

# SLEEP DISORDERS

## CLASSIFICATION

- Circadian rhythm disorders (eg, jet lag)
- **Insomnia** (difficulty initiating or maintaining sleep, or poor quality sleep)
- Parasomnias (disorders of arousal, partial arousal, and sleep stage transition)
- Hypersomnia of central origin (eg, narcolepsy)
- **Sleep-related breathing disorders** (central and obstructive sleep apnea and sleep-related hypoventilation-hypoxia syndromes)
- **Sleep-related movement disorders** (eg, RLS, periodic limb movement disorder)

**Bolded** disorders are covered here. Others are covered in *JAGS* 2009;57:761–789.

## INSOMNIA

### Risk Factors and Aggravating Factors

Treatable Associated Medical and Psychiatric Conditions: adjustment disorders, anxiety, bereavement, cough, depression, dyspnea (cardiac or pulmonary), GERD, nocturia, pain, paresthesias, Parkinson disease, stress, stroke

Medications That Cause or Aggravate Sleep Problems: alcohol, antidepressants,  $\beta$ -blockers, bronchodilators, caffeine, clonidine, corticosteroids, diuretics, L-dopa, methyldopa, nicotine, phenytoin, progesterone, quinidine, reserpine, sedatives, sympathomimetics including decongestants

### Management

- For most patients, behavioral tx should be initial tx. Medications are usually not the best solution.<sup>cw</sup> Despite benefits of hypnotics on sleep quality, total sleep time, and frequency of nighttime awakening, these are small compared to the risk of adverse cognitive or psychomotor events. Combined behavioral tx and pharmacotherapy is more effective than either alone.
- Sleep improvements are better sustained over time with behavioral tx, including discontinuing pharmacotherapy after acute tx.

### Nonpharmacologic

- Stimulus control

Measures recommended to improve sleep hygiene:

- During the daytime:
  - Get out of bed at the same time each morning regardless of how much you slept the night before.
  - Exercise daily but not within 2 h of bedtime.
  - Get adequate exposure to bright light during the day.
  - Decrease or eliminate naps, unless necessary part of sleeping schedule.
  - Limit or eliminate alcohol, caffeine, and nicotine, especially before bedtime.
- At bedtime:
  - If hungry, have a light snack before bed (unless there are symptoms of GERD or it is otherwise medically contraindicated), but avoid heavy meals at bedtime.
  - Don't use bedtime as worry time. Write down worries for next day and then don't think about them.
  - Sleep only in your bedroom.
  - Control nighttime environment, ie, comfortable temperature, quiet, dark.
    - Wear comfortable bedclothes.
    - If it helps, use soothing noise (eg, a fan or other appliance or a "white noise" machine).
    - Remove or cover the clock.
    - No television watching in the bedroom.
    - Avoid reading e-books or tablets with light-emitting device. Standard Kindle doesn't emit light.
  - Maintain a regular sleeping time, but don't go to bed unless sleepy.
  - Develop a sleep ritual (eg, hot bath 90 min before bedtime followed by preparing for bed for 20–30 min, followed by 30–40 min of relaxation, meditation, or reading).
  - If unable to fall asleep within 15–20 min, get out of bed and perform soothing activity, such as listening to soft music or reading (but avoid exposure to bright light or computer screens).

- CBT combines multiple behavioral approaches (eg, sleep restriction, stimulus control, cognitive tx); preliminary evidence supports that this also can be delivered either by telephone or via the Internet. More effective than tai chi.
- Sleep restriction: reduce time in bed to estimated total sleep time (min 5 h) and increase by 15 min/wk when ratio of time asleep to time in bed is  $\geq 90\%$ . During the period of sleep restriction, daytime sleepiness may be increased and reaction time may be slower. Effect size is comparable to CBT.
- Relaxation techniques—physical (progressive muscle relaxation, biofeedback); mental (imagery training, mindfulness meditation, hypnosis)
- Bright light: 10,000 lux for 30 min/d upon awakening for difficulty initiating sleep; 2,500 lux for 2 h/d in evening for difficulty maintaining sleep

#### Pharmacologic—Principles of Prescribing Medications for Sleep Disorders

- Combine with behavior tx rather than give medication alone.
- Use lowest effective dose.
- All increase risk of falls.
- Do not use OTC antihistamines to treat insomnia in older adults.
- For patients with anxiety at bedtime, consider SSRIs or buspirone.
- For sleep-onset insomnia, use a shorter-acting agent (eg, zolpidem, zaleplon). For sleep-maintenance insomnia, use a longer-acting agent (eg, eszopiclone, zolpidem ER, doxepin).
- Use intermittent dosing (2–4 $\times$ /wk).
- Prescribe medications for short-term use (no more than 3–4 wk).
- D/C medication gradually.
- Be alert for rebound insomnia after discontinuation.

Useful Medications for Sleep Disorders in Older Adults

Class, Medication	Usual Dose	Formulations	Half-life	Comments (Metabolism, Excretion)
<b>Antidepressant, sedating</b>				
Trazodone <sup>▲</sup> ( <i>Desyrel</i> )	25–50 mg	T: 50, 100, 150, 300	12 h	Moderate orthostatic effects; effective for insomnia with or without depression (L)
Doxepin ( <i>Silenor</i> )	3 mg	T: 3, 6	15.3 h	May cause next-day sedation; many potential drug interactions
<b>Benzodiazepines, intermediate-acting<sup>a</sup></b>				May impair next-day performance, including driving; may cause aggressive behavior
Estazolam <sup>▲</sup> ( <i>ProSom</i> )	0.5–1 mg	T: 1, 2	12–18 h	Rapidly absorbed, effective in initiating sleep; slightly active metabolites that may accumulate (K)
Lorazepam <sup>▲</sup> ( <i>Ativan</i> )	0.25–2 mg	T: 0.5, 1, 2	8–12 h	Effective in initiating and maintaining sleep; associated with falls, memory loss, rebound insomnia (K)
Temazepam <sup>▲</sup> ( <i>Restoril</i> )	7.5–15 mg	C: 7.5, 15, 30	8–10 h <sup>b</sup>	Daytime drowsiness may occur with repeated use; effective for sleep maintenance; delayed onset of effect (K)
<b>Nonbenzodiazepines<sup>a</sup></b>				May impair next-day performance, including driving; may increase the risk of infections
Eszopiclone ( <i>Lunesta</i> )	1 mg	T: 1, 2, 3	5–6 h	CYP3A4 interactions; avoid administration with high-fat meal; not for tx of anxiety (L)

Zaleplon <sup>▲</sup> ( <i>Sonata</i> )	5 mg	C: 5, 10	1 h	Avoid taking with alcohol or food (L)
Zolpidem <sup>▲</sup> ( <i>Ambien</i> )	5 mg	T: 5, 10	1.5–4.5 h <sup>c</sup>	CYP3A4 interactions; Confusion and agitation may occur but are rare (L)
( <i>Ambien CR</i> )	6.25 mg	T: 6.25, 12.5	1.6–5.5 h	Do not divide, crush, or chew
( <i>Zolpimist</i> )	5 mg	Spr: 5 mg/spr	2–3 h	Spray over tongue; absorption more rapid
( <i>Intermezzo</i> )	1.75 mg	SL: 1.75, 3.5	2.4 h	SL: For middle-of-the-night insomnia
( <i>Eduar</i> )	5 mg	T: 5, 10 (sl)	2.8 h	
<b>Orexin Receptor Agonist</b>				
Suvorexant ( <i>Belsomra</i> )	10–20 mg	T: 5, 10, 15, 20	12 h	Metabolized by CYP3A4; can impair next-day driving
<b>Hormone and Hormone Receptor Agonists</b>				
Melatonin <sup>▲</sup>	0.3–5 mg	Various	1 h	May be best taken 3-5 h before bedtime. Not regulated by FDA
Ramelteon ( <i>Rozerem</i> )	8 mg within 30 min of bedtime	T: 8	Ramelteon: 1–2.6 h; active metabolite: 2–5 h	Do not administer with or immediately after high-fat meal (L, K)
Tasimelteon ( <i>Hetlioz</i> )	20 mg hs	T: 20		Indicated for non-24-h sleep-wake disturbance; very expensive (L)

<sup>a</sup> May cause severe allergic reactions and complex sleep-related behavioral disturbances

<sup>b</sup> Can be as long as 30 h in older adults

<sup>c</sup> 3 h in older adults; 10 h in those with hepatic cirrhosis

## SLEEP APNEA

### Definition

Repeated episodes of apnea (cessation of airflow for  $\geq 10$  sec) or hypopnea (transient reduction [ $\geq 30\%$  decrease in thoracoabdominal movement or airflow and with  $\geq 4\%$  oxygen desaturation, or an arousal] of airflow for  $\geq 10$  sec) during sleep with excessive daytime sleepiness or altered cardiopulmonary function. Predicts future strokes and cognitive impairment. HF (in men), and all-cause mortality (if severe).

### Classification

Obstructive (OSA) (90% of cases): Airflow cessation as a result of upper airway closure in spite of adequate respiratory muscle effort

- Mild Apnea-Hypopnea Index (AHI): 5–15
- Moderate: AHI 15–30
- Severe: AHI:  $>30$

Central (CSA): Cessation of respiratory effort

Mixed: Features of both obstructive and central

### Associated Risk Factors

Family hx, increased neck circumference, male gender, Asian ethnicity, hx of hypothyroidism (in women), obesity, smoking, upper airway structural abnormalities (eg, soft palate, tonsils), HTN, HF, atrial fibrillation, stroke, chronic lung diseases, including asthma

### Clinical Features

Excessive daytime sleepiness, snoring, choking or gasping on awakening, morning headache, nocturia

## Evaluation

- Epworth Sleepiness Scale ([www.umm.edu/sleep/epworth\\_sleep.htm](http://www.umm.edu/sleep/epworth_sleep.htm)) is useful for documenting and monitoring daytime sleepiness.
- Full night's sleep study (polysomnography) in sleep laboratory is indicated for those who habitually snore and either report daytime sleepiness or have observed apnea.
- "Out-of-center" sleep testing can be used if high pretest probability of moderate-to-severe OSA but should not be used if patients with comorbid conditions (eg, HF) that predispose to a sleep-related breathing disorder or another sleep disorder
- Results are reported as AHI, which is the number of episodes of apneas and hypopneas per hour of sleep.
- Medicare reimbursement threshold for CPAP based on a minimum of 2 h sleep by polysomnography is AHI (1)  $\geq 15$  or (2)  $\geq 5$  and  $\leq 14$  with documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders, or insomnia, or documented HTN, ischemic heart disease, or hx of stroke.
- No need for re-titration if asymptomatic, adherent patients with stable weight<sup>CW</sup>

## Management

### Nonpharmacologic

- Patient education including information about increased risk of motor vehicle crashes
- Weight loss (eg, using very low-calorie diet) with active lifestyle counseling is effective in mild and moderate OSA. Benefit is less in severe OSA.
- Avoidance of alcohol or sedatives
- Lying in lateral rather than supine position (if normalization of AHI in nonsupine position is confirmed by sleep study); may be facilitated by soft foam ball in a backpack or devices that use vibratory feedback.
- Exercise (eg, 150 min/wk [4 d/wk] moderate intensity aerobic exercise, even in the absence of weight loss, can improve symptoms.
- Oral appliances that keep the tongue in an anterior position during sleep or keep the mandible forward; less effective than CPAP in reducing AHI score but may be better tolerated. Generally used in mild to moderate OSA (AHI  $< 30$ ) for patients who do not want CPAP.
- For moderate sleep apnea ( $> 15$  and  $< 30$  AHI), oropharyngeal exercises, including tongue, soft palate, and lateral pharyngeal wall, performed daily improves symptoms and reduces AHI score.
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- Positive airway pressure (PAP) is initial tx for clinically important sleep apnea. PAP may also improve the metabolic syndrome associated with OSA. PAP can be delivered through several modes:
  - Continuous (CPAP) by nasal mask, nasal prongs, or mask that covers the nose and mouth is the simplest and best studied. Other modes have not been shown to be superior. A short course (14 d) of eszopiclone may facilitate adherence when initiating CPAP.
  - Bilevel (BPAP) uses 2 preset (inspiratory and expiratory) levels of pressure.
  - Autotitrating (APAP) changes PAP in response to change in air flow, circuit pressure, or vibratory snore.
  - Nasal (NPAP) (*Provent*) is a 1-way valve inserted into each nostril that creates resistance during exhalation.
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- Bariatric surgery improves but does not cure moderate or severe OSA.

### Pharmacologic (Should not be used as primary tx)

- Modafinil (*Provigil*) 200 mg qam for excessive daytime sleepiness (CYP3A4 inducer and CYP2C19 inhibitor) [T: 100, 200]; use in addition to (not instead of) CPAP

### Surgical

- Palatal implants (for mild to moderate OSA)
- Tracheostomy (indicated for patients with severe apnea who cannot tolerate positive pressure or when other interventions are ineffective)
- Uvulopalatopharyngoplasty (curative in fewer than 50% of cases). Less invasive alternatives include laser-assisted uvulopalatoplasty, radiofrequency ablation, and maxillomandibular advancement. All decrease the AHI but have not been demonstrated to be superior to medical management.
- Hypoglossal nerve stimulation with an implantable neurostimulator device
- Maxillofacial surgery (rare cases)

## SLEEP-RELATED MOVEMENT DISORDERS

### Nocturnal Leg Cramps

Stretches of the calf and hamstrings (24 inches from wall, lean forward to wall, heels on floor, hold for 10–30 sec, repeat 5×) nightly before bedtime may help. Avoid dehydration. Despite evidence of effectiveness, quinine is not recommended for nocturnal leg cramps because of the potential for serious though uncommon AEs. Small studies have supported the use of vitamin B complex, verapamil, and diltiazem. Gabapentin has been used but with little evidence to support its effectiveness. There is no evidence to support the effectiveness of magnesium.

**Restless Legs Syndrome** (RLS; the majority will also have periodic limb movement disorder)

#### Diagnostic Criteria

- A compelling urge to move the limbs, usually associated with paresthesias or dysesthesias
- Motor restlessness (eg, floor pacing, tossing and turning in bed, rubbing legs)
- Vague discomfort, usually bilateral, most commonly in calves
- Symptoms occur while awake and are exacerbated by rest, especially at night
- Symptoms relieved by movement—jerking, stretching, or shaking of limbs; pacing

Secondary Causes: Iron deficiency, spinal cord and peripheral nerve lesions, uremia, diabetes, Parkinson disease, venous insufficiency, medications/drugs (eg, TCAs, SSRIs, lithium, dopamine antagonists, caffeine)

#### Nonpharmacologic Treatment

- Sleep hygiene measures (p ###).
- Avoid alcohol, caffeine, nicotine.
- Rub limbs.
- Use hot or cold baths, whirlpools.
- Vibrating pad (*Relaxis*) available by prescription only (FDA approved)

#### Pharmacologic Treatment

- Exclude or treat iron deficiency (treat if ferritin <75 mcg/L), peripheral neuropathy.
- If possible, avoid SSRIs, TCAs, lithium, and dopamine antagonists.

Start at low dosage, increase as needed. AASM recommendations:

- Standard medications (best benefit/burden and higher quality of evidence): Dopamine agonists pramipexole (begin at 0.125 mg) or ropinirole (begin at 0.25 mg) 1 h before time of usual onset of symptoms (**Table 93**).
- Guideline medications (less favorable benefit/burden or lower quality of evidence)
  - Carbidopa-levodopa (*Sinemet*) 25/100 mg, 1–2 h before bedtime. Symptom augmentation may develop earlier in the day (eg, afternoon instead of evening) and may be more severe with carbidopa-levodopa; tx may require reducing dosage or switching to dopamine agonist
  - Gabapentin ER formulation, gabapentin enacarbil (*Horizant*) 600 mg [T: 600] daily at 5 PM, has been FDA approved for RLS
  - Pregabalin (*Lyrica*) 300 mg/d [C: 25, 50, 75, 100, 150, 200, 225, 300]
  - Low-dose opioids
  - Cabergoline (*Dostinex*) beginning 0.25 mg twice per wk; [T: 0.5] may also be effective but has potential for causing valvular heart disease.
- Optional medications (lower quality of evidence): carbamazepine (**Table 94**), clonidine, and for patients with low ferritin levels, iron supplementation.
- If refractory, can use combination tx.
- If symptoms worsen with long-term tx (augmentation), switch tx regimen.

**Periodic Limb Movement Disorder** (a minority will also have RLS)

#### Diagnostic Criteria

- Insomnia or excessive sleepiness
- Repetitive, highly stereotyped limb muscle movements (eg, extension of big toes with partial flexion of ankle, knee, and sometimes hip) that occur during nonREM sleep
- Polysomnographic monitoring showing >15 episodes of muscle contractions per hour and associated arousals or awakenings
- No evidence of a medical, mental, or other sleep disorder that can account for symptoms

Treatment: Indicated for clinically significant sleep disruption or frequent arousals documented on a sleep study.

- Nonpharmacologic: See sleep hygiene measures, p ###.
- Pharmacologic: See RLS, Pharmacologic Treatment, above.

### **Rapid-Eye Movement (REM) Sleep Behavior Disorder**

- Loss of atonia during REM sleep (ranging from simple limb twitches to acting out dreams), exaggeration of features of REM sleep (eg, nightmares), and intrusion of aspects of REM sleep into wakefulness (eg, sleep paralysis)
- High risk of developing neurodegenerative disorder (eg, Parkinson disease, multisystem atrophy, Lewy body dementia)

Evaluation: If needed, in-laboratory video polysomnography

Nonpharmacologic Treatment: change sleeping environment to reduce risk of injury

Pharmacologic Treatment: clonazepam 0.25–1 mg hs, high-dose melatonin 3–6 mg; if associated with Parkinson disease, L-dopa, or pramipexole

## **SLEEP DISORDERS IN LONG-TERM-CARE FACILITIES**

### **Risk Factors**

- Medical and medication factors (Insomnia, p ###)
- Environmental factors (eg, little physical activity, infrequent daytime bright light exposure, extended periods in bed, nighttime noise and light interruptions)

### **Nonpharmacologic Treatment**

- Morning bright light tx
- Exercise (eg, stationary bicycle, Tai Chi) and physical activity
- Reduction of nighttime noise and light interruptions
- Multicomponent interventions combining the above and a bedtime routine

### **Pharmacologic**

One small study in a long-term-care facility demonstrated benefit of a supplement (5 mg melatonin, 225 mg magnesium, and 11.25 mg zinc, mixed with 100 g of pear pulp) 1 h before bedtime.