that is not better explained by another breathing-related sleep disorder. The documentation of increased arterial pCO_2 levels to greater than 55 mmHg during sleep or a 10 mmHg or greater increase in pCO_2 levels (to a level that also exceeds 50 mmHg) during sleep in comparison to awake supine values, for 10 minutes or longer, is the gold standard for diagnosis. However, obtaining arterial blood gas determinations during sleep is impractical, and non-invasive measures of pCO_2 have not been adequately validated during sleep and are not widely used during polysomnography in adults. Prolonged and sustained decreases in oxygen saturation (oxygen saturation of less than 90% for more than 5 minutes with a nadir of at least 85%, or oxygen saturation of less than 90% for at least 30% of sleep time) in the absence of evidence of upper airway obstruction are often used as an indication of sleep-related hypoventilation; however, this finding is not specific, as there are other potential causes of hypoxemia, such as that due to lung disease.

Functional Consequences of Sleep-Related Hypoventilation

The consequences of sleep-related hypoventilation are related to the effects of chronic exposure to hypercapnia and hypoxemia. These blood gas derangements cause vasoconstriction of the pulmonary vasculature leading to pulmonary hypertension, which, if severe, can result in right-sided heart failure (cor pulmonale). Hypoxemia can lead to dysfunction of organs such as the brain, blood, and heart, leading to outcomes such as cognitive dysfunction, polycythemia, and cardiac arrhythmias. Hypercapnia can depress ventilatory drive, leading to progressive respiratory failure.

Differential Diagnosis

Other medical conditions affecting ventilation. In adults, the idiopathic variety of sleep-related hypoventilation is very uncommon and is determined by excluding the presence of lung diseases, skeletal malformations, neuromuscular disorders, and other medical and neurological disorders or medications that affect ventilation. Sleep-related hypoventilation must be distinguished from other causes of sleep-related hypoxemia, such as that due to lung disease.

Other breathing-related sleep disorders. Sleep-related hypoventilation can be distinguished from obstructive sleep apnea hypopnea and central sleep apnea based on clinical features and findings on polysomnography. Sleep-related hypoventilation typically shows more sustained periods of oxygen desaturation rather that the periodic episodes seen in obstructive sleep apnea hypopnea and central sleep apnea. Obstructive sleep apnea hypopnea and central sleep apnea also show a pattern of discrete episodes of repeated airflow decreases that can be absent in sleep-related hypoventilation.

Comorbidity

Sleep-related hypoventilation often occurs in association with a pulmonary disorder (e.g., interstitial lung disease, COPD), with a neuromuscular or chest wall disorder (e.g., muscular dystrophies, post-polio syndrome, cervical spinal cord injury, obesity, kyphoscoliosis), or,

most relevant to the mental health provider, with medication use (e.g., benzodiazepines, opiates). Congenital central alveolar hypoventilation often occurs in association with autonomic dysfunction and may occur in association with Hirschsprung's disease. COPD, a disorder of lower airway obstruction usually associated with cigarette smoking, can result in sleep-related hypoventilation and hypoxemia. The presence of coexisting obstructive sleep apnea hypopnea is thought to exacerbate hypoxemia and hypercapnia during sleep and wakefulness. The relationship between congenital central alveolar hypoventilation and idiopathic sleep-related hypoventilation is unclear; in some individuals, idiopathic sleep-related hypoventilation may represent cases of late-onset congenital central alveolar hypoventilation.

Relationship to International Classification of Sleep Disorders

The *International Classification of Sleep Disorders,* 2nd Edition (ICSD-2), combines sleep-related hypoventilation and sleep-related hypoxemia under the category of sleep-related hypoventilation/hypoxemic syndromes. This approach to classification reflects the frequent co-occurrence of disorders that lead to hypoventilation and hypoxemia. In contrast, the classification used in DSM-5 reflects evidence that there are distinct sleep-related pathogenetic processes leading to hypoventilation.

Circadian Rhythm Sleep-Wake Disorders

Diagnostic Criteria

A. A persistent or recurrent pattern of sleep disruption that is primarily due to an alteration of the circadian system or to a misalignment between the endogenous circadian rhythm and the sleep–wake schedule required by an individual's physical environment or social or professional schedule.
B. The sleep disruption leads to excessive sleepiness or insomnia, or both.
C. The sleep disturbance causes clinically significant distress or impairment in social, occupational, and other important areas of functioning.

Coding note: For ICD-9-CM, code **307.45** for all subtypes. For ICD-10-CM, code is based on subtype.

Specify whether:

307.45 (G47.21) Delayed sleep phase type: A pattern of delayed sleep onset and awakening times, with an inability to fall asleep and awaken at a desired or conventionally acceptable earlier time.

Specify if:

Familial: A family history of delayed sleep phase is present.

Specify if:

Overlapping with non-24-hour sleep-wake type: Delayed sleep phase type may overlap with another circadian rhythm sleep-wake disorder, non-24-hour sleep-wake type.

307.45 (G47.22) Advanced sleep phase type: A pattern of advanced sleep onset and awakening times, with an inability to remain awake or asleep until the desired or conventionally acceptable later sleep or wake times.

Specify if:

Familial: A family history of advanced sleep phase is present.

307.45 (G47.23) Irregular sleep-wake type: A temporally disorganized sleep-wake pattern, such that the timing of sleep and wake periods is variable throughout the 24-hour period.

307.45 (G47.24) Non-24-hour sleep-wake type: A pattern of sleep-wake cycles that is not synchronized to the 24-hour environment, with a consistent daily drift (usually to later and later times) of sleep onset and wake times.

307.45 (G47.26) Shift work type: Insomnia during the major sleep period and/or excessive sleepiness (including inadvertent sleep) during the major awake period associated with a shift work schedule (i.e., requiring unconventional work hours).

307.45 (G47.20) Unspecified type

Specify if:

Episodic: Symptoms last at least 1 month but less than 3 months.

Persistent: Symptoms last 3 months or longer.

Recurrent: Two or more episodes occur within the space of 1 year.

Delayed Sleep Phase Type

Diagnostic Features

The delayed sleep phase type is based primarily on a history of a delay in the timing of the major sleep period (usually more than 2 hours) in relation to the desired sleep and wake-up time, resulting in symptoms of insomnia and excessive sleepiness. When allowed to set their own schedule, individuals with delayed sleep phase type exhibit normal sleep quality and duration for age. Symptoms of sleep-onset insomnia, difficulty waking in the morning, and excessive early day sleepiness are prominent.

Associated Features Supporting Diagnosis

Common associated features of delayed sleep phase type include a history of mental disorders or a concurrent mental disorder. Extreme and prolonged difficulty awakening with morning confusion is also common. Psychophysiological insomnia may develop as a result of maladaptive behaviors that impair sleep and increase arousal because of repeated attempts to fall asleep at an earlier time.

Prevalence

Prevalence of delayed sleep phase type in the general population is approximately 0.17% but appears to be greater than 7% in adolescents. Although the prevalence of familial delayed sleep phase type has not been established, a family history of delayed sleep phase is present in individuals with delayed sleep phase type.

Development and Course

Course is persistent, lasting longer than 3 months, with intermittent exacerbations throughout adulthood. Although age at onset is variable, symptoms begin typically in adolescence and early adulthood and persist for several months to years before diagnosis is established. Severity may decrease with age. Relapse of symptoms is common.

Clinical expression may vary across the lifespan depending on social, school, and work obligations. Exacerbation is usually triggered by a change in work or school schedule that requires an early rise time. Individuals who can alter their work schedules to accommodate the delayed circadian sleep and wake timing can experience remission of symptoms.

Increased prevalence in adolescence may be a consequence of both physiological and behavioral factors. Hormonal changes may be involved specifically, as delayed sleep phase is associated with the onset of puberty. Thus, delayed sleep phase type in adolescents should be differentiated from the common delay in the timing of circadian rhythms in this age group. In the familial form, the course is persistent and may not improve significantly with age.

Risk and Prognostic Factors

Genetic and physiological. Predisposing factors may include a longer than average circadian period, changes in light sensitivity, and impaired homeostatic sleep drive. Some individuals with delayed sleep phase type may be hypersensitive to evening light, which can serve as a delay signal to the circadian clock, or they may be hyposensitive to morning light such that its phase-advancing effects are reduced. Genetic factors may play a role in the pathogenesis of familial and sporadic forms of delayed sleep phase type, including mutations in circadian genes (e.g., *PER3*, *CKIe*).

Diagnostic Markers

Confirmation of the diagnosis includes a complete history and use of a sleep diary or actigraphy (i.e., a wrist-worn motion detector that monitors motor activity for prolonged periods and can be used as a proxy for sleep-wake patterns for at least 7 days). The period covered should include weekends, when social and occupational obligations are less strict, to ensure that the individual exhibits a consistently delayed sleep-wake pattern. Biomarkers such as salivary dim light melatonin onset should be obtained only when the diagnosis is unclear.

Functional Consequences of Delayed Sleep Phase Type

Excessive early day sleepiness is prominent. Extreme and prolonged difficulty awakening with morning confusion (i.e., sleep inertia) is also common. The severity of insomnia and excessive sleepiness symptoms varies substantially among individuals and largely depends on the occupational and social demands on the individual.

Differential Diagnosis

Normative variations in sleep. Delayed sleep phase type must be distinguished from "normal" sleep patterns in which an individual has a late schedule that does not cause personal, social, or occupational distress (most commonly seen in adolescents and young adults).

Other sleep disorders. Insomnia disorder and other circadian rhythm sleep-wake disorders should be included in the differential. Excessive sleepiness may also be caused by other sleep disturbances, such as breathing-related sleep disorders, insomnias, sleep-related movement disorders, and medical, neurological, and mental disorders. Overnight polysomnography may help in evaluating for other comorbid sleep disorders, such as sleep apnea. The circadian nature of delayed sleep phase type, however, should differentiate it from other disorders with similar complaints.

Comorbidity

Delayed sleep phase type is strongly associated with depression, personality disorder, and somatic symptom disorder or illness anxiety disorder. In addition, comorbid sleep disorders, such as insomnia disorder, restless legs syndrome, and sleep apnea, as well as depressive and bipolar disorders and anxiety disorders, can exacerbate symptoms of insomnia and excessive sleepiness. Delayed sleep phase type may overlap with another circadian rhythm sleep-wake disorder, non-24-hour sleep-wake type. Sighted individuals with non-24-hour sleep-wake type disorder commonly also have a history of delayed circadian sleep phase.

Advanced Sleep Phase Type

Specifiers

Advanced sleep phase type may be documented with the specified "familial." Although the prevalence of familial advanced sleep phase type has not been established, a family history of advanced sleep phase is present in individuals with advanced sleep phase type. In this type, specific mutations demonstrate an autosomal dominant mode of inheritance. In the familial form, onset of symptoms may occur earlier (during childhood and early adulthood), the course is persistent, and the severity of symptoms may increase with age.

Diagnostic Features

Advanced sleep phase type is characterized by sleep-wake times that are several hours earlier than desired or conventional times. Diagnosis is based primarily on a history of an advance in the timing of the major sleep period (usually more than 2 hours) in relation to the desired sleep and wake-up time, with symptoms of early morning insomnia and excessive daytime sleepiness. When allowed to set their schedule, individuals with advanced sleep phase type will exhibit normal sleep quality and duration for age.

Associated Features Supporting Diagnosis

Individuals with advanced sleep phase type are "morning types," having earlier sleep-wake times, with the timing of circadian biomarkers such as melatonin and core body temperature rhythms occurring 2–4 hours earlier than normal. When required to keep a conventional schedule requiring a delay of bedtime, these individuals will continue to have an early rise time, leading to persistent sleep deprivation and daytime sleepiness. Use of hypnotics or alcohol to combat sleep-maintenance insomnia and stimulants to reduce daytime sleepiness may lead to substance abuse in these individuals.

Prevalence

The estimated prevalence of advanced sleep phase type is approximately 1% in middle-age adults. Sleep-wake times and circadian phase advance in older individuals, probably accounting for increased prevalence in this population.

Development and Course

Onset is usually in late adulthood. In the familial form, onset can be earlier. The course is typically persistent, lasting more than 3 months, but the severity may increase depending on work and social schedules. The advanced sleep phase type is more common in older adults.

Clinical expression may vary across the lifespan depending on social, school, and work obligations. Individuals who can alter their work schedules to accommodate the advanced circadian sleep and wake timing can experience remission of symptoms. Increasing age tends to advance the sleep phase, however, it is unclear whether the common age-associated advanced sleep phase type is due solely to a change in circadian timing (as seen in the familial form) or also to age-related changes in the homeostatic regulation of sleep, resulting in earlier awakening. Severity, remission, and relapse of symptoms suggest lack of adherence to behavioral and environmental treatments designed to control sleep and wake structure and light exposure.

Risk and Prognostic Factors

Environmental. Decreased late afternoon/early evening exposure to light and/or exposure to early morning light due to early morning awakening can increase the risk of advanced sleep phase type by advancing circadian rhythms. By going to bed early, these individuals are not exposed to light in the phase delay region of the curve, resulting in perpetuation of advanced phase. In familial advanced sleep phase type, a shortening of the endogenous circadian period can result in an advanced sleep phase, although circadian period does not appear to systematically decrease with age.

Genetic and physiological. Advanced sleep phase type has demonstrated an autosomal dominant mode of inheritance, including a *PER2* gene mutation causing hypophosphorylation of the PER2 protein and a missense mutation in *CKI*.

Culture-Related Diagnostic Issues

African Americans may have a shorter circadian period and larger magnitude phase advances to light than do Caucasians, possibly increasing the risk for development of advanced sleep phase type in this population.

Diagnostic Markers

A sleep diary and actigraphy may be used as diagnostic markers, as described earlier for delayed sleep phase type.

Functional Consequences of Advanced Sleep Phase Type

Excessive sleepiness associated with advanced sleep phase can have a negative effect on cognitive performance, social interaction, and safety. Use of wake-promoting agents to combat sleepiness or sedatives for early morning awakening may increase potential for substance abuse.

Differential Diagnosis

Other sleep disorders. Behavioral factors such as irregular sleep schedules, voluntary early awakening, and exposure to light in the early morning should be considered, particularly in older adults. Careful attention should be paid to rule out other sleep-wake disorders, such as insomnia disorder, and other mental disorders and medical conditions that can cause early morning awakening.

Depressive and bipolar disorders. Because early morning awakening, fatigue, and sleepiness are prominent features of major depressive disorder, depressive and bipolar disorders must also be considered.

Comorbidity

Medical conditions and mental disorders with the symptom of early morning awakening, such as insomnia, can co-occur with the advance sleep phase type.

Irregular Sleep-Wake Type

Diagnostic Features

The diagnosis of irregular sleep-wake type is based primarily on a history of symptoms of insomnia at night (during the usual sleep period) and excessive sleepiness (napping) during the day. Irregular sleep-wake type is characterized by a lack of discernable sleep-wake

circadian rhythm. There is no major sleep period, and sleep is fragmented into at least three periods during the 24-hour day.

Associated Features Supporting Diagnosis

Individuals with irregular sleep-wake type typically present with insomnia or excessive sleepiness, depending on the time of day. Sleep and wake periods across 24 hours are fragmented, although the longest sleep period tends to occur between 2:00 A.M. and 6:00 A.M. and is usually less than 4 hours. A history of isolation or reclusion may occur in association with the disorder and contribute to the symptoms via a lack of external stimuli to help entrain a normal pattern. Individuals or their caregivers report frequent naps throughout the day. Irregular sleep-wake type is most commonly associated with neurodegenerative disorders, such as major neurocognitive disorder, and many neurodevelopmental disorders in children.

Prevalence

Prevalence of irregular sleep-wake type in the general population is unknown.

Development and Course

The course of irregular sleep-wake type is persistent. Age at onset is variable, but the disorder is more common in older adults.

Risk and Prognostic Factors

Temperamental. Neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, and Huntington's disease, and neurodevelopmental disorders in children increase the risk for irregular sleep-wake type.

Environmental. Decreased exposure to environmental light and structured daytime activity can be associated with a low-amplitude circadian rhythm. Hospitalized individuals are especially prone to such weak external entraining stimuli, and even outside the hospital setting, individuals with major neurocognitive disorder (i.e., dementia) are exposed to significantly less bright light.

Diagnostic Markers

A detailed sleep history and a sleep diary (by a caregiver) or actigraphy help confirm the irregular sleep-wake pattern.

Functional Consequences of Irregular Sleep-Wake Type

Lack of a clearly discernible major sleep and wake period in irregular sleep-wake type results in insomnia or excessive sleepiness, depending on the time of day. Disruption of the caregiver's sleep also often occurs and is an important consideration.

Differential Diagnosis

Normative variations in sleep. Irregular sleep-wake type should be distinguished from a voluntary irregular sleep-wake schedule and poor sleep hygiene, which can result in insomnia and excessive sleepiness.

Other medical conditions and mental disorders. Other causes of insomnia and daytime sleepiness, including comorbid medical conditions and mental disorders or medication, should be considered.

Comorbidity

Irregular sleep-wake type is often comorbid with neurodegenerative and neurodevelopmental disorders, such as major neurocognitive disorder, intellectual disability (intellectual developmental disorder), and traumatic brain injury. It is also comorbid with other medical conditions and mental disorders in which there is social isolation and/or lack of light and structured activities.

Non-24-Hour Sleep-Wake Type

Diagnostic Features

The diagnosis of non-24-hour sleep-wake type is based primarily on a history of symptoms of insomnia or excessive sleepiness related to abnormal synchronization between the 24-hour light-dark cycle and the endogenous circadian rhythm. Individuals typically present with periods of insomnia, excessive sleepiness, or both, which alternate with short asymptomatic periods. Starting with the asymptomatic period, when the individual's sleep phase is aligned to the external environment, sleep latency will gradually increase and the individual will complain of sleep-onset insomnia. As the sleep phase continues to drift so that sleep time is now in the daytime, the individual will have trouble staying awake during the day and will complain of sleepiness. Because the circadian period is not aligned to the external 24-hour environment, symptoms will depend on when an individual tries to sleep in relation to the circadian rhythm of sleep propensity.

Associated Features Supporting Diagnosis

Non-24-hour sleep-wake type is most common among blind or visually impaired individuals who have decreased light perception. In sighted individuals, there is often a history of delayed sleep phase and of decreased exposure to light and structured social and physical activity. Sighted individuals with non-24-hour sleep-wake type also demonstrate increased sleep duration.

Prevalence

Prevalence of non-24-hour sleep-wake type in the general population is unclear, but the disorder appears rare in sighted individuals. The prevalence in blind individuals is estimated to be 50%.

Development and Course

Course of non-24-hour sleep-wake type is persistent, with intermittent remission and exacerbations due to changes in work and social schedules throughout the lifespan. Age at onset is variable, depending on the onset of visual impairment. In sighted individuals, because of the overlap with delayed sleep phase type, non-24-hour sleep-wake type may develop in adolescence or early adulthood. Remission and relapse of symptoms in blind and sighted individuals largely depend on adherence to treatments designed to control sleep and wake structure and light exposure.

Clinical expression may vary across the lifespan depending on social, school, and work obligations. In adolescents and adults, irregular sleep-wake schedules and exposure to light or lack of light at critical times of the day can exacerbate the effects of sleep loss and disrupt circadian entrainment. Consequently, symptoms of insomnia, daytime sleepiness, and school, professional, and interpersonal functioning may worsen.

Risk and Prognostic Factors

Environmental. In sighted individuals, decreased exposure or sensitivity to light and social and physical activity cues may contribute to a free-running circadian rhythm. With the

high frequency of mental disorders involving social isolation and cases of non-24-hour sleep-wake type developing after a change in sleep habits (e.g., night shift work, job loss), behavioral factors in combination with physiological tendency may precipitate and perpetuate this disorder in sighted individuals. Hospitalized individuals with neurological and psychiatric disorders can become insensitive to social cues, predisposing them to the development of non-24-hour sleep-wake type.

Genetic and physiological. Blindness is a risk factor for non-24-hour sleep-wake type. Non-24-hour sleep-wake type has been associated with traumatic brain injury.

Diagnostic Markers

Diagnosis is confirmed by history and sleep diary or actigraphy for an extended period. Sequential measurement of phase markers (e.g., melatonin) can help determine circadian phase in both sighted and blind individuals.

Functional Consequences of Non-24-Hour Sleep-Wake Type

Complaints of insomnia (sleep onset and sleep maintenance), excessive sleepiness, or both are prominent. The unpredictability of sleep and wake times (typically a daily delay drift) results in an inability to attend school or maintain a steady job and may increase potential for social isolation.

Differential Diagnosis

Circadian rhythm sleep-wake disorders. In sighted individuals, non-24-hour sleep-wake type should be differentiated from delayed sleep phase type, as individuals with delayed sleep phase type may display a similar progressive delay in sleep period for several days.

Depressive disorders. Depressive symptoms and depressive disorders may result in similar circadian dysregulation and symptoms.

Comorbidity

Blindness is often comorbid with non-24-hour sleep-wake type, as are depressive and bipolar disorders with social isolation.

Shift Work Type

Diagnostic Features

Diagnosis is primarily based on a history of the individual working outside of the normal 8:00 A.M. to 6:00 P.M. daytime window (particularly at night) on a regularly scheduled (i.e., non-overtime) basis. Symptoms of excessive sleepiness at work, and impaired sleep at home, on a persistent basis are prominent. Presence of both sets of symptoms are usually required for a diagnosis of shift work type. Typically, when the individual reverts to a day-work routine, symptoms resolve. Although the etiology is slightly different, individuals who travel across many time zones on a very frequent basis may experience effects similar to those experienced by individuals with shift work type who work rotating shifts.

Prevalence

The prevalence of shift work type is unclear, but the disorder is estimated to affect 5%–10% of the night worker population (16%–20% of the workforce). Prevalence rises with advancement into middle-age and beyond (Drake et al. 2004).

Development and Course

Shift work type can appear in individuals of any age but is more prevalent in individuals older than 50 years and typically worsens with the passage of time if the disruptive work hours persist. Although older adults may show similar rates of circadian phase adjustment to a change in routine as do younger adults, they appear to experience significantly more sleep disruption as a consequence of the circadian phase shift.

Risk and Prognostic Factors

Temperamental. Predisposing factors include a morning-type disposition, a need for long (i.e., more than 8 hours) sleep durations in order to feel well rested, and strong competing social and domestic needs (e.g., parents of young children). Individuals who are able to commit to a nocturnal lifestyle, with few competing day-oriented demands, appear at lower risk for shift work type.

Genetic and physiological. Because shift workers are more likely than day workers to be obese, obstructive sleep apnea may be present and may exacerbate the symptoms.

Diagnostic Markers

A history and sleep diary or actigraphy may be useful in diagnosis, as discussed earlier for delayed sleep phase type.

Functional Consequences of Shift Work Type

Individuals with shift work type not only may perform poorly at work but also appear to be at risk for accidents both at work and on the drive home. They may also be at risk for poor mental health (e.g., alcohol use disorder, substance use disorder, depression) and physical health (e.g., gastrointestinal disorders, cardiovascular disease, diabetes, cancer). Individuals with a history of bipolar disorder are particularly vulnerable to shift work type–related episodes of mania resulting from missed nights of sleep. Shift work type often results in interpersonal problems.

Differential Diagnosis

Normative variations in sleep with shift work. The diagnosis of shift work type, as opposed to the "normal" difficulties of shift work, must depend to some extent on the severity of symptoms and/or level of distress experienced by the individual. Presence of shift work type symptoms even when the individual is able to live on a day-oriented routine for several weeks at a time may suggest the presence of other sleep disorders, such as sleep apnea, insomnia, and narcolepsy, which should be ruled out.

Comorbidity

Shift work type has been associated with increased alcohol use disorder, other substance use disorders, and depression. A variety of physical health disorders (e.g., gastrointestinal disorders, cardiovascular disease, diabetes, cancer) have been found to be associated with prolonged exposure to shift work.

Relationship to International Classification of Sleep Disorders

The *International Classification of Sleep Disorders,* 2nd Edition (ICSD-2), differentiates nine circadian rhythm sleep disorders, including jet lag type.

Parasomnias

Parasomnias are disorders characterized by abnormal behavioral, experiential, or physiological events occurring in association with sleep, specific sleep stages, or sleep-wake transitions. The most common parasomnias—non–rapid eye movement (NREM) sleep arousal disorders and rapid eye movement (REM) sleep behavior disorder—represent admixtures of wakefulness and NREM sleep and wakefulness and REM sleep, respectively. These conditions serve as a reminder that sleep and wakefulness are not mutually exclusive and that sleep is not necessarily a global, whole-brain phenomenon.

Non–Rapid Eye Movement Sleep Arousal Disorders

Diagnostic Criteria

A. Recurrent episodes of incomplete awakening from sleep, usually occurring during the first third of the major sleep episode, accompanied by either one of the following:

   1. **Sleepwalking:** Repeated episodes of rising from bed during sleep and walking about. While sleepwalking, the individual has a blank, staring face; is relatively unresponsive to the efforts of others to communicate with him or her; and can be awakened only with great difficulty.
   2. **Sleep terrors:** Recurrent episodes of abrupt terror arousals from sleep, usually beginning with a panicky scream. There is intense fear and signs of autonomic arousal, such as mydriasis, tachycardia, rapid breathing, and sweating, during each episode. There is relative unresponsiveness to efforts of others to comfort the individual during the episodes.

B. No or little (e.g., only a single visual scene) dream imagery is recalled.

C. Amnesia for the episodes is present.

D. The episodes cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication).

F. Coexisting mental and medical disorders do not explain the episodes of sleepwalking or sleep terrors.

Coding note: For ICD-9-CM, code **307.46** for all subtypes. For ICD-10-CM, code is based on subtype.

Specify whether:

307.46 (F51.3) Sleepwalking type

Specify if:

With sleep-related eating

With sleep-related sexual behavior (sexsomnia)

307.46 (F51.4) Sleep terror type

Diagnostic Features

The essential feature of non–rapid eye movement (NREM) sleep arousal disorders is the repeated occurrence of incomplete arousals, usually beginning during the first third of the major sleep episode (Criterion A), that typically are brief, lasting 1–10 minutes, but may be protracted, lasting up to 1 hour. The maximum duration of an event is unknown. The eyes are typically open during these events. Many individuals exhibit both subtypes of arousals on different occasions, which underscores the unitary underlying pathophysiology. The subtypes reflect varying degrees of simultaneous occurrence of wakefulness and NREM sleep, resulting in complex behaviors arising from sleep with varying degrees of conscious awareness, motor activity, and autonomic activation.

The essential feature of *sleepwalking* is repeated episodes of complex motor behavior initiated during sleep, including rising from bed and walking about (Criterion A1). Sleepwalking episodes begin during any stage of NREM sleep, most commonly during slow-wave sleep and therefore most often occurring during the first third of the night. During episodes, the individual has reduced alertness and responsiveness, a blank stare, and relative unresponsiveness to communication with others or efforts by others to awaken the individual. If awakened during the episode (or on awakening the following morning), the individual has limited recall for the episode. After the episode, there may initially be a brief period of confusion or difficulty orienting, followed by full recovery of cognitive function and appropriate behavior.

The essential feature of *sleep terrors* is the repeated occurrence of precipitous awakenings from sleep, usually beginning with a panicky scream or cry (Criterion A2). Sleep terrors usually begin during the first third of the major sleep episode and last 1–10 minutes, but they may last considerably longer, particularly in children. The episodes are accompanied by impressive autonomic arousal and behavioral manifestations of intense fear. During an episode, the individual is difficult to awaken or comfort. If the individual awakens after the sleep terror, little or none of the dream, or only fragmentary, single images, are recalled. During a typical episode of sleep terrors, the individual abruptly sits up in bed screaming or crying, with a frightened expression and autonomic signs of intense anxiety (e.g., tachycardia, rapid breathing, sweating, dilation of the pupils). The individual may be inconsolable and is usually unresponsive to the efforts of others to awaken or comfort him or her. Sleep terrors are also called "night terrors" or "pavor nocturnus."

Associated Features Supporting Diagnosis

Sleepwalking episodes can include a wide variety of behaviors. Episodes may begin with confusion: the individual may simply sit up in bed, look about, or pick at the blanket or sheet. This behavior then becomes progressively complex. The individual may actually leave the bed and walk into closets, out of the room, and even out of buildings. Individuals may use the bathroom, eat, talk, or engage in more complex behaviors. Running and frantic attempts to escape some apparent threat can also occur. Most behaviors during sleepwalking episodes are routine and of low complexity. However, cases of unlocking doors and even operating machinery (driving an automobile) have been reported. Sleepwalking can also include inappropriate behavior (e.g., commonly, urinating in a closet or wastebasket). Most episodes last for several minutes to a half hour but may be more protracted. Inasmuch as sleep is a state of relative analgesia, painful injuries sustained during sleepwalking may not be appreciated until awakening after the fact.

There are two "specialized" forms of sleepwalking: sleep-related eating behavior and sleep-related sexual behavior (sexsomnia or sleep sex). Individuals with *sleep-related eating* experience unwanted recurrent episodes of eating with varying degrees of amnesia, ranging from no awareness to full awareness without the ability to not eat. During these episodes, inappropriate foods may be ingested. Individuals with sleep-related eating disorder may find evidence of their eating only the next morning. In *sexsomnia,* varying degrees of

sexual activity (e.g., masturbation, fondling, groping, sexual intercourse) occur as complex behaviors arising from sleep without conscious awareness. This condition is more common in males and may result in serious interpersonal relationship problems or medicolegal consequences.

During a typical episode of sleep terrors, there is often a sense of overwhelming dread, with a compulsion to escape. Although fragmentary vivid dream images may occur, a story-like dream sequence (as in nightmares) is not reported. Most commonly, the individual does not awaken fully, but returns to sleep and has amnesia for the episode on awakening the next morning. Usually only one episode will occur on any one night. Occasionally several episodes may occur at intervals throughout the night. These events rarely arise during daytime naps.

Prevalence

Isolated or infrequent NREM sleep arousal disorders are very common in the general population. From 10% to 30% of children have had at least one episode of sleepwalking, and 2%–3% sleepwalk often. The prevalence of sleepwalking disorder, marked by repeated episodes and impairment or distress, is much lower, probably in the range of 1%–5%. The prevalence of sleepwalking episodes (not sleepwalking disorder) is 1.0%–7.0% among adults, with weekly to monthly episodes occurring in 0.5%–0.7%. The lifetime prevalence of sleepwalking in adults is 29.2%, with a past-year prevalence of sleepwalking of 3.6%.

The prevalence of sleep terrors in the general population is unknown. The prevalence of sleep terror episodes (as opposed to sleep terror disorder, in which there is recurrence and distress or impairment) is approximately 36.9% at 18 months of age, 19.7% at 30 months of age, and 2.2% in adults.

Development and Course

NREM sleep arousal disorders occur most commonly in childhood and diminish in frequency with increasing age. The onset of sleepwalking in adults with no prior history of sleepwalking as children should prompt a search for specific etiologies, such as obstructive sleep apnea, nocturnal seizures, or effect of medication.

Risk and Prognostic Factors

Environmental. Sedative use, sleep deprivation, sleep-wake schedule disruptions, fatigue, and physical or emotional stress increase the likelihood of episodes. Fever and sleep deprivation can produce an increased frequency of NREM sleep arousal disorders.

Genetic and physiological. A family history for sleepwalking or sleep terrors may occur in up to 80% of individuals who sleepwalk. The risk for sleepwalking is further increased (to as much as 60% of offspring) when both parents have a history of the disorder.

Individuals with sleep terrors frequently have a positive family history of either sleep terrors or sleepwalking, with as high as a 10-fold increase in the prevalence of the disorder among first-degree biological relatives. Sleep terrors are much more common in monozygotic twins as compared with dizygotic twins. The exact mode of inheritance is unknown.

Gender-Related Diagnostic Issues

Violent or sexual activity during sleepwalking episodes is more likely to occur in adults. Eating during sleepwalking episodes is more commonly seen in females. Sleepwalking occurs more often in females during childhood but more often in males during adulthood.

Older children and adults provide a more detailed recollection of fearful images associated with sleep terrors than do younger children, who are more likely to have complete amnesia or report only a vague sense of fear. Among children, sleep terrors are more common in males than in females. Among adults, the sex ratio is even.

Diagnostic Markers

NREM sleep arousal disorders arise from any stage of NREM sleep but most commonly from deep NREM sleep (slow-wave sleep). They are most likely to appear in the first third of the night and do not commonly occur during daytime naps. During the episode, the polysomnogram may be obscured with movement artifact. In the absence of such artifact, the electroencephalogram typically shows theta or alpha frequency activity during the episode, indicating partial or incomplete arousal.

Polysomnography in conjunction with audiovisual monitoring can be used to document episodes of sleepwalking. In the absence of actually capturing an event during a polysomnographic recording, there are no polysomnographic features that can serve as a marker for sleepwalking. Sleep deprivation may increase the likelihood of capturing an event. As a group, individuals who sleepwalk show instability of deep NREM sleep, but the overlap in findings with individuals who do not sleepwalk is great enough to preclude use of this indicator in establishing a diagnosis. Unlike arousals from REM sleep associated with nightmares, in which there is an increase in heart rate and respiration prior to the arousal, the NREM sleep arousals of sleep terrors begin precipitously from sleep, without anticipatory autonomic changes. The arousals are associated with impressive autonomic activity, with doubling or tripling of the heart rate. The pathophysiology is poorly understood, but there appears to be instability in the deeper stages of NREM sleep. Absent capturing an event during a formal sleep study, there are no reliable polysomnographic indicators of the tendency to experience sleep terrors.

Functional Consequences of Non-REM Sleep Arousal Disorders

For the diagnosis of a NREM sleep arousal disorder to be made, the individual or household members must experience clinically significant distress or impairment, although parasomnia symptoms may occur occasionally in nonclinical populations and would be subthreshold for the diagnosis. Embarrassment concerning the episodes can impair social relationships. Social isolation or occupational difficulties can result. The determination of a "disorder" depends on a number of factors, which may vary on an individual basis and will depend on the frequency of events, potential for violence or injurious behaviors, embarrassment, or disruption/distress of other household members. Severity determination is best made based on the nature or consequence of the behaviors rather than simply on frequency. Uncommonly, NREM sleep arousal disorders may result in serious injury to the individual or to someone trying to console the individual. Injuries to others are confined to those in close proximity; individuals are not "sought out." Typically, sleepwalking in both children and adults is not associated with significant mental disorders. For individuals with sleep-related eating behaviors, unknowingly preparing or eating food during the sleep period may create problems such as poor diabetes control, weight gain, injury (cuts and burns), or consequences of eating dangerous or toxic inedibles. NREM sleep arousal disorders may rarely result in violent or injurious behaviors with forensic implications.

Differential Diagnosis

Nightmare disorder. In contrast to individuals with NREM sleep arousal disorders, individuals with nightmare disorder typically awaken easily and completely, report vivid storylike dreams accompanying the episodes, and tend to have episodes later in the night. NREM sleep arousal disorders occur during NREM sleep, whereas nightmares usually occur during REM sleep. Parents of children with NREM sleep arousal disorders may misinterpret reports of fragmentary imagery as nightmares.

Breathing-related sleep disorders. Breathing disorders during sleep can also produce confusional arousals with subsequent amnesia. However, breathing-related sleep disorders are also characterized by characteristic symptoms of snoring, breathing pauses, and

daytime sleepiness. In some individuals, a breathing-related sleep disorder may precipitate episodes of sleepwalking.

REM sleep behavior disorder. REM sleep behavior disorder may be difficult to distinguish from NREM sleep arousal disorders. REM sleep behavior disorder is characterized by episodes of prominent, complex movements, often involving personal injury arising from sleep. In contrast to NREM sleep arousal disorders, REM sleep behavior disorder occurs during REM sleep. Individuals with REM sleep behavior disorder awaken easily and report more detailed and vivid dream content than do individuals with NREM sleep arousal disorders. They often report that they "act out dreams."

Parasomnia overlap syndrome. Parasomnia overlap syndrome consists of clinical and polysomnographic features of both sleepwalking and REM sleep behavior disorder.

Sleep-related seizures. Some types of seizures can produce episodes of very unusual behaviors that occur predominantly or exclusively during sleep. Nocturnal seizures may closely mimic NREM sleep arousal disorders but tend to be more stereotypic in nature, occur multiple times nightly, and be more likely to occur from daytime naps. The presence of sleep-related seizures does not preclude the presence of NREM sleep arousal disorders. Sleep-related seizures should be classified as a form of epilepsy.

Alcohol-induced blackouts. Alcohol-induced blackouts may be associated with extremely complex behaviors in the absence of other suggestions of intoxication. They do not involve the loss of consciousness but rather reflect an isolated disruption of memory for events during a drinking episode. By history, these behaviors may be indistinguishable from those seen in NREM sleep arousal disorders.

Dissociative amnesia, with dissociative fugue. Dissociative fugue may be extremely difficult to distinguish from sleepwalking. Unlike all other parasomnias, nocturnal dissociative fugue arises from a period of wakefulness during sleep, rather than precipitously from sleep without intervening wakefulness. A history of recurrent childhood physical or sexual abuse is usually present (but may be difficult to obtain).

Malingering or other voluntary behavior occurring during wakefulness. As with dissociative fugue, malingering or other voluntary behavior occurring during wakefulness arises from wakefulness.

Panic disorder. Panic attacks may also cause abrupt awakenings from deep NREM sleep accompanied by fearfulness, but these episodes produce rapid and complete awakening without the confusion, amnesia, or motor activity typical of NREM sleep arousal disorders.

Medication-induced complex behaviors. Behaviors similar to those in NREM sleep arousal disorders can be induced by use of, or withdrawal from, substances or medications (e.g., benzodiazepines, nonbenzodiazepine sedative-hypnotics, opiates, cocaine, nicotine, antipsychotics, tricyclic antidepressants, chloral hydrate). Such behaviors may arise from the sleep period and may be extremely complex. The underlying pathophysiology appears to be a relatively isolated amnesia. In such cases, substance/medication-induced sleep disorder, parasomnia type, should be diagnosed (see "Substance/Medication-Induced Sleep Disorder" later in this chapter).

Night eating syndrome. The sleep-related eating disorder form of sleepwalking is to be differentiated from night eating syndrome, in which there is a delay in the circadian rhythm of food ingestion and an association with insomnia and/or depression.

Comorbidity

In adults, there is an association between sleepwalking and major depressive episodes and obsessive-compulsive disorder. Children or adults with sleep terrors may have elevated scores for depression and anxiety on personality inventories.

Relationship to International Classification of Sleep Disorders

The *International Classification of Sleep Disorders,* 2nd Edition, includes "confusional arousal" as a NREM sleep arousal disorder.

Nightmare Disorder

Diagnostic Criteria **307.47 (F51.5)**

A. Repeated occurrences of extended, extremely dysphoric, and well-remembered dreams that usually involve efforts to avoid threats to survival, security, or physical integrity and that generally occur during the second half of the major sleep episode.
B. On awakening from the dysphoric dreams, the individual rapidly becomes oriented and alert.
C. The sleep disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The nightmare symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication).
E. Coexisting mental and medical disorders do not adequately explain the predominant complaint of dysphoric dreams.

Specify if:

During sleep onset

Specify if:

With associated non–sleep disorder, including substance use disorders
With associated other medical condition
With associated other sleep disorder

Coding note: The code 307.47 (F51.5) applies to all three specifiers. Code also the relevant associated mental disorder, medical condition, or other sleep disorder immediately after the code for nightmare disorder in order to indicate the association.

Specify if:

Acute: Duration of period of nightmares is 1 month or less.
Subacute: Duration of period of nightmares is greater than 1 month but less than 6 months.
Persistent: Duration of period of nightmares is 6 months or greater.

Specify current severity:

Severity can be rated by the frequency with which the nightmares occur:

Mild: Less than one episode per week on average.
Moderate: One or more episodes per week but less than nightly.
Severe: Episodes nightly.

Diagnostic Features

Nightmares are typically lengthy, elaborate, storylike sequences of dream imagery that seem real and that incite anxiety, fear, or other dysphoric emotions. Nightmare content typically focuses on attempts to avoid or cope with imminent danger but may involve themes that evoke other negative emotions. Nightmares occurring after traumatic experiences may replicate the threatening situation ("replicative nightmares"), but most do not. On awakening, nightmares are well remembered and can be described in detail. They arise

almost exclusively during rapid eye movement (REM) sleep and can thus occur throughout sleep but are more likely in the second half of the major sleep episode when dreaming is longer and more intense. Factors that increase early-night REM intensity, such as sleep fragmentation or deprivation, jet lag, and REM-sensitive medications, might facilitate nightmares earlier in the night, including at sleep onset.

Nightmares usually terminate with awakening and rapid return of full alertness. However, the dysphoric emotions may persist into wakefulness and contribute to difficulty returning to sleep and lasting daytime distress. Some nightmares, known as "bad dreams," may not induce awakening and are recalled only later. If nightmares occur during sleep-onset REM periods (*hypnagogic*), the dysphoric emotion is frequently accompanied by a sense of being both awake and unable to move voluntarily (*isolated sleep paralysis*).

Associated Features Supporting Diagnosis

Mild autonomic arousal, including sweating, tachycardia, and tachypnea, may characterize nightmares. Body movements and vocalizations are not characteristic because of REM sleep–related loss of skeletal muscle tone, but such behaviors may occur under situations of emotional stress or sleep fragmentation and in posttraumatic stress disorder (PTSD). When talking or emoting occurs, it is typically a brief event terminating the nightmare.

Individuals with frequent nightmares are at substantially greater risk for suicidal ideation and suicide attempts, even when gender and mental illness are taken into account.

Prevalence

Prevalence of nightmares increases through childhood into adolescence. From 1.3% to 3.9% of parents report that their preschool children have nightmares "often" or "always". Prevalence increases from ages 10 to 13 for both males and females but continues to increase to ages 20–29 for females (while decreasing for males), when it can be twice as high for females as for males. Prevalence decreases steadily with age for both sexes, but the gender difference remains. Among adults, prevalence of nightmares at least monthly is 6%, whereas prevalence for frequent nightmares is 1%–2%. Estimates often combine idiopathic and posttraumatic nightmares indiscriminately.

Development and Course

Nightmares often begin between ages 3 and 6 years but reach a peak prevalence and severity in late adolescence or early adulthood. Nightmares most likely appear in children exposed to acute or chronic psychosocial stressors and thus may not resolve spontaneously. In a minority, frequent nightmares persist into adulthood, becoming virtually a lifelong disturbance. Although specific nightmare content may reflect the individual's age, the essential features of the disorder are the same across age groups.

Risk and Prognostic Factors

Temperamental. Individuals who experience nightmares report more frequent past adverse events, but not necessarily trauma, and often display personality disturbances or psychiatric diagnosis.

Environmental. Sleep deprivation or fragmentation, and irregular sleep-wake schedules that alter the timing, intensity, or quantity of REM sleep, can put individuals at risk for nightmares.

Genetic and physiological. Twin studies have identified genetic effects on the disposition to nightmares and their co-occurrence with other parasomnias (e.g., sleeptalking).

Course modifiers. Adaptive parental bedside behaviors, such as soothing the child following nightmares, may protect against developing chronic nightmares.