

Sleep HealthCenters® Newsletter

David P. White, MD, Editor January 2006

Dear Colleague,

In this issue of the Sleep HealthCenters® Newsletter, we present circadian rhythm sleep disorders (CRSD) in clinical practice. Dr. Roger Smith discusses the diagnosis and treatment of CRSD, which are associated with increased risk of accidents, injuries and impaired quality of life. He also discusses circadian effects on human performance, which extend far beyond these diagnoses.

In the CEO Corner, we introduce our newly renovated and expanded Faulkner Sleep HealthCenter®. We are also happy to welcome new medical staff: Anjali Patwardhan, MD, Geoffrey Gilmartin, MD, and Suzanne Halsey, NP, and announce Dr. Cynthia Dorsey's new role as our Director of Behavioral Sleep Medicine. As we continue to pursue American Academy of Sleep Medicine accreditation at all of our facilities, we are proud to announce that our Bedford and Malden facilities have recently become accredited.

If you have any questions about sleep disorders, our services, or our Faulkner facility, please feel free to contact us.

Sincerely,

David P. White, MD
Corporate Medical Director
Sleep HealthCenters® LLC




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Circadian Rhythm Sleep Disorders in Clinical Practice

By Roger S. Smith, DO

Dr. Smith is the Medical Director of the Sleep HealthCenter® at Weymouth. He is board certified in sleep medicine and is an osteopathic physician and surgeon. He is an Adjunct Clinical Instructor at Stanford University Medical School, a Clinical Instructor in Medicine at Harvard Medical School and has completed a Sleep Medicine Fellowship at the Stanford University Sleep Disorders Clinic.



Circadian rhythm sleep disorders (CRSD) are commonly found in the general population. Unfortunately, they are also associated with increased risk of accidents, injuries, impaired quality of life and other morbidity, including sleep problems. Treatment is readily available and most often effective. This article will serve as an introduction to CRSD diagnosis and treatment.

Many biologic processes follow a rhythmic pattern with a period of about 24 hours. Examples include the sleep-wake process, body temperature fluctuation, growth hormone, cortisol and melatonin secretion to name a few. These circadian (circa = about, dies = a day) rhythms are primarily orchestrated by a paired group of several thousand specialized neurons located in the hypothalamus called the suprachiasmatic nuclei (SCN). Circadian physiology and pathophysiology is quite complex, beyond the scope of this letter and better-described elsewhere (1).

Diagnosis

The CRSD are thoroughly reviewed in the International Classification of Sleep Disorders-2nd edition (2). Common CRSD include:

1. Delayed sleep phase disorder
2. Advanced sleep phase disorder
3. Free-running (nonentrained) type
4. Jetlag disorder
5. Shift-work disorder

General criteria for all CRSD includes 1) a persistent or recurrent pattern of sleep disturbance, due primarily to alterations of the circadian timekeeping system and/or misalignment between the endogenous circadian rhythm and exogenous factors that affect the timing or duration of sleep, 2) the circadian related disruption also leads to insomnia, excessive daytime sleepiness, or both, 3) the sleep disturbance is associated with impairment of social, occupational, or other areas of functioning, and 4) is not due to another medical or sleep disorder. Specific features of each disorder are briefly described below.

Delayed sleep phase disorder is characterized by sleep-wake times that are usually delayed more than two hours. In other words, these patients go to sleep later and wake up later than the conventional or socially acceptable times. The disorder is common in adolescents and young adults. There is a positive family history in approximately 40% of the individuals affected by delayed sleep phase disorder. Exact mechanisms responsible for this problem are unknown. There does seem to be some biologic predisposition in teens, as has been described in the literature by Mary Carskadon, PhD, from Brown University.

In advanced sleep phase disorder, patients are often falling asleep and waking up much earlier than the conventional or socially acceptable times of day. (continued on page 2)


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 - Sleep HealthCenters® opens newly renovated and expanded Faulkner Sleep HealthCenter®
 - Sleep HealthCenters® welcomes new staff: Anjali Patwardhan, MD, Geoffrey Gilmartin, MD, and Suzanne Halsey, NP
 - Dr. Cynthia Dorsey assumes new role as Director of Behavioral Sleep Medicine
 - Sleep HealthCenters® Bedford and Malden facilities receive American Academy of Sleep Medicine (AASM) Accreditation
- ▶ Research Activities

Sleep HealthCenters® is a network of sleep medicine centers staffed by experts in the field of sleep medicine. Our integrated care system provides all the services needed to diagnose and treat patients with the entire array of sleep disorders including obstructive sleep apnea, insomnia, narcolepsy and restless legs syndrome. Sleep HealthCenters® has locations throughout eastern Massachusetts and is affiliated with the Brigham and Women's Hospital, Beth Israel Deaconess Medical Center, Faulkner Hospital, McLean Hospital and Hallmark Health.

Sleep HealthCenters® locations include Newton, Boston, Jamaica Plain, Bedford, Malden, Beverly and Weymouth.

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Referral forms are available on our website.

Sleep HealthCenters® Newsletter

(continued from page 1) This disorder increases in prevalence with age. It is commonly found in the elderly population, and again, the precise mechanisms underlying the pathophysiology are unknown.

Free-running type (AKA nonentrained type) is frequently found in blind patients or those in temporal isolation. Greater than 50% of totally blind patients will demonstrate a free-running circadian rhythm sleep disorder. Typically, these patients are going to bed and waking up 1-3 hours later everyday. On sleep logs, their sleep episodes demonstrate a very characteristic pattern which progressively marches or free runs around the 24-hour clock. These patients are also described as having a circadian rhythm period longer than 24 hours, hence its former name: non-24 hour sleep-wake disorder or hypnnycthemeral syndrome.

Jetlag disorder is well known and tends to be quite obvious. The disturbance in sleep is closely associated with air travel across two or more time zones. Essentially, the patient's sleep remains disturbed until the internal body clock becomes synchronized with the new time zone. A commonly suggested acclimation rate is one day for each time zone crossed. Although all humans will experience circadian rhythm disruption with air travel across time zones, the intensity of symptoms vary depending upon the individual, direction and degree of travel.

Shift-work disorder affects a great number of people across the world. In the United States alone, an estimated 20% of the work force is actively engaged in shift-work. Shift-work disorder is very similar to jet lag disorder. The sleep problem is associated with a work schedule that overlaps and displaces the usual time for sleep. Several studies have shown that shift workers are at significantly greater risk of work related accidents and injuries as well as automobile accidents (3).

Treatment

Treatment of CRSD generally involves four major principles:

1. Balance the physiology, patient and third party needs
2. Approximate normal/natural sleep
3. Phase-shift
4. Provide patient education

It is very important to develop a balance, or compromise, between the needs of the patient, the limits of physiology, and any third party needs. Circadian rhythm treatment plans are more likely to succeed if all three of these are addressed and balanced properly. Third party needs include, for example, the Department of Transportation regulations governing the employment of your patient who is a long-haul truck driver and shift worker.

Clinical presentations of CRSD patients vary greatly and it can be quite confusing to develop a standard treatment plan that addresses all variations. One method that helps overcome this challenge is to focus on approximating normal/natural sleep. For example, simply recommending adequate sleep hygiene (see www.sleephealth.com) can address many of the various problems CRSD patients encounter. Judiciously prescribing medications like sedative hypnotics or stimulants can also help to approximate normal/natural sleep.

Phase-shifting the circadian rhythm is one of the mainstays of treatment in CRSD. It involves shifting the abnormal sleep-wake phase to a more conventional or socially acceptable time. There are a number of ways to cause phase shifts in humans. Gradually shifting the sleep-wake times by about 30-60 minutes everyday is usually very effective and is called Chronotherapy. This method is best used in combination with bright light.

Phase shifting with bright light can phase advance or delay the circadian rhythm by 1-3 hours per day. The degree and direction of the shift is governed by the phase response curve to light (4). The degree of shift also depends on the intensity (usually 2,500 to 10,000 lux), duration (between 30 minutes to 3 hours) and the wavelength (optimally between 450-510 nm) of the light pulse.

The risk/benefit profile of light is very favorable. Certainly caution is recommended and the patient should never look directly into a light source unless the specific light device has been tested for this purpose (such as a light box). Further information regarding this technique is described in the literature (5).

Phase-shifting can also be done with melatonin. It can cause a phase advance or delay and also has its own phase response curve similar to light (6). This technique has been effective in treating blind patients (7). The risk/benefit profile, however, is somewhat unknown.

Clearly, melatonin has been used by many people without significant known adverse effects, but it is also unregulated by the FDA.

Other forms of phase-shifting have been attempted in humans but have not been as successful as the previously mentioned techniques. Examples include diet, activity, homeopathic remedies and medications. More information on phase-shifting techniques are reviewed in the literature (8).

Lastly, patient education is vital in the treatment of circadian rhythm sleep disorders. Patients with these disorders are at increased risk for accidents and injuries. The supporting literature on this point is rather extensive. Most likely, this increased risk is due to the combination of circadian rhythm disruption and sleep deprivation. Shift work sleep disorder patients may also be at increased risk for cardiovascular disease (9), breast cancer (10), and gastrointestinal disease (11). Additional patient education covering the basics of sleep, circadian rhythms and treatment rationale tends to improve compliance and outcome.

In summary, CRSD are very common in the general population and include significant increased health risks but are also relatively straightforward to treat. Diagnosis and treatment includes 1) performing a comprehensive history and physical exam, 2) ruling out underlying sleep disorders, 3) developing a balance between physiology, patient and third party needs, 4) approximating normal natural sleep (which includes sleep hygiene, and possibly medication use), 5) phase-shifting the abnormal or undesired sleep-wake episode to a more desired or socially acceptable time using a combination of chronotherapy and light, and 6) providing patient education regarding risk management and treatment rationale.

For a fully referenced version of this article, visit the Sleep HealthCenters® website: www.sleephealth.com



Other Aspects of Circadian Rhythms

Circadian rhythms in medical practice extend far beyond the ICSD diagnoses. Perhaps the largest area of interest relates to the circadian effects on human performance.

Exceeding the limits of our physiology yields adverse consequences, and circadian rhythm (CR) physiology is no exception. Research over the last 30 years has demonstrated significantly increased accident and injury rates secondary to CR disruption and sleep deprivation. Both physical and cognitive performance are adversely effected. A number of high-profile accidents, such as the grounding of the Exxon Valdez, have been linked to circadian rhythm disruption and sleep deprivation. Research continues to document evidence supporting this dangerous association in humans, from astronauts to medical interns (12).

Sleep Medicine experts have therefore been called upon to consult with NASA and the aerospace industry, elite athletes (NFL, US Olympic teams, etc.), the Department of Transportation, and many US corporations. Application of this CR information may lead to a significant competitive advantage by increasing productivity, decreasing accidents/injuries, decreasing liability, containing costs, and generally optimizing physical and cognitive performance (13).

Other areas of interest include the apparent association between CR and increased morbidity and mortality rates. This link has been documented with disorders such as myocardial infarction, stroke, asthma, seizure disorder, sudden death, and acute aortic dissection, which have all demonstrated diurnal patterns of incidence (14). CR appears to influence the clinical outcome of

certain pharmacologic treatment strategies. Dosing medication at specific times of the day has shown promise over standard dosing in treating hypertension, ischemia, asthma, arthritis, diabetes and cancer. Circadian rhythms also impact laboratory medicine. For example, a 10-20% variation in blood levels of common chemistries (TSH, PSA, bilirubin, creatine kinase, etc.) can be found throughout the 24-hour day.

We at SHC invite you to contact us, or check out our website at www.sleephealth.com for more information on circadian rhythms in clinical practice.

For a fully referenced version of this article, visit the Sleep HealthCenters® website: www.sleephealth.com



CEO Corner

Paul S. Valentine
President and
Chief Executive Officer

We are happy to announce the opening of our newly renovated and expanded Faulkner Sleep HealthCenter®. This neurological sleep program is affiliated with Brigham and Women's/Faulkner Hospital's Neurology Department and is located on the 5th floor of the Faulkner Hospital. The increased capacity allows us to provide better access to patients by offering shorter wait times for sleep studies. On Friday, December 16th, we held an open house and provided tours of our new lab to local providers.

As Sleep HealthCenters® continues to grow, we are expanding our medical team and are pleased to welcome our newest members: Anjali Patwardhan, MD, Geoffrey Gilmartin, MD, and Suzanne Halsey, NP. Dr. Patwardhan is board certified in internal medicine, pulmonary disease and critical care medicine and she completed her sleep medicine fellowship at the Boston University School of Medicine. She sees patients in both our Newton and Beverly locations. Dr. Gilmartin is the new Medical Director of our Sleep HealthCenter® affiliated with Beth Israel Deaconess Medical Center. He is board certified in internal medicine, pulmonary disease, critical care medicine and sleep medicine. Suzanne Halsey has family practice experience and has worked with patients in a variety of settings including hospitals, clinics and home care. She sees patients in our Malden and Weymouth facilities.

Dr. Cynthia Dorsey, Clinical Director of the Sleep HealthCenter® affiliated with McLean Hospital and board certified in psychology and sleep medicine, has decided to join us full-time as our Director of Behavioral Sleep Medicine. She will specialize in treating patients with insomnia and other behavioral sleep-related disorders. In addition, Dr. Dorsey will be working closely with Dr. Kelly Carden to expand our research efforts in the pharmaceutical and medical device areas. Dr. Dorsey will continue to see patients in our Newton facility and will begin seeing patients in our Bedford facility in February.

As discussed in a previous newsletter (March 2004), Sleep HealthCenters® values accreditation by the American Academy of Sleep Medicine (AASM). We believe that the accreditation process confirms our organization's efforts to instill and maintain consistent standard operating procedures focused at the highest level of patient care. We are proud to announce that we were recently notified that our Bedford and Malden facilities have received AASM accreditation, joining three of our other facilities. In early 2006, we will be pursuing accreditation at both the Faulkner and Beverly facilities.

Please contact us at 1-877-SLEEPHC (1-877-753-3742) if you are interested in taking a tour of our newly renovated Faulkner facility or if you have any questions about the services we offer. We look forward to continuing to service your patients at our sleep medicine centers.

Research Activities

Sleep HealthCenters® and their related research affiliations are actively recruiting patients for the following studies:

Apnea Positive Pressure Long-Term Efficacy Study (APPLES) A NIH-funded study examining the long-term effects on quality of life, neurocognitive function, sleepiness and mood of using Continuous Positive Airway Pressure (CPAP) to treat sleep apnea. The Sleep HealthCenter® affiliated with Brigham and Women's Hospital is recruiting patients age 18 or older who suspect they may have sleep apnea but have not been previously treated with CPAP or surgery. Subjects will be enrolled for six months (maximum of seven months) and will receive monetary compensation. *Study contact: Denise Clarke 617-527-3501 ext. 146.*

Restless Legs Syndrome A research study of a new drug is being tested (in the form of a patch) for Restless Legs Syndrome. The Sleep HealthCenter® affiliated with Brigham and Women's Hospital is recruiting individuals age 18-75 who suffer from Restless Legs Syndrome (achy, creepy-crawly sensations in the legs, which get worse at night). Males and females are eligible. Participation in this study requires 14 clinic visits over an eight-month period. There will be no overnight stays. Up to \$600 for participation. *Study contact: Erin Johnson 617-527-3501 ext. 115.*