

Preface



Kenneth P. Wright, Jr., PhD
Guest Editor

This issue of *Sleep Medicine Clinics* provides state-of-the-art reviews by physiologists, geneticists, molecular biologists, neuroscientists, psychologists, psychiatrists, and physicians on the basics of circadian physiology and circadian rhythm sleep disorders (CRSDs). Circadian biology is a rapidly changing field at the cutting edge of the molecular regulation of complex behaviors and disorders. Circadian clock genes are present in many tissues throughout the body, and disruption of these clock genes may be involved in impaired physiological function. Circadian rhythm sleep disorders (CRSDs) are a specialized class of sleep disorders associated with disruption of internal circadian physiology and/or a misalignment between internal biological time and environmental time. There are six CRSDs currently recognized in the International Classification of Sleep Disorders (ICSD-2): non-24-hour disorder (free-running type); irregular sleep-wake phase disorder (irregular sleep-wake type); advanced sleep phase disorder (advanced sleep phase type); delayed sleep phase disorder (delayed sleep phase type); jet lag (jet lag type); and shift-work disorder (shift-work type). The ICSD-2 also recognizes CRSDs secondary to medical conditions and drug or substance abuse, as well as a general category: CRSD Not Otherwise Specified (NOS).

The authors have made this issue a success. It was a great pleasure to work with my colleagues involved in writing articles for this issue. They are among the most influential and widely respected researchers and clinicians in their respective fields. I am grateful for the time and effort they devoted to the reviews in this issue. The articles provide synthesis and well balanced views on

the state of the art in circadian biology and treatment of CRSDs.

The internal circadian timekeeping system evolved to regulate and modulate physiological and behavioral processes across the 24-hour solar day-night cycle so that a multitude of the organism's physiological and behavioral processes occur at an appropriate environmental time. Drs. Gillette and Abbott review the neurophysiology of the circadian timekeeping system in mammals, including inputs to the master internal circadian clock located in the suprachiasmatic nuclei (SCN) of the hypothalamus and the outputs from the SCN that influence physiology and behavior. Drs. Dijk and Archer provide an overview of how sleep and circadian systems interact to influence human physiology and behavior and discuss cutting-edge research on the role of circadian clock genes in sleep physiology and cognitive function during sleep deprivation. Drs. Laposky and Turek cover recent advances in circadian biology using animal models, providing evidence that misalignment and disruption of circadian rhythms lead to adverse health consequences. The articles by Drs. Gillette and Abbott; Dijk and Archer; and Laposky and Turek provide the fundamentals of circadian rhythms to improve understanding of mechanisms underlying CRSDs.

The influence of internal circadian phase on disease severity and the consequences of circadian misalignment on cardiovascular disease, asthma, cancer, epilepsy, diabetes, and obesity are reviewed by Dr. Litinski and colleagues. Dr. Litinski and coauthors also discuss chronotherapy, which is the application of circadian principles to time treatment according to internal biological time to maximize the effectiveness of

treatment outcomes and/or minimize side effects. Drs. Duffy and Czeisler provide an update on how environmental light exposure influences the human circadian timing system, highlighting the importance of biological timing, duration, intensity, wavelength, and prior history of light exposure for resetting the timing of the internal circadian clock. Dr. Rajaratnam and colleagues discuss the role of the endogenous melatonin rhythm in human physiology, as well as the use of exogenous melatonin and melatonin analogs to influence circadian physiology. The articles by Drs. Duffy and Czeisler and Rajaratnam and coauthors provide circadian principles upon which current treatments of CRSDs are based. The remaining reviews provide insight into the pathophysiology and treatment of CRSDs. Drs. Uchiyama and Lockley provide a perspective on non-24-hour disorder in sighted and blind individuals, which results in chronic circadian misalignment akin to non-affected healthy humans experiencing chronic jet lag. As the number of older adults continues to increase, so does the prevalence of neurological disorders associated with CRSDs. Drs. Zee and Vitiello review what is known about irregular sleep-wake rhythm disorder, a condition that results in sleep and wakefulness episodes that occur across the 24-hour day and lead not only to sleep and wakefulness impairments in the individuals inflicted but also their caregivers. Dr. Auger provides a synthesis of advance sleep phase disorder, which is most common in older adults and results in bed and wake times earlier than desired; whereas Dr. Lack and coauthors provide insight into delayed sleep phase disorder, which is most common in adolescence and young adults and often results in bed and wake times later than desired. Delayed sleep phase can also result in shortened sleep duration and lead to impaired school and work performance. Drs. Eastman and Burgess discuss the negative impact of jet lag, which afflicts millions of jet-setters worldwide, and ways to make jet

travel easier. Drs. Akerstedt and Wright review the consequences of schedule-induced sleepiness and insomnia associated with shift work. Some individuals appear to have clinically meaningful impairments associated with their work schedule that require intervention to improve safety and, perhaps, health. Drs. Wirz-Justice, Bromundt, and Cajochen review evidence for the influence of circadian disruption in psychiatric disorders and suggest that stabilizing biological timing and sleep may improve treatment outcomes. Lastly, Dr. Levy and colleagues provide a historical perspective of winter depression and discuss a model for understanding the pathophysiology and treatment of this cyclic psychiatric disorder that negatively impacts individuals especially at latitudes far from the equator.

Recognition of CRSDs and their treatment options is required for reducing the negative impact of circadian disruption and circadian misalignment common in modern society. Available treatments for CRSDs are based primarily on principles learned from laboratory-based circadian science. The challenge for circadian science and medicine is to translate these basic circadian principles into more effective treatments, not only for CRSDs but also for other conditions where circadian disruption contributes to disease processes and symptoms. Future implementation of circadian medicine requires large-scale clinical trials and the implementation of circadian assessment tools to improve the understanding of disease processes and the most effective treatments.

Kenneth P. Wright, Jr., PhD
Department of Integrative Physiology
Sleep and Chronobiology Laboratory
University of Colorado at Boulder
1725 Pleasant Street, Clare Small 114
Boulder, CO 80309, USA