



Pretest and Objective

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Educational Objective

After studying the ACADEMIC HIGHLIGHTS, you will be able to:

- Diagnose and treat daytime sleepiness and nighttime wakefulness, particularly in shift workers, in the primary care setting.

This pretest is designed to facilitate your study of the material.

1. **Activities that disrupt biological processes such as the ultradian, homeostatic, and circadian processes do not directly influence the development of a sleep disorder.**
 - a. True
 - b. False

Pretest answer and Posttest on page 211.

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ACADEMIC HIGHLIGHTS

Sleepiness Versus Sleeplessness: Shift Work and Sleep Disorders in the Primary Care Setting

This ACADEMIC HIGHLIGHTS section of *The Primary Care Companion to The Journal of Clinical Psychiatry* presents the highlights of the teleconference series “Differential Diagnosis and Management of Excessive Sleepiness,” held April 5, 7, and 22, 2004. The teleconference and this ACADEMIC HIGHLIGHTS were supported by an unrestricted educational grant from Cephalon, Inc. This report was prepared by Physicians Postgraduate Press, Inc.

The teleconference was chaired by **Thomas Roth, Ph.D.**, Henry Ford Hospital Sleep Center, Detroit, Mich. The faculty were **Karl Doghramji, M.D.**, Department of Psychiatry and Human Behavior and the Sleep Disorder Center, Thomas Jefferson University, Philadelphia, Pa.; **Paul Doghramji, M.D.**, Brookside Family Practice, Pottstown, Pa.; **Jonathan R. L. Schwartz, M.D.**, Integris Sleep Disorders Center of Oklahoma, Oklahoma City; and **James K. Walsh, Ph.D.**, Sleep Medicine and Research Center, St. Luke’s Hospital, Chesterfield, Mo.

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Characteristics of Normal Sleep

Thomas Roth, Ph.D., explained that sleep is a fundamental behavior characterized by minimum movement, reduced responsiveness to stimuli, reversibility, and species-specific diurnal timing.¹ Normal human sleep consists of 2 alternating states, rapid eye movement (REM) and non-REM (NREM), in which the brain cycles between slow and mixed frequency and high and low voltage.²

Dr. Roth said that researchers believe that the body actively regulates sleep through 3 hypothesized sleep processes.¹ The first process is the homeostatic process. In this process, the level of sleepiness is determined by the amount of prior sleep and waking. The circadian process organizes the sleep

phases with the light and dark cycles, causing sleepiness at night and wakefulness during the day. The ultradian process is the 90- to 120-minute cycles of NREM and REM sleep that the body experiences 3 to 6 times per night. Dr. Roth commented that activities that disrupt these biological processes, such as shift work, directly influence the development of sleep disorders.

REFERENCES

1. Roth T, Roehrs T. Sleep organization and regulation. *Neurology* 2000;54(suppl 1): S2-S7
2. Carskadon M, Dement W. Normal human sleep: an overview. In Kryger MH, Roth T, Dement WC, eds. *Principles and Practices of Sleep Medicine*, 3rd ed. Philadelphia, Pa: Saunders; 2000:43-52

Excessive Sleepiness, Insomnia, and Shift Work Sleep Disorder in the Psychiatric Setting

Karl Doghramji, M.D., explained that sleep disturbances such as insomnia, fatigue, and daytime somnolence are frequent complaints in patients with psychiatric disorders. For example, Sweetwood and colleagues¹ found the overall prevalence of sleep disturbances to be 58% among male psychiatric patients and 21% among healthy controls. Similarly, in a European survey² of almost 1900 depressed subjects, 73% reported tiredness and

63% reported sleep problems during the 6 months prior to the study.

Insomnia, fatigue, and daytime somnolence often accompany psychiatric disorders such as depression. Sleep disturbances may also be the result of poor sleep hygiene, medical conditions, and circadian rhythm disorders such as shift work sleep disorder.

Dr. Doghramji emphasized that the recognition and management of sleep

Table 1. Items Assessed on the Epworth Sleepiness Scale^a

<p>Patient is asked to rate the chance of dozing in the following situations:</p> <ol style="list-style-type: none"> 1. Sitting and reading 2. Watching television 3. Sitting inactive in a public place such as a theater 4. Riding as a passenger in a car for more than an hour without a break 5. Lying down to rest in the afternoon 6. Sitting and talking to someone 7. Sitting quietly after lunch (when no alcohol has been drunk) 8. Sitting in a car while stopped in traffic
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^aBased on Johns.⁸

disorders is crucial because of the severity of the consequences associated with these disorders. Daytime sleepiness is associated with slower response time, instability of attention, deterioration of performance, and cognitive slowing. Daytime sleepiness has also been found to negatively affect memory and the ability to distinguish between essential and nonessential daily tasks.^{3,4}

While insomnia is a common sleep disorder worldwide, it is rarely the chief complaint of patients visiting physicians. Sufferers do, however, seem to be troubled by their insomnia, as 40% resort to self-medication with alcohol, over-the-counter agents, or both.⁵ Similarly, excessive sleepiness is also underreported, yet in the latter case, the primary reason may be related to poor subjective awareness of the objective consequences of sleepiness in the human brain and body.

Sleep Scales

Dr. Doghramji pointed out that several tests and scales, both subjective and objective, have been developed to determine the degree of daytime sleepiness in patients with sleep disturbances. One popular subjective scale is the Stanford Sleepiness Scale.⁶ Patients are asked to rate their level of sleepiness on a scale of 1 to 7, with 1 being the most alert (“feeling active, vital, alert, wide awake”) and 7 being the least alert (“no longer fighting sleep, sleep onset soon; having dreamlike thoughts”). Dr.

Doghramji commented that this scale is not considered to be very accurate because, as noted by Rosenthal and colleagues,⁷ many patients lack full awareness of their level of sleepiness.

The concern for the lack of accuracy in the Stanford Sleepiness Scale led to the development of another subjective scale, the Epworth Sleepiness Scale (ESS).⁸ The ESS is a self-administered questionnaire that assesses the patient’s likelihood of falling asleep during the course of the day in normal, everyday situations (Table 1). Patients are asked to rate the likelihood of falling asleep on a scale of 0 to 3 (0 = would never fall asleep, 3 = high chance of falling asleep). Test takers who score a 10 or more on the ESS are advised to seek the council of a physician to determine the cause of excessive sleepiness.

Dr. Doghramji related that objective tests are probably more effective and more sensitive in assessing sleepiness than subjective scales. Objective tests are commonly used in special settings such as sleep disorder clinics. One of the most common objective tests is the MSLT, in which patients are given opportunities to take 5 naps during the course of the day. A score of 5 or below on the MSLT indicates a pathologic level of sleepiness in which an individual may be unable to resist the urge to fall asleep and may even lack the premonition that they are sleepy. This test relies on the presumption that the speed of falling asleep is inversely proportional to the degree of daytime alertness. For example, a patient who is able to fall asleep after 2 or 3 minutes is considered more sleepy than a patient who falls asleep after 10 or 20 minutes.

A variant of the MSLT is the Maintenance of Wakefulness Test. This test asks patients to stay awake during nap subtests, rather than fall asleep. Since patients are asked to remain awake, some investigators consider the Maintenance of Wakefulness Test to be more directly proportional to the level of wakefulness during everyday situations than the MSLT.

Psychiatric scales may also be useful in identifying sleep disorders. Dr. Doghramji identified both the Hamilton Rating Scale for Depression (HAM-D)⁹ and the Profile of Mood States (POMS)¹⁰ as possible tests for patients complaining of sleep problems. The retardation factor of the HAM-D assesses the degree of retardation or anergy in psychiatric patients, while the fatigue/inertia subscale of the POMS is commonly used to assess levels of fatigue and sleepiness in patients.

Dr. Doghramji remarked that while a number of scales can be used to identify the presence or absence of insomnia—for example, the HAM-D—the most direct method to accomplish this task is to ask the patient. Careful and systematic questions about how long it takes a patient to fall asleep, the number of awakenings during the course of the night, and whether the patient remains awake the rest of bedtime hours or wakes earlier than desired, may provide physicians with insight into a patient’s general sleep patterns. Dr. Doghramji added that physicians should ask about the quality of sleep in patients with insomnia. Many patients may sleep for 8 hours but wake up feeling insufficiently rested. Asking a patient’s bed partner, if available, may also be more informative than asking the patient. Bed partners usually can provide insight into a patient’s sleep habits at night and sleepiness during the day that may be unknown to the patient.

Shift Work Sleep Disorder

Dr. Doghramji continued with a discussion on shift work sleep disorder. Individuals who work shift schedules often vary their bedtimes from one day to the next to such an extent that the body is unable to adapt properly to the change in schedule. This varying schedule often leads to complaints of both sleepiness and insomnia. Psychological and psychiatric symptoms, including depression, malaise, diminished motivation, and impaired concentration frequently afflict shift

Table 2. Factors Contributing to Shift Work Sleep Disorder

Increasing age
Possible existence of an underlying sleep disorder such as sleep apnea or narcolepsy
Self-treatment or self-medication (long naps, or using caffeine to stay awake or alcohol to fall asleep)
Direction in and degree to which shift changes occur (slow or clockwise shift changes may be more easily tolerated than rapid or counterclockwise shifts)

workers with sleep disorders¹¹ and many shift workers also suffer gastrointestinal disturbances and other medical afflictions as well.¹²

Simply working a shift work schedule does not necessitate the presence of a sleep disorder, i.e., a condition in which there is impairment in daytime functioning and disturbance with sleep initiation or maintenance. But a number of factors do predispose shift workers to developing sleep disorders (Table 2). The first factor is age. As workers age, they are often unable to adapt to rapid changes in shift schedules, leaving them vulnerable to insomnia and daytime sleepiness. The presence of a preexisting sleep disorder may also result in shift work sleep disorder. For example, the presence of sleep apnea has been found to be higher among shift workers such as bus drivers than non-shift workers.¹³ A third factor is a worker's individual coping strategies to manage shift work schedules. Excessive caffeine to stay awake, alcohol to fall asleep, as well as long naps in the wrong part of the day may all impact a worker's ability to manage sleepiness and result in a sleep disorder. A final factor involves the shift changes themselves. Shifts that rotate in a clockwise fashion are more easily tolerated than shifts that rotate counterclockwise.^{14,15} Additionally, rapidly rotating shifts may be more likely to negatively affect workers than shifts that are nonvariable or that rotate more slowly.¹⁶

Dr. Doghramji outlined proper treatment for shift work sleep disorder. Physicians should reinforce proper

sleep hygiene and advise patients to try to schedule work so that the changes in sleep scheduling between one day and the next are not dramatic (i.e., no more than a few hours from one night to the next). Additionally, shift workers may benefit from "power naps," or naps taken during certain times of the day, that are short in duration and timed in such a way that they do not interfere with nocturnal sleep. Shift workers are also often treated with a combination of bright lights, stimulants, wake-promoting agents, and hypnotics in order to adjust their rhythms.

Conclusion

Daytime sedation and insomnia are common in psychiatric patients and those who work irregular shifts. Unfortunately, they are often unrecognized by physicians as well as patients. Dr. Doghramji concluded by saying that a high clinical index of suspicion should be maintained by physicians when patients complain of sleepiness or insomnia, especially among those who work shift schedules or have psychiatric disorders. Both subjective and objective tests are available to aid clinicians in quantifying and identifying sleep disorders.

REFERENCES

1. Sweetwood H, Grant I, Kripke DF, et al. Sleep disorder overtime: psychiatric correlates among males. *Br J Psychiatry* 1980; 136:456-462
2. Tylee A, Gastpar M, Lepine J-P, et al. DEPRES II (Depression Research in European Society II): a patient survey of the symptoms, disability and current management of depression in the community. *Int Clin Psychopharmacol* 1999;14:139-151
3. Alapin I, Fichten CS, Libman E, et al. How is good and poor sleep in older adults and college students related to daytime sleepiness, fatigue, and the ability to concentrate? *J Psychosom Res* 2000; 49:381-390
4. Leger D, Guilleminault C, Bader G, et al. Medical and socio-professional impact of insomnia. *Sleep* 2002;25:625-629
5. Ancoli-Israel S, Roth T. Characteristics of insomnia in the United States: results of the 1991 National Sleep Foundation Survey I. *Sleep* 1999;22 (suppl 2): S347-S353
6. Hoddes E, Zarcone V, Smythe H, et al. Quantification of sleepiness: a new approach. *Psychophysiology* 1973;10: 431-436

7. Rosenthal L, Nykamp K, Day R, et al. The detection of brief daytime sleep episodes. *Sleep* 1999;22:211-214
8. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. *Sleep* 1991;14:540-545
9. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960;23: 56-62
10. McNair DM, Lorr M, Droppleman LF. *Manual for the Profile of Mood States*. San Diego, Calif: Educational and Industrial Testing Service; 1971
11. Gordon NP, Cleary PD, Parker CE, et al. The prevalence and health impact of shiftwork. *Am J Public Health* 1986;76: 1225-1228
12. Segawa K, Nakazawa S, Tsukamoto Y, et al. Peptic ulcer is prevalent among shift workers. *Dig Dis Sci* 1987;32: 449-453
13. Hui DS, Chan JK, Ko FW, et al. Prevalence of snoring and sleep-disordered breathing in a group of commercial bus drivers in Hong Kong. *Intern Med J* 2002; 32:149-157
14. Lavie P, Tzischinsky O, Epstein R, et al. Sleep-wake cycle in shift workers on a clockwise and counterclockwise rotation system. *Isr J Med Sci* 1992;28:636-644
15. Knauth P. The design of shift systems. *Ergonomics* 1993;36:15-28
16. Akerstedt T. Shift work and disturbed sleep/wakefulness. *Occup Med* 2003;53: 89-94

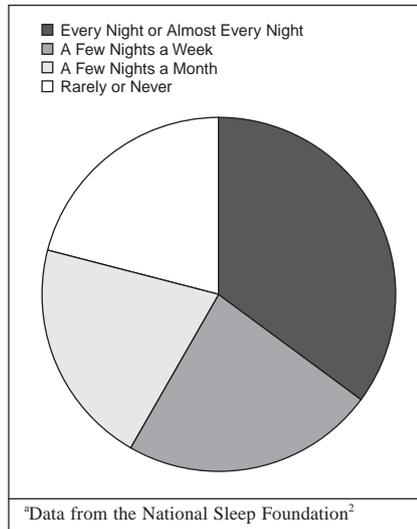
Insomnia and Shift Work

Paul Doghramji, M.D., stressed that physicians need to be aware of the prevalence and consequences of insomnia and sleepiness and should be motivated to take action to diagnose and treat these disorders. Hatoum and colleagues¹ reported that up to a third of the general population will experience insomnia and daytime sleepiness. The National Sleep Foundation found in its 2002 Sleep in America Poll² that 35% of respondents reported symptoms of insomnia (trouble falling or staying asleep, waking too early, or waking feeling unrefreshed) every or almost every night. Another 23% of respondents reported having 1 or more of these symptoms a few nights a week (Figure 1).

Insomnia

Dr. Doghramji explained that few of the patients who present with symptoms of insomnia in the primary care setting are treated for insomnia. For example, one study¹ found that 13.5% of

Figure 1. Respondents to the 2002 Sleep in America Poll Who Reported at Least 1 Symptom of Insomnia (N=1010)^a



patients had a diagnosis of insomnia and 32% had a diagnosis of insomnia with daytime sleepiness, but only 5.5% and 11.6% of these patients, respectively, received prescription medication. In another study,³ fewer than a third of patients with insomnia received medication, and patients who had a diagnosis of current depression were found to be more likely to receive treatment than patients with only a diagnosis of insomnia.

One reason that insomnia frequently goes untreated is that patients seldom complain of insomnia or daytime sleepiness. Patients will usually mention feeling tired or fatigued. Dr. Doghramji emphasized that even though the detection of sleep disturbances is often difficult in the primary care setting, patients complaining of fatigue or feeling worn out should be considered as possibly suffering from a sleep disorder.

Dr. Doghramji warned that untreated insomnia and daytime sleepiness can have potentially life-threatening consequences. Patients with insomnia have been found to have a high degree of functional impairment and higher health care costs than patients without insomnia.³ Excessive sleepiness is also considered to be as-

sociated with high rates of morbidity, illness, and life-threatening accidents.

In Dr. Doghramji's experience, patients typically visit their primary care physician for 1 of 3 reasons—for an acute visit for a particular reason, a follow-up visit for a chronic condition, or a complete physical examination—and it is during any of these visits that physicians should investigate any suspected sleep disorders.

Complaints of sleepiness should not lead to an automatic diagnosis of insomnia, Dr. Doghramji cautioned. Physicians need to rule out other various medical and psychological conditions that may cause sleepiness as well as other preexisting sleep disorders such as restless legs syndrome (Table 3).

To make a diagnosis of sleep disorder, it is important for the physician to query the patient closely about his or her sleep and daily habits, instructed Dr. Doghramji (Table 4).

Shift Work

Our society functions on a 24 hours per day, 7 days per week schedule, and therefore many people in the United States must work shifts other than daytime shifts, commented Dr. Doghramji. According to a survey by the U.S. Bureau of Labor Statistics⁴ of almost 100 million full-time workers, 14.5% work shifts. Examples of workers who are likely to be scheduled for shifts are truck drivers, factory workers, doctors, nurses, and restaurant employees.

Working a shift work schedule may result in shift work sleep disorder, but not everyone who works a shift work schedule will suffer from shift work sleep disorder. Ohayon and colleagues⁵ conducted a study of sleep disturbances in 817 hospital staff workers who worked 1 of 3 schedules: fixed daytime shift, rotating daytime shift, or shift or nighttime work. Disrupted sleep occurring 2 nights or more a week was reported by 29.7% of employees scheduled for rotating daytime shifts. These workers also reported significantly more difficulty in initiating sleep than fixed daytime workers (20.1% and

Table 3. Possible Causes of Excessive Sleepiness

Primary Disorder
Narcolepsy
Recurrent hypersomnia
Kleine-Levin syndrome
Secondary Disorder
Behavioral disorders
(Inadequate sleep hygiene)
Mental disorders
(Mood disorders, psychosis)
Drug-related side effects
Movement disorders
(Restless legs syndrome)
Circadian rhythm disorders
(Shift work sleep disorder)
Neurologic disorders
(Parkinson's disease)
Sleep disorders
(Insomnia, sleep apnea)

Table 4. Questions to Determine Sleep Disorders

1. Are you having trouble getting to sleep?
2. Are you having trouble staying asleep?
3. Are you waking up in the middle of the night or too early in the morning?
4. Do you feel that your sleep is unrefreshing?
5. If I were to leave the room and turn off the light, how long would it take you to fall asleep?
6. Do you suffer from any sleep disorders such as sleep apnea?
7. How likely are you to fall asleep during the day?
8. How long do you typically sleep at night?
9. What is your typical sleep schedule?
10. Do you snore?
11. Do you work a shift schedule?

12%, respectively). Almost a fourth of shift or nighttime workers met the diagnostic criteria for a circadian rhythm disorder ($p \leq .01$ vs. the fixed daytime group).

Treatment

Dr. Doghramji then reviewed his strategy for treating sleep disorders such as those caused by shift work. He explained that first he suggests that a patient discontinue shift work if possible, or if a patient must work a shift schedule, that he or she try to work the same shift every day and keep weekend sleep schedules as close to weekday sleep schedules as possible. By minimizing irregularities in one's sleep

cycle, he said, the patient may be able to keep his or her circadian clock steady.

Since shift work sleep disorder is a man-made problem, sometimes using a man-made agent is beneficial, commented Dr. Doghramji. For example, sleeping agents such as benzodiazepine receptor agonists may be an appropriate treatment for patients whose body clock is consistently trying to be awake when a patient is trying to sleep. Likewise, wake-promoting agents may be appropriate for patients experiencing excessive daytime sedation as a result of a shift work sleep disorder.

Conclusion

Dr. Doghramji concluded by emphasizing that physicians must keep in mind that most patients will not complain of a sleep disorder, but a good portion of patients are in fact suffering from one. Primary care physicians are given the unique opportunity, in the guise of routine patient visits, to query patients complaining of fatigue about the possibility of a sleep disorder and to treat these patients accordingly.

REFERENCES

1. Hatoum HT, Kania CM, Kong SX, et al. Prevalence of insomnia: a survey of the enrollees at five managed care organizations. *Am J Manag Care* 1998;4:79-86
2. National Sleep Foundation. 2002 Sleep in America Poll. Washington, DC: National Sleep Foundation; 2002. Available at: <http://www.sleepfoundation.org/img/2002SleepInAmericaPoll.pdf>. Accessed June 3, 2004
3. Simon GE, Von Korff M. Prevalence, burden, and treatment of insomnia in primary care. *Am J Psychiatry* 1997;154:1417-1423
4. US Bureau of Labor Statistics, US Department of Labor. Table 5. Shifts usually worked: full-time wage and salary workers by occupation and industry, May 2001. Available at: <http://www.bls.gov/news.release/flex.t05.htm>. Accessed June 3, 2004
5. Ohayon MM, Lemoine P, Arnaud-Briant V, et al. Prevalence and consequence of sleep disorders in shift worked population. *J Psychosom Res* 2002;53:577-583

Management of Nighttime Wakefulness With Hypnotics

According to James K. Walsh, Ph.D., despite the fact that the percentage of patients with insomnia who receive pharmacologic treatment is relatively low, between 70% and 80% of patients with chronic insomnia should be considered to be potential candidates for pharmacologic treatment. Clear indications for pharmacotherapy include short-term and transient insomnias, such as shift work sleep disorder. Potential indications are primary insomnia and secondary insomnia due to medical and psychological conditions (see Table 3).

Dr. Walsh commented that physicians have seen a shift in prescribing trends for insomnia during the 1990s, with a decrease (53.7%) in hypnotic medication prescriptions and an increase (146%) in prescriptions for antidepressants with sedating effects.¹ However, he added, very little is known about the efficacy and safety of sedating antidepressants in insomnia. Few trials have been conducted on the use of sedating antidepressants in non-depressed patients with insomnia, and some antidepressants are associated with potentially serious side effects such as anticholinergic effects.

Hypnotic Medications

Hypnotic medications are effective treatments with few serious side effects,

asserted Dr. Walsh. A review of several studies² showed that patients prescribed hypnotics report more positive effects and fewer adverse effects than patients treated with over-the-counter medications. The hypnotics currently prescribed in the United States are benzodiazepines, with the exception of zolpidem and zaleplon, Dr. Walsh explained. These nonbenzodiazepines are similar to benzodiazepines in that they act on similar receptor sites; however, evidence³ suggests that zolpidem and zaleplon are more selective in terms of binding properties and have fewer side effects than benzodiazepines. Dr. Walsh added that some studies^{4,5} have also found that nonbenzodiazepine hypnotics may be as effective when taken on a nonnightly basis as when taken on a nightly basis.

Meta-analyses^{6,7} have found that hypnotics are significantly efficacious in reducing sleep latency, increasing total sleep time, reducing the number of awakenings during the night, and improving sleep quality.

Although hypnotics are typically prescribed for the short-term treatment of insomnia, a small percentage of patients are treated with hypnotics for a year or more. Currently, only one long-term trial⁸ has been conducted on the efficacy of a hypnotic. After 6 months

of treatment, eszopiclone, a benzodiazepine receptor antagonist, was found to be significantly more effective than placebo in improving sleep latency, increasing total sleep time, and decreasing awakenings after sleep onset. Patients treated with eszopiclone also rated their alertness as being significantly improved with treatment.

Side Effects Associated With Hypnotics

Dr. Walsh emphasized that while hypnotics are effective for treating insomnia, physicians need to be aware of the side effects. Hypnotics are highly dose-dependent, with headache, drowsiness, and dizziness considered to be the most common side effects.

Another occasional concern is rebound insomnia. Rebound insomnia may occur on the first night of treatment discontinuation. Rebound insomnia, Dr. Walsh said, can be simply avoided by tapering the dose over a couple of nights.

Residual sedation is also a common side effect with long-acting hypnotics. Dr. Walsh recommended prescribing short-acting hypnotics to avoid residual sedation, but added that with patients who are anxious or hyperaroused, the use of long-acting hypnotics may not be problematic.

Conclusion

Dr. Walsh concluded by emphasizing that while sedating antidepressants are commonly prescribed to treat insomnia, more research is needed on the safety and efficacy of antidepressants in nondepressed patients. Hypnotics have been found to be efficacious in the treatment of acute insomnia and may also be effective in the long-term treatment of chronic insomnia. Research is also being done with treatments that utilize γ -aminobutyric acid (GABA) agonists and GABA reuptake inhibitors as well as corticotropin-releasing hormone (CRH) antagonists and 5-HT₂ antagonists.

REFERENCES

- Walsh JK, Schweitzer PK. Ten-year trends in the pharmacological treatment of insomnia. *Sleep* 1999;22:371-375
- Balter MB, Uhlenhuth EH. The beneficial and adverse effects of hypnotics. *J Clin Psychiatry* 1991;52(suppl 7):16-23
- Wagner J, Wagner ML. Non-benzodiazepines for the treatment of insomnia. *Sleep Med Rev* 2000;4:551-581
- Hajak G, Bandelow B, Zulley J, et al. "As needed" pharmacotherapy combined with stimulus control treatment in chronic insomnia: assessment of a novel intervention strategy in a primary care setting. *Ann Clin Psychiatry* 2002;14:1-7
- Walsh JK, Roth T, Randazzo A, et al. Eight weeks of non-nightly use of zolpidem for primary insomnia. *Sleep* 2000; 23:1087-1096
- Nowell PD, Mazumdar S, Buysse DJ, et al. Benzodiazepines and zolpidem for chronic insomnia: a meta-analysis of treatment efficacy. *JAMA* 1997;278: 2170-2177
- Holbrook AM, Crowther R, Lotter A, et al. Meta-analysis of benzodiazepine use in the treatment of insomnia. *CMAJ* 2000; 162:225-233
- Krystal AD, Walsh JK, Laska E, et al. Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. *Sleep* 2003;26:786-787

Management of Daytime Sleepiness

Jonathan R. L. Schwartz, M.D., reported that even though a consensus statement for the treatment of narcolepsy has been published,¹ there is no real consensus among clinicians on how to treat excessive daytime sleepiness. Many physicians base their choice of treatment on previous therapeutic successes and/or failures. Since there is no standard by which to judge medication use, they may use too low a dosage of medication to optimally treat the patient, perhaps in an effort to avoid side effects they have seen in other patients.

Dr. Schwartz also stressed that some patients suffer from more than one type of sleep disorder (Figure 2). Therefore, patients may begin to see an improvement when treated for one disorder, only to find their condition worsen as other untreated conditions manifest themselves. Dr. Schwartz added that because of the possibility of multiple sleep problems, physicians should make nonpharmacologic treatment recommendations, such as proper

sleep hygiene, in addition to pharmacologic treatments.

Pharmacotherapy

In selecting an appropriate medication, the goal of treatment should be a significant improvement in daytime alertness that allows a patient to return to his or her normal daily functioning without the burden of serious side effects. Dr. Schwartz commented that physicians should emphasize that daytime medication is not a substitute for getting enough sleep and should explain to patients what to expect from treatment.

Amphetamines. Amphetamines, which were developed in the 1930s, are effective in maintaining wakefulness. Dr. Schwartz noted, however, that few large-scale controlled studies have been conducted with amphetamines, a deficiency that has resulted in poor documentation of the benefit-to-risk ratio.

Methylphenidate. Methylphenidate is another stimulant used in the treat-

ment of excessive sleepiness. As with amphetamines, few studies exist that examine the efficacy of methylphenidate in patients with excessive sleepiness. Methylphenidate is more commonly studied as a treatment for attention-deficit/hyperactivity disorder.

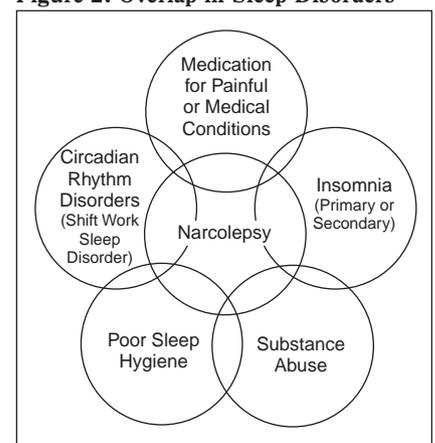
Pemoline. Pemoline, previously used as an entry-level stimulant, is seldom prescribed to patients due to the risk of hepatotoxicity.² And while the risk with pemoline is rare, hepatotoxicity can be fatal, explained Dr. Schwartz.

Modafinil. Modafinil, which became available in the United States in 1999, is the most widely studied treatment for excessive sleepiness. Studies have found modafinil to be an effective treatment not only for narcolepsy³ but also for ongoing sleepiness in patients with obstructive sleep apnea treated with nasal continuous positive airway pressure (CPAP).⁴

Dr. Schwartz added that modafinil is the only therapy that has received a formal treatment indication for sleepiness associated with shift work sleep disorder and persistent sleepiness despite CPAP therapy in sleep apnea. Several studies^{3,5,6} have found modafinil to have significantly superior benefit-to-risk ratio and efficacy and safety profiles when compared with placebo.

γ -Hydroxybutyric Acid. γ -Hydroxybutyric acid (GHB), marketed as sodium oxybate, was approved in 2002

Figure 2. Overlap in Sleep Disorders



for the treatment of cataplexy. It is a liquid medication and is usually dosed at bedtime and in the middle of the night. GHB may also be effective in treating daytime sleepiness. Studies^{7,8} indicate that although sleep time remains unchanged, sleep appears to be less fragmented and symptoms of daytime sleepiness are alleviated in many patients treated with GHB.

Follow-Up Care for Sleep Disorders

Dr. Schwartz advised physicians to follow up with patients during the first few weeks of treatment to assess efficacy and patient adherence to medication as well as examine patients for potential side effects. After the initial follow-up, if patients are significantly improved, physicians should follow-up with patients at least every 6 months to gauge the efficacy of the medication and to screen for other sleep disorders that may have become apparent.

When treating a patient with the traditional stimulants (amphetamines and methylphenidate), physicians should watch carefully for side effects. The most common ones are related either to the nervous system (e.g., headache, tremor, anxiety, or mood disturbances) or to the cardiovascular system (e.g., blood pressure problems, arrhythmia, or, occasionally, exacerbation of angina). Patients may develop a tolerance for these medications especially when given at high doses.

Conclusion

First and foremost, the appropriate diagnosis of excessive sleep needs to

be made before pharmacologic treatment is prescribed, concluded Dr. Schwartz. After initiating an appropriate treatment plan, physicians should follow-up with patients to ensure that a medication is effective and safe and that the treatment plan, including sleep hygiene measures, is being followed.

REFERENCES

1. Littner, M, Johnson SF, McCall WV, et al. Practice parameters for the treatment of narcolepsy: an update for 2000. *Sleep* 2001;24:451-466
2. Pratt DS, Dubois RS. Hepatotoxicity due to pemoline (Cylert): a report of two cases. *J Pediatr Gastroenterol Nutr* 1990;10: 239-241
3. US Modafinil in Narcolepsy Multicenter Study Group. Randomized trial of modafinil as a treatment for the excessive daytime somnolence of narcolepsy. *Neurology* 2000;54:1116-1175
4. Schwartz JRL, Hirshkowitz M, Erman MK, et al. Modafinil as an adjunct therapy for daytime sleepiness in disruptive sleep apnea: a 12-week, open-label study. *Chest* 2003;124:2192-2199
5. Beusterien KM, Rogers AE, Walsleben JA, et al. Health-related quality of life effects of modafinil for treatment of narcolepsy. *Sleep* 1999;22:757-765
6. Mittler MM, Harsh J, Hirshkowitz M, et al. Long-term efficacy and safety of modafinil (Provigil) for the treatment of excessive daytime sleepiness associated with narcolepsy. *Sleep Med* 2000;1: 231-243
7. Mamelak M, Scharf MB, Woods M. Treatment of narcolepsy with gamma-hydroxybutyrate: a review of clinical and sleep laboratory findings. *Sleep* 1986;9:285-289
8. Scharf MB, Brown D, Woods M, et al. The effects and effectiveness of gamma-hydroxybutyrate in patients with narcolepsy. *J Clin Psychiatry* 1985;46:222-225

Drug Names: methylphenidate (Ritalin, Concerta, and others), modafinil (Provigil), pemoline (Cylert), sodium oxybate (Xyrem), zaleplon (Sonata), zolpidem (Ambien).

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For the CME Posttest for this article, see pages 211-212.



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1. **The ultradian process is hypothesized to be:**
 - a. The amount of prior sleep and waking that determines a person's level of sleepiness
 - b. Organization of sleepiness and wakefulness by light and dark cycles
 - c. The cycles of rapid eye movement (REM) and non-REM sleep
 - d. None of the above
2. **All of the following are factors that may contribute to shift work sleep disorder *except*:**
 - a. Increase in age
 - b. The existence of an underlying sleep disorder
 - c. Self-medication with caffeine or alcohol
 - d. Working long daytime shifts
3. **Studies have found that about _____% of full-time U.S. workers work shifts, and _____ who work rotating daytime shifts reported trouble falling asleep compared with those who work a fixed time.**
 - a. 15; many
 - b. 3; very few
 - c. 60; many
 - d. 75; very few
4. **Little is known about the short-term use of hypnotics in the treatment of insomnia.**
 - a. True
 - b. False
5. **Physicians should first follow up with patients prescribed medication for sleepiness after:**
 - a. 5 days
 - b. 6 months
 - c. A few weeks
 - d. 1 year

Answer to Pretest: 1. b



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Circle the one correct answer for each question.

- 1. a b c d
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