NEUROLOGY IN PRACTICE

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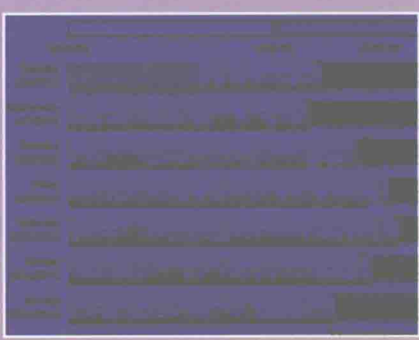
Sleep Medicine in Neurology



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Sleep Medicine in Neurology

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Sleep Medicine in Neurology

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Series Foreword

The genesis for this book series started with the proposition that, increasingly, physicians want direct, useful information to help them in clinical care. Textbooks, while comprehensive, are useful primarily as detailed reference works but pose challenges for uses at the point of care. By contrast, more outline-type references often leave out the "hows and whys" - pathophysiology, pharmacology - that form the basis of management decisions. Our goal for this series is to present books, covering most areas of neurology, that provide enough background information to allow the reader to feel comfortable, but not so much as to be overwhelming; and to associate that with practical advice from experts about care, combining the growing evidence base with best practices.

Our series will encompass various aspects of neurology, with topics and the specific content chosen to be accessible and useful.

Chapters cover critical information that will inform the reader of the disease processes and mechanisms as a prelude to treatment planning. Algorithms and guidelines are presented, when appropriate. "Tips and Tricks" boxes provide expert suggestions, while other boxes present cautions and warnings to avoid pitfalls. Finally, we provide "Science Revisited" sections that review the most important and relevant science background material, and references and further reading sections that guide the reader to additional material.

We welcome feedback. As additional volumes are added to the series, we hope to refine the content and format so that our readers will be best served.

Our thanks, appreciation, and respect go out to our editors and their contributors, who conceived and refined the content for each volume, assuring a high-quality, practical approach to neurological conditions and their treatment.

Our thanks also go to our mentors and students (past, present, and future), who have challenged and delighted us; to our book editors and their contributors, who were willing to take on additional work for an educational goal; and to our publisher, Martin Sugden, for his ideas and support, for wonderful discussions and commiseration over baseball and soccer teams that might not quite have lived up to expectations. We would like to dedicate the series to Marsha, Jake and Dan; and to Janet, Laura and David. And also to Steven R. Schwid, MD, our friend and colleague, whose ideas helped to shape this project and whose humor brightened our lives, but he could not complete this goal with us.

Robert A. Gross
Jonathan W. Mink
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Preface

For centuries of scientific exploration, sleep was considered a "black box." Though theories about what happens when humans and animals sleep have been observed in the writings of the ancient Greek philosophers through Rene Descartes and Thomas Willis and into the 19th century, little understanding of the biology of sleep occurred until the 20th century. Over the last 75 years, there has been an explosion of knowledge about the physiological processes in the brain that occur during sleep and the disorders that disrupt normal sleep.

The goal for this book is to review the clinical disorders of sleep for neurologists, but the subject material is likely relevant for a clinical practitioner of any specialty with an interest in sleep medicine. In today's medical community, assessment of sleeping problems continues to be a mystery for many clinicians, mostly related to a dearth of sleep-related education in medical school and training programs. However, much information is now available about the links between sleep disorders and other medical conditions, including factors relevant to many clinicians' daily practice. For instance, as neurologists consider modifiable risk factors for stroke prevention, methods of helping patients minimize headache frequency, and improving quality of life for patients with dementia, they should be considering disorders of sleep and how to address them. Hopefully, upon reviewing the chapters of this text, the reader will feel more comfortable conversing with their patients about sleep disorders and discussing possible treatment options.

Certification for sleep medicine in the United States requires a year-long fellowship after completing one of several residency programs, including neurology, internal medicine, psychiatry, and pediatrics. We are unable to replicate that learning process in this (or any) book. However, our hope is that this text provides a readable, clinically relevant source of information about sleep and its disorders, useful for any stage of medical practice from resident to attending physician. Particular tips, tricks, and cautions are highlighted in boxes throughout each chapter to increase the reader's yield. This book introduces the topic of sleep medicine in the first chapter, discussing some of the background history and growth of the field. The second and third chapters review the clinical approach to the patient with a sleep problem and the possible options for subjective and objective testing. The following chapters describe in detail each of the major sleep disorders, including insomnia, parasomnias, hypersomnia, sleep-disordered breathing, and limb symptoms. In addition, there are chapters devoted to the specific relationships between sleep and neurological disorders and the effects of sleep disorders on cognition and driving. The final chapter reviews aspects of pediatric sleep medicine, particularly highlighting those that differ from their adult counterparts.

As a neurologist who didn't even know sleep medicine was a subspecialty of neurology until late in my residency, I can only hope that the readers of this book, from whatever specialty, end up finding sleep medicine as exciting as I do.

Douglas B. Kirsch, MD
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Acknowledgments

Thanks go:

To Julie Elliott, from Oxford for keeping us all running like Swiss clocks ... on time.
To Drs. Gross and Mink, for resuscitating a project nearing asystole.
To My parents, who let me choose my own adventure, while providing guidance along the way.
To Ryan, who smiles at me when I wake him up in the morning and when I put him to bed at night.
And to Erin, who supports what I do and amazingly enough loves me for who I am.

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Introduction to Sleep Medicine

Douglas B. Kirsch, MD, FAASM

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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 papyri 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.[1]

> '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.[2]

> '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

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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."[3] 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.[4]

★ 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

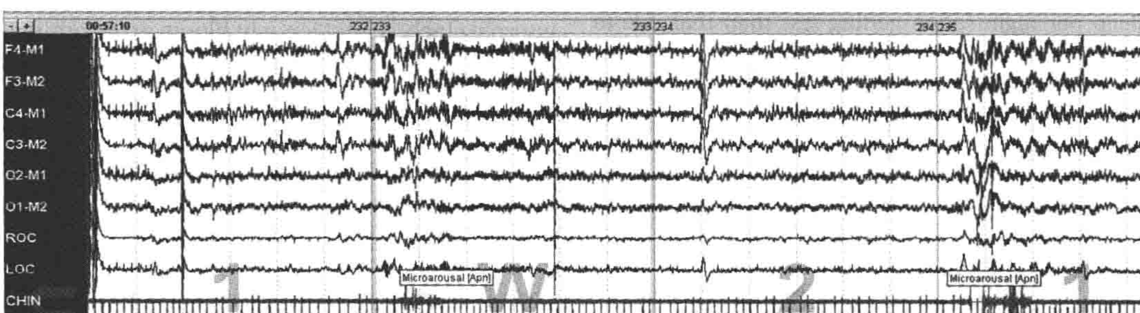

Figure 1.1 Two-minute epoch of in-laboratory polysomnography (Nihon Khoden, Foothill Ranch, CA) from a 55-year-old man with obstructive sleep apnea. The top six leads are EEG (right and left frontal, central, and occipital), followed by two eye leads (right and left), the chin lead, ECG with heart rate 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.