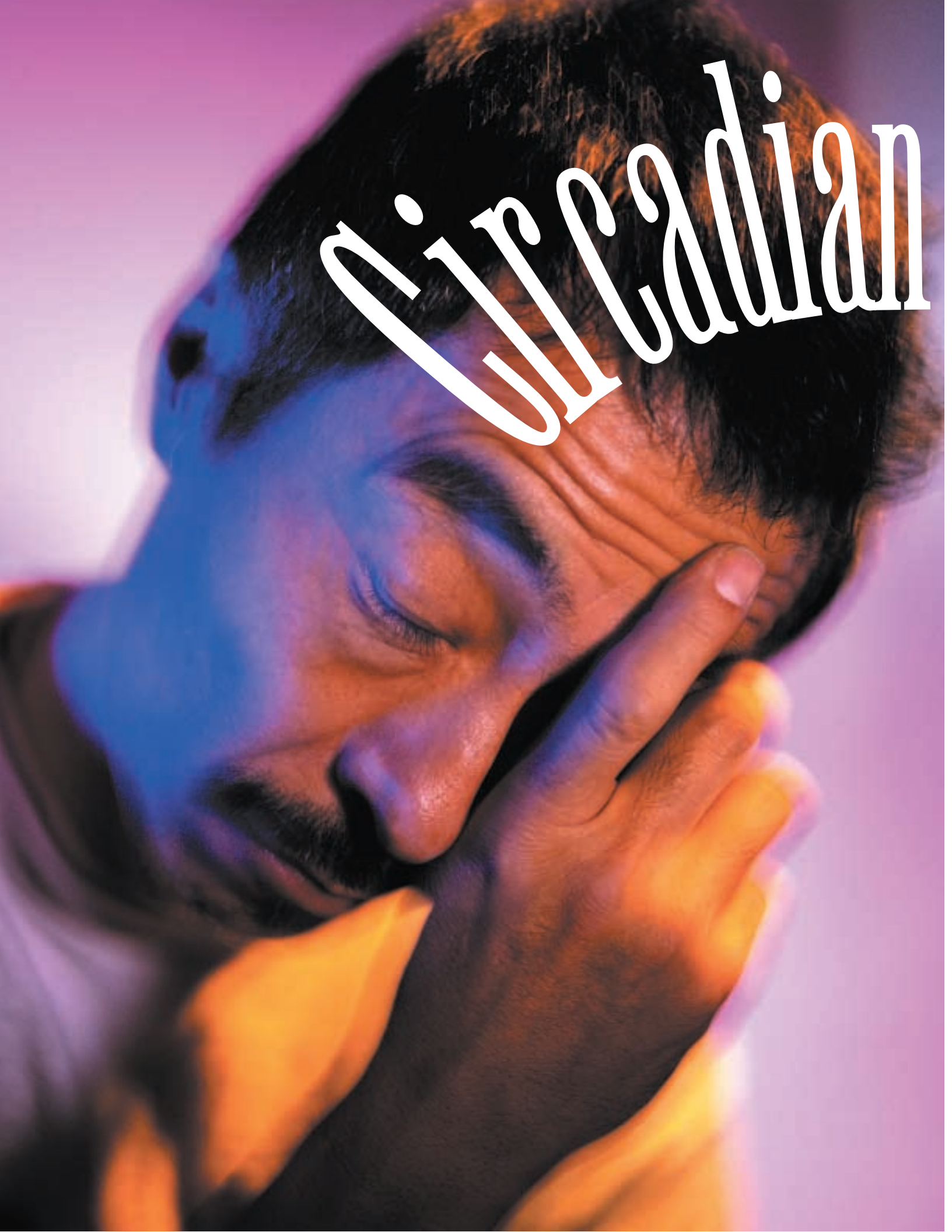
Circadian

RICHARD EVANS WILLS, MD, MA, FACSM

JAMES A WOODMANSEE, MD

MICHAEL NORTON, DC

rhythm sleep disorders

For more than 25 million Americans, including surgical technologists, who have non-traditional work schedules, sleep deprivation is a constant struggle. Hospitals can hardly shut down when employees need shut eye, but working odd shifts and call create hazards of their own. Shift workers are more likely to gain weight, get a cold or the flu, experience high blood pressure, heart problems, stomach problems and menstrual irregularities, have trouble remembering and concentrating, and become involved in a workplace or automobile accident. All of these risks are likely, at some point, to affect job performance.[5]

Sleep deprivation isn't just a problem among shift workers. More than 65 percent of Americans reported that they don't get at least eight hours of sleep each night, which leads to irritability, impatience, anxiety and depression.[5] In addition, about one-third of the adult population in the United States experience occasional or persistent sleep disturbances, making this one of the most common health problems in America.

Physiology of sleep

In the human natural sleep-wake cycle, sleep most naturally occurs between midnight and 7 am, and again between 1 pm and 4 pm. Most adults sleep seven to eight hours per night. The timing, duration, and internal structure of sleep can vary among apparently healthy individuals and as a function of age.[1]

Physiological activity during sleep occurs in two states: rapid eye movement (REM) sleep, also known as dreaming or "D" sleep, and non-rapid eye movement (NREM), also known as orthodox, synchronized or "S" sleep.[1] NREM is then divided into four stages. Stage one is the transition from wakefulness and is characterized by disappearance of the regular alpha patterns. This pattern shows slow, rolling eye movements. NREM stage two, is characterized by spikes called K complexes. During this time, REM activity is absent. In NREM stage three, eye movement activity is absent and EMG levels are reduced. Finally, NREM stage 4 is slow wave, delta or deep sleep.

Circadian rhythmicity

Natural 24-hour cycles of endocrine, thermoregulatory, cardiac, pulmonary, renal, gastrointestinal, and cognitive functions are called circadian rhythms.[1] These functions are controlled by a small group of cells in the brain called the suprachiasmatic nucleus (SCN). The SCN lies in the supraoptic region of the hypothalamus, just superior to where the optic nerves cross. Understandably, then, this circadian "pacemaker" is influenced by light and darkness.

The principal properties of the endogenous circadian pacemaker are its intrinsic period, phase, amplitude, and resetting capacity.[1] Although exposure to light can shift the natural circadian pacemaker, the timing and intensity of the light are actually more vital. The human circadian pacemaker can be reset within two to three days by regulating the proper time of light exposure.[1]

Two principal neurobiologic systems govern the sleep-wake cycle. Intrinsic abnormalities in these systems or extrinsic (environmental, drug, or illness-related) disturbances can lead to sleep or circadian rhythm disorders. It is important to evaluate circadian variations to distinguish between those sleep disorders passively evoked by periodic environmental or behavioral changes, such as shift work disorder and jet lag, and those controlled by endogenous pathways, such as variations in plasma cortisol levels.[1]

Shift work sleep disorder

About 7 million Americans work at night, either on a permanent or rotating schedule. Studies of shift workers indicate that the circadian timing system of the average night-shift worker fails to adapt successfully to such work schedules. This leads to a misalignment between the desired work-rest schedule and the output of the pacemaker and in disturbed daytime sleep. In addition to the health risks involved, the consequent sleep loss and circadian disruption produce decreased alertness and performance and cause increased safety hazards among night-shift workers.

Treatment must be aimed at minimizing both circadian disruption and sleep deprivation. The work schedule must: favor a phase delay in clockwise direction of shift rotation; minimize the frequency of shift rotation so that shifts do not rotate more than once every two to three weeks; and reduce the number of consecutive days worked at night from seven to four or five. Future approaches may include strategic use of bright-light exposure to facilitate rapid adaptation to night-shift work.

Rapid time zone change (jet lag) syndrome

More than 60 million people will, at some time, experience trans-meridian air travel, which is often associated with excessive daytime sleepiness, sleep onset insomnia, and very frequent arousals from sleep, particularly in the latter half of the night. Gastrointestinal discomfort is also common. These symptoms can last typically two to 14 days depending on the number of time zones crossed, as well as the direction of the travel and the traveler's age. Globetrotters who spend more time outdoors reportedly adapt more

quickly than those who remain inside due to bright-light exposure.

Sleep disorders

Sleep disorders can be divided into three major groups: dyssomnias, parasomnias, and medical psychiatric sleep disorders. (Table 1)[1] Shift work disorder and jet lag are both dyssomnias, sleep disorders that are characterized by a change in the quality, amount or routine of sleep. Parasomnias are abnormal events that occur during sleep, such as nightmares and sleep walking. Infection, cardiopulmonary disease, musculoskeletal disorders, and neurological, cerebrovascular or endocrine problems can also disrupt sleep.

Patients with either insomnia or hypersomnia may present with a sleep timing rather than a sleep generation disorder.[1] Sleep time disorders can be either organic, from a defect in the circadian pacemaker, or environmental, due to disruption of exposure to stimuli from the environment. Regardless of etiology, the symptoms reflect the influence of the underlying circadian pacemaker on sleep-wake function. An effective therapeutic approach should aim to adjust the stimuli at an appropriate phase.[1]

Generally, patients visit the physician for the following reasons: chronic fatigue and daytime sleepiness; an acute or chronic inability to sleep adequately at night; and a behavioral manifestation during sleep. Disruption or disturbance of nocturnal sleep is directly related to decreased alertness and cognitive impairment—often a serious patient concern.

In taking a history from a patient, the duration, severity, and consistency of the complaint are important, along with the patient's estimate, in the case of insomnia, of the consequences of reported sleep loss on subsequent waking function. It is also important to gather information from friends and family members in assessing the severity of the complaint. Most patients will under-report potentially embarrassing symptoms, such as heavy snoring or falling asleep while driving.

Abnormal synchronization of the circadian pacemaker to the 24-hour day can be assessed clinically by studying patients under standardized behavioral and environmental conditions.[1] Exogenous factors, such as variations in light exposure, room temperature, activity level, posture, nutritional intake, can all provoke physiologic responses. These must be held constant to assess the phase and amplitude of endogenous circadian rhythms.[1] These patients are studied for 30 to 50 hours of enforced semirecumbent wakefulness in a constant indoor room light, while their daily nutritional and fluid intake is equally divided into hourly snacks. During these tests, body temperature cycle serves as a reliable marker of the output of the endogenous circadian pacemaker.[1]

Reduce shift-worker stress and fatigue

A National Institute for Occupational Safety and Health (NIOSH) offers two publications that present workplace strategies for reducing shift-worker stress and fatigue. The first publication is designed to decrease stress on the job. The second addresses safety and health problems associated with working rotating, evening, or night shifts that can disrupt the body's internal circadian rhythm.

Circadian rhythm disorders can result in sleep deprivation that can lead to on-the-job injury and errors, physical illness, and stress. Order free copies of Stress at Work (Publication No. 99-101) and Plain Language About Shiftwork (Publication No. 97-145) by calling NIOSH at 800-35-NIOSH (800-356-4674). The documents are also available online by accessing the following sites: ***www.cdc.gov/niosh/pdfs/97-145.pdf***, ***www.cdc.gov/niosh/pdfs/stress.pdf***

Table 1 Sleep disorder groups

Dyssomnias

- A *Intrinsic sleep disorders*
  - 1 Psychophysiologic insomnia
  - 2 Idiopathic insomnia
  - 3 Narcolepsy
  - 4 Recurrent or idiopathic hypersomnia
  - 5 Posttraumatic hypersomnia
  - 6 Sleep apnea syndromes
  - 7 Periodic limb movement disorder
  - 8 Restless legs syndrome
- B *Extrinsic sleep disorders*
  - 1 Inadequate sleep hygiene
  - 2 Environmental sleep disorder
  - 3 Attitude insomnia
  - 4 Adjustment sleep disorder
  - 5 Sleep-onset association disorder
  - 6 Food allergy insomnia
  - 7 Nocturnal eating (drinking) syndrome
  - 8 Drug or alcohol dependent sleep disorders
- C *Circadian rhythm sleep disorders*
  - 1 Time zone change (jet lag) syndrome
  - 2 Shift work sleep disorder
  - 3 Delayed sleep phase syndrome
  - 4 Advanced sleep phase syndrome
  - 5 Non 24-hour sleep-wake disorder

Parasomnias

- A *Arousal disorders*
  - 1 Confusional arousals
  - 2 Sleepwalking
  - 3 Sleep terrors
- B *Sleepwake transition disorders*
  - 1 Rhythmic movement disorder
  - 2 Sleep talking
  - 3 Nocturnal leg cramps
- C *Parasomnias usually associated with REM sleep*
  - 1 Nightmares
  - 2 Sleep paralysis
  - 3 Impaired sleep-related penile erections
  - 4 Sleep-related painful erections
  - 5 REM sleep-related cardiac arrhythmias
  - 6 REM sleep behavior disorder
- D *Other parasomnias*
  - 1 Sleep bruxism
  - 2 Sleep paralysis
  - 3 Nocturnal paroxysmal dystonia

Sleep disorders associated with medical/psychiatric disorders

- A *Associated with mental disorders*
  - 1 Acute stress
  - 2 Depression
  - 3 Schizophrenia
- B *Associated with neurologic disorders*
  - 1 Cerebral degenerative disorders
  - 2 Parkinsonism
  - 3 Fatal familial insomnia
  - 4 Sleep-related epilepsy
  - 5 Sleep-related headaches
- C *Associated with other medical disorders*
  - 1 Sleeping sickness
  - 2 Nocturnal cardiac ischemia
  - 3 Chronic obstructive pulmonary disease
  - 4 Sleep-related asthma
  - 5 Sleep-related gastroesophageal reflux
  - 6 Peptic ulcer disease
  - 7 Fibromyalgia

Diagnosis and assessment

The measurement of all physiological activity during the stages of sleep is called polysomnography. This includes measuring brain activity with an electroencephalogram (EEG), movement of the eyes with an electro-oculogram (EOG), contraction of muscles with an electromyogram (EMG), respiration (as in effort, airflow, and oxygen saturation) with respirometer, and heart rate and function with an electrocardiogram.[2]

Assessment of daytime functioning as an index of the adequacy of sleep can be made with the multiple sleep latency test (MSLT). This test involves repeated measurement of sleep latency under standardized conditions during a day following quantified nocturnal sleep. The average latency across four to six tests is taken as an objective measure of daytime sleep tendency. MSLT measures the direct transition from wakefulness to REM sleep, which is indicative of specific pathologic conditions such as narcolepsy.

Given the circadian influence, diagnostic and therapeutic procedures may be affected by time of day. Patient samples may include blood pressure, body temperature, dexamethasone suppression test, and serum cortisol levels. The timing of chemotherapy administration has been reported to have an effect on the outcome of treatment. Few physicians realize the extent to which routine measures are affected by the time (sleep-wake state) when measurement is made. Both the toxicity and effectiveness of drugs can vary during the day—particularly with anesthetic agents, which are specific to the time of day administered to the patient.

Conclusion

Understanding the role of circadian rhythmicity in the pathophysiology of illness may lead to improvements in diagnosis and treatment. Examples of circadian rhythmic variations have been reported in the incidence of acute myocardial infarction, sudden cardiac death and stroke, which are leading causes of death in the United States.[4] Platelet aggregation, which is increased after arising in the early morning hours, has shown an increase in peak cardiovascular events. By understanding the role of circadian rhythmicity in the acute destabilization of chronic conditions such as atherosclerotic disease, there could be a great improvement in the understanding of this type of pathophysiology.[4]

Finally, it should be noted that the risk of errors and accidents due to inattention and or sleepiness varies markedly with the time of day. Single-vehicle truck accidents, industrial errors and accidents, that typically occur during the latter half of the night, coincide with maximal sleep drive within the brain. The physician must be increasingly aware of the public health risks associated with the ever-increasing demands made by the duty-rest recreation schedules in our round-the-clock society.

About the authors

Richard E Wills, MD, MBA, ACSM, is the medical director and program director of Steven's Henager Physician Assistant Program and professor of clinical medicine. James A Woodmansee, MD, practices obstetrics and family medicine in Provo, Utah. Michael Norton, DC, is the owner of Chiropractic Health and Fitness and adjunct professor of medicine at Steven's Henager College in Salt Lake City, Utah.

References

1. *Harrison's Principles Of Internal Medicine.* 13th ed. New York: McGraw-Hill; 1992.
2. Copstead LE, Banasik JL. *Pathophysiology: Biological and Behavioral Perspectives.* 2nd ed. Philadelphia: Saunders; 2000.
3. Guyton AC. *Textbook Of Medical Physiology.* 8th ed. Philadelphia: Saunders; 1991.
4. Strub RL, Black FW. *The Mental Status Examination In Neurology.* 4th ed. Philadelphia: FA Davis Company; 2000.
5. National Sleep Foundation web site. ***www.sleepfoundation.org*** Accessed 11/30/00