Sleep Disorders

September 2017

Sleep-Related Breathing Disorders
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Deepa Burman, MD, FAAFP, FAASM, is a clinical assistant professor in the department of family medicine at the University of Pittsburgh Medical Center (UPMC). She is the director of the sleep program at the UPMC McKeesport Hospital; she also is director of resident research and scholarly activity and co-director of the obesity medicine track at UPMC McKeesport Family Medicine Residency Program. Dr Burman is board certified by the American Board of Family Medicine and has a certificate of added qualifications in sleep medicine; she also is a diplomate of the American Board of Obesity Medicine. Dr Burman serves on the American Board of Internal Medicine Sleep Medicine Test Writing Committee. She has been involved in several peer reviewed oral presentations and publications, and has been an invited speaker at family medicine conferences about sleep disorders and fatigue management in medical professionals. Dr Burman has authored book chapters on sleep disorders and other primary care topics.

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Foreword

I hope you slept well last night, enjoyed pleasant dreams, and awoke refreshed. Sleep is essential.

Shakespeare’s sleepless Prospero recognizes that although the real world will dissolve away, eventually life will be surrounded and completed by sleep (and death), “…We are such stuff / As dreams are made on, and our little life / Is rounded with a sleep….” (The Tempest, Act 4, Scene 1).

Similarly, Hamlet bemoans the unfairness of life as he contemplates sleep (and death), “…To die, to sleep, / To sleep, perchance to dream; ay, there’s the rub!” (The Tragedy of Hamlet, Prince of Denmark, Act 3, Scene 1).

Poor sleep plagues many of our patients, and all of us have at one time or another endured sleepless episodes that darken our outlook and affect our ability to function. This edition of FP Essentials™ addresses the common problem of sleep disorders.

Section One covers sleep-related breathing disorders. I was interested to read about the differences between obstructive and central sleep apnea, and to learn when to consider ordering a home sleep test instead of formal polysomnography in the sleep laboratory. Section Two discusses the links between insomnia and other diseases, and emphasizes the importance of cognitive behavioral therapy in managing this common but challenging disorder. Section Three addresses restless legs syndrome and provides useful management tips. Section Four focuses on shift work sleep disorder and jet lag, both of which disrupt circadian rhythms but often can be effectively managed with appropriately timed bright light exposure and oral melatonin.

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Karl T. Rew, MD, Associate Medical Editor
Assistant Professor, Departments of Family Medicine and Urology
University of Michigan Medical School, Ann Arbor

Learning Objectives

1. Recognize which patients are at risk for sleep-disordered breathing and obtain the appropriate type of sleep testing for them.
2. Advise patients about the advantages and disadvantages of the various options for managing obstructive sleep apnea, including positive airway pressure and mandibular advancement devices.
3. Apply the criteria from the International Classification of Sleep Disorders—Third Edition (ICSD-3), to diagnose chronic insomnia disorder.
4. Recommend cognitive behavioral therapy for insomnia (CBT-I) and brief behavioral treatment for insomnia (BBTI) as first-line treatments for insomnia disorders.
5. Test for iron deficiency anemia in patients with restless legs syndrome (RLS) and prescribe oral iron therapy when indicated.
6. Select and prescribe appropriate pharmacotherapy for patients with RLS.
7. Diagnose shift work sleep disorder and instruct patients about the risk of associated medical disorders and cognitive impairment.
8. Advise travelers about online calculators that can help them appropriately time their use of bright light and oral melatonin to minimize the effects of jet lag.
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Editorial Mission
The mission of FP Essentials is to provide practicing family physicians, family medicine residents, and other clinicians and trainees with high-quality, cost-effective educational content that emphasizes new advances in clinical practice.

Objectives
1. To provide learners with information on advances in clinical practice to aid them in providing up-to-date care for their patients.
2. To assist learners in preparing for the American Board of Family Medicine (ABFM) certification and recertification examinations. Each monthly edition of FP Essentials is part of a 9-year curriculum that presents topics with areas of emphasis similar to those on the ABFM examinations.
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4. To present the content of FP Essentials in both print and online formats, thus enabling learners to have access to information anywhere, anytime.

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1. More than half of moderate to severe obstructive sleep apnea in adults is attributable to which one of the following risk factors?
   - A. Enlarged tonsils.
   - B. Myotonic dystrophy.
   - C. Obesity.
   - D. Retrognathia.

2. For which one of the following patients, all of whom have frequent daytime sleepiness, would an unattended portable home sleep test be indicated?
   - A. A nurse with hypertension who frequently works night shifts.
   - B. A young patient with depression and suspected narcolepsy.
   - C. An elderly patient with coronary artery disease and congestive heart failure.
   - D. An obese diabetes patient with a high pretest probability of severe obstructive sleep apnea.

3. Which one of the following statements about alternatives to positive airway pressure therapy for managing obstructive sleep apnea (OSA) is true?
   - A. Acetazolamide reduces daytime sleepiness.
   - B. Bariatric surgery can improve OSA in patients with body mass index of 40 kg/m² or greater.
   - C. Custom-fabricated mandibular advancement devices are not covered by Medicare.
   - D. Mandibular advancement devices can be used in patients with 3 to 4 healthy teeth in each arch.

4. Which one of the following is the most common sleep disorder in the family medicine population?
   - A. Insomnia.
   - B. Narcolepsy.
   - C. Obstructive sleep apnea.
   - D. Restless legs syndrome.

5. Which one of the following is a risk factor for the development of insomnia?
   - A. Depression.
   - B. Higher socioeconomic status.
   - C. Male sex.
   - D. Younger age.

6. Which one of the following drugs is recommended management of restless legs syndrome?
   - A. Diphenhydramine.
   - B. Metoclopramide
   - C. Pramipexole.
   - D. Prochlorperazine.

7. Which one of the following is associated with a lower risk of shift work sleep disorder?
   - A. High sleep reactivity.
   - B. Male sex.
   - C. Postshift morning light exposure.
   - D. Resuming normal daytime activities on weekends.

8. Bright light for 3 to 6 hours during the start of a night shift is a reasonable management of shift work sleep disorder.
   - A. True.
   - B. False.
Pretest Answers

**Question 1:** The correct answer is C.
Approximately 60% of moderate to severe obstructive sleep apnea is attributable to obesity. See page 11.

**Question 2:** The correct answer is D.
Home sleep testing is appropriate for patients with all of the following: a high pretest probability of moderate to severe OSA; no comorbid conditions that may affect accuracy (eg, severe pulmonary disease, neuromuscular disease, congestive heart failure); and no clinical suspicion of other sleep disorders (eg, central sleep apnea, narcolepsy, periodic limb movement disorders, parasomnias, circadian rhythm sleep disorders); and in patients who cannot undergo full polysomnography because of immobility or critical illness. See Table 4.

**Question 3:** The correct answer is B.
In patients with obstructive sleep apnea (OSA) and severe obesity (body mass index of at least 40 kg/m²), bariatric surgery can be considered when conservative treatments have failed. Bariatric surgery can resolve or improve obstructive sleep apnea. See page 20.

**Question 4:** The correct answer is A.
Insomnia is the most common sleep disorder in the family medicine population. See page 22.

**Question 5:** The correct answer is A.
The most common cause of insomnia in patients evaluated by a physician is depression. See page 23.

**Question 6:** The correct answer is C.
Because of their favorable adverse effect profiles, nonergot dopamine agonists (eg, pramipexole, ropinirole) are the main pharmacotherapy options for restless legs syndrome. See page 31.

**Question 7:** The correct answer is B.
Risk factors for shift work sleep disorder include advancing age, female sex, and postshift morning light exposure such as may occur during a long commute home or morning social obligations. See page 34.

**Question 8:** The correct answer is A.
Bright light for 3 to 6 hours during the start of shift can be helpful in managing shift work sleep disorder. See page 35.
Key Practice Recommendations

1. Patients with unexplained daytime sleepiness should be assessed for suspected obstructive sleep apnea.

2. For patients with chronic insomnia, recommend cognitive behavioral therapy for insomnia as the initial treatment.

3. In patients with symptomatic restless legs syndrome (RLS) and a serum ferritin level less than 50 ng/mL, prescribe iron replacement therapy.

4. For patients with RLS who require drug treatment, prescribe a dopamine agonist (ie, pramipexole, ropinirole) or a gabapentinoid (ie, gabapentin, pregabalin, gabapentin enacarbil). (This is an off-label use of pregabalin.)

5. For patients with jet lag or shift work sleep disorder, prescribe or recommend use of melatonin and light therapy. (This is an off-label use of melatonin.)

6. For patients with shift work sleep disorder and excessive sleepiness, consider prescribing modafinil or armodafinil.

Evidence Ratings and Sources

1. Evidence rating: SORT C
   Website: http://annals.org/aim/article/1892620/diagnosis-obstructive-sleep-apnea-adults-clinical-practice-guideline-from-american

2. Evidence rating: SORT A
   Website: http://www.aasmnet.org/jcsm/ViewAbstract.aspx?pid=27286

3. Evidence rating: SORT C
   Website: http://journals.sagepub.com/doi/pdf/10.1177/1054773810388557

4. Evidence rating: SORT A
   Source: Sleep, reference 167.
   Website: https://academic.oup.com/sleep/article/35/8/1039/2558916/The-Treatment-of-Restless-Legs-Syndrome-and

5. Evidence rating: SORT A
   Source: Sleep Med Rev.
   Website: http://www.smrv-journal.com/article/S1087-0792(08)00044-0/fulltext

6. Evidence rating: SORT B
   Website: http://www.smrv-journal.com/article/S1087-0792(12)00025-1/fulltext
Sleep Disorders

### Strength of Recommendation Taxonomy (SORT)

<table>
<thead>
<tr>
<th>Strength of Recommendation</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>• Recommendation based on consistent and good-quality patient-oriented evidence.¹</td>
</tr>
<tr>
<td>B</td>
<td>• Recommendation based on inconsistent or limited-quality patient-oriented evidence.¹</td>
</tr>
<tr>
<td>C</td>
<td>• Recommendation based on consensus, usual practice, opinion, disease-oriented evidence,² or case series for studies of diagnosis, treatment, prevention, or screening.</td>
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</tbody>
</table>

¹Patient-oriented evidence measures outcomes that matter to patients: morbidity, mortality, symptom improvement, cost reduction, and quality of life. Disease-oriented evidence measures intermediate, physiologic, or surrogate end points that may or may not reflect improvement in patient outcomes (eg, blood pressure, blood chemistry, physiologic function, pathologic findings).  

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Sleep-related breathing disorders or sleep-disordered breathing are characterized by abnormal respiration during sleep. They are grouped into obstructive sleep apnea (OSA), central sleep apnea, sleep-related hypoventilation, and sleep-related hypoxemia disorder. OSA is a common disorder encountered in the family medicine setting that is increasingly being recognized because of the obesity epidemic and greater public and physician awareness. OSA is characterized by recurrent episodes of partial or complete closure of the upper airway resulting in disturbed breathing during sleep. It is associated with decreased quality of life and significant medical comorbidities. Untreated OSA can lead to a host of cardiovascular diseases including coronary artery disease, stroke, and atrial fibrillation. Patients who report symptoms of snoring, witnessed apneas, or daytime sleepiness should be screened for sleep apnea. In-laboratory attended diagnostic polysomnography or portable home sleep testing can be used to diagnose sleep apnea. Continuous positive airway pressure (CPAP) therapy is the first-line treatment for OSA in adults. Other modalities include mandibular advancement devices, surgery, or upper airway stimulation therapy. Adjunctive therapy should include weight loss in overweight patients, avoidance of sedatives and alcohol before sleep, and possibly positional therapy.

Case 1. Chad is a 45-year-old man, who comes to your office reporting that he has been falling asleep during meetings at work. He goes to sleep at 10 pm and gets up at 6 am. He does not drink caffeinated beverages. Body mass index is 29 kg/m^2 and he is in good physical condition except for poorly controlled hypertension. He does not report symptoms of depression. Chad’s bed partner has not noticed apneas but states that Chad snores “loudly enough to shake the windows out of their frames.”

Sleep apnea is a common disorder characterized by abnormalities of respiration during sleep, causing patients to temporarily discontinue or decrease breathing during sleep.

Types
In the International Classification of Sleep Disorders—Third Edition (ICSD-3), the sleep-related breathing disorders are divided into four groups:

- Obstructive sleep apnea (OSA) disorders,
- Central sleep apnea syndromes,
- Sleep-related hypoventilation disorders, and
- Sleep-related hypoxemia disorder.

The diagnosis often is based on the predominating disorder shown on a sleep study; however, this may vary from night to night as well as over time in individual patients.

Table 1 defines common terms used in a sleep study as they relate to various sleep disorders.

OSA Disorders

Definition. Obstructive sleep apnea disorders are characterized by 5 or more episodes/hour of complete or partial upper airway closure during sleep, with respiratory effort during at least a portion of the event, as measured by the apnea-hypopnea index (AHI). The AHI also determines the severity of OSA in adults:

- Normal: fewer than 5 events/hour,
- Mild OSA: 5 to 14.9 events/hour,
- Moderate OSA: 15 to 29.9 events/hour, and
- Severe OSA: 30 or more events/hour.

Pathophysiology. The pathophysiology of upper airway narrowing in OSA is multifactorial. A common underlying mechanism is excessive bulk of soft tissues coupled with craniofacial anatomy that reduces the cross-sectional area of the upper airway lumen.

Risk factors. The major predisposing factor for OSA is excess body weight. Approximately 60% of moderate to severe OSA is attributable to obesity. In a longitudinal analysis of a subset (n = 690) of the Wisconsin Sleep Cohort with a 4-year follow-up, a 10% increase in weight was associated with sixfold greater odds of developing sleep-disordered breathing among individuals initially without the condition.

Obstructive sleep apnea also can occur in non-obese patients, often because of structural abnormalities, such as a maxillomandibular malformation.
Sleep Disorders

(retrognathia or micrognathia) or adenotonsillar enlargement. Structural etiologies are a common cause of OSA in Asian patients. Postmenopausal women have a 3 times higher risk of moderate or severe OSA than premenopausal women, independent of age, body mass index (BMI), and other potential confounding factors. Endocrine disorders, such as acromegaly and hypothyroidism, are risk factors for OSA, but there are no clear data on the value of endocrine testing in patients with OSA. Some evidence suggests that sleep apnea in patients with hypothyroidism may be reversible with adequate treatment.

Obstructive sleep apnea is common in patients with neurologic disorders that affect peripheral muscles, such as myotonic dystrophy. Children with Down syndrome are at increased risk of OSA, with a shown prevalence of 31% to 83%. The characteristic facial features of Down syndrome—midfacial and mandibular hypoplasia, relative macroglossia, a shortened palate, and narrowed nasopharynx—are all anatomic risk factors for OSA; hypotonia also may contribute to airway collapse during sleep.

In patients with HIV infection, OSA risk increases when weight gain and lipodystrophy associated with the use of highly active antiretroviral therapy lead to impingement on the upper airway. In addition, inflammation related to HIV infection increases OSA risk. Obstructive sleep apnea often is aggravated by alcohol consumption or use of sedating drugs before sleep. Zolpidem and triazolam can decrease nocturnal oxygen saturation in patients with OSA.

Table 2 shows factors that increase the risk of sleep apnea as well as key questions and observations for evaluating high-risk patients.

### Screening recommendations

Guideline recommendations regarding screening for OSA vary. The American College of Physicians (ACP) 2013 clinical practice guideline suggests clinicians target clinical assessments to individuals with unexplained daytime sleepiness.

<table>
<thead>
<tr>
<th>Terminology</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Apnea</td>
<td>A cessation of airflow (≥90% decrease in oral thermistor signal compared with baseline) of a minimum duration of 10 seconds in adults and two breaths in children. Apneas are classified as obstructive, mixed, or central, based on the pattern of respiratory effort</td>
</tr>
<tr>
<td>Hypopnea</td>
<td>A reduction in airflow (≥30% drop in signal excursion) of a minimum duration of 10 seconds in adults and two breaths in children. The reduction in airflow must be accompanied by a ≥3% desaturation and an arousal or a ≥4% desaturation (Medicare criteria)</td>
</tr>
<tr>
<td>Respiratory effort-related arousal</td>
<td>A sequence of breaths characterized by a decrease in flow of &lt;30%, or increasing respiratory effort (esophageal manometry), inspiratory flattening in the nasal pressure or PAP device flow channel, or an increase in end-tidal PCO₂ (in children) leading to an arousal from sleep</td>
</tr>
<tr>
<td>Apnea-hypopnea index</td>
<td>Number of apneas and hypopneas recorded per hour of sleep</td>
</tr>
<tr>
<td>Respiratory disturbance index</td>
<td>Number of apneas and hypopneas per hour of recording time on a portable home sleep test</td>
</tr>
<tr>
<td>Periodic limb movement index</td>
<td>Number of periodic limb movements per hour of sleep</td>
</tr>
<tr>
<td>Phase delay</td>
<td>Moving bedtime and wake time later in the day</td>
</tr>
<tr>
<td>Phase advance</td>
<td>Moving bedtime and wake time earlier in the day</td>
</tr>
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</table>

PAP = positive airway pressure.

The United States Preventive Services Task Force (USPSTF) states that current evidence is insufficient to assess the balance of benefits and harms of screening for OSA in asymptomatic adults.\textsuperscript{20} The American Academy of Sleep Medicine (AASM) recommends that physicians ask all patients, especially high-risk populations, about signs and symptoms of OSA.\textsuperscript{4,21}

The ACP recommends polysomnography in patients with suspected OSA.\textsuperscript{22} For patients without serious comorbid conditions, portable home sleep testing is recommended when polysomnography is not available. The AASM recommends that routine health maintenance examinations include questions about OSA and an assessment for risk factors, including obesity, retrognathia, and comorbid health conditions such as hypertension, coronary artery disease, and arrhythmias.\textsuperscript{4} Positive findings should trigger a comprehensive sleep evaluation.

Laboratory blood testing typically is not indicated unless a particular condition such as hypothyroidism is suspected. Patients with severe nocturnal hypoxemia may have polycythemia and elevation of serum bicarbonate levels.\textsuperscript{23}

**Diagnosis.** In addition to the in-laboratory attended sleep study (diagnostic polysomnography), which is considered the gold standard for diagnosis of OSA, the portable home sleep test is now included in the diagnostic criteria for adult OSA.\textsuperscript{4}

*Figure 1 shows results of a polysomnography demonstrating OSA associated with severe hypoxemia.*

### Central Sleep Apnea Syndromes

**Definition.** The central sleep apnea syndromes are characterized by reduction or cessation of airflow because of absent or reduced respiratory effort.\textsuperscript{1} Central apneas or hypopneas may occur in a cyclical fashion (Cheyne-Stokes respiration) or intermittent fashion.

**Pathophysiology.** In healthy individuals, PaCO\textsubscript{2} rises by 2 to 8 mm Hg during nonrapid eye movement sleep, likely because of loss of the wakefulness drive, reduction of the hypercapnic and hypoxic ventilatory drives, and increased upper airway resistance. During wakefulness, hypocapnia does not cause cessation of breathing because of the presence of the wakefulness stimulus to breathing, but during nonrapid eye movement sleep, ventilation depends completely on metabolic control. If the PaCO\textsubscript{2} falls below a value called the apnea threshold that is characteristic for each individual, a central apnea occurs.\textsuperscript{24} Occasional central apneas are normal.

**Risk factors.** Central sleep apnea commonly is seen in patients with Chiari malformation, acute ischemic stroke, multiple system atrophy, and congestive heart failure, and with use of opioid drugs.\textsuperscript{1,25-27}

**Diagnosis.** Central sleep apnea is diagnosed using a sleep study when five or more central apneas or hypopneas occur per hour of sleep with symptoms, in the absence of Cheyne-Stokes respiration, discussed below.\textsuperscript{1} The number of central sleep apneas or hypopneas should be greater than 50% of the total number of apneas and hypopneas.

The most important predisposing factors for central sleep apnea are the presence of congestive heart failure, stroke, and possibly renal failure.\textsuperscript{1}

**Cheyne-Stokes respiration.** Cheyne-Stokes respiration is a breathing pattern characterized by three or more consecutive cycles of recurrent central apneas or central hypopneas, alternating with a respiratory phase exhibiting a crescendo-

---

**Table 2**

<table>
<thead>
<tr>
<th>Comorbid health conditions associated with increased risk of OSA</th>
<th>Key questions and observations during examination of high-risk patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>Breathing pauses</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Daytime sleepiness</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>Frequent morning headaches</td>
</tr>
<tr>
<td>High-risk occupation/commercial driving</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Nocturnal arrhythmias</td>
<td>Obesity</td>
</tr>
<tr>
<td>Obesity</td>
<td>Retrognathia</td>
</tr>
<tr>
<td>Preoperative clearance for bariatric surgery</td>
<td>Snoring</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td></td>
</tr>
<tr>
<td>Refractory hypertension</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
</tr>
</tbody>
</table>

\textit{OSA = obstructive sleep apnea.}

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decrescendo pattern of flow, with a cycle length that typically lasts 45 to 60 seconds.\textsuperscript{1,28}

The prevalence of Cheyne-Stokes respiration in the setting of chronic congestive heart failure has been shown to be 25% to 40%.\textsuperscript{1,29} Central sleep apnea with Cheyne-Stokes respiration has been shown to occur in 26% to 50% of patients during the acute period after stroke.

\textbf{Obesity Hypoventilation Syndrome}

During the past 30 years, the prevalence of obesity has markedly increased in the United States, leading to many comorbidities associated with excess weight.

Obesity hypoventilation syndrome is the triad of obesity, daytime hypoventilation, and sleep-disordered breathing, in the absence of an alternative neuromuscular, mechanical, or metabolic explanation.\textsuperscript{1,30}

\textbf{Diagnosis.} Diagnosing obesity hypoventilation syndrome requires documentation of daytime hypoventilation (\(P_{aCO_2}\) greater than 45 mm Hg), in the presence of obesity (ie, BMI greater than 30 kg/m\(^2\) for adults; BMI greater than the 95th percentile for age and sex for children).\textsuperscript{1}

In addition, the hypoventilation cannot be fully attributed to an underlying cardiopulmonary or neurologic disease. Central nervous system depressants, such as alcohol, anxiolytics, and hypnotics, may further worsen respiratory impairment.\textsuperscript{1,31}

Therapy directed at improving sleep-disordered breathing may be effective in reversing daytime respiratory failure.\textsuperscript{30} However, it is not universally successful, and information regarding longer-term clinical outcomes is limited. Weight reduction strategies are necessary to reduce comorbid conditions and improve quality of life, but data regarding their effectiveness and durability in obesity hypoventilation syndrome are sparse.

\textbf{Office-Based Tools}

\textbf{Questionnaires, Scores, and Classifications}

The STOP-Bang questionnaire (Table 3) is easy to use and has been validated in surgical and sleep practice patients as a screening tool for OSA. Its sensitivity is greater than 90%; its specificity ranges between 25% and 85%, with higher values seen in obese men.\textsuperscript{32-34}

The Sleep Apnea Clinical Score (SACS) is based on snoring, witnessed apneas, neck circumference, and systemic hypertension.\textsuperscript{35} It has been validated in adult family medicine patients in a prospective cohort study.\textsuperscript{36} The authors found that in patients with OSA and an AHI greater than 10 events/hour, a sleep apnea

\begin{figure}
\centering
\includegraphics[width=\textwidth]{Figure1.png}
\caption{Obstructive Sleep Apnea Recorded During an In-Laboratory Attended Sleep Study}
\textbf{Figure} shows an in-laboratory, attended polysomnography recording with electroencephalogram (EEG) and eye channels, chin and leg leads, electrocardiogram, snore channel, oximetry, respiratory effort from chest and abdomen belts, and nasal oral airflow. The portions marked in yellow represent an EEG arousal after a breathing event. Oximetry channel shows a desaturation of \(>4\%\) and airflow channels show a decrease in airflow \(>90\%\) (apnea).
\end{figure}

\textit{Image provided by Deepa Burman, MD, FAAFP, FAASM.}
clinical score greater than 15 was 40% sensitive and 90% specific, with a positive predictive value of 73% and a negative predictive value of 69%.

The Mallampati classification, which grades oropharyngeal appearance on a 4-point scale, has been shown to predict polysomnographic confirmation of OSA. Each 1-point increase in the score was associated with an odds ratio of 2.5 (95% CI = 1.2 to 5.0) for OSA and predicted a 5-point higher AHI (coefficient = 5.2; 95% CI = 0.2 to 10), independent of many other physical findings and symptoms. However, another study did not show evidence that the Mallampati score was of added value for diagnosing OSA.

The Epworth Sleepiness Scale (ESS) measures subjective daytime sleepiness using a short questionnaire. The Wisconsin Sleep Cohort Study found that only 37% of patients with severe OSA (AHI of 30 events/hour or more) showed excessive daytime sleepiness, and that mortality associated with long-term OSA was independent of subjective sleepiness.

The Berlin Questionnaire was evaluated in a cross-sectional study that sampled adults from the general population of Norway. It had a sensitivity of 37.2% and a specificity of 84% when using an AHI cutoff of 5 events/hour or greater. When using an AHI cutoff of 15 events/hour or greater, the sensitivity increased to 43% but its specificity dropped to 79.7%.

**Effect of Neck Size and Weight**

Increasing neck circumference predicts a higher AHI, but is not independent of BMI. Obstructive sleep apnea becomes more severe in patients whose BMI increases, and OSA may improve with weight reduction. However, the effect of weight gain on increasing OSA severity is greater than the effect of weight loss on decreasing its severity. The consequences of weight change are more evident in men than women. In one cohort, a 10% weight gain predicted a 32% increase in AHI, and a 10% weight loss predicted a 26% decrease in AHI. Weight loss is less effective in reducing a patient’s AHI when craniofacial abnormalities play a prominent role in the pathogenesis of OSA.

**Sleep Studies for Diagnosis of Sleep Apnea**

Diagnostic polysomnography is the gold standard for the diagnosis of sleep apnea and the classification of its severity. It is a noninvasive comprehensive recording of physiologic parameters including electroencephalography; electrooculography; electromyography of the chin and leg; electrocardiography; pulse oximetry with or without carbon dioxide monitoring; and respiratory parameters including nasal airflow, oral airflow, and chest and abdominal breathing effort, as well as audio and video recording (Figure 1).

An unattended portable home sleep test measures fewer physiologic parameters than diagnostic polysomnography, but it is considered an acceptable test to diagnose OSA. It measures the respiratory disturbance index (akin to the AHI), defined as apneas or hypopneas per hour of recording time. In a 2008 ruling, the Centers for Medicare and Medicaid Services (CMS) allowed patients to qualify for continuous positive airway pressure (CPAP) treatment on the basis of a diagnosis by home sleep testing, provided certain guidelines are followed.
Common home sleep testing devices monitor ventilation, oximetry, electrocardiography or heart rate, and pulse oximetry. Their major limitation is the lack of measured sleep because of the absence of electroencephalography channels; thus, they may underdiagnose or underestimate severity of disease when the patient has reduced sleep efficiency. Therefore, although a positive home sleep test result can be used to diagnose OSA, any patient with a negative result should undergo formal in-laboratory attended polysomnography.

When used appropriately, home sleep testing devices have the potential advantage of reducing costs, improving convenience for the patient by avoiding an overnight stay in a sleep laboratory, and increasing access to care for patients unable or unwilling to undergo polysomnography. Table 4 lists criteria for identifying patients in whom home sleep testing is appropriate.

**Sleep Apnea and Chronic Diseases**

Obstructive sleep apnea is a risk factor for hypertension, coronary artery disease, congestive heart failure, stroke, arrhythmias, and premature death. These associations are more evident in men and middle-aged individuals.

Among patients with OSA and resistant hypertension, CPAP has a relatively large effect on blood pressure reduction. A systematic review and meta-analysis showed a weighted mean decrease in systolic and diastolic blood pressure of 2.58 and 2.01 mm Hg, respectively, in those treated with CPAP. This finding supports the importance of aggressively screening for OSA in patients with resistant hypertension as well as ensuring treatment adherence in those with OSA.

The Sleep Heart Health Study (SHHS) showed that patients with OSA had an increased risk for stroke and other manifestations of cardiovascular disease. Among older men, severe nocturnal hypoxemia is a significant risk factor for stroke; measures of overnight oxygen saturation may better identify those at elevated risk than measures of apnea frequency. One study showed that CPAP management reduced mortality rates after ischemic stroke in patients with OSA.

Arrhythmias, particularly atrial fibrillation, are observed commonly in association with OSA. OSA and atrial fibrillation share many common risk factors; therefore, the presence of one may promote the development of the other. OSA also decreases the effectiveness of pharmacotherapy and ablative therapy for atrial fibrillation. Patients with atrial fibrillation should be screened for OSA, and OSA management should be initiated as soon as it is diagnosed.

Obstructive sleep apnea appears to be a risk factor for the development of type 2 diabetes, independent of obesity,

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**Table 4**

<table>
<thead>
<tr>
<th>Patients for Whom Home Sleep Testing Is Appropriate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home sleep testing is appropriate for patients with all of the following:</td>
</tr>
<tr>
<td>A high pretest probability of moderate to severe obstructive sleep apnea</td>
</tr>
<tr>
<td>No comorbid conditions that may affect accuracy (eg, severe pulmonary disease, neuromuscular disease, congestive heart failure)</td>
</tr>
<tr>
<td>No clinical suspicion of other sleep disorders (eg, central sleep apnea, narcolepsy, periodic limb movement disorders, parasomnias, circadian rhythm sleep disorders)</td>
</tr>
<tr>
<td>Home sleep testing also is appropriate for patients who:</td>
</tr>
<tr>
<td>Cannot undergo full polysomnography because of immobility or critical illness</td>
</tr>
</tbody>
</table>

primarily in blacks and whites. However, one study showed that PAP therapy did not improve glycemic control in patients with relatively well controlled type 2 diabetes and OSA.

Obstructive sleep apnea may increase the severity of depression. Because OSA leads to daytime sleepiness, patients commonly experience functional impairment, as manifested by poor job performance, loss of employment, impaired family relationships, and reduction in overall quality of life.

Sleep Apnea and Pulmonary Hypertension

Some patients with OSA have an increased vascular response to nocturnal episodes of acidosis and hypoxemia, with remodeling of the pulmonary vascular bed. The incidence of pulmonary hypertension in patients with OSA has been estimated to be between 20% to 40%. One long-term case series showed that patients with OSA and pulmonary hypertension had stable pulmonary pressures over 5 years when treated with CPAP. In a small 12-week randomized crossover trial, effective CPAP therapy resulted in lower pulmonary arterial systolic pressure when compared with sham treatment.

Sleep Apnea and Surgery

Perioperative patients are at high risk of apneic episodes. The surgical team should be made aware of patients having risk factors for OSA. When possible, high-risk patients should have a consultation before surgery with a sleep subspecialist. Postoperative orders should include continuous pulse oximetry monitoring with an alarm as a precaution against unobserved respiratory failure. Follow-up to ensure ongoing OSA treatment after discharge also is essential.

Quality of Life

Obstructive sleep apnea impairs quality of life for patients (and their bed partners), but the severity of impairment is not directly proportional to the severity of the condition. Management with CPAP improves quality of life, as measured by the 36-Item Short Form Health Survey (SF-36) and the Calgary Sleep Apnea Quality of Life Index (SAQLI). Relative to healthy age- and sex-matched counterparts, patients with OSA have impaired health-related quality of life; management with CPAP is associated with an improvement in this measure. Other treatment modalities have not been rigorously studied.

Sleep Apnea and Driving

Unintentional injuries, including motor vehicle crashes, are the fourth leading cause of death in the United States. Inattentiveness, fatigue, and sleepiness are increasingly recognized as contributing factors. The risk of motor vehicle crashes is significantly increased among those with OSA; although the true increase in risk is difficult to determine, a meta-analysis has shown a 2 times greater rate in patients with OSA compared to patients without OSA. Patients with suspected or confirmed OSA should be counseled about drowsy driving and the risks of excessive sleepiness.

Sleep Medicine Subspecialist Consultation

Referral to a sleep medicine subspecialist may be considered for refractory cases of OSA, difficulty with adherence to CPAP therapy, or when there is suspicion for disorders other than OSA.

Managing Sleep Apnea in Adults

Table 5 shows an overview of OSA management options.

PAP Therapy

Since 1981, PAP has been the mainstay of OSA management in adults. The various modes of delivering PAP are shown in Table 6. Positive airway pressure treatment pressurizes the pharyngeal airway, creating a pneumatic splint that
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Table 5
Management Options for OSA

<table>
<thead>
<tr>
<th>Modality</th>
<th>Key Aspects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PAP therapy</strong></td>
<td>First-line treatment</td>
</tr>
<tr>
<td>Gold standard in moderate to severe cases</td>
<td>Main limitation is the patient's willingness to accept therapy and remain adherent</td>
</tr>
<tr>
<td>An option in mild cases</td>
<td>Many variants are available, such as CPAP, bilevel PAP, and autoadjusting PAP therapy</td>
</tr>
<tr>
<td></td>
<td>PAP acts to splint the airway open, preventing collapse while sleeping</td>
</tr>
<tr>
<td><strong>Mandibular advancement device</strong></td>
<td>Device inserted in the mouth</td>
</tr>
<tr>
<td>Standard for primary snoring</td>
<td>Types include: tongue-retaining and mandibular-repositioning devices</td>
</tr>
<tr>
<td>Guideline for patients with mild to moderate OSA who prefer it, are not candidates for CPAP, or cannot tolerate CPAP</td>
<td>Acts by repositioning the mandible and tongue</td>
</tr>
<tr>
<td></td>
<td>A minimum of 6 to 10 teeth in each arch are needed</td>
</tr>
<tr>
<td></td>
<td>Not recommended as first-line treatment in patients with severe OSA, but may be considered if a patient is unable to tolerate PAP therapy or has not benefited from surgery</td>
</tr>
<tr>
<td>Surgery</td>
<td>Various options are available (eg, maxillary mandibular advancement, uvulopalatopharyngoplasty, and palatal implants); alternatively, surgery can be part of a multilevel or stepwise approach</td>
</tr>
<tr>
<td>Can serve as a treatment option in patients having difficulty tolerating PAP therapy or in patients with identifiable surgical target</td>
<td>Historically, tracheostomy was the primary treatment option available for sleep apnea</td>
</tr>
<tr>
<td>Also can serve as an optional adjunct to treatment of OSA in obese patients. Evaluation of potential patients includes fiberoptic evaluation of upper airway. Patients should be advised about potential complications and the availability of alternative treatment options</td>
<td>Other adjuncts to primary treatment</td>
</tr>
<tr>
<td></td>
<td>Weight loss; armodafinil or modafinil for residual sleepiness; topical nasal corticosteroids* for rhinitis; positional therapy. Can cause insomnia if taken late during the day</td>
</tr>
<tr>
<td><strong>Oxygen therapy</strong></td>
<td>Oxygen therapy has not been shown to improve outcomes in OSA</td>
</tr>
<tr>
<td>Not recommended as primary treatment</td>
<td>It may be useful in management of severe hypoxemia untreated by PAP therapy</td>
</tr>
</tbody>
</table>

*OSA is an off-label use of some corticosteroids.

CPAP = continuous positive airway pressure; OSA = obstructive sleep apnea; PAP = positive airway pressure.

Information from various sources.

Prevents it from collapsing during sleep. Studies have shown that CPAP increases upper airway size, especially in the lateral dimension. Although the pneumatic splint is the main mechanism of action, an increase in lung volume because of CPAP treatment also may increase upper airway size or stiffen the upper airway walls, making them less collapsible.

Numerous studies have shown that PAP can decrease the AHI to less than 5 to 10 events/hour in the majority of patients.

**Strategies to improve adherence.** Despite many advances in technology, a major challenge facing clinicians is improving adherence to PAP management. Comfort measures used in most PAP devices to help improve adherence include:

- A ramp allowing pressure to gradually build up at a preset level over a set time,
- Pressure relief, which is a small drop in pressure during exhalation,
- Heated humidification, and
- Liners to decrease air leaks and improve mask fit.
A variety of interfaces and masks are available. Often, a trial of several masks is needed to find one that a patient can use comfortably. If the patient wakes to use the bathroom during the night, disconnection of the hose from the mask, rather than taking off the mask, is encouraged. Masks that are removed in the middle of the night often are not replaced.

Newer PAP machines have internal memory and removable memory media (eg, smart cards, memory sticks, disks).\textsuperscript{72} The removable media can store extensive information on adherence and patterns of use. Some devices use a modem to send information to a central location so that physicians can obtain patient data on an ongoing basis. Other devices communicate with a central location using wireless technology.

Comprehensive programs of education for the patient and the bed partner, early contact and interventions, a simple CPAP help line, and group education have improved adherence in some studies.\textsuperscript{73-75}

**Medicare Coverage**

Current Medicare coverage requirements for OSA management typically are accepted by most commercial insurance providers. These guidelines include an AHI of 5 events/hour or greater in the context of at least one of the following: hypertension, cardiac disease, history of stroke, insomnia, excessive daytime sleepiness, depression, or cognitive dysfunction. In addition, Medicare covers treatment of individuals with an AHI of 15 events/hour or greater even in the absence of associated comorbid conditions. Medicare guidelines require that obstructive hypopneas be defined by an oxygen desaturation greater than 4% and exclude the diagnosis for arousal without desaturation. Medicare also requires clinician documentation of patient adherence (use of therapy for at least 4 hours/night for 70% of the time) and effectiveness to cover treatment beyond 12 weeks.\textsuperscript{76}

**Mandibular Advancement Devices**

Mandibular advancement devices (MADs), also known as oral appliances, are devices inserted into the mouth with the aim to protrude the mandible and treat snoring or OSA.\textsuperscript{77,78} A candidate for a MAD should first be examined by a qualified dentist to determine whether such an appliance is feasible and safe from a dental standpoint. Patients typically should have at least 6 to 10 healthy teeth in each arch to use a MAD, must be able to open their jaw adequately for device insertion, and must have the ability to voluntarily protrude the mandible. Although mild temporomandibular joint dysfunction may improve with MAD use, moderate to severe temporomandibular joint disease and inadequate protrusive ability may be contraindications to use of these devices. Moderate to severe bruxism also is a contraindication in most patients because it can damage the MAD. However, in some patients, bruxism will improve with adequate OSA management.

Somewhat similarly, tongue-retaining devices splint the tongue in place to keep the airway open. There is insufficient evidence of their effectiveness, and they are not used commonly.\textsuperscript{77,79}

Although results differ considerably among studies, MAD management has been shown to be successful in approximately 50% of patients with mild to moderate OSA, using an AHI of fewer than 10 events/hour as the measure of success.\textsuperscript{77} Although MADs

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**Table 6**

**Positive Airway Pressure Machines: Modes and Mechanisms**

<table>
<thead>
<tr>
<th>Mode</th>
<th>Mechanism of Pressure Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP</td>
<td>Continuous pressure during exhalation and inhalation</td>
</tr>
<tr>
<td>BIPAP</td>
<td>Separate pressures during exhalation (lower) and inhalation (higher). A backup rate can be added for patients with ineffective breathing efforts</td>
</tr>
<tr>
<td>Autotitrating positive airway pressure</td>
<td>Pressure fluctuates between minimum and maximum set limits based on device-specific algorithms to eliminate sleep-disordered breathing. Both continuous (auto-CPAP) and bilevel (auto-BiPAP) modes are available</td>
</tr>
</tbody>
</table>

BiPAP = bilevel positive airway pressure; CPAP = continuous positive airway pressure.

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typically are less effective than CPAP in reducing the AHI, their effects on quality of life and subjective sleepiness are similar to those of CPAP, perhaps because of better adherence. Center for Medicare and Medicaid Services has recognized certain types of MADs as reasonable and necessary for management of OSA. Only custom-fabricated MADs are covered. Coverage requires a face-to-face clinical evaluation before a Medicare-covered sleep test.

Common adverse effects of MAD therapy are noted in Table 7.

Surgery

Some patients with sleep apnea find it difficult to adhere to PAP therapy, prompting them to seek surgical alternatives. There is insufficient evidence to support any particular surgery for the management of OSA, and data on outcomes such as quality of life and cardiovascular benefits also are lacking. However, surgical therapy can improve tolerance and success of CPAP or a MAD.

Tracheostomy was the first management available for OSA. It bypasses all upper airway obstruction and hence it is effective, but it should be considered only when all other options have failed. Other surgical options include maxillomandibular advancement, nasal reconstruction, uvulopalatopharyngoplasty, and genioglossus (tongue muscle) advancement. All patients considered for surgery to correct snoring or OSA should undergo polysomnography. Fiberoptic examination of the nose, pharynx, and hypopharynx often is useful. Patients should be advised about surgical success rates and complications; the availability of alternative management options, such as PAP and MAD therapy; and the levels of effectiveness and success rates of the various management options.

Upper Airway Stimulation

The onset of an episode of apnea is accompanied by a reduction in drive to the upper airway muscles, and upper airway patency is strongly correlated with the activation of the genioglossus muscle. Upper airway stimulation has shown promise in feasibility trials.

Weight Loss and Bariatric Surgery

More than 70% of patients with OSA are obese, and BMI is closely correlated with AHI. Therefore, weight loss is a main goal in OSA management. Unfortunately, many diet programs fail because OSA itself causes metabolic changes that can preclude weight loss. In addition, initiation of CPAP may actually lead to weight gain, perhaps because of a decrease in nighttime work of breathing or sympathetic stimulation. In patients with severe obesity (BMI of at least 40 kg/m²), bariatric surgery can be considered when conservative treatments have failed. Bariatric surgery can resolve or improve OSA. A recent meta-analysis showed that bariatric surgery and nonsurgical weight loss have significant beneficial effects on OSA, but the former may offer greater improvements in BMI and AHI. Bariatric surgery in obese patients with OSA has resulted in an improvement in more than 75% of patients and improvement or resolution in 84% after 2 years.

Pharmacotherapy

There is insufficient evidence to recommend the use of drug therapy in the treatment of OSA. A Cochrane review of 25 drugs showed that 10 had some effect on the severity of OSA and four altered symptoms of sleepiness, although in most individuals, the changes were only modest. A topical nasal steroid was well tolerated, reduced the severity of sleep apnea, and improved subjective daytime alertness in individuals with OSA and rhinitis. Acetazolamide reduced the number of respiratory events per hour of sleep, but did not reduce daytime sleepiness and was poorly tolerated long-term. (This is an off-label use of these drugs.)

<table>
<thead>
<tr>
<th>Major</th>
<th>Minor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes in dental occlusion</td>
<td>Excessive salivation</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>Temporomandibular joint tenderness</td>
</tr>
<tr>
<td>Gum irritation</td>
<td>Tongue pain</td>
</tr>
<tr>
<td>Temporomandibular joint</td>
<td>Tooth pain</td>
</tr>
<tr>
<td>dysfunction or pain</td>
<td></td>
</tr>
<tr>
<td>Tooth movement</td>
<td></td>
</tr>
</tbody>
</table>

**OSA in Children**

Obstructive sleep apnea in children should be suspected when they show nocturnal symptoms of snoring, gasping, increased work of breathing or paradoxical breathing, restless sleep, witnessed apneas, or mouth breathing. In children, the obstruction is caused primarily by hypertrophy of the tonsils and adenoids, typically at ages 4 to 8 years.

Daytime symptoms of sleep apnea in children often are nonspecific (hyperactivity, difficulty concentrating or learning, behavioral problems, excessive daytime sleepiness, and moodiness), but when present along with nighttime symptoms, such symptoms may help alert clinicians to clinically significant OSA.

A history of prematurity is associated with an increased risk of OSA, and a family history of OSA also may be a risk factor. Other groups at risk include children with uncontrolled epilepsy, neuromuscular disorders, Prader-Willi syndrome, and complex medical conditions, such as achondroplasia, Chiari malformation, Ehlers-Danlos syndrome, mucopolysaccharidoses, and Down syndrome.

On physical examination, findings of tonsillar hypertrophy, obesity, midface deformity, macrognathia, or mandibular hypoplasia may strengthen the suspicion of OSA. There is little evidence linking tonsillar size evaluated subjectively during physical examination with OSA severity as determined by polysomnography. In clinical practice, techniques such as lateral neck x-ray, flexible nasopharyngoscopy, and cephalometry, magnetic resonance imaging study, or computed tomography scan of the upper airway should be reserved for more complex cases.

Because the history and physical examination alone are poorly correlated with a diagnosis of OSA in children, polysomnography often is the diagnostic study of choice. At present there are no good randomized controlled trials on the use of pediatric unattended home sleep tests for diagnosing sleep apnea. Obtaining polysomnography can be challenging because children may experience difficulty sleeping in a laboratory environment or cooperating with the setup. Staffing and laboratory hours might need to be extended to suit children’s schedules because they typically go to bed earlier and need more sleep than adults. One parent typically remains with the child at all times. Respiratory scoring in children also is different from that in adults. Apneic or hypopneic events in children are scored when they are of at least 2 breaths in duration, even if they are less than 10 seconds in duration. Children can have clinical complications of OSA with a much lower AHI than adults, and treatment is recommended for children with an AHI of more than 2 events/hour of sleep.

In children with OSA, combined tonsillectomy and adenoidectomy has been the standard and initial treatment of choice, especially in those with adenotonsillar hypertrophy and no contraindications to surgery. Recent studies using postoperative polysomnography have shown cure rates in children ranging from 24.2% to 93%.

Positive airway pressure therapy is recommended in children with OSA if adenotonsillectomy cannot be performed or if the condition persists postoperatively. The effectiveness of PAP therapy is severely limited by adherence in children, so PAP is used primarily in patients without an identifiable surgical target.

Mandibular advancement devices similarly are poorly tolerated by most children, but weight loss is recommended for obese children with OSA. Craniofacial surgery may be helpful in complex cases in which patients are unable to tolerate CPAP. Tracheostomy is reserved for children with severe craniofacial malformations who cannot be treated with other methods.

**Case 1, cont’d.** Chad’s STOP-Bang score is 4, with 1 point each for snoring, tiredness, pressure, and sex, consistent with intermediate risk of obstructive sleep apnea. Diagnostic polysomnography confirms moderate OSA with an apnea-hypopnea index of 16 events/hour. A continuous positive airway pressure (CPAP) titration study is completed, and he starts to use the CPAP device. He initially does not tolerate the mask well, but after he changes to a different mask with heated humidification, he notes a considerable improvement in daytime sleepiness as well as improvement in blood pressure control.
Insomnia is the most common type of sleep disorder in the family medicine population. It is defined as a persistent difficulty initiating or maintaining sleep, or a report of nonrestorative sleep, accompanied by related daytime impairment. Insomnia is a significant public health problem because of its high prevalence and management challenges. There is increasing evidence of a strong association between insomnia and various medical and psychiatric comorbidities. Diagnosis of insomnia and treatment planning rely on a thorough sleep history to address contributing and precipitating factors as well as maladaptive behaviors resulting in poor sleep. Using a sleep diary or sleep log is more accurate than patient recall to determine sleep patterns. A sleep study is not routinely indicated for evaluation of insomnia. Cognitive behavioral therapy for insomnia (CBT-I) is the mainstay of treatment and is a safe and effective approach. The key challenge of CBT-I is the lack of clinicians to implement it. The newer generation nonbenzodiazepines (eg, zolpidem, zaleplon) are used as first-line pharmacotherapy for chronic insomnia. Newer drugs active on targets other than the gamma-aminobutyric acid receptor are now available, but clear treatment guidelines are needed.

Case 2. Patricia is a 69-year-old woman, who reports difficulty sleeping almost every night. She watches the evening news and then goes to bed at approximately midnight. Sometimes, she thinks that she lies in bed all night without sleeping. At other times, she sleeps for a brief period, then wakes up and cannot go back to sleep. She does not have a set time for waking in the morning. Sometimes, she is so tired that she naps during the day. Her friends suggested she ask you for a prescription for sleeping pills, but she is hesitant to take drugs.

Insomnia is the most common sleep disorder in the family medicine population. It is defined as a persistent difficulty initiating or maintaining sleep, or a report of nonrestorative sleep, accompanied by related daytime impairment. Insomnia is a significant public health problem because of its high prevalence and management challenges. There is increasing evidence of a strong association between insomnia and various medical and psychiatric comorbidities. Diagnosis of insomnia and treatment planning rely on a thorough sleep history to address contributing and precipitating factors as well as maladaptive behaviors resulting in poor sleep. Using a sleep diary or sleep log is more accurate than patient recall to determine sleep patterns. A sleep study is not routinely indicated for evaluation of insomnia. Cognitive behavioral therapy for insomnia (CBT-I) is the mainstay of treatment and is a safe and effective approach. The key challenge of CBT-I is the lack of clinicians to implement it. The newer generation nonbenzodiazepines (eg, zolpidem, zaleplon) are used as first-line pharmacotherapy for chronic insomnia. Newer drugs active on targets other than the gamma-aminobutyric acid receptor are now available, but clear treatment guidelines are needed.

Types

The International Classification of Sleep Disorders—Third Edition (ICSD-3) classifies insomnia in three groups:

- **Chronic insomnia disorder,**
- **Short-term insomnia disorder,** and
- **Other insomnia disorders.**

Chronic Insomnia Disorder

Diagnosing chronic insomnia disorder requires the presence of one of the following over at least 3 months for a minimum of 3 times/week:

- Difficulty initiating or maintaining sleep,
- Waking up earlier than desired, or
- Resistance to going to bed on an appropriate schedule.

In addition, one or more of the following daytime symptoms related to the insomnia needs to be present:

- Fatigue or malaise,
- Attention, concentration, or memory impairment,
- Impaired social, family, occupational, or academic performance,
- Mood disturbance or irritability,
- Daytime sleepiness,
- Behavioral conditions (eg, hyperactivity, impulsivity, aggression),
- Reduced motivation, energy, or initiative,
- Proneness for errors or accidents, or
- Concerns about or dissatisfaction with sleep.

In chronic insomnia disorder, the sleep-wake complaints cannot be explained purely by inadequate opportunity (ie, not enough time allotted for sleep) or inadequate circumstances (ie, the environment is not safe, dark, quiet, comfortable enough) for sleep. Subtypes of chronic insomnia disorder are beyond the scope of this edition of FP Essentials but can be found elsewhere.

The 3P behavioral model of insomnia distinguishes predisposing (individual variants), precipitating (stressors), and perpetuating (maladaptive behaviors and cognitions) factors that contribute to insomnia.
Thus, an individual may be prone to insomnia because of personal traits, may experience short-term insomnia because of precipitating stresses, and may develop a persistent and chronic insomnia as a consequence of pathologic coping strategies and poor sleep hygiene.

**Short-Term Insomnia Disorder**

Short-term insomnia disorder is insomnia of less than 3 months’ duration.¹

**Other Insomnia Disorders**

The diagnosis of other insomnia disorders is reserved for individuals who report difficulty initiating and maintaining sleep and yet do not meet the full criteria for chronic insomnia disorder or short-term insomnia disorder.¹ In some patients, this diagnosis is assigned on a provisional basis when more information is needed to establish a diagnosis of chronic insomnia disorder or short-term insomnia disorder. This diagnosis should be used sparingly, given its nonspecific nature.

**Prevalence**

Insomnia occurs on at least a few nights per year in 33% to 35% of the US adult population.¹ insurg with symptoms of attributable impairment is present in 10% of the population. Specific insomnia disorders occur in 5% to 10% of the population.¹ insurg

Chronic insomnia disorder is more common in women; individuals in lower socioeconomic strata; and patients with medical conditions (eg, chronic pain, diabetes, cancer), psychiatric conditions (eg, anxiety, depression, panic disorders), or substance use disorders.¹ It may occur at any age but is diagnosed more commonly in older adults; this is likely because of age-related deterioration in sleep continuity, increases in medical comorbidities, and use of drugs that increase the risk of insomnia. In adolescents, insomnia prevalence rates are 3% to 12%, depending on the diagnostic criteria, with higher frequency in girls than boys after puberty.

**Primary Versus Secondary Insomnia**

Insomnia can be a primary sleep disorder or secondary to an underlying medical, psychiatric, or substance abuse disorder.¹ Many symptoms and associated features of primary and secondary insomnias overlap, making differentiation among such subtypes difficult.

Even when insomnia arises secondary to another condition, it often develops an independent course over time and may remain as a clinically significant condition, even if the primary condition is adequately managed.¹ Management of the insomnia can improve the sleep disturbance and the comorbid conditions. Therefore, insomnia seems best viewed as a comorbid disorder that warrants separate attention in terms of management.

**Risk Factors**

Risk factors for insomnia include older age, female sex, comorbid conditions, shift work, unemployment, and lower socioeconomic status.¹ Some studies suggest that single, divorced, and separated individuals have higher insomnia rates than married counterparts. The most common cause of insomnia in patients evaluated by a physician is depression. Insomnia occurs in the majority of patients (80%) with major depressive disorder. Persistent insomnia symptoms increase by a factor of 4 the likelihood of developing major depression within a 1-year period.

The most common comorbidities associated with insomnia are psychiatric disorders, including anxiety, depression, panic disorder, adjustment disorder, somatoform disorders, and personality disorders.¹ Medical conditions that commonly co-occur with insomnia include arthritis, cancer, hypertension, chronic pain, coronary heart disease, and diabetes. Common drugs associated with insomnia are shown in Table 8.

**Screening Tools**

A detailed sleep history is the cornerstone of evaluation of insomnia.¹ Most questionnaires for diagnosing insomnia have not been validated in the family medicine population.

The Insomnia Severity Index (ISI)¹⁰⁹ is a 7-item questionnaire to assess the nature, severity, and effect of insomnia and monitor treatment response in adults.

The Pittsburgh Sleep Quality Index (PSQI)¹¹⁰ is a 24-item self-report measure of general sleep quality over the preceding 1-month period. It evaluates seven domains: duration of sleep, sleep disturbance, sleep latency, daytime dysfunction because of sleepiness, sleep efficiency, need for drugs to sleep, and overall sleep quality. Poor sleep correlates with a global score of greater than 5. The PSQI is used predominantly in research because of complexity of scoring and use.

The 30-item Dysfunctional Beliefs and Attitudes about Sleep (DBAS) questionnaire is a self-rating...
survey to assess negative cognitions about sleep. A shorter, 16-item version (DBAS-16) has been validated in a private behavioral sleep medicine clinic.

Sleep diaries are an important tool in the evaluation of insomnia, but data on their predictive value have not been published. Although diaries are not necessary to establish the presence of insomnia, they can help define its severity and reveal etiologies (e.g., inadequate sleep hygiene, delayed sleep phase syndrome, psychophysiologic insomnia). A 2-week sleep diary can provide a more accurate estimate of the patient’s sleep quantity than is possible from patient recall and can reveal sleep-wake patterns, such as an irregular sleep schedule and nap schedule.

Although sleep testing is not indicated for the routine assessment of insomnia, diagnostic polysomnography should be conducted for patients who report symptoms of other sleep disorders (e.g., periodic limb movement disorder, sleep-disordered breathing) or who do not benefit from standard insomnia treatment.

### Comorbidities Associated With Insomnia

Increasing evidence suggests a relatively strong association between insomnia and risk of future cardiovascular events. In a large-scale, nationwide population-based study in Taiwan, individuals with insomnia had an approximately 80% risk of acute myocardial infarction, stroke, and both compared with those without insomnia, after adjustment for confounders.

In addition to its association with major depression and dysthymic disorder, insomnia commonly occurs with bipolar disorder during depressive and manic episodes. Although some manic patients will describe a decreased need for sleep, others report being distressed by an inability to sleep. Sleep loss from any reason, including jet lag and work schedules, may contribute to the onset or progression of manic episodes in patients with bipolar disorder.

Most patients with panic disorder will at times experience distressing panic episodes that awaken them from sleep. This pattern may lead to considerable anticipatory anxiety about going to sleep, which can in turn cause sleep insufficiency and more anxiety. Insomnia also is a risk factor for adverse outcomes in depression, including suicidal ideation in adolescents.

### Management

Insomnia management aims to improve the amount and quality of sleep, and enhance daytime function. The two major evidence-based forms of management for chronic insomnia are cognitive behavioral therapy and pharmacotherapy. Whenever drugs are prescribed, management goals and expectations should be discussed along with safety, adverse effects, potential for dose escalation, and risk of rebound insomnia. Long-term drug management should be accompanied by consistent follow-up and ongoing monitoring for effectiveness, adverse effects, and new comorbid conditions. Table 9 summarizes the nonpharmacologic therapies, and Table 10 shows drugs used to manage insomnia.

### Nonpharmacologic Therapy

#### Cognitive behavioral therapy for insomnia.

Cognitive behavioral therapy for insomnia (CBT-I) is the recommended initial management of chronic insomnia. It produces meaningful improvements in sleep outcomes as shown in the sleep diary, and can produce sustained benefits without the risk of tolerance or adverse effects that can be associated with
<table>
<thead>
<tr>
<th>Type</th>
<th>Key Aspects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biofeedback: provides visual or auditory feedback to help patients control physiologic parameters and reduce somatic arousal</td>
<td>Three types of biofeedback have been specifically tested for the treatment of insomnia: EMG, theta EEG, and sensorimotor rhythm EEG</td>
</tr>
<tr>
<td>Cognitive behavioral therapy for insomnia: combines cognitive therapy with behavioral interventions</td>
<td>Components: sleep education, stimulus control techniques, sleep restriction techniques, cognitive therapy techniques, possibly relaxation training</td>
</tr>
<tr>
<td>Cognitive therapy: identifies, challenges, and replaces dysfunctional beliefs and attitudes regarding sleep and sleep loss</td>
<td>Challenges unhelpful beliefs and fears about sleep Unhelpful beliefs and fears about sleep increase arousal and tension, impeding sleep and further reinforcing the dysfunctional beliefs Typical beliefs may include an overestimation of the numbers of hours of sleep necessary to be rested; an apprehensive expectation that sleep cannot be controlled; a fear of missing opportunities for sleep Thought journaling is used to reduce rumination Behavioral experiments can be used to test beliefs about sleep</td>
</tr>
<tr>
<td>Relaxation techniques: uses techniques to decrease waking arousal and facilitate sleep at night</td>
<td>Muscular tension and cognitive arousal are incompatible with sleep Specific techniques may include progressive muscle relaxation, guided imagery, paced breathing</td>
</tr>
<tr>
<td>Sleep hygiene: promotes behaviors that help sleep, and discourages behaviors that interfere with sleep</td>
<td>Specific recommendations vary across studies Typical recommendations include: Do not try to sleep if not sleepy Avoid stimulants (eg, caffeine, nicotine) Limit alcohol intake Maintain a regular sleep schedule 7 nights/week Avoid naps Get regular exercise at least 6 hours before sleep Keep the bedroom dark and quiet</td>
</tr>
<tr>
<td>Sleep restriction: increases homeostatic sleep drive by reducing time in bed; maintains a consistent wake time in the morning to reinforce circadian rhythms</td>
<td>Based on experimental evidence that sleep is regulated by circadian and homeostatic processes Restricts time awake in bed by setting strict bedtime and rising schedules limited to the average number of hours of actual sleep reported in one night Maintains a fixed wake time, regardless of actual sleep duration If after 10 days, sleep efficiency is &lt;85%, further restrict bedtime by 15 to 30 minutes Increase time in bed by advancing bedtime by 15 to 30 minutes when the time spent asleep is at least 85% of time in bed</td>
</tr>
<tr>
<td>Stimulus control: prescribes behaviors that strengthen the associations between the environment and sleep</td>
<td>Based on operant and classical conditioning principles, and the idea that nonsleep activities and the bedroom environment can serve as stimuli that interfere with sleep Recommendations include: Go to bed only when sleepy Use the bed and bedroom for sleep only Do not read, watch television, talk on the telephone, worry, or plan activities in the bedroom If unable to fall asleep within 10 to 20 minutes, leave the bed and the bedroom; return only when feeling sleepy again Set the alarm and wake up at a regular time every day Do not use the snooze button on the alarm Do not nap during the day</td>
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</tbody>
</table>

EEG = electroencephalogram; EMG = electromyography. Information from various sources.
Table 10
Pharmacotherapy for Insomnia

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Main Adverse Effects</th>
<th>Relative Contraindications</th>
<th>Drugs and Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nonbenzodiazepine sedatives/hypnotics</strong></td>
<td>First-line hypnotics, Margin of safety or therapeutic index is wide</td>
<td>Sedation, anterograde amnesia, ataxia, sleep walking, sleep violence or sleep-related eating disorders, respiratory depression Rebound insomnia, tolerance, and abuse may occur</td>
<td>Zolpidem 5 to 10 mg at bedtime</td>
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<tr>
<td></td>
<td></td>
<td>Concomitant illnesses (eg, OSA, substance use disorder, advanced liver disease)</td>
<td>Zolpidem CR 6.25 to 12.5 mg at bedtime</td>
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<td></td>
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<td></td>
<td>Eszopiclone 1 to 3 mg at bedtime</td>
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<td></td>
<td>Zaleplon 5 to 20 mg at bedtime</td>
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<td></td>
<td></td>
<td>(Zaleplon and sublingual zolpidem also have been used in studies with middle-of-the-night dosing if the individual has at least 4 hours of time in bed remaining after administration)</td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
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<tr>
<td>Agonists at benzodiazepine</td>
<td>Sedation; anterograde amnesia; ataxia, sleep walking, sleep</td>
<td>Concomitant illnesses, such as OSA, substance use disorder, or advanced liver disease</td>
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<tr>
<td>receptor GABA-A site</td>
<td>violence or sleep-related eating disorders; respiratory</td>
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<tr>
<td></td>
<td>depression</td>
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<tr>
<td>Short-term use in insomnia due to</td>
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<tr>
<td>anxiety</td>
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<tr>
<td>Duration of action differs across</td>
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<td></td>
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<tr>
<td>drugs</td>
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<tr>
<td><strong>Sedative antidepressants</strong></td>
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<tr>
<td>Sedative nature due to central</td>
<td>Somnolence, headache, dizziness, nausea</td>
<td>Hypersensitivity</td>
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<td>anticholinergic or antihistaminic</td>
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<tr>
<td>activity</td>
<td></td>
<td>Use of MAOIs within 14 days</td>
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<td></td>
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<tr>
<td></td>
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<td>For doxepin: dry mouth, constipation, narrow-angle glaucoma, and urinary retention</td>
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<td></td>
<td></td>
<td>Trazodone to be used with caution in those at risk of falls because of orthostatic hypotension</td>
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<tr>
<td><strong>Orexin receptor antagonists</strong></td>
<td>Drowsiness, headaches, sleep paralysis, hypnagogic</td>
<td>Narcolepsy (absolute contraindication)</td>
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<tr>
<td></td>
<td></td>
<td>Should be avoided in patients with</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>depression</td>
<td></td>
</tr>
<tr>
<td><strong>Melatonin receptor agonist</strong></td>
<td>Headache, dizziness, somnolence, fatigue, nausea</td>
<td>History of angioedema with ramelteon</td>
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<tr>
<td></td>
<td></td>
<td>Concurrent use of fluvoxamine</td>
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<tr>
<td></td>
<td></td>
<td>Use in severe liver failure</td>
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</tr>
</tbody>
</table>

\(^{a}\)Insomnia is an off-label use of other benzodiazepines.

\(^{b}\)This is an off-label use of this drug.

FDA = Food and Drug Administration; GABA-A = gamma-aminobutyric acid A; MAOI = monoamine oxidase inhibitor; OSA = obstructive sleep apnea.
pharmacologic approaches. CBT-I can improve several polysomnography measurements: sleep-onset latency (the amount of time from lights out until the time the patient actually falls asleep), wake after sleep onset (a measurement of sleep fragmentation), and sleep efficiency (the percentage of total time in bed that is actually spent sleeping). These benefits have been shown to be maintained at early and late follow-up. CBT-I initially causes small improvements in total sleep time. Although 70% to 80% of patients with insomnia experience long-term improvement with CBT-I, and it can be implemented by family physicians in the office setting, this therapy is not commonly practiced because of lack of awareness, training, time, and reimbursement.

There are not enough clinicians able to implement CBT-I, so validated online programs can be useful. Programs include SHUTi, Sleepio, and others (http://www.sleepreviewmag.com/2014/12/online-options-insomnia-therapy/). Such programs have been shown to be a cost-effective alternative to in-person CBT-I; compared to no treatment or other non-CBT treatments, they are superior in improving sleep efficiency and daytime functioning.

### Brief behavioral treatment for insomnia

Brief behavioral treatment for insomnia (BBTI) is a short-term, targeted course of counseling to change behaviors. It includes four sessions, two of which may be telephone sessions, and uses a hard copy workbook that facilitates its concise delivery format and ease of training clinicians. BBTI has shown effectiveness in treating older adults with insomnia.

This tool has a strong behavioral focus and is based on a physiologic model of sleep regulation, which provides a sound empirical rationale for patients and physicians. It is simple enough to be taught in a short time and is as effective as established treatments. Table 11 outlines the four basic principles of BBTI for insomnia.

### Sleep hygiene education

Sleep hygiene education is an adjunct intervention for adults with insomnia that can be used along with other behavioral interventions. There is insufficient evidence that this education is effective as sole therapy.

### Stimulus control and sleep restriction

Stimulus control and sleep restriction are subsets of CBT-I. The objective of stimulus control therapy is to train...
the patient with insomnia to reassociate the bed and bedroom with sleep and to reestablish a consistent sleep-wake schedule. Sleep restriction involves curtailing the amount of time in bed to the actual amount of time spent asleep, creating a mild sleep deprivation, and then subsequently lengthening sleep time as sleep efficiency improves.

**Lifestyle and integrative therapy.** Regular moderate-intensity exercise has been shown to improve the quality of sleep in older patients. One randomized controlled trial showed that tai chi and low-impact aerobic exercise can reduce daytime sleepiness and improve sleep quality in older adults with moderate sleep disturbances. Current evidence is not sufficient to support or refute the use of acupuncture for treating insomnia. The findings of a meta-analysis suggest that listening to music may improve subjective sleep quality in individuals experiencing insomnia symptoms, but no effect was seen on other aspects of sleep or on related physiologic and psychologic aspects of daytime function. None of the participants had a formal diagnosis of insomnia, so effectiveness of music for improving sleep in adults with diagnosed insomnia disorder is unknown.

Relaxation training involves methods to reduce somatic tension or intrusive thoughts at bedtime that interfere with sleep. It has shown promise in a few randomized controlled trials for insomnia management.

**Pharmacotherapy**

Benzodiazepine receptor agonists commonly are prescribed for insomnia. Benzodiazepine receptor agonists further open chloride ion channels and facilitate gamma-aminobutyric acid inhibitory activity. Some have a benzodiazepine chemical structure (eg, estazolam, flurazepam, lorazepam, temazepam, triazolam) and others do not (eg, eszopiclone, zaleplon, zolpidem). At appropriate doses, the benzodiazepine receptor agonist hypnotics reduce sleep latency, and most of them increase total sleep time (except for zaleplon). The newer generation nonbenzodiazepines (eg, zolpidem, zaleplon) are used as first-line pharmacotherapy for chronic insomnia. Because of their potential adverse effects, benzodiazepines and other sedative-hypnotics should not be used in older adults as first-line management for insomnia, agitation, or delirium.

The 2005 National Institutes of Health (NIH) state-of-the-science report on the management of chronic insomnia concluded that the benzodiazepine receptor agonists are the only drugs with an established scientific basis (ie, clearly defined risk and benefit by dose) for use in managing insomnia. Common over-the-counter sleep drugs contain diphenhydramine, which is not recommended for insomnia treatment because of its adverse effects and minimal evidence for improved sleep. Other commonly prescribed drugs such as trazodone and quetiapine also are not recommended for insomnia management because of their potential adverse effects and minimal evidence for improved sleep. (This is an off-label use of trazodone and quetiapine.) The benefits of hypnotic drugs are small, and many have an unfavorable risk-benefit ratio.

Pharmacotherapy for insomnia during pregnancy typically is contraindicated because of the potential adverse or teratogenic effects of such drugs, so CBT-I and BBTI are the mainstays of insomnia treatment in pregnant women.

**Sleep Medicine Subspecialist Consultation**

Consultation with a sleep medicine subspecialist for insomnia is indicated if the diagnosis is unclear; when there is no response to therapy; when further testing for a comorbid condition, sleep disorder, circadian rhythm disturbance, or movement disorder is warranted; and when formal CBT-I is necessary.

Case 2, cont’d. Given Patricia’s age and the presence of maladaptive sleep behaviors, it is reasonable to adopt a nonpharmacologic treatment approach. You arrange for her to start brief behavioral treatment for insomnia and plan to see her in follow-up.

---

**Table 11**

**Brief Behavioral Treatment for Insomnia**

<table>
<thead>
<tr>
<th>Main Interventions</th>
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<tbody>
<tr>
<td>Reduce time in bed</td>
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<tr>
<td>Get up at the same time every day of the week, regardless of sleep duration</td>
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</tr>
<tr>
<td>Do not go to bed unless sleepy</td>
<td></td>
</tr>
<tr>
<td>Do not stay in bed unless asleep</td>
<td></td>
</tr>
</tbody>
</table>

Restless legs syndrome (RLS) is a common disorder that often is underdiagnosed and undertreated. Patients with RLS describe an urge to move their legs, especially in the evenings and during periods of inactivity. The prevalence of clinically significant RLS is approximately 2% to 3% in adults in Europe and North America. RLS can be an independent disorder or may occur in conjunction with other conditions (e.g., iron deficiency, pregnancy, chronic renal failure). Diagnosis is based on clinical history. Routine polysomnography typically is not recommended unless there is suspicion of other sleep disorders (e.g., obstructive sleep apnea). Management includes a combination of supportive measures, dopaminergic drugs, gabapentinoids, opioids, or benzodiazepines. Good sleep hygiene can help prevent development of insomnia related to RLS. Avoiding alcohol and reducing caffeine intake is recommended. If iron stores are low, iron supplementation may improve symptoms. The main pharmacologic options for RLS management are dopaminergic agonists (e.g., pramipexole and ropinirole); gabapentinoids also are good options. Patients may experience augmentation, an increase in RLS symptom severity with increasing drug dosage, which is the main complication of dopaminergic drugs. There is no evidence to support use of vibratory devices that provide stimulation to the lower extremities.

Case 3. Cecilia is a 39-year-old woman, who comes to your office describing a painful sensation in her legs that is relieved by moving the legs or walking. This sensation often prevents her from falling asleep. She had iron deficiency anemia when she was younger. Her bed partner states Cecilia is restless and kicks her legs frequently during sleep.

Diagnosis
The diagnosis of restless legs syndrome (RLS) is clinical.1 The criteria include an urge to move the legs (in some patients, arms or other body parts may be involved), typically accompanied by uncomfortable and unpleasant sensations.1,134 These symptoms occur predominantly in the evening, and begin or worsen during periods of rest or inactivity, such as lying down or sitting. They are partially or totally relieved by movement, such as walking or stretching. To diagnose RLS, the symptoms should cause concern; distress; sleep disturbance; or impairment in mental, physical, social, occupational, educational, behavioral, or other important areas of functioning.

Prevalence
Restless legs syndrome occurs in approximately 5% to 10% of Europeans and North Americans.1 Prevalence increases with age up to 60 to 70 years, except in Asian populations, where an age-related increase has not been shown.1 Frequency (i.e., 1 to 2 times/week), severity (i.e., moderate to severe distress), differential diagnosis, and impact have been applied to population-based studies, which indicate the prevalence of clinically significant RLS to be 2% to 3% in Europe and North America, but lower in Asia.

Risk Factors
Restless legs syndrome appears to be heritable. In 40% to 92% of patients, a family history can be shown, and studies in twins show a high concordance rate.1,135 Genome studies have found a positive association with sequence variants on chromosomes 6p, 2p, and 15q.136 Other genome-wide association studies have identified three genomic regions associated with RLS.137 Obesity is associated with an increased likelihood of RLS.138 Physical activity is effective in improving symptoms.139 Smoking is associated with increased RLS risk, but only among women.140 Consumption of coffee or caffeinated beverages also has been linked to RLS although controlled studies are lacking.141

Drug-Induced RLS
The following classes of drugs may precipitate or exacerbate RLS:142,143:
- First-generation (sedating) antihistamines (e.g., diphenhydramine),
Sleep Disorders

- Antinausea drugs (eg, prochlorperazine),
- Dopamine receptor blockers (eg, metoclopramide), and
- Antidepressants (including selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors; one exception is bupropion).

During Pregnancy

The prevalence of RLS among pregnant women ranges from 11% to 31%. Typically, there is complete remission of symptoms soon after delivery; however, in some patients, symptoms may continue into the postpartum period. Risk factors include a strong family history, low serum iron and ferritin levels, and a high estrogen level during pregnancy. Vitamin D deficiency and calcium metabolism also may play a role.

If iron stores are not replenished between pregnancies, iron levels tend to decrease with each pregnancy. This depletion may be one reason multiparity is associated with a higher risk of RLS. It has been suggested that high estrogen, elevated prolactin, and elevated progesterone levels during pregnancy may trigger RLS, although one study showed no difference between the estrogen levels in women with and without RLS. That study also has suggested that genetic factors and smoking during pregnancy may trigger RLS.

Initial treatment for pregnant women with RLS should include nonpharmacologic approaches along with dietary supplementation. Pharmacotherapy during pregnancy is difficult and challenging, considering the risks to mother and fetus. However, in some patients, RLS may be severe enough to require drug therapy.

Periodic Limb Movements During Sleep and Akathisia

Other movement disorders may mimic or be closely related to RLS. The presence of involuntary periodic limb movements during sleep (PLMS), which can be diagnosed using a sleep study, is supportive of but not diagnostic for RLS. Approximately 90% of individuals with RLS experience PLMS, but less than 50% of individuals with PLMS also have RLS. Similar to RLS, akathisia is an internal desire to move, but it is not necessarily associated with discomfort in the legs and is not worse at night. Akathisia is most commonly associated with the use of neuroleptic drugs.

RLS and Parkinson Disease

Restless legs syndrome and Parkinson disease respond to dopaminergic drugs, which is suggestive of underlying dopamine dysfunction in both conditions. In addition, there is now evidence that the nigrostriatal system, primarily involved in Parkinson disease, also is affected in RLS. Furthermore, an association of RLS with the parkin mutation has been suggested. However, clinical association studies and functional imaging have produced mixed findings.

RLS and Other Medical Conditions

A large meta-analysis has confirmed the intimate relationship between PLMS noted during polysomnography and attention-deficit/hyperactivity disorder (ADHD). Not only do children with ADHD experience PLMS and RLS more frequently, but children with PLMS have a higher prevalence of ADHD. A link between ADHD and RLS or PLMS is further supported by data suggesting that dopaminergic drugs improve not only the limb symptoms, but also the ADHD symptoms in children with RLS and PLMS.

In patients with end-stage renal disease, RLS is associated with an increased mortality rate. Symptoms of RLS can resolve after successful kidney transplantation.

Effects on Quality of Life

Patients with RLS experience greater humanistic and economic burden than individuals without RLS. Patients with RLS have worse health outcomes and lower health-related quality of life, and use more health care resources than unaffected individuals.

A population-based study showed that 36-Item Short Form Health Survey (SF-36) scores of patients with moderate to severe RLS were significantly lower than with population norms. These measures included vitality, physical limitations on normal role activities, pain, physical functioning, and general health. Also reduced but to a smaller degree were
the remaining dimensions of social functioning, emotional limitations on normal role activities, and mental health.

**Management**

Iron deficiency is the most important reversible cause of RLS and should be treated with iron replacement therapy.\(^{160}\) Deficiencies of vitamin B\(_{12}\), folate, vitamin D, and magnesium also should be treated.

**Role of Iron**

Iron is a cofactor in the activity of tyrosine hydroxylase, the rate-limiting enzymatic step in the conversion of tyrosine to dopamine. Iron content in the substantia nigra and the putamen are lower in patients with RLS than in unaffected individuals.\(^{161}\) Levels of ferritin in the cerebrospinal fluid are significantly lower in patients with RLS than in healthy individuals as well, although serum levels are similar between the two groups.\(^{162}\) Serum iron stores (as measured by serum ferritin) have been shown to correlate inversely with RLS severity. Patients with a serum ferritin level of less than 50 ng/mL in the setting of RLS should be treated with iron replacement therapy.\(^{160}\)

**Nonpharmacologic Therapy**

Insufficient evidence exists for yoga, acupuncture, pneumatic compression devices, near infrared light therapy, cognitive behavioral therapy, valerian (Valeriana officinalis), or Chinese herbs in managing RLS.\(^{163}\) Likewise, there is insufficient evidence to determine whether acupuncture is more effective for RLS than no management or other therapies.\(^{164}\)

Regular physical activity can improve RLS symptoms, although the specific type and duration need to be elucidated, as does the mechanism of effect.\(^{163,165}\)

If RLS occurs during management with a selective serotonin reuptake inhibitor, switching to a different class of drug may be helpful.\(^{165}\)

A device that provides vibratory stimulation to the legs has been tested in patients with RLS, but there is no compelling evidence of benefit from the currently available data.\(^{166}\)

**Pharmacotherapy**

Because of their favorable adverse effect profiles, nonergot dopamine agonists (eg, pramipexole, ropinirole) are the main pharmacotherapy options for RLS.\(^{167}\) Gabapentinoids (eg, gabapentin, pregabalin [Lyrica]) also are good options. (This is an off-label use of pregabalin.) One advantage of pramipexole is its longer duration of action. These dopamine agonists are associated with addictive patterns (eg, compulsive gambling, eating, spending, or sexual behavior). Rotigotine (Neupro) is a nonergot dopamine receptor agonist available as a transdermal system. Other drugs used to manage RLS include carbidopa-levodopa, benzodiazepines, and opioids. (This is an off-label use of carbidopa-levodopa, benzodiazepines, and some opioids.) Table 12 summarizes pharmacotherapy for RLS.

The main complication of long-term use of dopaminergic drugs for RLS is augmentation, whereby symptoms of RLS become more severe, start earlier in the evening, and spread to other body parts.\(^{147}\) If augmentation occurs, ferritin levels should be reevaluated and iron stores replenished if necessary. Any new drugs or lifestyle changes that may be exacerbating symptoms should be considered. In mild cases, the dose of a dopamine agonist can be split between an early daytime dose and a nighttime dose. In severe cases, dopamine agonists can be discontinued and replaced with gabapentin or pregabalin. Gabapentinoids have not been associated with augmentation.

**Case 3, cont’d.** Because of Cecilia’s history of anemia, you evaluate the complete blood count and ferritin level. She has iron deficiency anemia, so you prescribe an oral iron supplement. Because she has a painful variant of restless legs syndrome, you tell her you can prescribe gabapentin if symptoms do not resolve with iron supplementation.
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Key Aspects</th>
<th>Adverse Effects</th>
<th>Drug and Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine agonists&lt;sup&gt;a&lt;/sup&gt;</td>
<td>First-line treatment</td>
<td>Nausea, orthostatic hypotension, vomiting, daytime fatigue and somnolence, compulsive or impulsive behavior, tolerance, and augmentation</td>
<td>Pramipexole 0.125 to 0.5 mg Ropinirole 0.25 to 4 mg Rotigotine transdermal patch 1 mg/24 hours; increase dose once a week to a maximum of 3 mg/24 hours</td>
</tr>
<tr>
<td>Dopamine precursors</td>
<td>Quick onset and short duration of action</td>
<td>Morning rebound or augmentation in early evening, daytime somnolence</td>
<td>Carbidopa-levodopa&lt;sup&gt;b&lt;/sup&gt; 25 mg/100 mg, one tablet Carbidopa-levodopa CR 25 mg/100 mg, one tablet</td>
</tr>
<tr>
<td>Opioids&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Useful in severe cases when patients do not benefit from other drugs</td>
<td>Constipation, dependence, respiratory depression at high doses Use with caution in patients with sleep apnea who snore</td>
<td>Oxycodone&lt;sup&gt;b&lt;/sup&gt; 5 to 15 mg</td>
</tr>
<tr>
<td>Benzodiazepine receptor agonists&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Can be used in mild cases, particularly in younger patients Used to improve quality of sleep and reduce periodic limb movements associated with arousals Insufficient evidence and a high incidence of adverse effects limit their use</td>
<td>Sedation; ataxia; anterograde amnesia; sleepwalking, sleep violence, or sleep-related eating disorders; respiratory depression Rebound insomnia, tolerance, and abuse may occur</td>
<td>Clonazepam&lt;sup&gt;b&lt;/sup&gt; 1 mg 30 minutes before bedtime</td>
</tr>
<tr>
<td>Gabapentinoids (alpha&lt;sub&gt;2&lt;/sub&gt;-delta calcium channel ligand anticonvulsants)</td>
<td>More potent and fewer adverse effects than dopaminergic agonists Useful in neuropathic RLS</td>
<td>Daytime fatigue, somnolence, dizziness</td>
<td>Gabapentin 600 mg Gabapentin enacarbil 600 mg Pregabalin&lt;sup&gt;b&lt;/sup&gt; 50 to 450 mg</td>
</tr>
<tr>
<td>Iron supplementation</td>
<td>Iron deficiency (and conditions involving iron deficiency, such as end-stage renal disease, pregnancy, gastric surgery) has been associated with secondary RLS Most clinicians recommend achieving a ferritin level of &gt;50 ng/mL Take on an empty stomach with vitamin C</td>
<td>Constipation, nausea, gastrointestinal upset, dark stools</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>This is an off-label use of other drugs in this class.

<sup>b</sup>This is an off-label use.

<sup>c</sup>This is an off-label of some drugs in this class.

RLS = restless legs syndrome.

Shift work sleep disorder is a common problem in industrialized countries because of the need for occupations and services to continue to function 24 hours/day. Approximately 20% of employed adults in the United States are engaged in shift work. Shift work sleep disorder is diagnosed if there is a report of insomnia or excessive sleepiness for at least 3 months associated with a recurring work schedule that overlaps the usual time for sleep. Shift work is associated with an increased occurrence of metabolic disorders, such as insulin resistance, diabetes, dyslipidemia, and metabolic syndrome, and it has been implicated in weight gain and cognitive impairment. There is evidence of increased absenteeism in night workers compared with day workers. A planned sleep schedule, timed bright light exposure, timed melatonin administration, and stimulants or drugs promoting alertness can be used to manage shift work sleep disorder. Jet lag is characterized by a misalignment between internal circadian rhythms and local time caused by rapid travel across at least two time zones. Not all travelers experience jet lag; risk factors include age, number of time zones crossed, and circadian preference. Management includes timed melatonin along with optional timed and dosed bright light exposure.

Case 4. Your final patient of the day is Stephen, a 28-year-old man, who is sleeping in the examination room. When you enter, he wakes up and apologizes for falling asleep. He says he just finished working for 30 consecutive hours and has had difficulty adjusting to his current job, which has a variable schedule and involves frequent overnight work. He has difficulty sleeping and feels tired all the time. He has never taken any drugs for sleep. He asks if there is anything that he can do to improve concentration while he is working and to improve sleep quality when he is not.

Shift Work Sleep Disorders

In human beings, many physiologic and behavioral processes occur on a circadian cycle slightly longer than 24 hours. Misalignment between the internal circadian rhythm and external factors results in a variety of disorders called circadian rhythm sleep-wake disorders. Shift work sleep disorder manifests with excessive sleepiness or insomnia associated with a work schedule that overlaps the usual time for sleep.

Approximately 20% of employed adults in the United States are engaged in shift work. This proportion may be even higher if workers with early morning shifts or irregular shifts are included. However, not all individuals exposed to shift work develop shift work sleep disorder. Many factors, including scheduling differences, shift frequency, shift duration, family and social responsibilities, and differences in sleep and circadian physiology, can affect an individual’s response to shift work.

Workers with regularly rotating shift schedules face additional challenges related to the speed and direction of shift rotations. Rapid shift rotations (eg, multiple shift changes within a week) are associated with reduced total sleep duration compared with slower rotations.

Diagnosis

Shift work sleep disorder is diagnosed if a patient reports insomnia or excessive sleepiness for at least 3 months, accompanied by a reduction of total sleep time, associated with a recurring work schedule that overlaps the usual time for sleep. Monitoring with actigraphy (a noninvasive method of monitoring human rest and activity cycles using a watch-shaped electronic device) or a 2-week sleep diary (including work and free days) should show a disturbed sleep and wake pattern. Routine use of polysomnography is not indicated.

There are many types of shift work schedules, including evening shifts, night shifts, early morning shifts, rotating shifts, split shifts, on-call overnight duty, and long duration work shifts that include work hours at night. However, night shifts, early morning shifts, and rotating shifts most commonly lead to reported sleep disturbance. In addition to impairment of performance at work, reduced alertness because of
Sleep Disorders

Sleep disturbances can affect safety during the work schedule and on the commute to and from work. Typically, the sleep disturbance lasts only for the duration of the shift work schedule, but in some individuals, it may persist longer.

Prevalence

Although the actual prevalence of clinically significant sleep disturbance and excessive daytime sleepiness because of work schedules is not clear, the total number of night-shift workers suggests that up to 2% to 5% of the general population may be affected. The prevalence of shift work sleep disorder among rotating- and night-shift workers has been estimated to be between 10% and 38%.

Normal sleepers with a sensitive sleep system (called high sleep reactivity) are more prone to transient sleep disturbance and increased wake-time sleepiness in response to a single night of circadian misalignment. Rotating-shift workers with high sleep reactivity are at substantially higher risk of such disturbances. They also experience escalations in depression and anxiety symptoms attributable to work-related changes in sleep-wake experiences.

Pathophysiology

One model proposes that disturbances to sleep and alertness in circadian rhythm sleep-wake disorders can be explained by disruptions of two biologic processes: Process C and Process S. According to this model, a homeostatic process resulting in sleep drive that is dependent on the amount of time since the last sleep episode (Process S) interacts with a process controlled by the suprachiasmatic circadian pacemaker that is independent of sleep (Process C). Physiologic and behavioral variables determine the time courses.

In a traditional work schedule, individuals sleep when their sleep drive is high and circadian alertness signal is low. Shift workers may experience a misalignment in these rhythms. Night shift workers often attempt to sleep during the day, when their alertness signal is high, resulting in curtailed, fragmented sleep. They then may have trouble staying alert during work, because of rising melatonin levels that promote sleep.

Risk Factors

Risk factors for shift work sleep disorder include advancing age, female sex, and postshift morning light exposure such as may occur during a long commute or morning social obligations. Exacerbating factors can include long shifts (which cause fatigue) and the common practice of resuming normal daytime activities and nighttime sleep on weekends.

Clockwise (forward) rotation of shifts is better tolerated than counterclockwise (backward) rotation, because of the body’s natural tendency to phase delay. In other words, staying up later tends to be easier than getting up earlier.

Chronic Diseases and Shift Work Sleep Disorder

Shift work is associated with an increased occurrence of metabolic disorders, such as insulin resistance, diabetes, dyslipidemia, and metabolic syndrome. It is still unknown whether circadian disruption or sleep restriction is responsible for these metabolic changes. Pivotal studies indicate that sleep restriction alone can lead to drastic changes in metabolism. Among women who have worked as registered nurses, a longer career duration of rotating night shift work is associated with a statistically significant but small absolute increase in risk of coronary heart disease. Working rotating night shifts for extended periods also has been shown to be associated with an increase in breast cancer risk of 36% to 60% in a large prospective study of nurses. Other studies of shift workers show a threefold increased risk for duodenal ulcers and increased cardiovascular morbidity and mortality.

Cognitive Function

Exposure to shift work is associated with a chronic cognitive impairment. This association is highly significant for exposures to rotating shift work exceeding 10 years, and the recovery of cognitive functioning after having ceased any form of shift work takes at least 5 years. Cognitive and memory deficits have been seen in male industrial workers who had been exposed to shift work relative to those who had not. These associations were independent of age and self-reported sleep quality.

Weight Management

Shift work has been implicated in weight gain, and it has been suggested that obesity in part mediates the relationship between shift work and various other morbidities. Investigators have postulated that shift work may promote weight gain through behavioral dysregulation, such as a lack of time to exercise,
in addition to hormonal and dietary factors related to circadian rhythm disruption and sleep deprivation.\textsuperscript{181,186} The interactions between education, sleep, workplace stress, shift work duration, and other social determinants of health to better understand the complex relationships among unconventional work hours, metabolism, and weight need to be studied further.\textsuperscript{187}

*Quality of Life and Work Performance*

Shift work is associated with reduced dexterity and efficiency,\textsuperscript{188} impaired threat detection,\textsuperscript{189} and lower productivity.\textsuperscript{190} There also is evidence of increased absenteeism in night workers compared with day workers, particularly for those experiencing insomnia or excessive sleepiness.\textsuperscript{191} The negative impact of shift work can affect the family system as well as the individual’s quality of life. Studies show a 57% higher divorce rate,\textsuperscript{192} reduced job satisfaction, and less family and social interaction.\textsuperscript{191}

*Management*

**Nonpharmacologic therapy.** A variety of nonpharmacologic therapies can be helpful in managing shift work sleep disorder:\textsuperscript{193}
- Bright light for 3 to 6 hours during the start of shift,
- Short scheduled naps (preshift or during shift),
- Avoidance of bright light on the way home in the morning after work (use dark goggles if the trip home is after sunrise),
- A quiet and dark sleep environment at home during sleep,
- Oral melatonin in the morning before bedtime (This is an off-label use of melatonin.), and
- Going to bed upon arrival at home.

**Pharmacotherapy.** Stimulants or alerting drugs at the start of the shift can be helpful, including:\textsuperscript{193}
- Caffeine (100 to 200 mg) every 3 to 4 hours, (This is an off-label use of caffeine.)
- Modafinil 200 mg or armodafinil 150 mg taken 30 to 60 minutes before start of a night shift,
- Using hypnotics before daytime sleep can increase total sleep time but has not been shown to improve alertness at night.

*Graduate Medical Education Duty Hours*

In an attempt to decrease medical errors, the Accreditation Council for Graduate Medical Education (ACGME) placed formal limits on all US medical resident work hours in 2003, including an 80-hour work week averaged over 4 weeks, and specified standards for supervision for accredited residency programs.\textsuperscript{194} These limits were extended in 2011 to include a maximum of 16 continuous hours of direct patient care for first-year residents. There has been conflicting evidence about whether the reduction in duty hours improves patient safety. One concern is that the shortened work days for first-year residents necessitate increased handoffs, which may in turn result in more medical errors.\textsuperscript{195}

New ACGME duty hour rules that went into effect July 2017 increased the limit of total hours on duty to 24 hours on-task plus 4 hours to manage transitions of care. Residents may stay past the time limit for educational or research purposes in some circumstances, but the additional time will be counted toward the 80-hour weekly limit.\textsuperscript{196} Findings from studies of medical personnel have shown an increased number of injuries associated with the use of sharp instruments and items,\textsuperscript{197} drug and diagnostic errors,\textsuperscript{198} and increased patient mortality rates associated with extended and unconventional shift schedules.\textsuperscript{199}

Performance impairment during a heavy call rotation, assessed with sustained attention, vigilance, and simulated driving tasks, is comparable to that seen with a 0.04% to 0.05% blood alcohol concentration.\textsuperscript{200} Moreover, residents may have limited ability to judge this impairment, especially for certain tasks.

Results of a national multicenter randomized trial of a policy regulating surgery resident duty hours show that flexible, less restrictive policies can be safe for patients and reduce handoffs.\textsuperscript{201}

*Jet Lag*

Jet lag is characterized by a misalignment between internal circadian rhythms and local time caused by rapid travel across at least two time zones.\textsuperscript{1} Eastward travel requires adaptation by a phase advance (bedtime and wake time move to an earlier time) and adaptation is more difficult than for westward travel. Westward travel requires adaptation by phase delay (bedtime and wake time move to a later time), which often is easier because of the body’s intrinsic tendency for phase delay. Most individuals require approximately 1 day of adaptation for each time zone crossed.

Jet lag is diagnosed when a patient reports insomnia or excessive daytime sleepiness, accompanied by a reduction of total sleep time, associated with rapid travel across at least two time zones.\textsuperscript{1} Symptoms may
include impairment of daytime function, general malaise, or somatic symptoms (eg, gastrointestinal disturbance) within 1 to 2 days after travel.

Data from athletes show detrimental effects of long travel on maximal power production (eg, vertical jumps). In another study, the use of artificial bright light alongside sleep hygiene recommendations had negligible effects on the recovery of physical performance after simulated air travel. Therefore, the benefit of minimizing travel-induced sleep disruption may be limited to attenuating travel fatigue.

One study has shown cognitive performance deficits and higher cortisol levels in airline cabin crew who experienced repeated exposure to jet lag for more than 3 years, compared with ground crew working for the same company. There were no such effects in aircrew who had been exposed for 3 years or less.

Long-term exposure to short recovery periods (5 days or less) from jet lag is associated with lower cognitive performance, higher salivary cortisol, and a smaller volume of the right temporal lobe. These findings were interpreted as showing a cumulative effect of chronic exposure to circadian disruption on cerebral structures and cognitive function.

Management

Direct overnight flights provide more opportunity to sleep during travel than do itineraries with multiple stops. Eyeshades and earplugs or noise-canceling headphones may help sleep during flight. Alcohol should be avoided during the flight; although alcohol shortens sleep latency, it disrupts sleep continuity. On arrival, it often is recommended to immediately adapt to the sleep and wake times of the new time zone. Staying awake until bedtime in the new time zone should promote sleep.

Avoiding bright light exposure at the wrong times (when it would induce the wrong phase shift), and receiving light exposure at the proper times (to induce the desired phase shift) at the new destination are recommended. Taking oral melatonin before the desired sleep period may be helpful. Travelers can use online calculators (eg, jetlagrooster available at http://www.jetlagrooster.com/) to plan the appropriate times to use bright light and melatonin to adjust to a specific change in time zones.

Eastward travel: Travelers should take melatonin at the local bedtime until adjusted. Morning use of stimulants also has been studied. One study showed that taking 150 mg of armodafinil each morning increased wakefulness after eastward travel through six time zones. (Jet lag is an off-label use of melatonin, stimulants, and armodafinil.)

Westward travel: Travelers should take melatonin during the second half of the night. Daytime bright light exposure can be beneficial when adjusting after westward travel, but bright light exposure should be avoided for 3 hours before bedtime.

Case 4, cont’d. You discuss shift work sleep disorder with Stephen. You explain the importance of avoiding morning light exposure when he is coming off a night shift, and instruct him to avoid resuming normal daytime activities and nighttime sleep on his days off. Together, you decide to initiate a program of using 3 to 6 hours of bright light exposure at the beginning of his work shifts, avoiding bright light on the way home after working, and taking melatonin before sleep.
References


Sleep Disorders


References


Sleep Disorders


References


Sleep Disorders


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196. Accreditation Council for Graduate Medical Education. Common program requirements. The learning and working environment (duty hours). Available at https://www.acgmecommon.org/.


**Suggested Reading**


1. Which one of the following is most consistent with a diagnosis of severe obstructive sleep apnea?
   - A. Apnea-hypopnea index of 30 events/hour.
   - B. Epworth Sleepiness Scale score of 0.
   - C. Mallampati class I.
   - D. STOP-Bang questionnaire score of 2.

2. More than half of moderate to severe obstructive sleep apnea in adults is attributable to which one of the following risk factors?
   - A. Enlarged tonsils.
   - B. Myotonic dystrophy.
   - C. Obesity.
   - D. Retrognathia.

3. Which one of the following factors is associated with an increased risk of obstructive sleep apnea?
   - A. Down syndrome.
   - B. Hyperthyroidism.
   - C. Premenopausal status.
   - D. Underweight.

4. Which one of the following sets of data meets the criteria for obesity hypoventilation syndrome?
   - A. Body mass index (BMI) of 25 kg/m$^2$ and daytime Paco$_2$ of 40 mm Hg.
   - B. BMI of 25 kg/m$^2$ and daytime Paco$_2$ of 50 mm Hg.
   - C. BMI of 35 kg/m$^2$ and daytime Paco$_2$ of 40 mm Hg.
   - D. BMI of 35 kg/m$^2$ and daytime Paco$_2$ of 50 mm Hg.

5. Which one of the following tools produces a score that reflects oropharyngeal appearance on a 4-point scale?
   - A. Berlin Questionnaire.
   - B. Epworth Sleepiness Scale.
   - C. Mallampati classification.
   - D. STOP-Bang questionnaire.

6. For which one of the following patients, all of whom have frequent daytime sleepiness, would an unattended portable home sleep test be indicated?
   - A. A nurse with hypertension who frequently works night shifts.
   - B. A young patient with depression and suspected narcolepsy.
   - C. An elderly patient with coronary artery disease and congestive heart failure.
   - D. An obese diabetes patient with a high pretest probability of severe obstructive sleep apnea.

7. Which one of the following statements about positive airway pressure (PAP) management of sleep apnea is true?
   - A. Heated humidification of PAP decreases adherence.
   - B. Medicare coverage for PAP therapy requires an apnea-hypopnea index (AHI) of 30 events/hour or more.
   - C. PAP stiffens the upper airway walls, leading to a decrease in lateral upper airway dimension.
   - D. PAP decreases the AHI to less than 5 to 10 events/hour in the majority of patients.

8. Which one of the following statements about alternatives to positive airway pressure therapy for managing obstructive sleep apnea (OSA) is true?
   - A. Acetazolamide reduces daytime sleepiness.
   - B. Bariatric surgery can improve OSA in patients with body mass index of 40 kg/m$^2$ or greater.
   - C. Custom-fabricated mandibular advancement devices are not covered by Medicare.
   - D. Mandibular advancement devices can be used in patients with 3 to 4 healthy teeth in each arch.

9. Which one of the following is most helpful in diagnosing children with suspected sleep apnea?
   - A. Genetic testing.
   - B. Imaging of the upper airway.
   - C. Nasopharyngoscopy.
   - D. Symptoms.
10. Which one of the following is the most common sleep disorder in the family medicine population?
   ❑ A. Insomnia.
   ❑ B. Narcolepsy.
   ❑ C. Obstructive sleep apnea.
   ❑ D. Restless legs syndrome.

11. Symptoms need to be present for which one of the following durations to meet the diagnostic criteria for chronic insomnia disorder?
   ❑ A. 3 months.
   ❑ B. 6 months.
   ❑ C. 9 months.
   ❑ D. 12 months.

12. Which one of the following is a risk factor for the development of insomnia?
   ❑ A. Depression.
   ❑ B. Higher socioeconomic status.
   ❑ C. Male sex.
   ❑ D. Younger age.

13. Which one of the following is the recommended initial management of chronic insomnia disorder?
   ❑ A. Cognitive behavioral therapy.
   ❑ B. Sleep hygiene.
   ❑ C. Trazodone.
   ❑ D. Zolpidem.

14. Which one of the following statements about restless legs syndrome (RLS) is true?
   ❑ A. Clinically significant RLS is present in 10% to 15% of North American adults.
   ❑ B. Obesity reduces its likelihood.
   ❑ C. Polysomnography is needed to make a definitive diagnosis.
   ❑ D. Symptoms are relieved by movement.

15. Which one of the following is most likely to improve restless legs syndrome symptoms?
   ❑ A. Caffeine consumption.
   ❑ B. Pregnancy.
   ❑ C. Regular exercise.
   ❑ D. Smoking in women.

16. Which one of the following drugs is recommended management of restless legs syndrome?
   ❑ A. Diphenhydramine.
   ❑ B. Metoclopramide
   ❑ C. Pramipexole.
   ❑ D. Prochlorperazine.

17. Shift work sleep disorder can be diagnosed if there is a reduction of total sleep time associated with a recurring work schedule that overlaps the usual time for sleep, along with a report of insomnia or excessive sleepiness that has lasted for which one of the following durations or longer?
   ❑ A. 3 months.
   ❑ B. 6 months.
   ❑ C. 9 months.
   ❑ D. 12 months.

18. Which one of the following is associated with a lower risk of shift work sleep disorder?
   ❑ A. High sleep reactivity.
   ❑ B. Male sex.
   ❑ C. Postshift morning light exposure.
   ❑ D. Resuming normal daytime activities on weekends.

19. Bright light for 3 to 6 hours during the start of a night shift is a reasonable management of shift work sleep disorder.
   ❑ A. True.
   ❑ B. False.

20. Which one of the following statements is true of jet lag?
   ❑ A. Drinking alcohol during a long flight improves sleep continuity.
   ❑ B. Most individuals require about 1 day of adaptation for each three time zones crossed.
   ❑ C. Staying awake until bedtime in the new time zone promotes sleep.
Question 1: The correct answer is A.
Obstructive sleep apnea (OSA) disorders are characterized by 5 or more episodes/hour of complete or partial upper airway closure during sleep, with respiratory effort during at least a portion of the event, as measured by the apnea-hypopnea index (AHI). The AHI also determines the severity of OSA in adults: normal = fewer than 5 events/hour; mild OSA = 5 to 14.9 events/hour; moderate OSA = 15 to 29.9 events/hour; severe OSA = 30 or more events/hour. See page 11.

Question 2: The correct answer is C.
Approximately 60% of moderate to severe obstructive sleep apnea is attributable to obesity. See page 11.

Question 3: The correct answer is A.
Children with Down syndrome are at increased risk of obstructive sleep apnea, with a shown prevalence of 31% to 83%. See page 12.

Question 4: The correct answer is D.
Diagnosing obesity hypoventilation syndrome requires documentation of daytime hypoventilation ($P_{aco_2}$ greater than 45 mm Hg), in the presence of obesity (ie, body mass index [BMI] greater than 30 kg/m$^2$ for adults; BMI greater than the 95th percentile for age and sex for children). See page 14.

Question 5: The correct answer is C.
The Mallampati classification, which grades oropharyngeal appearance on a 4-point scale, has been shown to predict polysomnographic confirmation of obstructive sleep apnea. See page 15.

Question 6: The correct answer is D.
Home sleep testing is appropriate for patients with all of the following: a high pretest probability of moderate to severe OSA; no comorbid conditions that may affect accuracy (eg, severe pulmonary disease, neuromuscular disease, congestive heart failure); and no clinical suspicion of other sleep disorders (eg, central sleep apnea, narcolepsy, periodic limb movement disorders, parasomnias, circadian rhythm sleep disorders); and in patients who cannot undergo full polysomnography because of immobility or critical illness. See Table 4.

Question 7: The correct answer is D.
Numerous studies have shown that positive airway pressure can decrease the apnea-hypopnea index to less than 5 to 10 events/hour in the majority of patients. See page 18.

Question 8: The correct answer is B.
In patients with obstructive sleep apnea (OSA) and severe obesity (body mass index of at least 40 kg/m$^2$), bariatric surgery can be considered when conservative treatments have failed. Bariatric surgery can resolve or improve obstructive sleep apnea. See page 20.

Question 9: The correct answer is D.
Daytime symptoms of sleep apnea in children often are nonspecific (hyperactivity, difficulty concentrating or learning, behavioral problems, excessive daytime sleepiness, and moodiness), but when present along with nighttime symptoms, such symptoms may help alert clinicians to clinically significant obstructed sleep apnea. See page 21.

Question 10: The correct answer is A.
Insomnia is the most common sleep disorder in the family medicine population. See page 22.

Question 11: The correct answer is A.
Diagnosing chronic insomnia disorder requires the presence of symptoms over at least 3 months for a minimum of 3 times/week. See page 22.

Question 12: The correct answer is A.
The most common cause of insomnia in patients evaluated by a physician is depression. See page 23.

Question 13: The correct answer is A.
Cognitive behavioral therapy for insomnia is the recommended initial management of chronic insomnia. See page 24.

Question 14: The correct answer is D.
Restless legs syndrome symptoms are partially or totally relieved by movement, such as walking or stretching. See page 29.

Question 15: The correct answer is C.
Physical activity is effective in improving restless legs syndrome symptoms. See page 29.

Question 16: The correct answer is C.
Because of their favorable adverse effect profiles, nonergot dopamine agonists (eg, pramipexole, ropinirole) are the main pharmacotherapy options for restless legs syndrome. See page 31.

Question 17: The correct answer is A.
Shift work sleep disorder is diagnosed if a patient reports insomnia or excessive sleepiness for at least
3 months, accompanied by a reduction of total sleep time, associated with a recurring work schedule that overlaps the usual time for sleep. See page 33.

Question 18: The correct answer is B.
Risk factors for shift work sleep disorder include advancing age, female sex, and postshift morning light exposure such as may occur during a long commute home or morning social obligations. See page 34.

Question 19: The correct answer is A.
Bright light for 3 to 6 hours during the start of shift can be helpful in managing shift work sleep disorder. See page 35.

Question 20: The correct answer is C.
Staying awake until bedtime in the new time zone should promote sleep. See page 36.
Notes
The following topics appear in this month’s edition of the AAFP FP Audio™ program:

**Clinical Topic:** Diagnosis of Inflammatory Bowel Disease  
**Clinical Topic:** Management of Inflammatory Bowel Disease  
**Journal Notes:** Colonoscopy for Colorectal Cancer Screening  
**Editor’s Q&A:** Microscopic Colitis

The next edition of AAFP FP Essentials™ will be:

**Spine Conditions**