

# Introduction to Sleep Medicine

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## Introduction

Sleep medicine is a field which has had exponential growth over the last 25 years. Interest has blossomed from both medical practitioners and the general public on the impact sleep has on human function and long-term health. Sleep clinics and laboratories have become more common and an enlarging market of consumer goods for home analysis of sleep has developed. This chapter will introduce you to the field of sleep medicine, describe normal sleep, and provide a basic outline of the sleep disorders.

The American Medical Association recognized sleep medicine as a specialty in 1995. The field of sleep medicine is currently composed of physicians from many specialties. In fact, physicians from six American Board of Medical Specialties (ABMS) primary boards are able to sit for the board examination in sleep medicine: the American Boards of Psychiatry and Neurology, Internal Medicine, Pediatrics, Anesthesiology, Family Medicine, and Otolaryngology. This blend of primary specialties leads to a vibrant subspecialty with a variety of interests ranging from airway anatomy to snoring surveys.

### CAUTION

As of 2013, to qualify to sit for the ABMS examination, an Accreditation Council for Graduate Medical Education (ACGME)-certified Sleep Medicine Fellowship must be completed. Before 2013, entry could be obtained via a practice-based experimental pathway.

## A brief history of sleep and sleep medicine

Sleep has been of interest to cultures for thousands of years. Ancient Egyptians devoted sections of papyrus to the interpretation of dreaming. In the ancient Greek culture, Aristotle wrote a work entitled *On Sleep and Sleeplessness* devoted to sleep and waking; he also believed that ingesting food caused sleepiness through “fumes” that were carried through the blood vessels into the brain. Hippocrates, considered by some to be the father of Greek medicine, wrote this about sleep and its relationship to health.<sup>1</sup>

‘With regard to sleep – as is usual with us in health, the patient should wake during the day and sleep during the night. If this rule be anywise altered it is so far worse: but there will be little harm provided he sleep in the morning for the third part of the day; such sleep as takes place after this time is more unfavorable; but the worst of all is to get no sleep either night or day; for it follows from this symptom that the insomnolency is connected with sorrow and pains, or that he is about to become delirious.’

The Bible discusses the prophecies that occurred through dreaming, most notable in the story of Joseph. A religious text from the Judaic faith, written by a scholar known as Maimonides in the 1100s, stated the following, which still holds true today.<sup>2</sup>

‘The day and night consist of 24 hours. It is sufficient for a person to sleep one-third thereof which is eight hours. These should be at the end

of the night so that from the beginning of sleep until the rising of the sun will be eight hours. Thus he will arise from his bed before the sun rises.'

It is not until the 17th century that medical theories around sleep clearly resurface after the long Dark Ages. Rene Descartes developed a hydraulic model of sleep, involving movement of the pituitary gland. Thomas Willis described patients with symptoms of narcolepsy and restless legs syndrome. The science of circadian rhythms was brought to light in the mid-18th century by Jean Jacques d'Ortous de Mairan, when he described that a heliotrope plant kept a stable pattern of opening its blooms for the day, even when kept in a dark environment without the sun for a cue.

Multiple theories about sleep circulated in the 19th century: sleep was related to changes in blood flow, sleep was caused by an increase in toxins in the blood, or sleep was initiated by physical changes in the newly discovered neurons. Increasing research was done on the changes in temperature in the human body. William Hammond, a physician during the Civil War, wrote *Sleep and Its Derangements* in 1869, primarily discussing insomnia; likely the first text on the subject in the Americas.

In 1925, Hans Berger measured the electrical activity of the human brain, via his "Elektrenkephalogramm". Two groups, one at Harvard University and one at the University of Chicago, used this device to perform the majority of sleep-related research in the late 1930s. Alfred Loomis's group at Harvard categorized sleep into stages A to E, from the electrical brain rhythm of wakefulness to stages of deep non-rapid eye movement (NREM) sleep, in order of resistance to change by disturbance. Nathaniel Kleitman and his student Eugene Aserinsky discovered rapid eye movement (REM) sleep in 1953 at the University of Chicago after observation of episodic eye movements during sleep in infants. They developed the electrooculogram (EOG) to better characterize the eye movements, noting both rapid and slow eye motions. Kleitman and William Dement then applied these studies to demonstrate the recurring pattern of REM and NREM sleep; sleep was no longer a purely homogenous state with low-frequency electroencephalogram (EEG) readings, much to the surprise of many others working in the field.

In 1967, Allan Rechtschaffen and Anthony Kales, as well as others, developed a scoring manual for

human sleep. *A Manual of Standardized Terminology, Techniques, and Scoring System for Sleep Stages of Human Subjects* was published in 1968 with the hope that it would "markedly increase the comparability of results reported by different investigators." This monograph formally defined the polysomnogram and clarifying the stages of sleep (wakefulness, movement time, stages 1–4 [NREM sleep], and REM sleep). The Multiple Sleep Latency Test was developed at Stanford in the early 1980s to evaluate narcoleptics and their daytime sleep propensity. In 2008, the scoring manual for sleep was reviewed, updated and renamed (*AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*); another update was undertaken in 2012.

The modern clinic for evaluating and treating patients with sleep disorders was developed at Stanford University in its Sleep Disorders Clinic which had initially began in the 1960s, closed, and then re-opened in 1970. Other sleep clinics began to spread across the United States, eventually grouping together to form the American Academy of Sleep Medicine. The number of sleep laboratories or centers has grown steadily since the mid-1990s and today there are an estimated 3000–3500 sleep laboratories operating in the United States.

### Normal sleep

Thomas Edison once said: "In my opinion sleep is a habit, acquired by the environment. Like all habits, it is generally carried to extremes. The man that sleeps four hours soundly is better off than the dreamy sleeper of eight hours."<sup>3</sup> However, recent data have demonstrated that not only is 8 hours of sleep not a detriment for most people, it is a necessary component for optimal functioning. People who obtain insufficient sleep are prone to difficulties with attention, may suffer from cognitive and mood problems, and appear to be at higher risk for co-morbid medical disorders and death, particularly in those with less than 6 hours of sleep per night. However, epidemiological studies of sleep times suggest not only that people with inadequate sleep times are more likely to die sooner, but that people with excessive sleep times (more than 9 hours per night) are also at increased risk, potentially due to underlying illness.<sup>4</sup>

### ★ TIPS AND TRICKS

In the general population, excessive daytime sleepiness is most commonly caused by insufficient nighttime sleep rather than a primary sleep disorder. Adequate sleep is often traded for work or social activities. A brief review of the patient's sleep schedule may be helpful.

Sleep changes over the course of our lives. Newborn babies spend about 50% of their total sleep in REM sleep, and in fact enter sleep via REM sleep, which is not considered normal in adults. Newborns also sleep in short episodes initially (as any new parent is aware), though they may obtain 12–18 hours of sleep over the course of the day. During the first few months of life, infants consolidate sleep into longer blocks which occur at night, attempting to acquire 14–15 hours of sleep per day. As children reach school age (5–10 years old), their daily sleep demand decreases to 10–11 hours. Teenagers require 8.5–9.25 hours of sleep per night (often getting less than that due to school commitments and social interests), and adults need 7–9 hours. In rare confirmed cases, it appears that humans with certain genetics are “short sleepers” and require less sleep than the average. Much more commonly, modern adults obtain less sleep than they require to perform optimally, distracted by long work schedules or the wealth of available entertainment options. Later in life, older adults generally require similar amounts of sleep (7–9 hours), though it becomes more difficult for them to maintain sleep consolidation with medical disorders and medications and napping may become more common.

### ☞ CAUTION

While many people expect older adults to require less sleep than young adults, sleep requirements are not dramatically different. Clinical attention should be paid to napping schedules, circadian pattern, and possible underlying sleep and medical disorders.

The clear purpose of sleep is not truly known, though each of us is acutely aware of its regenerative properties for alertness. However, many other

functions appear to occur during the night, most prominently memory processing, hormonal fluctuation, and metabolic changes. While one theory suggests that sleep allows an organism to save energy, functional brain scans during sleep reveal that the human brain is more active in some areas during REM sleep than when awake, and the energy savings appear to be about the number of calories in one cookie. The high neuronal activity observed in REM sleep may be part of the education process, strengthening and weakening synapses related to things we learned (or didn't learn) during the period of wakefulness preceding sleep. Alternatively, or perhaps adjunctively, memory extraction and filing may represent the notable magnetic resonance imaging (MRI) signal activity. The immune system appears positively affected by sleep; animal species that sleep longer appear to have fewer parasites and higher white blood cell counts.

Almost all living creatures have a circadian clock, so that certain functions of the organism occur at optimal times. As pointed out in the historical section, even the simple heliotrope flower has an internal clock, so that it might bloom at the optimal time each day (even if the sun is not present). Humans have a similar clock, such that our tendency is generally to sleep when it is dark outside and be awake during the sunlit portion of the day. Some mammals, such as mice, have a reversed clock, in which they have a tendency to be awake in the nocturnal portion of the cycle. Our circadian cycle is relevant from a physiological perspective, in that many hormones (growth hormone, melatonin, cortisol) appear at different times during our 24-hours cycle. However, our clock also affects how we respond to plane travel (jet-lag) and working non-standard shifts (night work, rotating shifts). Our sleep patterns in relationship to this clock also have a tendency to shift as we age, such that teenagers biologically tend to have a delayed sleep phase and older adults tend to have an advanced sleep phase.

### ★ TIPS AND TRICKS

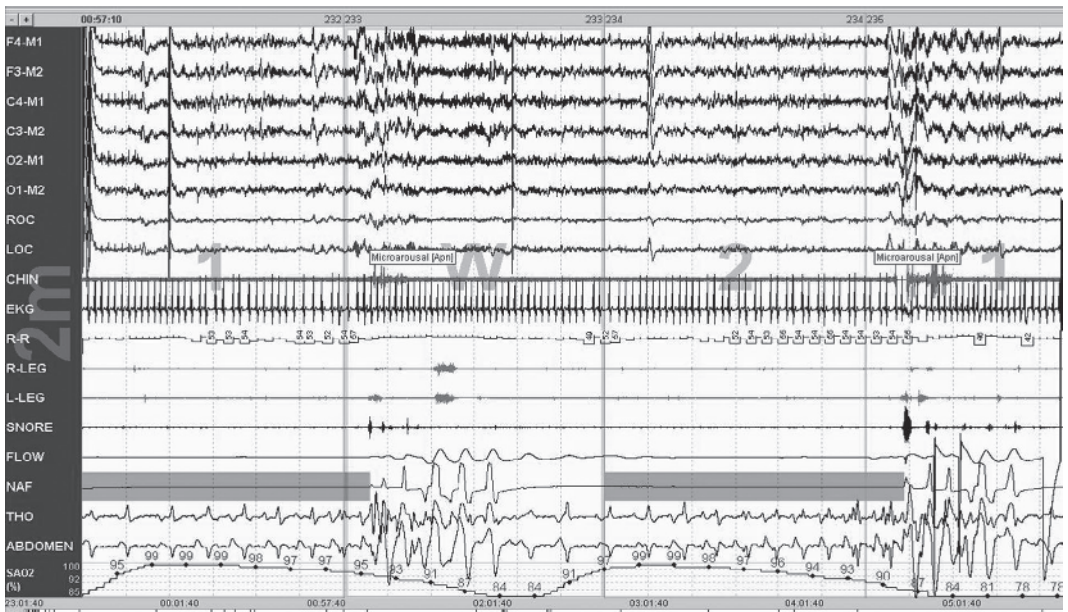
An easy way to remember the shift of the circadian sleep phase over the lifespan is to consider teenagers; they never want to get up in the morning to go to school, but are always

ready to stay up late at night to watch TV or play video games. Meanwhile, in Florida, you might find your grandmother walking the beach before the sun rises in the morning, but dozing off in her chair while watching TV in the early evening.

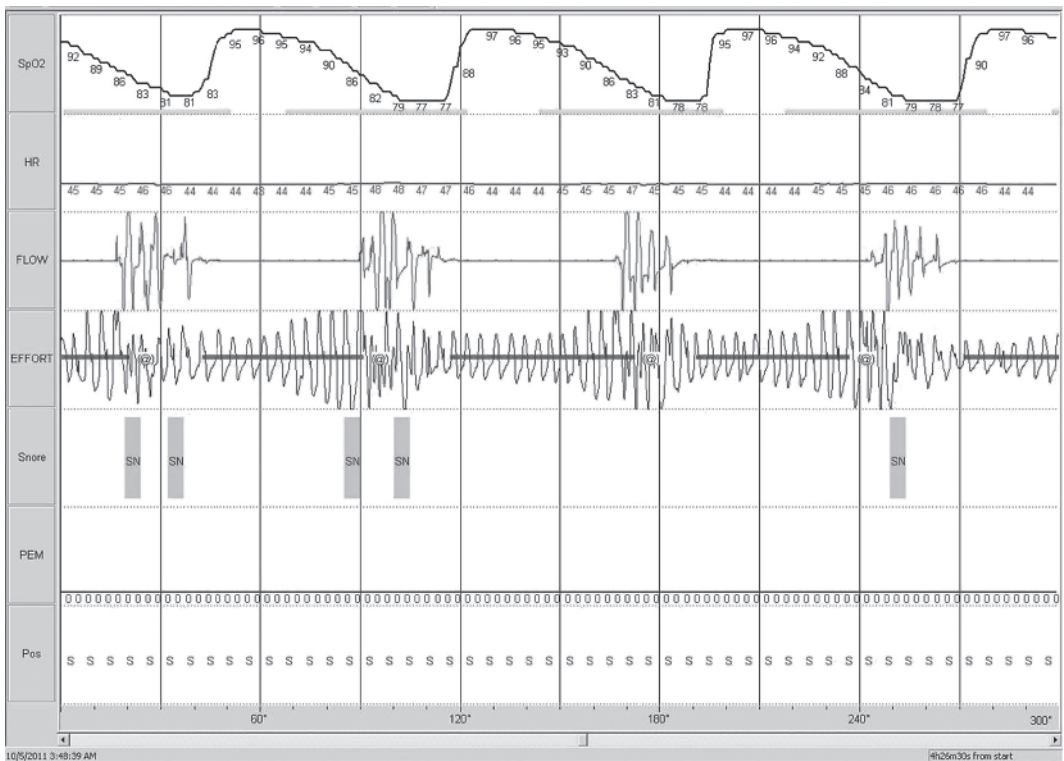
Currently, the clinical evaluation of sleep is performed most commonly by an in-laboratory polysomnogram (sleep study) (Figure 1.1). Via measurement of brain waves (EEG), eye movements (EOG), heart rate and rhythm (electrocardiography, EKG), muscle movement of chin and legs (electromyography, EMG), nasal pressure and airflow (nasal-oral thermistor), chest and thorax movement, and oximetry, these studies allow for assessment of sleep stage, breathing, and movements during sleep. Video monitoring is standard to allow for assessment of parasomnias and other behaviors. A polysomnographic technologist

places the leads on the patient, monitors them through the night, and unhooks them in the morning.

The overnight test typically runs overnight for a minimum of 6 hours, but often longer. These studies are visually scored in 30-sec increments. The current scoring manual categorizes sleep into several stages: wake, N1, N2, N3, and R. Stages N1–N3 are progressively deeper stages of what is considered NREM sleep. N1 is considered light sleep, usually what occurs when a person transitions from wake into sleep. The majority of NREM sleep during the night in a normal individual is stage N2. Stage N3, also known as slow-wave sleep, appears most frequently in children and young adults, lessening in frequency as we age. Stage R, also known as REM sleep, is a time of skeletal muscle atonia (except eye and breathing muscles) which is strongly associated with vivid dreaming. The breathing and heart rhythm in stage R tend to be more irregular in pattern. The majority of sleep (perhaps 75–80%) in a normal adult is spent in NREM sleep; episodes of



**Figure 1.1** Two-minute epoch of in-laboratory polysomnography (Nihon Khoden, Foothill Ranch, CA) from a 55-year-old man with obstructive sleep apnea. The top six leads are EEG (right and left frontal, central, and occipital), followed by two eye leads (right and left), the chin lead, EKG with heart rate below (R-R), two leg leads (right and left), snore channel, oronasal thermistor, nasal pressure transducer, effort bands (thorax and abdomen), and oxygen saturation. Two obstructive apneas are observed at the boxes in the NAF (nasal airflow) signal with absent nasal-oral airflow and continued respiratory effort. The respiratory events are associated with increased frequency signal (arousals) in the EEG signals and oxygen desaturations.



**Figure 1.2** This is a 5-minute epoch from a Stardust home sleep testing device (Respironics, Murrysville, PA) of a 64-year-old woman with obstructive sleep apnea. The top channel is oximetry, followed by heart rate, nasal pressure, respiratory effort, snoring, patient event marker (PEM), and position (in this case, supine). The epoch demonstrates repetitive apneas with absent nasal pressure and continuous respiratory effort.

REM sleep occur every 90–120 min and account for approximately 20–25% of the total sleep time.

In some cases, daytime studies are performed to evaluate the presence of daytime sleepiness or to assess the ability to maintain alertness (the Multiple Sleep Latency Test and the Maintenance of Wakefulness Test respectively). These will be covered more fully in the chapter on assessment of excessive daytime sleepiness. More recently, testing for obstructive sleep apnea has been done in the home rather than the laboratory (Figure 1.2); this home testing is undertaken via assessment of breathing, but most home monitors do not include an actual evaluation of sleep.

### Sleep disorders: a brief review

There are many ways to categorize sleep disorders. One is the *International Classification of Sleep Disorders*, currently in its second edition (ICSD-2). Box 1.1 lists the broad categories it uses.

#### Box 1.1 ICSD-2 sleep disorder categories

- Insomnia
- Sleep-related breathing disorders
- Hypersomnias of central origin
- Circadian rhythm sleep disorder
- Parasomnias
- Sleep-related movement disorders
- Isolated symptoms, apparently normal variants, and unresolved issues
- Other sleep disorders

An alternative method of categorization is to consolidate disorders into broader groups: disorders of sleep fragmentation (insomnia, sleep-disordered breathing), disorders of wake (hypersomnias,

circadian rhythms), and abnormal activities during sleep (sleep-related movement disorders and parasomnias). Whether you lump or split these disorders, it is important to understand how to appropriately assess and treat your patients. This section will briefly discuss the disorders, each of which will be reviewed in more detail in the chapters to follow.

### **Insomnias**

This group of disorders is defined by difficulty falling asleep, staying asleep, waking too early, or feeling unrefreshed in the morning, usually associated with some form of daytime impact. A nearly universal experience which may be related to stress, medical conditions, or medications, insomnia is generally time-limited, lasting only a few days or weeks. However, in approximately 10% of the United States population, the disorder is chronic.

### **Sleep-related breathing disorders**

Obstructive sleep apnea, central sleep apnea, and hypoventilation are the primary disorders relevant to neurologists in this section. Obstructive sleep apnea, the most common disorder diagnosed in sleep laboratories, is caused by collapse of the upper airway, resulting in arousals and daytime sleepiness. Particularly relevant is that patients with obstructive apnea are at increased risk for hypertension, coronary artery disease, and strokes. Central sleep apnea occurs when breathing stops with an open airway due to a disorder in the respiratory control circuit. While it most commonly occurs in patients with congestive heart failure, it may also arise transiently or permanently in patients after strokes or with other brain diseases. Hypoventilation, where gas exchange is insufficient to rid the body of carbon dioxide and bring in enough oxygen, appears in patients who suffer from certain cardiopulmonary disorders, obesity, or neuromuscular conditions, such as amyotrophic lateral sclerosis.

### **Hypersomnias**

The hypersomnias, particularly narcolepsy, are a common reason for referral to a sleep center, but are rarely the diagnosed disorder. Generally speaking, narcolepsy and idiopathic hypersomnia are fairly rare disorders resulting in significant daytime sleepiness causing impairment in function. The pentad of narcoleptic symptoms includes hypersomnia, sleep

paralysis, hypnagogic hallucinations, cataplexy, and insomnia (almost always in the form of sleep fragmentation). While not all patients with narcolepsy have cataplexy, when it occurs, it is typically pathognomic for the disorder. Idiopathic hypersomnia appears to have a different pathophysiology from narcolepsy and appears in two forms in the current ICSD-2, with long sleep time and without long sleep time, depending on whether the length of time of the primary nocturnal sleep is more or less than 10 hours.

### **Circadian rhythm sleep disorder**

As mentioned previously, humans have a circadian clock that dictates their preferred sleeping hours. However, when that preferred sleep time does not match with their expected schedule, a sleeping problem is likely to occur. These mismatches present in patients flying across several time zones (jet-lag), with work shifts that start very early in the morning, are overnight, or which rotate over the course of the week (shift work), or perhaps most commonly, when patients have a daytime schedule that does not meet with their biological desire to stay up late and sleep late (delayed sleep phase).

### **Parasomnias**

Confusional arousals, sleepwalking, sleep-related eating disorder, and enuresis (bedwetting) are some of the more common abnormal sleep-related behaviors, classified as parasomnias. Children are more prone to these disorders than adults in general. In specific parasomnias, such as REM-sleep behavior disorder, when patients enact dream-related behavior at a typical time of atonia, adults are the more common demographic, particularly those with underlying alpha-synucleinopathies.

### **Sleep-related movement disorders**

Sleep-related movement disorders include diagnoses such as restless legs syndrome (RLS), periodic limb movement disorder, and sleep-related bruxism (teeth grinding). They are typically characterized by simple stereotyped movements that disrupt sleep, though RLS is a more complex set of movements and was lumped in this group due to its association with periodic limb movements. Patients with RLS very commonly have periodic limb movements on their polysomnograms (about 80%), though only a small portion of patients with periodic limb

movements on polysomnograms (about 20%) have RLS. Sleep-related bruxism is most common in children and occurs in about 8% of adults.

### Isolated symptoms

This group is an assortment of unrelated diagnoses, including snoring, myoclonic jerks (sleep starts), and long and short sleepers. According to some reports, snoring occurs in 24% of adult women and 40% of adult men. However, there is ongoing debate as to whether snoring, in the absence of obstructive sleep apnea, is associated with morbidity. Myoclonic jerks which occur on the transition from wake to sleep are very common, generally benign, and are often only observed by the bed partner (unless, of course, you are falling asleep in a public place).

### Other sleep disorders

Lastly, the “Other sleep disorders” include those cases in which it is unclear what the final sleep disorder will be or when diagnoses appear to overlap. The most clear disorder in this category is environmental sleep disorder, in which a “physically measurable stimulus” causes disruption of sleep and a resultant fragmentation of sleep or daytime sleepiness.

### Helpful resources

While the hope is that this book will provide an in-depth review of important topics in sleep medicine, there are other resources that may expand the reader’s knowledge on a specific topic or be useful in the care of patients with sleep disorders.

- *American Academy of Sleep Medicine*: the AASM is “the only professional society dedicated exclusively to the medical subspecialty of sleep medicine.” This group has produced many practice parameters for sleep medicine as well as a standardized scoring manual for sleep: [www.aasmnet.org](http://www.aasmnet.org). The AASM also provides some useful information for patients at: <http://yoursleep.aasmnet.org/>.
- *American Thoracic Society*: this professional society, composed of many specialties including pulmonary and critical care physicians dedicated to the chest and lungs, provides good educational materials regarding sleep: [www.thoracic.org/clinical/sleep/index.php](http://www.thoracic.org/clinical/sleep/index.php).

- *Centers for Disease Control*: the US government has a website providing education on sleep topics, including insufficient sleep and sleep disorders: [www.cdc.gov/sleep/](http://www.cdc.gov/sleep/).
- *National Sleep Foundation*: this organization is “dedicated to improving sleep health and safety through education, public awareness, and advocacy.” It has resources for both physicians and patients on its website: [www.sleepfoundation.org](http://www.sleepfoundation.org).

### The future of sleep medicine

Sleep medicine has been a growing specialty in the last few decades with increasing interest from scientific researchers and the public. Demand from patients for consultation on sleeping problems is likely to continue to climb in the United States, in both adult and child populations. Changes are likely to occur in assessment and treatment modalities, with an increasing shift from the sleep laboratory towards home-based diagnosis and management. Sleep medicine physicians will need to implement long-term follow-up plans for patients with chronic disorders, such as those with insomnia or obstructive sleep apnea, similar to treatment for diabetes or hypertension.

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### Further reading

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