



Wake Me When It's Over: Sleep and Its Disorders

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The phenomenon of sleep is hardly less complex and inscrutable than those of cognition, respiration, digestion, and reproduction. Sleep is not just a temporary suspension of consciousness, but an intricate process, consisting of cyclical changes in many aspects of body chemistry and function, that must occur periodically to restore and maintain neurologic health. Numerous disorders of this process have been identified, from nightmares, jet lag, and insomnia, which we all sometimes experience, to less common but more serious ones such as obstructive sleep apnea, narcolepsy, and sudden infant death syndrome. This article surveys the physiology of normal sleep and discusses the nature, diagnosis, and treatment of some of its more important disorders.

The Physiology of Sleep

Until the 1950s, neurophysiologists considered sleep a largely passive state, in which the reduction or withdrawal of external and internal stimuli allowed for an idling or suspension of many neural functions. During the past 50 years, intensive study of sleep by means of electroencephalography (EEG), animal experimentation, and more recently positron-emission tomography (PET), along with observation of the effects of central nervous system (CNS) depressants and stimulants, has yielded a concept of sleep as an active process characterized by a regular succession of psychophysiological events.

Normal sleep is a cyclically recurring phenomenon, the length of the cycle determined by one of many internal rhythms or "biological clocks." The sleep-wake cycle parallels, but is not inherently tied to, other circadian rhythms such as those that determine fluctuations in body temperature and cortisol secretion. In persons isolated for many weeks and given no sensory clues as to the time of day, the period of each sleep-wake cycle gradually increases to 25-30 hours, or even longer. Individual variations in sleep biorhythms account for the difference between "morning persons" and "night owls" (more about this later).

Four stages or levels of normal sleep have been identified on the basis of EEG changes. In the waking state, the EEG typically shows low-voltage waves of moderate frequency (alpha waves) or high frequency (beta waves). In contrast, the EEG during most of the time spent in sleep is characterized by slower waves of higher voltage. The normal *sleep latency* (the interval between going to bed and falling asleep) varies from 15 seconds to 15 minutes. After falling asleep, one passes gradually from stage 1 to stage 4 over a period of about 45

minutes, each stage being characterized by waves of lower frequency and higher voltage than the preceding one. After about 30 minutes in stage 4, the sleeper gradually passes back through stage 3 to stage 2. A full night's sleep typically includes five to seven such cycles, but only the first one or two of these may reach stage 4.

During stage 1 sleep, the EEG shows theta waves, which have a frequency of 4-7 Hz (hertz, or cycles per second). In stage 2, so-called *sleep spindles* occur—brief intermittent bursts of faster (12-14 Hz) activity. The very slow (1-2 Hz) high-voltage waves of stages 3 and 4 are called delta waves. The deeper the stage of sleep, the more difficult it is for the sleeper to be aroused by external stimuli. About 50% of normal sleep is spent in stage 2.

During the four stages of sleep thus far described, the parasympathetic division of the autonomic nervous system is dominant. Pulse, blood pressure, and respiratory rates gradually decline, and gastrointestinal motility is increased. Voluntary muscles are relaxed but not inhibited; a normal sleeper changes position every 5-20 minutes.

Upon the return to stage 2 after an interval at deeper stages, a series of striking alterations occur. The sleeper passes into an entirely different state, in which many of the features characterizing stages 1-4 are sharply reversed. The EEG now shows low-voltage, high-frequency activity, as in the waking state. Cerebral blood flow and oxygen consumption are increased, and the sympathetic division of the autonomic nervous system becomes activated, with increases in pulse, blood pressure, and respiratory rate, and inhibition of gastrointestinal motility.

A profound loss of tone, amounting almost to paralysis, affects all the voluntary muscles except those controlling eye movements. While the rest of the sleeper's body lies immobile and inert, the eyes undergo spells of rapid, irregular movement. Hence this phase of sleep is called *rapid-eye-movement (REM) sleep*. In contrast, the four stages previously described are said to pertain to non-REM or NREM sleep. REM sleep was first reported by Aserinsky and Kleitman in 1953.

Periods of REM sleep typically occur with each return to stage 2—hence five to seven times during a full night's sleep—and they make up about 25% of the total period of sleep. The longer one sleeps, the more frequently periods of REM sleep occur, and the longer they last. During REM sleep, the subject is even less susceptible to arousal by external stimuli than in stage 4 sleep, but is more likely to awaken spontaneously.

Alcohol and barbiturates suppress REM sleep, while reserpine and lysergic acid diethylamide (LSD) increase it. After selective deprivation of REM sleep, experimental subjects experience a rebound period of increased REM sleep, which may persist for more than one night. REM sleep cycles also increase in frequency and duration during withdrawal from barbiturates, amphetamines, and narcotics.

Virtually everyone dreams nightly. However, it has been shown experimentally that dreams are remembered for only 8-15 minutes. Hence, unless one awakens during this brief period, all possibility of later recall of the dream is probably lost. Most dreaming occurs during REM sleep, but some mental activity (less vivid, more structured, and more plausible than dreaming) may occur during NREM sleep, and most nightmares occur during stages 3 and 4 of NREM sleep.

The sleep requirements of the human brain decline with age. While the newborn may sleep 16-20 hours a day, an elderly adult may get along on 4-5 hours of sleep in each 24-hour period. For most healthy adults, the sleep requirement remains fairly stable at 7-9 hours during the middle decades. In later life, sleep patterns change: more time is spent in REM sleep, less time in delta-wave sleep. After age 60, descent to stage 4 sleep may no longer occur. Elderly sleepers are subject to more frequent arousal, often related to psychological or medical factors (depression, joint pain, nocturia due to bladder or prostate problems).

The sleep pattern of infants is biphasic (a longer period of sleep at night, a nap in the afternoon), and in advanced age this pattern may return. Traces of the biphasic cycle may persist throughout the middle years. Many persons experience drowsiness in the afternoon and attribute it to the effects of eating lunch. The digestive process, however, actually tends to inhibit sleep, as will be discussed later. The tendency to doze in the early afternoon is culturally reinforced in tropical countries where the siesta is customary.

As mentioned earlier, sleep used to be considered a negative or idling process in which a postulated arousal or activating system was temporarily shut down. We now know that the onset of sleep is an active process, initiated in the brainstem, possibly in more than one neural center. During REM sleep, voluntary muscle tone is actively inhibited by a zone in the locus ceruleus of the pons. Hence sleep is radically different from coma, which does indeed represent a breakdown or failure of cortical activation and responsiveness due to CNS trauma or disease, or to toxic or vascular factors.

Several peptide neurotransmitters have been implicated in the initiation of sleep. Recent attention has focused on melatonin (*N*-acetyl-5-methoxytryptamine), a derivative of serotonin secreted by the pineal gland. Melatonin production rises as ambient light decreases. Serum levels increase tenfold just before sleep, reaching a peak around midnight. The 24-hour secretion of melatonin is higher in winter, when periods of daylight are shorter. Melatonin secretion declines with age, a fact that may account for altered sleep patterns in the elderly.

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Numerous disorders of sleep, some potentially fatal, have been identified and studied. These include insomnia, sleepwalking, bedwetting, nightmares, restless legs syndrome, narcolepsy, and sleep apnea syndrome. During the past decade, a number of sleep clinics, either free-standing or associated with other healthcare programs or facilities, have been established for the diagnosis and treatment of sleep disorders.

Experimental observations of normal and abnormal sleep, and diagnostic studies of persons with sleep disorders, are carried out in a sleep laboratory by *polysomnography*. While the subject lies in a comfortable bed in a dark, quiet room and sleeps or tries to sleep, a multichannel monitor continuously measures and records pulse, respirations, limb movements, and eye movements simultaneously with the EEG. In some cases other measurements may be made as well.

Insomnia

Insomnia has been defined as the inability to sleep long enough or deeply enough at night to maintain optimum CNS health and function during the day. Since sleep requirements vary markedly from person to person, no quantitative definition (so many minutes or hours in such-and-such a stage of sleep) is feasible. Moreover, the diagnosis of insomnia is generally based on the patient's own observations, and extensive studies have shown that these observations are often unreliable. One researcher studied a large group of self-professed insomniacs in a sleep laboratory and found that they had an average sleep latency of 15 minutes and an average duration of nighttime sleep of 7 hours. In exasperation, he postulated that many persons who claim that they suffer from insomnia actually sleep well, but dream that they are awake!

Be that as it may, insomnia is regarded as a significant and widespread public health problem. The prevalence of chronic insomnia (defined as inadequate sleep at least three nights a week for at least one month) may be as high as 15% in the general population. Besides leading to daytime drowsiness, difficulty concentrating, impairment of memory, irritability, and restlessness or anxiety, insomnia is believed to be responsible for much poor job performance and many industrial and automobile accidents.

Insomnia is not a single disorder, but rather a symptom with numerous possible causes. Various patterns of sleep disturbance occur. Difficulty in falling asleep (prolonged sleep latency) can result from mental preoccupation, emotional upset (anxiety, anger), ingestion of a large meal or use of CNS stimulants (caffeine, nicotine, or various medicines) shortly before

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bedtime, physical distress (pain, nausea), symptoms aggravated by recumbency (cough, gastroesophageal reflux, orthopnea), or disruption of the sleep-wake rhythm (jet lag, shift work, daytime napping).

Another type of insomnia, which consists of failure to attain stages 3 and 4, with frequent awakenings during the night, can also be due to emotionally induced restlessness or to physical factors such as chronic musculoskeletal problems (osteoarthritis, fibromyalgia) and nocturia due to urinary tract disease. A third type, called terminal insomnia, isn't as serious as it sounds. This refers to awakening in the early morning (two to three hours before intended rising time) with inability to fall back asleep. Terminal insomnia is a cardinal feature of clinical depression, but may occur in other conditions as well.

The elderly are particularly susceptible to insomnia, or at least to the subjective sense of not getting enough sleep at night. Many elderly persons complain of both prolonged sleep latency and frequent awakenings. This may be due in part to the higher incidence of physical illness in the elderly, as well as to the related fact that elderly persons are more likely to be taking one or more medicines capable of causing insomnia. Other possible causes include a reduction in physical activity during the day, the lack of a rigid schedule such as those imposed by a job or the responsibilities of homemaking and child-rearing, and the habit of taking catnaps during periods of idleness.

Alleviating insomnia begins logically with an attempt to find and eliminate its cause. Treatment of physical or emotional illness or correction of an unhealthy lifestyle may lead to improvement in sleep. Many medicines (decongestants, antidepressants, antihypertensives, nicotine patches prescribed to facilitate smoking cessation, even some antibiotics) can delay the onset of sleep or impair its quality. Changing medicines or dosage times may restore a healthy sleep pattern.

Standard advice for all sufferers from insomnia includes the following precepts of sleep hygiene:

1. Maintain as regular a schedule as possible, so as to avoid disrupting internal rhythms. Get up, eat meals, take medicines, and perform daily tasks at about the same time every day, but go to bed only when you are sleepy.
2. Follow a relaxing bedtime ritual, such as taking a warm bath, listening to quiet music, or doing light reading. Avoid strenuous exertion or emotionally stimulating activities during the late evening. Don't consume caffeine, nicotine, alcohol, or a heavy meal for several hours before bedtime.
3. Exercise regularly (but not in the evening). Physical fatigue is often conducive to better sleep.
4. Avoid taking daytime naps. If you must nap, do it at the same time every day, preferably in midafternoon.

5. Don't use your bed as a couch where you read, watch television, or eat. Go to bed only to sleep.

A number of non-drug measures (besides counting sheep and reading Jane Austen) have been found effective in some cases of insomnia. *Relaxation therapy* attempts to relieve bedtime wakefulness by a variety of techniques designed to reverse heightened physical, cognitive, or emotional arousal. These include progressive muscle relaxation, biofeedback, and attention focusing through meditation, controlled breathing, or other means. The rationale of *sleep restriction therapy* is to induce a mild state of sleep deprivation. This is done by limiting the subject's nightly time in bed to a period equivalent to the amount of sleep the subject has actually been getting. As sleep improves, hours in bed are gradually increased.

Prescription Hypnotics

Barbiturates

- butobarbital (Butisol)
- pentobarbital (Nembutal)

Benzodiazepines

- estazolam (Prosom)
- flurazepam (Dalmane)
- quazepam (Doral)
- temazepam (Restoril)
- triazolam (Halcion)

Other

- zaleplon (Sonata)
- zolpidem (Ambien)

The notion that insomnia is a disease that should be treated with medicine is deeply ingrained in Western society. Drugs that have a calming or relaxing effect are called *ataractics*, *sedatives*, or *tranquilizers*, and those that are intended to induce sleep are called *hypnotics* or *soporifics*. The search for a safe and effective hypnotic probably began before recorded time. But, until early in the present century, the pharmacopeia offered only alcohol, opiates, bromides, chloral hydrate, and a few other agents—all of them unpredictable, and most of them potentially toxic and habit-forming. In 1903 the first barbiturate was synthesized. Hypnotics and sedatives of that class dominated the treatment of insomnia and anxiety neuroses from then until mid-century, when the first phenothiazines and benzodiazepines became available.

Although the first dose of a barbiturate can generally put the most desperate insomniac to sleep, these drugs have many disadvantages. Because all barbiturates are habit-forming, physical dependence develops quickly. Withdrawal of a regular nighttime dose of a barbiturate after even a few days often results in rebound insomnia.

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Tolerance to barbiturates also develops rapidly, usually in less than two weeks. This means that a dose that was formerly effective soon ceases to induce sleep. Barbiturates are detoxified by one or more hepatic enzymes of the cytochrome P-450 system. Repeated administration of a barbiturate promotes formation of more enzyme. This results in more rapid clearing of the drug from the plasma, so that a therapeutic level cannot be attained without increase of dose. Switching to a different barbiturate may not help, since the same enzyme may show activity against many drugs within a class, and even some drugs in other classes. Repeatedly increasing the dose of a nighttime barbiturate to sustain its hypnotic effect, or just continuing the same dose for many months, is an unsound expedient.

During the 1950s, phenothiazine tranquilizers such as chlorpromazine (Thorazine) became available and quickly displaced barbiturates in the control of anxiety, besides proving valuable in the treatment of schizophrenia. But the usefulness of these drugs for nighttime sedation is limited by their tendency to cause orthostatic hypotension, and, with prolonged administration, to induce parkinsonlike side effects. The benzodiazepines, beginning with chlordiazepoxide (Librium) in 1961, provided better and safer means of treating many emotional disorders. Moreover, certain benzodiazepines were found to be more useful than barbiturates in treating insomnia.

Unlike barbiturates, which suppress REM sleep, benzodiazepine hypnotics reduce the amount of time spent in stage 3 and 4 NREM sleep, while increasing the total time spent in sleep. More importantly, although both tolerance and physical dependence can become a problem with benzodiazepines, these develop more slowly than with barbiturates.

The biological half-life of a drug is the period required for the plasma level of a single dose to decrease by one-half. Because some benzodiazepine hypnotics have a long biological half-life (as high as 24 hours for estazolam), regular nightly dosing can lead to gradual accumulation of a significant baseline plasma level, with resulting daytime drowsiness or "hang-over" effect. In addition, triazolam interacts with many other drugs, some of which (cimetidine, macrolide antibiotics) can cause marked increases in the blood level of triazolam at a normally therapeutic dosage.

Numerous hypnotics other than barbiturates and benzodiazepines have been synthesized and marketed during the past 30 years; most of these have fallen into disuse. Two products recently released, zaleplon and zolpidem, induce sleep by a novel mechanism involving CNS receptors for the neurotransmitter GABA (γ -aminobutyric acid). Both have relatively short half-lives, and are promoted for the short-term management of difficulty in falling asleep. Zolpidem, an imidazopyridine with a half-life of 2.5 hr, is marketed as Ambien; zaleplon, a pyrazolopyrimidine with a half-life of 1 hr, is marketed as Sonata. Residual daytime drowsiness and rebound insomnia after withdrawal are claimed to be minimal with these agents. Because the wholesale cost of a 10-mg tablet of either of these products is over \$2, they have been excluded from the formularies of many third-party payers.

Current medical practice guidelines strongly emphasize the importance of seeking reasons for insomnia rather than auto-

matically treating it with hypnotics. Physicians are advised to prescribe only small supplies of hypnotic drugs and to educate patients about their proper use and potential adverse effects. Sleeping medicines nonetheless continue to be heavily prescribed. By far the largest number of hypnotic prescriptions are for elderly patients, in whom they can aggravate existing disorders such as depression, dementia, and orthostatic hypotension, and can also interact with other medicines.

Nonprescription sleeping medicines, including nighttime medicines for sufferers of acute respiratory infections, exploit the sedative effects of antihistamines such as chlorpheniramine (Alka Seltzer Plus, Children's NyQuil, most TheraFlu products), diphenhydramine (Nytol, Sleepinal, Somnex, Tylenol PM), and doxylamine (NyQuil, Unisom). These products are moderately effective for occasional mild insomnia, but regular use can lead to habituation. In addition, although some are touted as treatments for nasal congestion and cough, they often make those symptoms worse by reducing the volume and increasing the viscosity of respiratory tract secretions.

Melatonin has shown some promise as a sleep aid in certain circumstances. Unlike most hormones, melatonin is readily absorbed from the digestive tract, and is a component of some foods. For that reason, therapeutic formulations of melatonin come under federal standards for foods rather than those for drugs. Testing of commercially available preparations of melatonin has indicated both wide variations in potency and the presence of possibly harmful contaminants. No adequately controlled studies of the efficacy and safety of melatonin have been published.

The direct hypnotic effect of melatonin apparently varies considerably from person to person. Limited studies suggest that it may increase the duration of restful nighttime sleep in the elderly, in whom melatonin secretion is normally reduced. There is conflicting evidence as to whether it can reset the circadian pacemaker so as to hasten recovery from jet lag or facilitate adaptation to night-shift work. High doses of melatonin result in prolonged elevation of the serum melatonin level and increased production of prolactin by the pituitary gland.

Narcolepsy

Narcolepsy is a relatively uncommon disorder characterized by attacks of irresistible sleepiness occurring during the daytime, often without warning, and lasting 0.5 to 30 minutes. This is a chronic disorder with an organic basis. It tends to run in families, and typically begins during the teen years. Attacks may be triggered by laughter or by strong emotion, such as anger or sexual arousal. They can occur even during purposeful activity, such as when carrying on a conversation, operating machinery, or driving a car, sometimes with disastrous results.

Often there is an abrupt loss of muscle tone (cataplexy), with buckling of the knees and a fall to the floor.

EEG studies support the notion that narcolepsy is an intrusion of REM sleep into the waking state. The victim may experience fleeting, vivid, dreamlike images while drifting off. Persons with narcolepsy "can fall asleep anywhere." In the sleep laboratory they display very short sleep latency (2 minutes or less) even during the daytime. Amphetamines, methylphenidate (Ritalin), and modafinil (Provigil) are generally effective in reducing or preventing sleep attacks.

Parasomnias

This term refers to a large group of behavioral phenomena associated with the sleeping state. These vary widely in incidence and significance. Only the more common and medically important will be discussed here.

A **nightmare** is a terrifying dream that often awakens the sleeper in a state of mental anguish and physical excitement. Most true nightmares differ from merely unpleasant dreams by occurring in the deeper stages of NREM sleep rather than in periods of REM sleep. A special form of nightmare is the **incubus**, in which one experiences intense anxiety accompanied by a feeling of respiratory oppression or inhibition and sometimes partial paralysis.

Children are subject to another variant, called **night terrors** or *pavor nocturnus*. Within 30 minutes after falling asleep, the child screams, sits up in bed, and displays evidence of intense panic—a frozen, wide-eyed posture, tachycardia, hyperventilation, diaphoresis, and shaking or crying. The period of distress may last from 5 to 15 minutes, during which the victim seems oblivious of others or their efforts to provide reassurance and consolation. In the morning there is amnesia for the event.

Night terrors occur upon sudden arousal from delta-wave (stage 3 and 4) NREM sleep. The manifestation of profound fear is apparently not tied to any specific dream experience or imagery. The phenomenon can be triggered by excessive fatigue or emotional excitement.

The term *hypnagogic* refers to the act of falling asleep, while *hypnopompic* refers to the act of awakening. Many persons experience brief dreamlike visual or auditory hallucinations during these periods. Such episodes are typically simple, unstructured, and without much emotional content, and do not correspond to periods of rapid eye movement. A **hypnagogic hallucination** may culminate in a sudden convulsive twitch that wakes the sleeper. **Sleep paralysis** (hypnopompic paralysis) occurs when one returns to a near-waking state before the muscle inhibition of REM sleep has ended. There is a frightening sense of being unable to move, often accompanied by a dream in which one cannot escape some imminent evil.

Sleepwalking or somnambulism affects about 18% of the population. It is more frequent in children and in males, and the peak incidence is around age 11. The sleepwalker arises from bed (usually during the first one-third of the night) and walks around in a sort of open-eyed trance, avoiding obstacles and sometimes engaging in purposeful activity such as getting a

drink of water. Arousing a sleepwalker is usually difficult, but there may be some mumbled responses to questions.

Sleepwalking occurs during stages 3 and 4 of NREM sleep, and is not typically accompanied by any dream experience. Eventually the sleepwalker returns to bed, and in the morning has no recollection of the event. Persons walking in their sleep occasionally suffer injury or death by stepping out of windows or wandering into a street full of traffic. Administration of a short-acting benzodiazepine at bedtime often suppresses sleepwalking behavior.

Sleeptalking (somniloquy) is the production of speech or speechlike utterances during sleep. The vocal sounds produced may be wholly incoherent and unintelligible, or on the other hand several grammatically correct sentences may be spoken. The sleeper may even appear to be carrying on a conversation. Although speech during sleep would be expected to correlate with dreaming, sleeptalking can occur during any stage of sleep.

Probably most people occasionally talk in their sleep. The incidence of sleeptalking is higher in children and in persons with other sleep disorders such as sleepwalking and REM movement disorder (discussed below). It may also reflect anxiety or organic illness (fever, delirium).

Enuresis is defined as bedwetting during sleep in a person in whom bladder control has previously been well established. Although some bedwetting may be due to urologic anomalies, urinary tract infection, diabetes mellitus, diabetes insipidus, or a seizure disorder, about 3-6% of children and a much smaller proportion of adults experience at least occasional bedwetting in the absence of any of these.

Sleep laboratory studies show that an episode of bedwetting is typically preceded by a period of restlessness occurring during a rapid ascent from NREM stage 4 sleep. This is followed by a brief calm interval, after which micturition occurs. Bedwetting does not ordinarily occur during dreaming, much less as a result of dreaming about water. When such dreams occur, they are apparently suggested by the sensation of wetness that follows loss of urine.

Bedwetting, like sleepwalking, is commoner in boys, and the two conditions often occur together. Bedwetting has been attributed by some observers to a delay of CNS maturation, but psychosocial factors are evident in some cases. For example, a child may begin bedwetting after the birth of a sibling, and bedwetting is said to occur in as many as 30% of institutionalized children.

Behavior modification techniques (an alarm bell triggered by wetness; making the child wash the sheets) are not only unduly punitive but ineffectual. A bedtime dose of a tricyclic antidepressant or a short-acting benzodiazepine is usually effective in preventing bedwetting. However, these are off-label uses of these drugs, which moreover are not approved for administration to prepubertal children.

Fibromyalgia syndrome, a musculoskeletal pain disorder that occurs almost exclusively in middle-aged women, merits discussion here because it is an important cause of insomnia. Sufferers complain of chronic muscular soreness and stiffness

Night Life: The Meaning of Dreaming

Dreaming, a mysterious and universal experience, has challenged thinkers for thousands of years. Prophetic dreams are recorded in the Old and New Testaments, and they figure prominently in the secular literature of all regions and eras. The ancient Greeks believed that a sick person who slept in a temple of Asklepios, the god of healing, would receive a therapeutic message from the god in a dream. In some primitive cultures, dreaming is thought to occur because the soul leaves the body during sleep and wanders in another realm or dimension. The English philosopher Bertrand Russell suggested that “what we call waking life may be only an unusual and persistent nightmare.”

It is a matter of common observation that some dreams incorporate residual material from recent waking experiences, and that others are triggered by sensory stimuli such as a dry mouth or a ringing telephone. But the exact significance and bearing of most dreams remain elusive. Books purporting to enable one to interpret one's dreams have been popular for centuries, and remain so today. Efforts at scientific interpretation date back at least as far as Aristotle.

This year marks the centennial of the publication of Sigmund Freud's pivotal work, *The Interpretation of Dreams*. Freud used dream analysis, along with hypnosis, free association, and other techniques, to unlock the subconscious. He established several basic concepts still considered valid today: dreaming is an active process whereby the subconscious mind endeavors to resolve conflicts and tensions within itself; the central figure in a dream generally

represents the dreamer; the objects and events dreamed about are often symbolic, disguising deeper meanings so as to protect the dreamer from feelings of anxiety or guilt.

An unfortunate weakness of Freud's thinking was his tendency to adopt a single, simplistic explanation for a broad range of phenomena and then cling rigidly to that explanation even when doing so meant forcing the facts to fit the theory. Most of his disciples (Adler, Jones, Jung, Ferenczi, Rank, and others) fell away from him one by one because he was incapable of modifying his views to accommodate or assimilate new data resulting from ongoing observation and experimentation. Having committed himself to the position that all dreams represent wish fulfillment, Freud stubbornly refused to acknowledge what every thinking person must recognize—that in some of our dreams, instead of acting out our wishes, we observe or experience circumstances or events that we fear or abhor. Probably even Freud would not have cared to have “all his dreams come true”!

Modern scientific studies of dreaming show that most dreams involve people (often friends, relatives, or associates), that their principal imagery is visual, and that they usually occur in familiar settings, but differ from our experience of reality in their lack of temporal continuity and logical coherence. One observer wryly notes that dreams with erotic content are far more abundant in the writings of psychoanalysts than in those of sleep physiologists. All mammals so far tested experience periods of REM sleep, which are believed to represent the equivalent of human dreaming.

in the neck, shoulders, back, and hips, which are aggravated by physical exertion, as in performing housework or occupational activities. Typically these symptoms are accompanied by insomnia, headaches, weakness, and fatigue.

Physical examination discloses several “trigger points” over the neck and back—sharply localized and symmetrically distributed spots where the pressure of the examiner's finger elicits marked tenderness. Joint pain and muscle spasm are absent, as are fever, swelling, and other objective signs of disease; x-ray studies and laboratory tests are negative. In some cases hypothyroidism or a preceding viral infection has been implicated, but no unitary theory of causation has been advanced.

Moreover, it is unclear whether muscle pain keeps the patient awake, or whether nighttime restlessness and insomnia from some other cause lead to chronic muscle soreness. Although depression has not been consistently associated with fibromyalgia syndrome, a bedtime dose of a tricyclic antidepressant is often effective in improving sleep and alleviating muscle pain. In addition, patients benefit from education, reassurance that the condition is not progressive or crippling, and a program of moderate exercise.

Restless legs syndrome (RLS) is a neuromuscular disorder that is also a frequent cause of insomnia. RLS is a recurring dysesthesia or feeling of discomfort in the legs (occasionally the arms), variously described as a tickling, tingling, aching, or crawling sensation, that can be temporarily relieved or assuaged by moving or massaging the affected extremities. Although it is most common and most distressing when the sufferer is lying in bed trying to sleep, it can occur during any period of protracted immobility, as when traveling in a car, bus, or plane, sitting in a theater, or reading or watching television. Getting out of bed and walking or taking a hot bath provides only temporary relief.

The origin of RLS is obscure; probably various mechanisms can be responsible. Most victims are over 50, but the condition sometimes occurs during pregnancy. A familial form has been identified, in which onset occurs at a younger age, and application of cold relieves the restlessness. Among causes identified in some persons are peripheral neuropathy, parkinsonism, iron deficiency, renal dialysis, and certain medicines. Symptoms may be made worse by caffeine or alcohol.

A variant of this disorder, sometimes occurring in conjunction with it, is **periodic limb movement disorder**

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(PLMD), in which a sleeping person is subject to violent movements (myoclonic jerks) of the legs occurring at regular intervals of 20-90 seconds. RLS and PLMD can interfere significantly with sleep by delaying sleep onset and causing frequent arousal. These disorders can be equally hard on the sufferer's bedfellow. Although the Food and Drug Administration (FDA) has not yet approved any drug for the treatment of RLS or PLMD, several agents have been found effective. These include dopaminergics used in the treatment of parkinsonism (carbidopa-levodopa, pergolide), clonazepam (a benzodiazepine), and gabapentin (an anticonvulsant).

Sleep bruxism is a stereotyped movement disorder characterized by grinding or clenching of the teeth during sleep. Although more common in children, it can occur at any age. When it occurs frequently, it can result in damage to occlusal surfaces of teeth and chronic pain in jaw muscles and temporomandibular joints.

Less common than these conditions is so-called **REM sleep behavior disorder**. Whereas REM sleep is normally associated with inhibition of voluntary muscle movement, persons with this disorder become vigorously mobile during REM sleep, as if "acting out" their dreams. They may injure themselves by falling out of bed or striking walls or furniture with flailing extremities. This condition, of unknown cause, occurs most often in men over 50, and usually responds to treatment with clonazepam.

Sleep Cycle Disorders

Neural control of the normal circadian sleep cycle is poorly understood. The role of rhythmic fluctuations in melatonin secretion was mentioned earlier. Recent studies have identified a genetically induced **sleep-advance syndrome** in several family groups. Persons with this disorder experience a consistent 3- to 4-hour advance in their sleep-wake cycle, becoming drowsy in the early evening and wakeful long before dawn. Both melatonin secretion and body temperature rhythms are correspondingly skewed. There is also a **sleep-delay syndrome** in which evening wakefulness, with prolonged sleep latency, is combined with sluggishness and difficulty getting started in the morning.

In other recent research, studies of persons with **night-eating syndrome** have provided insights into some neuroendocrine influences on sleep cycles. Night-eating syndrome consists of ravenous hunger at bedtime and during the night, associated with insomnia and morning anorexia. These symptoms are associated with abnormally low levels of both melatonin and leptin during nighttime hours. Leptin is a hormone, produced by adipose tissue, that signals the brain to turn off appetite as fat stores accumulate. Normally the leptin level rises

to inhibit appetite as night approaches. The incidence of night-eating syndrome is thought to be 1-2% in the general population, but among the severely obese it may exceed 25%.

Much more common are disturbances in the sleep-wake cycle resulting from temporary changes of sleeping behavior due to travel, work, or lifestyle. Persons who work on an evening or night shift may have difficulty in adjusting to the need to be awake and alert at night and to sleep during the day, unless their internal clock happens to be set that way already. It is estimated that some 20% of those making up the work force in this country work evenings or nights, and that they sleep an average of 7 hours less each week than those who work in the daytime. Frequent changes of shift are particularly stressful, and may lead to chronic drowsiness, irritability, and anxiety.

Jet lag refers to a transitory interruption of the sleep rhythm resulting from rapid travel across more than one time zone. Resetting of the internal clock to the new time zone can take as long as a week. Traveling eastward usually makes adjustment harder, because the traveler is still wakeful when night falls. With westward travel, adjusting by staying up late may prove less difficult.

To recalibrate the internal sleep rhythm after air travel or a change of shift, a full night's sleep usually works better than daytime napping. Using caffeine to remain awake in the daytime, or sleeping pills or alcohol to induce sleep at night, may only aggravate the problem. Long-term problems with sleep cycle adjustment can sometimes be helped by exposure to bright light in the early morning hours or by administration of melatonin.

Obstructive Sleep Apnea

Obstructive sleep apnea syndrome (OSAS), first clearly delineated in 1965, is a disorder in which breathing is repeatedly interrupted during sleep as the airway is intermittently obstructed by lax, excessively bulky, or malformed pharyngeal tissues (soft palate, uvula, and sometimes tonsils). The cardinal features of this disorder are loud snoring and recurrent apneic episodes during sleep followed by gasping inspiration with partial or complete arousal. The period of apnea may last as long as two full minutes, and may be accompanied by sinus bradycardia or atrioventricular block.

Not all snoring is an indication of significant respiratory tract obstruction during sleep. In fact, most of us breathe more noisily while asleep, at least part of the time, because of a normal relaxation of the tongue and palate. Mild degrees of obstructive apnea may occur for a few nights in otherwise normal persons who are suffering from respiratory infections or allergies. But in OSAS the problem is chronic and can have severe consequences.

As a result of nocturnal hypoxemia and shallow, non-refreshing sleep, persons subject to this disorder often suffer from daytime lethargy, difficulties with memory and concentration, and even personality change and accident-proneness. About 15% develop sustained pulmonary hypertension. Limited studies suggest that persons with this disorder have an impaired swallowing reflex, at least during sleep.

OSAS affects about 4% of men and 2% percent of women between the ages of 30 and 60, and its incidence increases with advancing age. Obesity, hypothyroidism, cigarette smoking, alcohol, and some hypnotics (particularly benzodiazepines) predispose to this disorder. Diagnosis is confirmed by polysomnography augmented by chin electromyography and continuous monitoring of arterial oxygen saturation. Diagnostic assessment includes evaluation of the shape and caliber of upper respiratory passages. Weight loss, smoking cessation, and avoidance of benzodiazepine hypnotics are advised for all patients. An appliance worn inside the mouth at night reduces symptoms in some patients by maintaining the lower jaw in a forward position. The nightly use of *continuous positive airway pressure* (CPAP), which provides a steady flow of room air at low pressure through the nose to overcome intermittent upper respiratory obstruction, is often effective, but the device keeps some patients awake. Some have benefited from surgical trimming and reshaping of the uvula and soft palate, which can be performed by laser or radiofrequency ablation under local anesthesia, or from mandibular osteotomy with genioglossus muscle advancement.

Sudden Infant Death Syndrome

Sudden infant death syndrome (SIDS; also called crib death or cot death) is defined as the sudden death of an apparently healthy infant that remains unexplained after all known possible causes have been ruled out through autopsy, death scene investigation, and review of the medical history. Most deaths apparently occur during sleep. SIDS is the leading cause of death in infants between one week and one year of age. The yearly death toll in the United States is 6000-7000. The peak age is 2-4 months, and the majority of deaths occur during the winter.

The definition of SIDS excludes death due to drugs or poisons, respiratory infection, aspiration of vomitus or formula, accidental strangulation or suffocation, and child abuse. SIDS strikes all races and socioeconomic levels. It is somewhat commoner in males, and the second child is more vulnerable than the first. Familial clustering has not been observed. Although SIDS cannot be predicted, statistical studies have identified certain risk factors, among them maternal smoking before and after birth, inadequate prenatal care, low birth weight, young maternal age, maternal hard drug use, and perhaps bottle feeding and gastric infection with *Helicobacter pylori*.

By far the most important known risk factor is sleeping in the prone (face-down) position. Sleeping on the side is less dangerous than sleeping prone, but more dangerous than sleeping supine (face-up). These facts have yet to be explained, but the incidence of SIDS in the United States has fallen markedly

Sleep Words: A Brief Etymologic Glossary

Hypnotic—‘Pertaining to sleep’, from Greek *hypnos* ‘sleep’. The word is sometimes derived from the name of Hypnos, god of sleep (twin brother of Thanatos or Death), but in fact the mythic figure was named from the common noun *hypnos*. *Hypnosis* and *hypnotism*, terms referring to a transitory trance-like state, come from the same source.

Incubus—This evocative word, from Latin *in* ‘on’ and *cubare* ‘to lie’, was coined in the Middle Ages for a nightmare in which one feels that someone or something is pressing down on one’s chest. Compare the German word for ‘nightmare’, *Alpdruck* ‘pressure of an Alp [i.e., a mountain, on one’s chest]’.

Insomnia—A Latin word for sleeplessness, from *in* ‘not’ + *somnus* ‘sleep’ + the suffix *-ia* ‘condition’. Somewhat inconveniently, this word is indistinguishable from the plural of *insomnium* ‘dream’.

Nightmare—A dream that arouses intense fear or distress. The second part of the term is unrelated to our term for a female horse. It comes from Middle English *mare* ‘female goblin’, which may perhaps be related to words denoting grinding (*mortar*), wasting (*marasmus*), and death (*mortal*). The same word appears in the French word for ‘nightmare’, *cauchemar*.

Sandman—A figure of folklore and fairy tales, who is supposed to sprinkle sand in children’s eyes to make them sleepy. For many centuries, when children have become drowsy and rubbed their eyes, their parents have told them that the sandman or dustman must be around. *Dustman* is the usual British term for a garbage collector. The folkloric term *sandman* may have arisen by confusion with the Middle English *sandesman* or *sendman* ‘messenger’, literally ‘sent man’.

Soporific—Latin *sopor* ‘poppy juice’ is related to Latin *opium* and Greek *opion*. By metonymy (which here denotes putting the effect for the cause), the classical Latin term acquired the meaning ‘sleep’. Soporific is a modern technical term meaning ‘sleep-inducing’, from *sopor* + *-ficare* ‘to make, promote, induce’ (modified from *facere* ‘to make’). A proprietary formulation of the hypnotic drug methaqualone was formerly marketed in this country under the name of Sopor. Because of its high abuse potential, this drug (as well as Quaalude, another brand of methaqualone) was eventually withdrawn. But *sopors*, often misspelled *soapers*, meanwhile became a street name for sleeping pills or “downers.”

since 1992, when the American Academy of Pediatrics first recommended that healthy infants be placed on their backs for sleep. In healthy infants, the supine position does not increase the risk of vomiting and aspiration, but for infants with gastroesophageal reflux, swallowing dysfunction, or unilateral vocal cord paralysis, the prone position may be safer.

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