

Patient Identification

Michael J. Thorpy, MD; Joseph A. Lieberman III, MD, MPH;
Thomas Roth, PhD; and Glenda S. Owens, RPh, MHA, CDM

Abstract

The homeostatic sleep drive and circadian arousal, each opposing the other, form the neurobiological bases of the sleep and wake states. Many factors can and do disrupt this cycle. Yet, excessive daytime sleepiness is not only common, and it often goes unrecognized. It can contribute to accidents, produce or exacerbate health conditions, reduce efficiency and productivity, interfere with social relationships, and diminish quality of life.

The spectrum of common sleep disorders includes circadian rhythm changes, shift-work requirements, obstructive sleep apnea, narcolepsy, and difficulty in initiating or maintaining sleep, also known as insomnia. In many cases, however, sleep deprivation is the choice of the patient, chosen in response to long commutes, academic rigor, or occupational matters. Regardless of the sleep disorder that a patient has, good sleep behavior or “sleep hygiene” is essential.

(*Am J Manag Care.* 2007;13:S132-S139)

Despite the high prevalence of excessive daytime sleepiness (EDS), it is still underrecognized and undertreated, despite the physical, mental, social, public health, and safety consequences. It can lead to or exacerbate health conditions, contribute to accidents, reduce efficiency and productivity, interfere with social relationships, and diminish quality of life. Therefore, EDS is a societal as well as a personal problem, with significant costs to the healthcare system, the workplace, and the wider society.

The purpose of this article is to delineate some of the ways to identify patients with EDS, show how the condition affects daily functioning, and evaluate the available pharmacologic and nonpharmacologic treatment methods. A case study will illustrate an approach to the problem, some of the clinical reasoning, and recommended treatment.

Physiological Basis of Sleep and Wakefulness

Although the function of sleep is not fully understood, the neurobiological basis of the sleep and wake states has been fairly well elucidated. Two major, opposing factors are at work: the homeostatic sleep drive and the circadian arousal response.^{1,2} The homeostatic sleep drive is at its nadir in the morning when after having slept, when it immediately begins to increase, and it rises over the course of the period of wakefulness. Sleep does not typically occur during the day because of the opposing effect of the circadian arousal signal, which also rises over the course of the day, and the result is a relatively even level of alertness. Alertness does vary during the day, with peaks about 3 hours after awakening and in the early evening. Most people have felt a mid-afternoon dip in alertness. Being overly tired in the early evening is not desirable, and people who fall asleep then, often with the excuse of “a busy day at work,” may be experiencing excessive sleepiness. As the arousal signal sharply diminishes at night with the secretion of melatonin, the sleep drive takes over, and sleep occurs, resetting the drive to its low level by morning.

The locus of circadian cycling, “the biological clock,” resides in the suprachiasmatic nucleus of the brain. The hypothalamus and the thalamus are integrally involved in wakefulness.¹ Neurons in the brainstem, hypothalamus, and basal forebrain cause arousal in the cerebral cortex

Address correspondence to: Michael J. Thorpy, MD, Professor of Neurology, Albert Einstein College of Medicine, Montefiore Medical Center, 111 East 210th St, Bronx, NY 10467. E-mail: thorpy@aecom.yu.edu.

and thalamus. During sleep, gamma-aminobutyric acid-containing neurons inhibit these cells. Arousal and sleep-inducing circuits inhibit each other, with sharp transitions, resulting in discrete sleep and wake states. This switch is stabilized by hypocretin (orexin) neurons in the lateral hypothalamus.

Excessive Sleepiness Versus Fatigue

Given the biological sleep drive and the brain circuits for arousal, it is important to distinguish excessive sleepiness as a pathologic condition from a state of fatigue.^{3,4} Sleepiness is a normal function, based on time of day and circadian phase. A mid-afternoon lull or outright sleepiness at night are normal. Pathological or “excessive” sleepiness is a condition in which sleepiness interferes with activities of daily living, such as work, child care, or driving a car.

Fatigue is a state of tiredness, not a drive for sleep (ie, without the excessive sleepiness).^{5,6} A problem arises when people complain about fatigue but really mean sleepiness. They often do not make the distinction and just present with the final common pathway complaint of “I’m tired all of the time.” Physicians need to be aware of how patients present and what terms they may use for what amounts to excessive sleepiness. They then have to distinguish whether a patient is fatigued or sleepy.

Of course, fatigue and excessive sleepiness can coexist. A medical illness, for example, can cause either or both.⁷ If a person has fatigue, it is worth looking for an underlying cause, which may be as obvious as prolonged physical or mental activity. If a patient is sleepy during the day, one must consider the factors affecting nocturnal sleep and what else may be causing the pathologic daytime sleepiness, such as a medical illness, behavioral factors, or a specific sleep disorder like obstructive sleep apnea (OSA).

A patient with primary insomnia presents an interesting example of fatigue without sleepiness.⁸ While a lack of sleep at night may cause daytime fatigue and tiredness, it is the same pathologic mechanism that prevents sleep initiation at night that keeps the person from falling asleep at inappropriate times during the day. Still, the person is not fully refreshed and may perform poorly from lack of sleep. On the other hand, disorders that fragment nighttime sleep, such as OSA or periodic limb

movement disorders, lead a person to have episodes of “microsleep” or unplanned naps.

Signs and Symptoms of Sleep Disturbance

EDS interferes with normal activities, possibly resulting in episodes of microsleep during waking hours, trouble waking up and staying awake, and unrefreshing sleep.^{7,9} Patients often present with fairly vague symptoms and may complain of tiredness, fatigue, lack of attention or concentration, lack of motivation, or making more mistakes at work. Patients may also say they wake up feeling unrefreshed. Clinicians should be aware that those general statements may imply excessive sleepiness. A patient may also report falling asleep at inappropriate times, such as on a bus to work or even while driving.

Signs of excessive sleepiness are rarely seen in a physician’s office. However, if a patient is asleep in the waiting room or falls asleep when left alone in an examination room, it is a good sign of excessive sleepiness. Ptosis and pupillary instability may also indicate an extreme state.¹⁰

EDS can be misdiagnosed as depression based on complaints of lack of energy or motivation, poor concentration, memory disturbances, and a reduced interest in life. Patients may be inappropriately prescribed a selective serotonin-reuptake inhibitor when the primary problem is really EDS.⁹

Assessing Sleep Quality in the Primary Care Setting

Because physicians and patients may both think of sleepiness as normal in today’s society, it falls on the primary care physician (PCP) to recognize the need to raise and evaluate the issue. Since many people are somewhat anxious and therefore more alert while at a physician’s office, the PCP will probably miss a sleep problem unless he or she specifically asks. Therefore, every patient should be asked these 2 simple questions: (1) How well are you sleeping? and (2) How alert are you across the day?

To determine if a patient has a significant impairment of alertness, a simple but slightly more detailed interview should reveal the problem.

1. Do you have difficulty falling asleep or remaining asleep at night?
2. Do you snore loudly or have gasping, choking episodes, or cessation of breathing at night?

3. Do you have discomfort in your legs that causes you to move them around in bed or at rest?
4. Has your bed partner said that your legs jerk while you are asleep at night?
5. Are you often very restless during sleep at night?
6. Do you have frequent nightmares?
7. Do you awaken feeling unrefreshed in the morning?
8. Are you often sleepy, fatigued, or tired during the daytime?
9. Do you doze in front of the TV or when reading?
10. Have you ever fallen asleep while driving?

This set of interview questions may appear to be just another onus on the already overburdened PCP, but medical literature emphasizes that given the extent and seriousness of potential negative outcomes of EDS, it serves the patient's health well to evaluate sleep issues.^{7,9}

Also, the Epworth Sleepiness Scale (ESS) may be useful to the clinician. It is a questionnaire that is quick and simple to administer and score in a primary care setting. This tool rates a patient's level of daytime sleepiness.¹¹ The standardized ESS scale results in an easily interpreted score that lets a physician quickly distinguish normal subjects from ones who may be diagnosed with various sleep disorders. ESS scores have been validated in patients with OSA, narcolepsy, and idiopathic hypersomnia. (Additional information on the ESS can be found in the *Managed Care Considerations* section of this supplement.)

Finally, simple observation may be helpful in detecting excessive sleepiness. Patients are usually alert while seeing a physician, but observing them in the waiting room may provide valuable information if they doze off there. The same may happen if they are left alone in an examination room for a while.

Causes of Excessive Sleepiness: Presentations and Underlying Etiologies

Causes of excessive sleepiness may be behavioral, medical, or primary sleep disorders. Behavioral etiologies mainly relate to sleep deprivation (voluntary sleep restriction) and/or irregular timing of sleep (circadian rhythm not synchronized

with the desired sleep-wake cycle, as in shift workers).⁹ Medical causes such as Parkinson's disease (PD), other central nervous system or metabolic and somatic diseases, movement disorders, chronic pain syndromes, psychiatric disorders, and side effects of a wide variety of medications are manifold.^{7,8} OSA, narcolepsy, insomnia, and shift-work sleep disorder (SWSD) are some examples of primary sleep disorders.⁷

According to sleep researcher Thomas Roth, PhD, nocturia may accompany disturbed sleep but is usually not the cause of it. If the patient awakes during the night, he or she may then go to the bathroom. But once the sleep disorder is corrected, he or she may sleep through to morning. If there is no sleep disorder and if one awakes to urinate, sleep is generally not disturbed much, and the person can get back to sleep relatively easily.

Physicians sometimes treat the obvious signs and symptoms and do not recognize the underlying sleep disturbance. The clinician should be aware that patients often do not complain of *excessive sleepiness* but may use terms such as *tiredness*, *fatigue*, or *lack of energy*.⁹ Other tip-offs may be complaints of the consequences of sleepiness (eg, difficulty concentrating or irritability) (**Table 1**).

Common Sleep Disorders

As listed by Thorpy,⁷ various common sleep disorders can be found in **Table 2**.

Insomnia. Insomnia, defined as difficulty in initiating or maintaining sleep, is more prevalent in women, the unemployed, and the elderly.¹³ Diagnosed or not, it is linked to a number of health problems, including comorbid physical conditions and psychiatric disorders. The National Health Interview Survey reports that people who sleep 7 or 8 hours per night make fewer doctor office visits and spend less days in the hospital than do those who sleep either more or fewer hours. Yet, according to one report, only about 5% of the more than 65 million persons with insomnia in the United States saw their doctor specifically for that complaint, and 69% did not mention insomnia when seeing their physicians for other reasons.¹² In another study of people with insomnia, more than half of their PCPs had no idea that the patient had problems sleep-

ing.¹² It is here, especially, that PCP vigilance can be invaluable.

SWSD. Almost 20% of the American workforce works alternative schedules that are either permanent or rotating, and, of those, 32% have symptoms that fit the minimum criteria for SWSD,¹³ a disorder of excessive sleepiness and/or insomnia caused by misalignment of the sleep-wake schedule and a person's circadian sleep-wake patterns. Night shifts are primarily composed of 4 occupational groups: those in public safety, including police and firefighters; healthcare workers; global workers manning telephones in far-flung time zones; and newspaper publishers and other graveyard-shift workers. The problem with SWSD is that it cannot only mask other symptoms, but precipitate them. In addition, SWSD is a risk factor for such comorbidities as depression and breast cancer, gastrointestinal ulcers, and heart disease.^{14,15}

Medical interns and residents subjected to long hours of work are considered vulnerable to SWSD. An early study found that interns reading electrocardiograms made up to twice the number of errors after working unrelieved for 24 hours or more than after a night's sleep.¹⁶ More recent studies have reported that, during simulated surgeries, surgical residents made up to twice the number of errors after working overnight than after a full night's sleep. Although few would doubt that sleep deprivation could lead to substantial decrements in performance and cognition in physicians, it was not until recently that serious inquiries into a system that routinely deprives medical personnel of sleep have begun. Of all hospital-based trainees, interns (physicians in their first postgraduate year of medical education) normally work the greatest number of weekly hours, with shifts often extended beyond 24 hours. A study was conducted that compared the number of errors made by interns working 2 different shift types. One shift was the more traditional extended-hours shift and the other was the "interventional" schedule that reduced work hours. Not surprising, interns made 22% more errors of a serious nature in the traditional work schedule. Potentially serious mistakes that were intercepted occurred 37% more frequently in the traditional schedule. Although the costs of medical errors made in critical care by sleep-deprived interns were

■ **Table 1. Spectrum of Clinical Presentations Indicative of Excessive Sleepiness**

Fatigue	Poor memory	Automatic behavior
Low energy	Reduced concentration	Frequent accidents
Laziness	Reduced attention	Drowsiness
Apathy	Irritability	Sleep attacks
Lethargy	Poor performance in work/school	
Reprinted with permission from Reference 7.		

not calculated in this study, few would argue that certain errors will translate into costs as well as endangering the lives of patients.

OSA. In the general population, the prevalence of OSA, defined as abnormal sleeping respirations from repeated episodes of obstruction in the upper airway associated with cessation or diminution of breathing, is about the same as that of asthma or diabetes, clinically significant in about 2% of women and 4% of men.¹⁷⁻²⁰ The need to waken to reinnervate the upper airway disrupts their sleep, contributing to the EDS. Sufferers of OSA may, in addition to EDS, experience decreased libido, impotence, depression, and, although a less reliable symptom of sleep apnea than previously thought, morning headaches.^{18,20}

Diagnosis is not straightforward. When considering OSA in the primary care setting as the cause of excessive sleepiness, a useful sign is the patient's neck size, with a neck circumference >17 inches in a male increasing the likelihood of OSA.²¹ Similarly, a crowded oropharynx with large tonsils and a small airway or even enlarged adenoids should raise suspicion of OSA. The condition is not confined to the obese, the elderly, and the postmenopausal, as OSA occurs in children, young women, and people with asthenic physiques.^{18,22} The expectation that OSA favors the overweight man abets its underdiagnosis in women and children.¹⁸ Men do, in fact, predominate, but that may occur at puberty, because before puberty numbers are approximately equal between the sexes.²² Risk factors for sleep-disordered breathing (SDB) in children include enlarged tonsils and adenoids; secondary risk factors were found to include exposure to secondhand smoke, chronic

■ **Table 2. Common Sleep Disorders**

<p>Insomnia</p> <ul style="list-style-type: none"> Adjustment sleep disorder Psychophysiological insomnia Idiopathic insomnia Insomnia due to mental disorder Inadequate sleep hygiene Insomnia due to medical condition Insomnia due to drug or substance use/abuse <p>Sleep-related breathing disorders</p> <ul style="list-style-type: none"> Central sleep apnea syndrome Cheyne Stokes breathing pattern Obstructive sleep apnea syndrome Sleep-related hypoventilation/hypoxemic syndrome <p>Hypersomnia not due to a sleep-related breathing disorder</p> <ul style="list-style-type: none"> Narcolepsy Idiopathic hypersomnia <p>Circadian rhythm sleep disorders</p> <ul style="list-style-type: none"> Jet lag Shift work Delayed sleep phase <p>Sleep-related movement disorders</p> <ul style="list-style-type: none"> Restless legs syndrome Periodic limb movement sleep disorder Sleep-related leg cramps Sleep-related bruxism Sleep-related rhythmic movement disorder

Adapted with permission from Reference 7.

rhinitis, family history of snoring or SDB, obesity, and African-American race or ethnicity. Yet, many obese people do not suffer from OSA, and about one third of those with OSA are not obese.¹⁸ When OSA exists, however, it carries physiologic effects beyond EDS. The oxygen desaturation it engenders can provoke hypertension, right-sided heart failure, or polycythemia (the proliferation of red blood cells). In children, SDB has been associated with such behavior problems as attention-deficit hyperactivity disorder, with which some children may, in fact, present.²²

Many studies report poor correlation between suspected and proven sleep apnea.¹⁸ Likewise, sleep questionnaires are often discrepant with objective

measures. It is for these reasons that laboratory-conducted sleep studies, available for both adults and children, are required for positive diagnosis and determination of severity. Some people with OSA have measurably smaller and narrower upper airways than those without the disorder. Parallel to the smaller airways, they may have neck diameters of 17 inches or more.²⁰ Thus far, techniques such as cephalometric roentgenography, somnifluoroscopy, flow-volume curves, acoustic-reflection studies, and Valsalva's and Müller's maneuvers, used to evaluate upper-airway anatomy and determine candidacy for such surgeries as uvulopalatopharyngoplasty, have not been as predictive as hoped.¹⁸ By far, the best way to diagnose OSA with certainty is with an overnight polysomnogram.²⁰

Narcolepsy. In this sleep disorder, loss of the neuropeptide hypocretin (orexin), apparently through autoimmune activity, is associated with abnormal and displaced phenomena such as muscle paralysis that normally occurs only during rapid eye movement (REM) sleep.²³ Documented narcolepsy is uncommon, with prevalence—0.09%—that approximates those of multiple sclerosis and PD.¹⁸ Although narcolepsy can manifest at any age, its usual age of onset is during adolescence or early adulthood. After onset it may progress for a short time and then stabilize, although it rarely or never clears up completely. Unanticipated sleep attacks last from seconds to minutes, usually occurring during times of reduced stimulation, such as when watching television or passively listening in on a conference call.

Narcolepsy is also associated with cataplexy, sleep paralysis, and hallucinations occurring at sleep onset (hypnagogic) or on awakening (hypnopompic).¹⁸ Although fewer than half of patients with narcolepsy report having all of these ancillary symptoms, EDS may precede their appearance, sometimes by decades. Between 65% and 70% of patients with narcolepsy also have cataplexy, defined as a sudden loss of muscle tone usually triggered by strong emotion. Sleep paralysis, a total paralysis of the body or selective muscle groups (eg, jaw, leg), occurs in up to 60% of patients with narcolepsy. Lasting from seconds to minutes, it can be very disturbing. The hallucinations that can accompany narcolepsy are reportedly vivid and often

nightmarish and occur in 12% to 50% of patients. However, both sleep paralysis and hallucinations lurking on the frontiers of sleep have been reported in people who do not have narcolepsy.

Narcolepsy may have a genetic footprint, although nongenetic factors suggested through the increased risk of narcolepsy in first-degree relatives are also involved in this complex disorder.^{18,24} Many patients with narcolepsy carry a specific human leukocyte antigen (HLA) allele otherwise detected in less than 30% of people. However, although this linkage of HLA to disease is suggestive, it is neither necessary for nor predictive of the finding of narcolepsy. A variation in one gene cannot account for the spectrum of symptoms attributed to narcolepsy.

Narcolepsy is thought to be a reflection of disruptions in the normal boundaries among wakefulness, REM sleep, and non-REM sleep, which impair control of both REM and non-REM sleep.¹⁸ Relatively discrete components of the state of sleep become disordered, intruding inappropriately into wakefulness. Cataplexy and sleep paralysis are manifestations of the atonia of REM sleep, and hypnagogic and hypnopompic hallucinations are components of REM-related dreaming.

Psychiatric Conditions and Sleep. Although sleep disorders and depression commonly coexist in a person, some would not routinely consider depression a sufficient reason for EDS.¹⁸ Yet, depression can cause patients to increase their time needed to fall asleep, the amount of time between deciding to sleep and actually doing so.²⁵ Depression can also increase nighttime wakefulness and early-morning awakening, and decrease the slow-wave sleep occurring during the deep sleep of stages 3 and 4. The prevalence of depression is high in people with EDS, and EDS is a risk factor for depression.¹⁸ In any case, depression can certainly interfere with the quality of sleep, as can anxiety, dementia, and post-traumatic stress disorder (PTSD).²⁰

Dementia, particularly Alzheimer's disease, is associated with sleep disorders.²⁵ Patients with dementia tend to have lower sleep efficiency, the ratio of total sleep time to time in bed, and more daytime napping. Dementia also alters the lengths of the stages of sleep. No effective therapy especially for sleep disorders arising from dementia has yet been devised.

PTSD and other anxiety disorders, schizophrenia, and bipolar disorder can cause problems in initiating or maintaining sleep.²⁵ Also known as manic-depressive illness, bipolar disorder affects about 2.6% of the population older than the age of 18, typically developing late in adolescence or early in adulthood—although first symptoms have appeared in childhood as well as in later life.²⁶ The daily amount of sleep a patient believes he/she requires during a manic episode is scant—maybe 3 hours, maybe none—and episodes will last a week or longer. In depressive episodes, a patient may sleep too much or, ironically, again be unable to sleep. Medication decisions can be complex and further complicated by sudden fluctuations in the patient's response; the expertise of a psychiatrist may be needed.

Medical Conditions Affecting Sleep. As anyone who has ever had nasal congestion can attest, breathing disruptions are even more difficult when trying to sleep. People with chronic obstructive pulmonary disease (COPD) have dips in oxygenation of arterial blood at night, producing hypoxia and arousals from sleep.²⁵ Orthopnea, a form of dyspnea that allows comfortable breathing only when the patient is sitting erectly or standing, might understandably impair sleep. Trauma to the heart or head can produce a Cheyne-Stokes breathing pattern, which makes it difficult to sleep. Nicotine disrupts sleep in a similar manner. People who smoke have more sleep disturbances, more difficulty falling asleep, and an increased risk of sleep apnea than those who don't smoke.

PD begets sleep/wake dysfunction in 98% of those who have it.²⁷ In terms of EDS and other sleep events, it is difficult to separate the effects of PD pathophysiology from those of treatment with dopamine-agonist (DA) agents, which are discussed below. They may have urinary frequency and find it hard to turn in bed, thereby fragmenting sleep. Inability to initiate and maintain sleep, likely arising from neuropathologic PD manifestations, will surely amplify any EDS and sleep events that accompany DA agents.

Conditions such as asthma, arthritis, congestive heart failure, frequent nocturia, and any chronic pain can, if not frankly prevent sleep, at least interfere with its continuity.²⁰ Constipation, gastroesophageal reflux disease, and pruritic skin con-

ditions are not conducive to sleep, nor are such lower urinary tract disorders as benign prostatic hypertrophy or detrusor instability.²⁵ Along with all of its other aches and pains, and because of some of them, advancing age also tends to create or amplify sleep dysfunctions. In addition, older patients consume a daily average of 5 to 9 medications, and some of these can interfere with sleep or wakefulness.

Drug-induced EDS

Hypnotics. The best-studied drugs that cause hypersomnia are long-acting sedative-hypnotics such as barbiturates, benzodiazepines, and nonbenzodiazepine hypnotics.¹⁸ Although benzodiazepines will initially decrease sleep latency and fragmentation, in OSA patients they may increase the arousal threshold and thereby exacerbate sleep apnea or COPD.²⁰ Antihistamines or tricyclic antidepressants may cause drowsiness and are sometimes prescribed for insomnia.¹⁸ In fact, tricyclic antidepressants may cause increased limb movement and disruption of sleep.²⁰

DAs. EDS is a common side effect of dopamine-receptor agonists used to treat people with PD or restless legs syndrome (RLS). Since 1999, DAs have been implicated in EDS, defined as episodes of sudden-onset sleep resistant to protective measures and thus distinguishable from EDS.^{27,28} A group of European researchers who analyzed publications between 1999 and 2001 that discussed sleep attacks in patients with PD concluded that sleep attacks are a class phenomenon in up to 30% of patients taking DAs.²⁹ Anyone being treated with DA therapies, particularly those involving pramipexole, ropinirole, or pergolide, is at risk for sleepiness.

Other risk factors for sleep events include concurrent sedating drugs, high levels of dopamine, OSA, and poor sleep hygiene.²⁸ Notably, a link between EDS and sleep attack has never been verified. This implies that, even in the absence of an awareness of EDS, a person being treated with a DA may at any time have an abrupt and irresistible sleep episode.

RLS and DA Treatment. Investigation of sleep disturbances among RLS patients taking DAs is much more limited.²⁸ When DAs are used for RLS,

the dosages are generally lower than those used for PD. In one report, a patient with RLS continued to experience EDS and occasional sleep attacks until pergolide was replaced by pramipexole.

REFERENCES

1. Saper CB, Scammell TE, Lu J. Hypothalamic regulation of sleep and circadian rhythms. *Nature*. 2005;437:1257-1263.
2. Ebert B, Wafford KA, Deacon S. Treating insomnia: current and investigational pharmacological approaches. *Pharmacol Ther*. 2006;112:612-629.
3. Lichstein KL, Means MK, Noe SL, Aguillard RN. Fatigue and sleep disorders. *Behav Res Ther*. 1997;35:733-740.
4. Hossain JL, Ahmad P, Reinish LW, Kayumov L, Hossain NK, Shapiro CM. Subjective fatigue and subjective sleepiness: two independent consequences of sleep disorders? *J Sleep Res*. 2005;14:245-253.
5. Bailes S, Libman E, Baltzan M, Amsel R, Schondorf R, Fichten CS. Brief and distinct empirical sleepiness and fatigue scales. *J Psychosom Res*. 2006;60:605-613.
6. Vgontzas AN, Chrousos GP. HPA axis and sleep. <http://www.endotext.org/adrenal/adrenal31/adrenal31.htm>. Accessed October 10, 2007.
7. Thorpy MJ. Which clinical conditions are responsible for impaired alertness? *Sleep Med*. 2005;6(suppl 1):S13-S20.
8. Kushida CA. Countermeasures for sleep loss and deprivation. *Curr Treat Options Neurol*. 2006;8:361-366.
9. Black J, Duntley SP, Bogan RK, O'Malley MB. Recent advances in the treatment and management of excessive daytime sleepiness. *CNS Spectr*. 2007;12(2 suppl 2):1-16.
10. Bitsios P, Schiza SE, Giakoumaki SG, Savidou K, Alegakis AK, Sifakas N. Pupil miosis within 5 minutes in darkness is a valid and sensitive quantitative measure of alertness: application in daytime sleepiness associated with sleep apnea. *Sleep*. 2006;29:1482-1488.
11. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*. 1991;14:540-545.
12. 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.
13. Drake CL, Roehrs T, Richardson G, Walsh JK, Roth T. Shift work sleep disorder: prevalence and consequences beyond that of symptomatic day workers. *Sleep*. 2004;27:1453-1462.
14. Davis S, Mirick DK, Stevens RG. Night shift work, light at night, and risk of breast cancer. *J Natl Cancer Inst*. 2001;93:1557-1562.
15. Schernhammer ES, Laden F, Speizer FE, et al. Rotating night shifts and risk of breast cancer in women participating in the nurses' health study. *J Natl Cancer Inst*. 2001;93:1563-1568.
16. Landrigan CP, Rothschild JM, Cronin JW, et al. Effect of reducing interns' work hours on serious medical errors in intensive care units. *N Engl J Med*. 2004;351:1838-1848.
17. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med*. 1993;328:1230-1235.
18. Mahowald MW. What is causing excessive daytime sleepiness? Evaluation to distinguish sleep deprivation from sleep disorders. *Postgrad Med*. 2000;107:108-123.

19. **Finlayson TL, Moyer CA, Sonnad SS.** Assessing symptoms, disease severity, and quality of life in the clinical context: a theoretical framework. *Am J Manag Care.* 2004;10:336-344.
20. **O'Hollaren MT.** Basics in clinical practice: recognizing and treating sleep disorders. *Medscape Today.* September 8, 2006. <http://www.medscape.com/viewprogram/5967>. Accessed September 7, 2007.
21. **Davies RJ, Stradling JR.** The relationship between neck circumference, radiographic pharyngeal anatomy, and the obstructive sleep apnoea syndrome. *Eur Respir J.* 1990;3:509-514.
22. **Johnson EO, Roth T.** An epidemiologic study of sleep-disordered breathing symptoms among adolescents. *Sleep.* 2006;29:1135-1142.
23. **Chemelli RM, Willie JT, Sinton CM, et al.** Narcolepsy in orexin knockout mice. *Cell.* 1999;98:437-451.
24. **Chabas D, Taheri S, Renier C, et al.** The genetics of narcolepsy. *Annu Rev Genomics Hum Genet.* 2003;4:459-493.
25. **Vij S, Gentili A.** Sleep disorder, geriatric. *emedicine.* August 4, 2005. <http://www.emedicine.com/med/topic3179.htm>. Accessed September 11, 2007.
26. **Spearing M.** Bipolar disorder. National Institute of Mental Health, NIH Publication No. 3679, 2002. <http://www.nimh.nih.gov/publicat/bipolar.cfm>. Accessed September 10, 2007.
27. **Simuni T.** Diagnosis and management of Parkinson's disease. *Medscape Today.* August 30, 2007. <http://www.medscape.com/viewprogram/7698>. Accessed September 5, 2007.
28. **Plowman BK, Boggie DT, Morreale AP, et al.** Sleep attacks in patients receiving dopamine-receptor agonists. *Am J Health Syst Pharm.* 2005;62:537-540.
29. **Homann CN, Suppan K, Wenzel K, et al.** The Bradykinesia Akinesia Incoordination Test (BRAIN TEST), an objective and user-friendly means to evaluate patients with parkinsonism. *Mov Disord.* 2000;15:641-647.