National Sleep Foundation

Sleep-Wake Cycle: Its Physiology and Impact on Health

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www.sleepfoundation.org

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No doubt, the consequences of sleep loss are significant. Historic tragedies have been linked to fatigue-related human error, among them the Exxon Valdez oil spill[1] and the NASA Challenger shuttle explosion.[2] The grave outcomes of events like these are just some of the reasons why improved understanding of the biology of sleep and wake can lead to improved quality of life and safety.

Emerging science and advances in technology now are allowing us to examine sleep at a level of detail never before possible. In addition to documenting the more obvious consequences of poor sleep, scientists are increasingly exploring what happens during sleep at the neurological and physiological level. And what they're recognizing is that sleep provides more benefits than previously thought and is absolutely crucial to promoting health and bodily function.

So why is sleep so important? Although we naturally think of sleep as a time of rest and recovery from the stresses of everyday life, research is revealing that sleep is a dynamic activity, during which many processes vital to health and well-being take place. New evidence shows that sleep is essential to helping maintain mood, memory, and cognitive performance. It also plays a pivotal role in the normal function of the endocrine and immune systems. In fact, studies show a growing link between sleep duration and a variety of serious health problems, including obesity, diabetes, hypertension, and depression.

It is no exaggeration to say that some of the most pressing problems we face as a society may be linked to poor sleep. Drowsiness in sleep-deprived drivers is likely the cause of more than 100,000 crashes, 71,000 injuries and more than 1,500 deaths each year.[3] In addition, sleep disorders are estimated to cost Americans over $100 billion annually in lost productivity, medical expenses, sick leave, and property and environmental damage.[4] On a personal level, we all know how miserable we feel after a night of poor sleep.

Despite the fact that at least 40 million Americans report having sleep problems, more than 60 percent of adults have never been asked about the quality of their sleep by a physician, and fewer than 20 percent ever initiated a discussion about it.[5] Clearly, sleep's impact on health and well being is under-recognized. But the growing body of knowledge about the complex structure, function, and mechanisms of sleep, as well as the consequences when sleep is lost or disturbed, should serve as a wake-up call for making sleep a public health priority.

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Mechanisms Controlling Sleep and Wakefulness

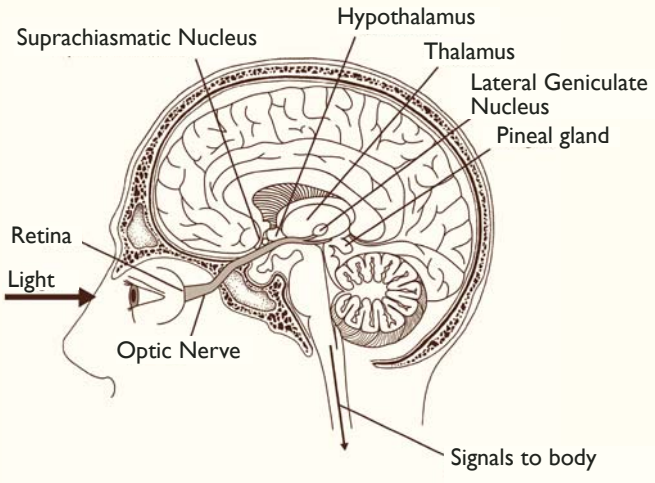
Mechanisms Controlling Sleep And Wakefulness

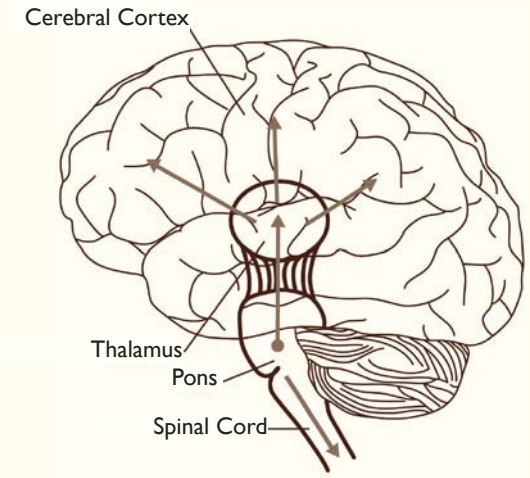
What makes us sleep at night and wake up each morning? To understand the importance of sleep, it is helpful to know something about the basic mechanisms of the sleep-wake cycle. This cycle, which consists of roughly 8 hours of nocturnal sleep and 16 hours of daytime wakefulness in humans, is controlled by a combination of two internal influences: sleep homeostasis and circadian rhythms.

Homeostasis is the process by which the body maintains a "steady state" of internal conditions such as blood pressure, body temperature, and acid-base balance. The amount of sleep each night is also under homeostatic control. From the time that we wake up, the homeostatic drive for sleep accumulates, reaching its maximum in the late evening when most individuals fall asleep. Although the neurotransmitters of this sleep homeostatic process are not fully understood, there is evidence to indicate that one may be the sleep-inducing chemical, adenosine. As long as we are awake, blood levels of adenosine rise continuously, resulting in a growing need for sleep that becomes more and more difficult to resist. Conversely, during sleep, levels of adenosine decrease, thereby reducing the need for sleep. Certain drugs, like caffeine, work by blocking the adenosine receptor, disrupting this process.

Sleep loss results in the accumulation of a sleep debt that must eventually be repaid. When we stay up all night, for example, our bodies will demand that we make up each hour of lost sleep—by napping or sleeping longer in later cycles—or suffer the consequences. Even the loss of one hour of sleep time that accumulates for several days can have a powerful negative effect on daytime performance, thinking, and mood.

Circadian rhythms refer to the cyclical changes—like fluctuations in body temperature, hormone levels, and sleep—that occur over a 24-hour period, driven by the brain's biological "clock." In humans, the biological clock consists of a group of neurons in the hypothalamus of the brain called the suprachiasmatic nucleus (SCN). These internal 24 hour rhythms in physiology and behavior are synchronized to the external physical environment and social/work schedules. In humans, light is the strongest synchronizing agent. Light and darkness are external signals that "set" the biological clock and help determine when we feel the need to wake up or go





to sleep. In addition to providing synchronization in time between various rhythms, the circadian clock also helps promote wakefulness.

Thus the homeostatic system tends to make us sleepier as time goes on throughout the waking period, regardless of whether it's night or day, while the circadian system tends to keep us awake as long as there is daylight, prompting us to sleep as soon as it becomes dark. Because of the complexity of this interaction, it is generally agreed that sleep quality and restfulness are best when the sleep schedule is regularly synchronized to the internal circadian rhythms and that of the external light-dark cycle—when we try to go to bed and wake up at around the same time each day, even on days off and weekends. Moreover, the circadian system is particularly intolerant of major alterations in sleep and wake schedules, as anyone who has traveled cross-country by plane or worked the graveyard shift can attest.

Disruptions of the Circadian System

What happens when circadian rhythms are disrupted? Not surprisingly, when we attempt to stay awake against the schedule dictated by our circadian clock, our mental and physical performance is greatly diminished. Conditions associated with a disruption of circadian rhythms include shift work, jet lag and other circadian rhythm sleep disorders.

In jet lag, times for sleep and wakefulness dictated by the internal circadian clock do not correspond with external cues in the new time zone. The result is excessive sleepiness, poor sleep, loss of concentration, poor motor control, slowed reflexes, nausea, and irritability. Those who perform shift work, particularly on night shifts, also may experience the effects of a disrupted circadian sleep-wake cycle; research shows that 10 to 20 percent of shift workers report falling asleep on the job. They also may suffer from diminished performance and alertness, and may be more prone to accidents. Strategies to re-align circadian rhythm, such as using light and melatonin can help. There is also evidence that taking a nap in the middle of a night shift may help. Naps—even as short as 20 minutes—can maintain or improve alertness, performance, and mood.

The Stages of Sleep

Although it's common to think of sleep as a time of "shutting down," sleep is actually an active physiological process. While metabolism generally slows down during sleep, all major organs and regulatory systems continue to function. In fact, sleep can be categorized into distinct

There are two types of sleep: ***rapid eye movement (REM) sleep*** and ***non-REM (NREM) sleep***. Changes in brain activity that take place are measured using an electroencephalogram (EEG).

NREM Sleep

NREM sleep is characterized by a reduction in physiological activity. As sleep gets deeper, the brain waves as measured by EEG get slower and have greater amplitude, breathing and heart rate slow down, and blood pressure drops. The NREM phase consists of four stages:[15]

- **Stage 1** is a time of drowsiness or transition from being awake to falling asleep. Brain waves and muscle activity begin to slow down during this stage. People in stage 1 sleep may experience sudden muscle jerks, preceded by a falling sensation.

- **Stage 2** is a period of light sleep during which eye movements stop. Brain waves become slower, with occasional bursts of rapid waves called sleep spindles, coupled with spontaneous periods of muscle tone mixed with periods of muscle relaxation. The heart rate slows and body temperature decreases.

- **Stages 3 and 4** (which together are called slow wave sleep), are characterized by the presence of slow brain waves called delta waves interspersed with smaller, faster waves. Blood pressure falls, breathing slows, and body temperature drops even lower, with the body becoming immobile.

  Sleep is deeper, with no eye movement and decreased muscle activity, though muscles retain their ability to function. It is most difficult to be awakened during slow wave sleep. People who are awakened during these stages of sleep may feel groggy or disoriented for several minutes after they wake up. It also is during this stage that some children experience bedwetting, night terrors, or sleepwalking.

REM Sleep

REM sleep is an active period of sleep marked by intense brain activity. Brain waves are fast and desynchronized, similar to those in the waking state. Breathing becomes more rapid, irregular, and shallow; eyes move rapidly in various directions and limb muscles become temporarily paralyzed. Heart rate increases and blood pressure rises. This also is the sleep stage in which most dreams occur.

Although the role each of these states plays in overall health is uncertain, having the right balance between them is believed to be important for obtaining restful, restorative sleep and for promoting processes such as learning, memory, mood, and ability to concentrate.

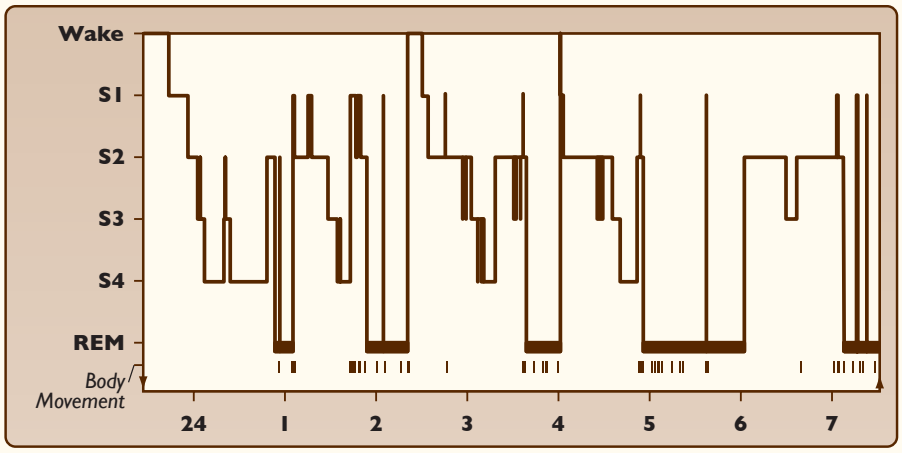
Sleep Architecture: The Right Mix of Sleep

Sleep research shows that adults of every age need, on average, a range of seven to nine hours of sleep each night, teenagers need about 9.5 hours, and infants generally require around 16 hours per day.[16] But just as important as the quantity of sleep is getting the right mix of REM and NREM sleep, as well as shallow and deep sleep. In normal sleep, REM and NREM sleep alternate throughout the night according to a predictable pattern referred to as the "sleep architecture."

A complete sleep cycle consists of NREM and REM cycles that alternate every 90 to 110 minutes and is repeated four to six times per night.[17] Adults, on average, spend more than half of their total daily sleep time in stage 2 sleep, about 20 percent in REM sleep, and the remaining time in the other stages, but the amount of time spent in any given stage is not constant over the course of a night.[18] The first sleep cycles each night contain fairly short periods of REM sleep and longer periods of slow wave sleep. As the night wears on, REM periods increase in length while the amount of slow wave sleep decreases. By morning, nearly all sleep is in stages 1, 2, and REM.[19]

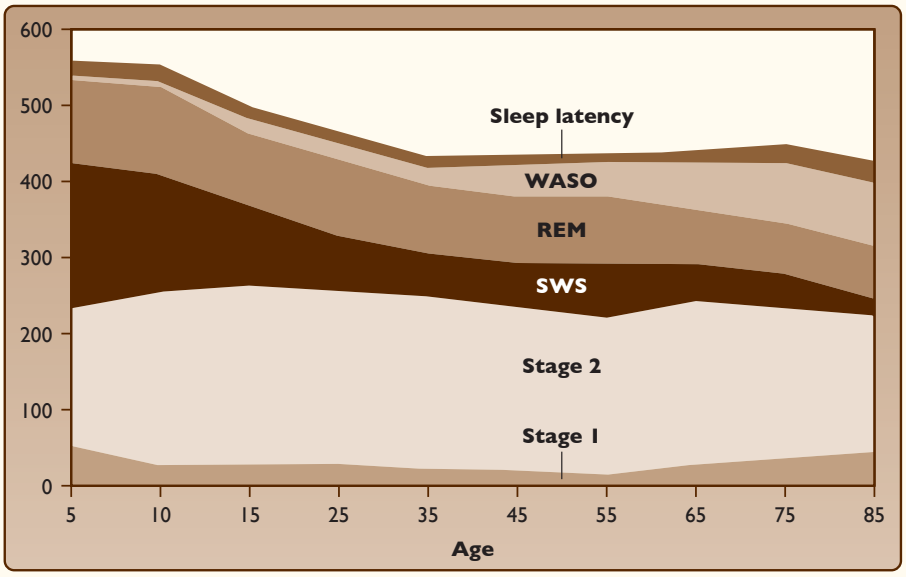
In addition to these nightly changes, the sleep architecture also varies over the course of a lifetime. Normal adults spend 20-25 percent of sleep time in REM, which is constant throughout adulthood, but newborn babies spend about half their time in REM sleep. Young children also have substantial amounts of deep NREM sleep, but as people age, the amounts of stages 3 and 4 NREM sleep decrease, with lighter sleep predominating. Although sleep may become more fragile in older people, the need for sleep does not decrease with age.[20]

Progression of sleep stages during a single night in a normal young adult.



Progression of sleep stages during a single night in a normal young adult. Reprinted from Principles and Practice of Sleep Medicine, Kryger M, Roth T, Dement WC, 4th ed., Normal Human Sleep: An Overview. Carskadon M, Dement WC, p18 ©2005 with permission from Elsevier.

Changes in sleep with age.



Time (in minutes) for sleep latency and wake time after sleep onset (WASO), and for rapid eye movement (REM) sleep and NREM sleep stages 1, 2, and slow wave sleep (SWS). (Ohayon M, Carskadon MA, Guilleminault C, et al; Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: Developing normative sleep values across the human lifespan. Sleep 2004;27:1255-1273). Permission granted by the Associated Professional Sleep Societies, LLC, April 2006. Reprinted from Principles and Practice of Sleep Medicine, 4th ed., Kryger M, Roth T, Dement WC, Normal Human Sleep: An Overview. Carskadon M, Dement WC p19, ©2005 with permission from Elsevier.

Why Sleep Matters: The Impact Of Sleep And Sleep Loss

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Although scientists still are trying to find out why people need sleep, research on the sleep of animals shows that sleep is necessary for survival. Some experts believe sleep allows the body to repair itself; during sleep many cells show increased production of proteins, the essential building blocks needed for cell growth and repair of damage from stress and ultraviolet rays. The fact that many biochemical and physiological processes take place during sleep has led to a consensus among researchers that adequate sleep is essential to health and wellness.

A look at the impact of sleep loss on physiological and cognitive functions can also help shed light on the purpose of sleep. Some of these functions include memory and attention, complex thought, motor response, and emotional control. But sleep loss does far more than make us grumpy and groggy. In the past few years, investigators have found that sleep loss may have harmful consequences for our immune and endocrine systems, as well as contribute to serious illnesses such as obesity, diabetes, and hypertension.

Sleep, Cognitive Performance, and Mood

The evidence that sleep deprivation adversely affects cognition and motor performance is striking. One study showed that people who were awake for up to 19 hours scored substantially worse on performance and alertness than those who were legally intoxicated.[21] Other studies have found:

- After one night of total sleep deprivation, subjects scored significantly lower on tests of judgment, simple reaction time, explicit recall, and inverse word reading.[22]
- Daytime alertness and memory are impaired by the loss of eight hours of sleep, especially when sleep loss is sustained over a few nights.[23]

Getting three, five, or less than seven hours of sleep a night for seven consecutive nights can significantly impair alertness and motor performance.[24] In addition, researchers at Stanford University found that people with mild to moderate sleep apnea, a health condition in which breathing stops periodically during sleep and disrupts sleep, did as badly or worse on reaction-time tests as those who would be considered to be inebriated in most states.[25]

It is well documented that sleep loss can adversely affect mood. We all know how irritable we become after a night spent tossing and turning. A growing body of medical evidence links inadequate sleep with anger, anxiety, and sadness. University of Pennsylvania researchers found that when study subjects were only allowed to sleep 4.5 hours a night for one week, they reported feeling more stressed, angry, sad, and mentally exhausted, with overall scores for mood and vigor declining steadily during the test period. When the subjects were allowed to get enough sleep, their mood scores improved dramatically.[26]

Hormones and Metabolism

Sleep is the time when the body secretes many important hormones that affect growth, regulate energy, and control metabolic and endocrine functions. For example, blood levels of the stress hormone, ***cortisol***, which can promote wakefulness, increase near the end of a complete sleep cycle. Growth hormone, which contributes to childhood growth and helps regulate muscle mass in adults, also is secreted during sleep. Follicle stimulating hormone and luteinizing hormone, both involved in reproduction, also are released during sleep; the sleep-dependent release of luteinizing hormone is thought to initiate puberty. Further, the sleep cycle affects secretion of hormones influencing appetite and weight. Sleep loss has powerful potential implications for obesity and diabetes, both of which have grown to epidemic proportions in recent years.

Obesity and Diabetes

According to the Centers for Disease Control and Prevention, about 65 percent of Americans now are overweight or obese. Why is the nation getting fatter? Most experts attribute it to our sedentary lifestyle combined with our caloric intake. But we're also getting less sleep than we used to, a factor whose role in obesity is just coming to light.

Researchers have measured the impact of sleep deprivation on certain hormones that affect the tendency toward obesity. For example, decreased slow wave sleep in young men is associated with decreased production in growth hormone.[27] Because growth hormone plays an important role during adulthood in controlling the body's proportions of fat and muscle, having less of it as men age increases the tendency toward becoming overweight and having a paunch in middle age. Other short term studies have found a correlation between inadequate sleep and insufficient levels of the hormone leptin, which regulates carbohydrate metabolism. Low levels of leptin cause the body to crave carbohydrates regardless of the amount of calories consumed.

The growing problem of obesity also is linked to diabetes. A 1999 study at the University of Chicago found that a sleep debt accumulated over a matter of days can impair sugar metabolism and disrupt hormone levels. After 11 healthy young adults were allowed only a restricted amount of sleep (four hours) for several nights, their ability to process blood glucose had declined, in some cases to a pre-diabetic state, prompting their bodies to produce more insulin.[28]

Immune System

We often automatically retreat to bed when we have a cold or sore throat, instinctively perceiving that sleep helps us heal. Growing evidence suggests this is not mere wishful thinking but scientific fact. The best evidence for sleep's impact on the immune system comes from a recent study showing that the effectiveness of flu vaccinations is severely delayed in individuals who are sleep deprived.

Flu shots were administered to men who had been restricted to just four hours of sleep per night for four straight nights and to those who had slept normally. Ten days after vaccination, those in the sleep-deprived group had a substantially lower immune response compared with those who got adequate

sleep, producing less than half as many flu-fighting antibodies.[29]

Cytokines, chemicals our immune systems use to help fight an infection, also are powerful sleep-inducers. This suggests that sleep may help the body conserve energy and other resources it needs to mount an immune response and fight disease.

Cardiovascular Disease

A growing amount of evidence shows a relationship between long and short term sleep loss and cardiovascular disease, including increased blood pressure and increased risk of stroke in addition to other long-term health consequences. Sleep deprivation has been associated with a rise in blood pressure during the night that lasts through the following day.[30] Evidence suggests an association between too much or too little sleep and an increased risk of coronary heart disease in women.[31]

There is a high prevalence of sleep apnea among people with cardiovascular problems. People with this common sleep disorder are at increased risk of hypertension, as well as sudden death from cardiac causes during the night.[32]

Sleep Disorders

- **Sleep paralysis:** being unable to talk or move for a brief period when falling asleep or waking up.
- **Hypnagogic hallucinations:** vivid and often frightening dreams and sounds reported when falling asleep.
- **Automatic behavior:** performing familiar tasks without full awareness or later memory of them.

Recent discoveries indicate that people with narcolepsy lack a neuropeptide in the brain called orexin (also known as hypocretin), which normally is released during wakefulness and stimulates arousal. The loss of orexin-producing neurons in people with narcolepsy is probably caused by an autoimmune or neurodegenerative process.[36]

It is estimated that 125,000 to 200,000 Americans suffer from narcolepsy; however, fewer than 50,000 are properly diagnosed, in part because physicians may not always consider narcolepsy when evaluating symptoms of sleepiness and problems with concentration, attention, memory, and performance. Once diagnosed, an important part of the treatment can be involvement in a patient support group such as those organized by the Narcolepsy Network (www.narcolepsynetwork.org). Regularly scheduled daytime naps, a regular nightly bedtime schedule and avoidance of heavy meals and alcohol are among the recommended behavioral approaches to treating narcolepsy. Stimulants, antidepressants, and other medications such as modafinil or methylphenidate can help control the symptoms of narcolepsy. Sodium oxybate, fluoxetine and venlafaxine (for adults and children) are used for treating cataplexy.[38] Because sodium oxybate improves nighttime sleep in these patients, it may also reduce their excessive daytime sleepiness.

Restless Legs Syndrome (RLS)

Recent research suggests that anywhere from 5 to15 percent of Americans suffer from restless legs syndrome, a condition characterized by uncomfortable sensations in the legs, including creeping, tingling, cramping, burning, and pain that tend to worsen upon lying down. People with RLS may find it difficult to relax and fall asleep because of their strong urge to walk or move to relieve the sensations in their legs. Although the cause is unknown, factors associated with RLS include:

- Family history
- Pregnancy
- Low iron or folate levels or anemia
- Chronic diseases, including kidney failure, diabetes, rheumatoid arthritis, and peripheral neuropathy
- Caffeine intake

Treatment options for people with RLS include both behavioral and pharmacological approaches. Making lifestyle changes, such as eating a balanced diet, avoiding caffeinated products and drinking alcohol in the evening, and practicing good ***sleep hygiene*** have been shown to help lessen the severity and impact of RLS symptoms. If an iron deficiency is identified as the cause of symptoms, iron supplements, vitamin B12, or folate (as indicated) may provide relief.[39]

Recent studies demonstrate that RLS may be caused by dopamine deficiency, a key chemical messenger in the brain responsible for smooth, coordinated movement and other motor and cognitive functions.[40] Some RLS patients have been found to respond positively to treatment

Sleep Disorders

Anything that disrupts normal sleep affects the sleep-wake cycle, potentially leading to an imbalance in sleep homeostasis and circadian factors that regulate sleep. For some people, poor sleep constitutes a medical problem. Each year, at least 40 million people in the United States suffer from chronic sleep disorders, and another 30 million are troubled by transient or occasional sleep problems.[33] These disorders account for an estimated $16 billion in medical costs alone, wreaking havoc on people's work lives, driving, and social activities.[34] The most prevalent sleep disorders include ***sleep apnea, narcolepsy, restless legs syndrome***, ***parasomnias,*** and ***insomnia***.

Sleep Apnea

An estimated 18 million Americans have sleep apnea, a serious, potentially life-threatening disorder characterized by episodes of interrupted breathing during sleep.

Obstructive sleep apnea, the more common type, occurs when air cannot flow into or out of the person's airway despite efforts to breathe. It usually is associated with fat buildup or loss of muscle tone with aging, which allow the windpipe to collapse during breathing.

Central sleep apnea occurs when the system that controls breathing is abnormal and there are decreased efforts to breathe during sleep.

In sleep apnea, the brain has to awaken the sufferer in order for breathing to start again. Frequent arousals from apneic events during the night prevent the person from getting enough deep, restorative sleep.

Because of the constant interruption of their normal sleep patterns, people with sleep apnea often feel very sleepy, causing problems with daytime concentration and performance. It recently has been shown that sleep apnea contributes to high blood pressure.[35] Risks for heart attack, irregular heartbeat, and stroke also are increased in those with sleep apnea. Other consequences of sleep apnea include depression, irritability, sexual dysfunction, learning and memory difficulties, and falling asleep while at work, on the phone, or driving.

Sleep apnea's association with obesity can create a vicious cycle for some patients, who may find it harder to exercise because of their sleepiness. Successful treatment, usually with nasal ***continuous positive airway pressure*** or CPAP, may reduce sleepiness, motivating patients to effectively lose weight and, in turn, help alleviate the breathing obstruction. People with sleep apnea should not take sedatives or sleeping pills, because they may prevent them from awakening to breathe.

Narcolepsy

About one in 2,000 people suffers from narcolepsy, a chronic neurological disorder that causes the sufferer to fall asleep at times when he or she wants to be awake. In addition to an overwhelming and recurring need to sleep at inappropriate times, narcolepsy may cause symptoms associated with REM sleep including:

- **Cataplexy**: a sudden loss of muscle control ranging from slight weakness (head droop, facial sagging, jaw drop, slurred speech, buckling of knees) to total collapse. It is commonly triggered by intense emotion (laughter, anger, surprise, fear) or strenuous physical activity.

with precursors of dopamine. Most recently, drugs classified as dopaminergic agonists such as ropinerole and pramipexole have become the treatment of choice for this debilitating sleep disorder.[41]

Parasomnias

When the transition from one sleep state to another doesn't progress in an orderly fashion or a person is aroused from sleep, bizarre and often complex behaviors known as parasomnias may occur. Parasomnias include sleepwalking, night terrors, and bedwetting, which are ***NREM disorders*** that occur early in the night. Night terrors are characterized by agitation, large pupils, sweating, and increased blood pressure. Many of the parasomnias are more common in children, who usually outgrow them and don't require treatment.

Superficially resembling night terrors but more common in adults is ***REM sleep behavior disorder***, which is characterized by vigorous or violent behaviors that occur later in the night. In this disorder, the temporary muscle paralysis that normally characterizes REM sleep is absent, allowing individuals to react to vivid dreams during sleep and potentially injure themselves or their bed partners. This disorder usually affects middle-aged or elderly individuals who frequently also have a neurological disorder. Fortunately, most of these parasomnias can be treated effectively.

A relative of the NREM parasomnias is ***sleep-related eating disorder,*** in which a person eats food during the night while he or she appears to be asleep. Two-thirds of patients with this disorder are women. It may be induced by taking certain medications, such as amitriptyline (a sedating anti-depressant) or zolpidem (a hypnotic), but it also may be triggered by other sleep disorders, such as obstructive sleep apnea or restless legs syndrome. Although many medicines have been tried to treat the disorder, their success has been limited.[42]

Insomnia

Insomnia is the complaint of difficulty initiating or maintaining sleep, waking too early and not being able to get back to sleep, or waking feeling unrefreshed and lethargic. Data presented at a recent NIH conference on management of chronic insomnia suggest that about 30 percent of the general population has complaints of sleep disruption, while approximately 10 percent have associated symptoms of daytime functional impairment.[43] The effects of insomnia can include daytime fatigue, impaired mood and judgment, poor performance, and an increased likelihood of accidents at home, in the workplace, and while driving.[44]

Insomnia occurs more often among women, the elderly, individuals of low socioeconomic status, and those who are widowed, divorced, or separated than in other individuals.[45] It may be ***primary***, or not directly associated with any other health condition or problem, or ***secondary*** to some underlying health condition, such as depression, heartburn, cancer, asthma, or arthritis, or as a result of medications or drugs, including alcohol and caffeine.

In some people insomnia is ***transient***, can last up to one month and may be caused by many things, among them jet lag, stress, a major life change such as a new job or loss of a relationship, environmental factors like noise, or even consuming too much caffeine.[46]

Chronic insomnia occurs when a person has insomnia a minimum of three nights a week for a month or longer. Chronic insomnia is present in either the primary or secondary forms mentioned above. In the secondary forms it usually is caused by a medical condition or medication taken for other disorders, or by alcohol consumption.[47]

Patients with chronic insomnia should be evaluated to ensure the sleep problem is not due to an underlying medical or psychiatric condition that may require treatment.

Depression and anxiety are the most common causes of insomnia. In addition, certain behaviors can contribute to insomnia, such as excessive caffeine intake, drinking alcohol or smoking cigarettes before bedtime, excessive daytime napping, and irregular or continually disrupted sleep-wake cycles. As yet, little is known about the neurobiology of insomnia; however, hyperactivity of the systems in the brain that cause arousal is believed to be involved.

As evidence mounts on the importance of sleep, the development of safe and effective treatment for insomnia continues to be a priority for sleep researchers. The approach to treatment for poor sleep generally falls into two categories: behavioral and pharmacologic.

Behavioral Approach to Insomnia Treatment

Behavioral approaches and sleep hygiene are the cornerstones of treatment for insomnia.

Lifestyle changes, such as decreasing caffeine and alcohol intake, adjusting exercise, regulating not only diet but the amount and time we eat (contrary to conventional wisdom, heavy meals actually keep us awake), and stopping smoking all can contribute to more regular sleep patterns. Caffeine and nicotine are stimulants that can make it difficult to sleep, and nicotine also may cause nightmares. Although many people think of alcohol as a sedative, it actually disrupts sleep, causing nighttime awakenings.

Good sleep hygiene is equally important to achieving quality restorative sleep. These practices include maintaining the same sleep and wake patterns every day, avoiding stimulants late in the day, ensuring adequate exposure to natural daylight, and maintaining an environment conducive to sleep—one that is dark, cool, and noise-free.

In the 1970s and 1980s, ***behavioral therapy*** techniques for sleep were developed and became popular.[48]

Stimulus-control therapy conditions the patient to associate the bed and bedroom with sleep only, instructing the individual to get out of bed if unable to sleep and to avoid eating, reading, or watching television in bed. ***Relaxation therapy*** includes muscle relaxation, biofeedback, meditation, and breathing techniques, all aimed at helping the patient fall asleep faster and stay asleep longer. ***Sleep-restriction therapy,*** as its name suggests, restricts the individual's time in bed, resulting in sleep deprivation that allows the individual to fall asleep.

At the physiological level, ***behavioral treatments*** work in the same way as medications—by decreasing the activity of the arousal systems in the brain producing wakefulness—and have been shown in some instances

to be as or more effective than most medications in treating insomnia. However, if this treatment is not satisfactory, a pharmacological approach may be recommended, especially when more immediate relief is needed, or to break a cycle of sleeplessness before it becomes a chronic problem.

Pharmacologic Approach to Insomnia Treatment

Over-the-Counter Products: A variety of over-the-counter products are promoted as sleep aids, but these drugs often have many side effects and may not provide effective and sustained relief. They include ***antihistamines*** such as diphenhydramine and doxylamine, which induce sleep, but also may lead to daytime drowsiness, blurred vision, and dry mouth. Researchers continue to investigate whether other nonprescription therapies, such as herbal remedies or nutritional supplements, may effectively treat insomnia. Because of its role in the circadian system of promoting sleep, the nutritional supplement ***melatonin*** has been widely touted as a sleep aid. However, clinical studies on the safety, efficacy, and dosing of melatonin have yielded inconsistent results. Because much is still unknown about its potential effects, it is recommended that people talk to their doctors before taking melatonin.

Prescription Sleep Medications: Until the 1960s, barbiturates, such as phenobarbital, were widely used as sedatives, despite their association with such dangerous side effects as addiction, tolerance, and overdosage. In 1964, ***benzodiazepines*** (also known as ***benzodiazepine receptor agonists***) were introduced and soon became the mainstay of pharmacologic treatment. Some benzodiazepines in use today include flurazepam, triazolam, and temazepam.

Benzodiazepines are central nervous system depressants that work by enhancing the actions of the inhibitory neurotransmitter gamma-aminobutyric acid ***(GABA)*** at its receptor. GABA is believed to be one of the factors that help promote sleep, and also is involved in cognitive, memory, and psychomotor functions. Because benzodiazepines bind nonspecifically to GABA receptors, they actually may be more active in reducing anxiety, inducing muscle relaxation, and inhibiting convulsions than in promoting sleep. Their side effects, such as memory loss, rebound insomnia, and drug dependence, may make them inappropriate for some people.[49]

In the early 1990s, a new generation of ***nonbenzodiazepines*** (or ***nonbenzodiazepine receptor agonists***) was introduced that target only certain receptor subtypes of the GABA complex. These drugs, which include zolpidem and zaleplon, have the advantage of being much shorter-acting compounds with less likelihood for daytime sleepiness or impairment of memory. However, they still may have some side effects, including rebound insomnia, dependence, drowsiness, dizziness, lightheadedness, and difficulty with coordination.[50]

Two medications for the treatment of insomnia—eszopiclone and ramelteon—recently received approval from the U.S. Food and Drug Administration (FDA). Based on published clinical reports, eszopiclone has demonstrated safety and efficacy of long term nightly use, and helps people fall asleep and stay asleep throughout the night.

Unlike other prescription sleep aids, ramelteon is thought to work by selectively affecting melatonin receptors (neurons) in the suprachiasmatic nucleus (SCN), a part of the brain that functions to regulate times for sleep and times for optimal alertness or wakefulness. This contrasts with other hypnotic medications that work by binding to GABA receptors, which reduce central nervous system (CNS) activity.[51] Ramelteon has been found to be effective in helping those who have difficulty falling asleep. Because there has been no evidence that ramelteon has a potential for abuse or dependence, it can be prescribed for long-term use in adults.

Evidence supports the efficacy of cognitive behavioral therapy and benzodiazepine receptor agonists in the treatment of chronic insomnia.[52] Very little evidence supports the efficacy of other treatments, despite their widespread use.

Conclusion

Unfortunately, sleep is sometimes given a low priority in modern life, taking a back seat to our busy schedules and lifestyles. Yet, as scientists in the field of sleep medicine continue to discover, sleep is a dynamic activity in its own right that is as essential to good health as diet and exercise, and as necessary for survival as food and water. Sleep research continues to expand and attract more notice from scientists and clinicians alike. However, more research and public education are needed to make sleep a top health priority. As one of the most crucial, yet most overlooked, indicators of overall health, it is important that doctors begin an ongoing dialogue with their patients about sleep.

Fpr more information about sleep and sleep-related issues, visit www.sleepfoundation.org

Glossary

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Circadian Rhythms: cyclical changes—like fluctuations in body temperature, hormone levels, and sleep—that occur over a 24-hour period, driven by the body's biological "clock"

Cortisol: one of several stress hormones produced by the adrenal cortex that is secreted near the end of sleep to stimulate alertness

GABA: short for gamma-aminobutyric acid, an amino acid in the central nervous system associated with the transmission of nerve impulses

Homeostasis: the process by which the body maintains a "steady state" of internal conditions such as blood pressure, body temperature, acid-base balance, and sleep

Hypothalamus: region of the forebrain below the thalamus, controlling body temperature, thirst, and hunger, and involved in sleep and emotional activity

Insomnia: sleep disorder characterized by an inability to sleep or to remain asleep for a reasonable period or waking feeling unrefreshed

Melatonin: hormone secreted by the pineal gland especially in response to darkness that promotes sleep

Narcolepsy: a sleep disorder characterized by sudden and uncontrollable episodes of deep sleep

Non-Rapid Eye Movement (NREM) Sleep: one of four initial sleep stages preceding REM sleep characterized by a reduction in physiological activity and a slowing of brain waves

Parasomnia: a category of sleep disorders in which abnormal physiological or behavioral events occur during sleep, including night terrors and sleepwalking

Pineal Gland: a small cone-shaped organ of the brain that secretes the hormone melatonin into the bloodstream

Receptor: a molecular structure within a cell or on the surface characterized by selective binding of a specific substance and a specific physiologic effect that accompanies the binding

Rapid Eye Movement (REM) Sleep: a recurring sleep state characterized by rapid eye movement and intense brain activity, during which dreaming occurs

Relaxation Therapy: a form of sleep behavioral therapy including muscle relaxation, biofeedback, meditation, and breathing techniques aimed at helping the patient fall asleep faster and stay asleep longer

Restless Legs Syndrome: a sleep disorder characterized by leg discomfort during sleep, which is only relieved by frequent movements of the legs

Sleep: a natural and periodic state of rest during which consciousness of the environment is suspended

Sleep Apnea: a serious, potentially life-threatening sleep disorder characterized by episodes of interrupted breathing during sleep

Sleep Architecture: the predictable pattern of alternating REM and NREM sleep that occurs throughout the night, consisting of four NREM phases and one REM phase

Sleep Hygiene: practices conducive to good sleep including maintaining the same sleep and wake patterns every day, avoiding stimulants late in the day, ensuring adequate exposure to natural daylight, and maintaining a cool, dark, and quiet sleep environment

Sleep-Restriction Therapy: a form of sleep behavioral therapy that restricts the individual's time in bed, resulting in sleep deprivation that allows the individual to fall asleep

Sleep-Wake Cycle: the biological pattern of alternating sleep and wakefulness, in humans roughly 8 hours of nocturnal sleep and 16 hours of daytime activity

Stimulus-Control Therapy: a form of sleep behavioral therapy that conditions the patient to associate the bed and bedroom with sleep

Suprachiasmatic Nucleus (SCN): a region in the hypothalamus that regulates circadian rhythms, acting as the body's sleep-wake center or "biological clock"

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