

A composite image featuring a woman lying in bed in the foreground, looking upwards. In the background, a semi-transparent, ghostly image of the same woman is shown sitting up on the bed, appearing to be in a state of wakefulness or distress. The scene is set in a bedroom with floral wallpaper and a window in the upper right. The overall mood is one of insomnia or sleeplessness.

# Treating insomnia

Tailor therapy to  
address hormonal  
changes, other factors

# across women's life stages

## Changes during menstruation, pregnancy, and menopause often impact sleep

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**M**s. A, age 44, reports a 3-month history of forgetfulness, difficulty concentrating, and insomnia. She says she can fall asleep but wakes up multiple times during the night and feels tired during the day. She has no history of a mood or anxiety disorder or medications that might be responsible for her symptoms.

Before her current insomnia began, Ms. A could sleep for 7 to 8 hours at night. Her husband suffers from obstructive sleep apnea (OSA), and his snoring occasionally would awaken her, but she slept well overall. Ms. A cannot identify anything that could be causing her sleep complaints. She states "The weird thing is that sometimes I am not sure if I'm cold or hot" and "I sometimes wake up drenched in sweat." She also reports recent changes in the timing of her otherwise regular menstrual flow.

Ms. A attributes her memory problems to her poor sleep. A recent audit at her company held her responsible for several accounting errors, and Ms. A is worried that she might lose her job. She denies symptoms that would suggest major depression. You are unable to elicit a history of limb movements or excessive snoring.

Compared with men, women have a 1.3- to 1.8-fold greater risk for developing insomnia.<sup>1,2</sup> Multiple factors contribute to this increased risk of insomnia, including:

- hormonal changes across the reproductive cycle<sup>3,4</sup>
- predilection to mood and anxiety disorders
- psychosocial factors, such as being single, separated, or widowed.<sup>5</sup>

Furthermore, the higher prevalence of psychiatric disorders during the reproductive stages may confer additional risk for sleep problems.

Insomnia has tremendous impact on health and quality of life, re-



## Insomnia in women

### Clinical Point

Women's life stages are marked by physiologic changes that impact insomnia risk

Table 1

## Sleep characteristics across the life span

Age	Sleep architecture	Total sleep time per 24 hours	Number of sleep periods per 24 hours
0 to 1	Sleep onset begins with REM. REM represents >50% of total sleep time	16 to 18 hours	6 to 9
>1 to 16	Fully developed REM and NREM sleep. Majority of sleep occurs during nighttime hours. Onset of a single consolidated sleep period usually occurs by age 5	Up to age 13: 12 hours Age >13 to 16: 8 hours	Age >1 to 5: 2 to 3 Age >5 to 16: 1
>16 to 50	Stage I: 2% to 5% Stage II: 45% to 55% Stage III: 3% to 8% Stage IV: 10% to 15% REM sleep: 20% to 25% Decreased SWS (stage III and stage IV) and delta wave activity	7 to 8 hours	1
>50	REM and light NREM sleep progressively decline and result in increased wake time	Variable	Variable

NREM: non-rapid eye movement; REM: rapid eye movement; SWS: slow wave sleep  
Source: Reference 3

sulting in reduced work productivity and increased absenteeism, accidents, and health care costs.<sup>6</sup> This article examines the factors that contribute to women's sleep difficulties throughout the life cycle, and suggests evaluation and treatment approaches appropriate for each phase.

### Sex differences in sleep

DSM-IV-TR criteria for primary insomnia include experiencing difficulty initiating or maintaining sleep, or nonrestorative sleep, for  $\geq 1$  month that:

- causes significant distress or impairment in social, occupational, or other important areas of functioning
- does not occur exclusively during the course of another sleep disorder
- does not occur exclusively during the course of a mental disorder
- is not due to the direct physiologic effects of a substance or a general medical condition.<sup>7</sup>

The lifetime prevalence rate of insomnia is 10% to 30%.<sup>8</sup> A meta-analysis of epidemiologic studies that included >1 million subjects concluded that insomnia is more prevalent in women, with a risk ratio of 1.4 for females vs males.<sup>9</sup>

For both men and women, sleep characteristics vary across the life span (Table 1).<sup>3</sup> Men experience more stage 1 sleep than women, who have more stage 3 and 4 sleep, according to studies of sleep architecture. This contrasts with polysomnography studies, which have reported women have better sleep quality compared with men. Sex differences may depend at least in part on how sleep is measured (ie, subjective vs objective).

A thorough evaluation of insomnia includes obtaining a detailed history from the patient and her bed partner, and asking about her hormonal status (Table 2).<sup>10</sup> Women's life stages are marked by physiologic changes related to the reproductive cycle, including onset of menstruation (menarche), pregnancy, the postpartum period, and menopause, each of which impacts insomnia risk.

### Menstruation's effect on sleep

The menstrual cycle is regulated by luteinizing and follicle-stimulating hormones, which are produced by the pituitary gland. Cyclic alterations in progesterone and estrogen levels throughout the menstrual cycle produce 3 distinct phases: follicular, ovulatory, and luteal.

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One small study that evaluated sleep diaries of 32 healthy women found a significant increase in sleep onset latency and decrease in sleep efficiency and quality during the luteal phase that was not related to the severity of other premenstrual symptoms.<sup>11</sup> Results from polysomnography studies have been mixed.<sup>12,13</sup> Evaluation of 138 sleep episodes among 9 healthy women revealed no significant variation across the menstrual cycle in subjective ratings of sleep quality and mood or objective measures of total sleep time, sleep efficiency, sleep latency, rapid eye movement (REM) sleep latency, and slow wave sleep.<sup>13</sup> However, given the limited number of studies, small sample sizes, exclusion of women from certain age groups, and subjects' varied length of the menstrual cycle, additional research is warranted.<sup>14</sup>

**Premenstrual syndrome (PMS)** is a constellation of physical and mood symptoms that appear during the last 1 or 2 weeks of the menstrual cycle and resolve by the end of menses. Premenstrual dysphoric disorder (PMDD) is a more severe form of PMS characterized by significant premenstrual mood disturbance and associated social or occupational impairment. Although PMS is not a DSM-IV-TR diagnosis, the term often is used in clinical settings. In DSM-IV-TR, PMDD is classified as a "depressive disorder not otherwise specified."

Sleep complaints are common in PMS and PMDD. Survey and polysomnography studies have reported increased sleep difficulties in the late luteal phase.<sup>1</sup>

**Treatment strategy.** Begin by obtaining a thorough history of your patient's menstrual cycle regularity, the temporal relationship of the sleep difficulties to the menstrual phase, and physical symptoms such as dysmenorrhea, headaches, breast tenderness, bloating sensations, and weight gain. Screen for PMDD symptoms, which include mood swings, feelings of deep sadness or despair, irritability, anxiety, poor concentration, and sleep difficulties. Treatment choices depend on the patient's stress level and severity of functional impairment (*Algorithm, page 30*).<sup>15,16</sup>

Table 2

## Evaluating women's insomnia: First steps

Take a detailed history from your patient and her bed partner
Obtain details of sleep onset, duration, quality of sleep, frequency and number of awakenings, daytime alertness, snoring, apnea, and limb movements
Ask about your patient's hormonal status
Screen for mood and anxiety symptoms
Assess prescription and nonprescription medication use, general medical conditions, substance use, and psychiatric disorders
Use sleep dairies and the Pittsburgh Sleep Quality Index <sup>10</sup> as objective sleep measures

Options include:

- sleep hygiene (establishing a regular sleep/wake schedule, limiting caffeine and alcohol, avoiding naps, eliminating noise and light from the bedroom, using the bed only for sleeping, and not looking at a clock while trying to sleep)
- behavioral therapy, such as cognitive-behavioral therapy (CBT) or sleep restriction therapy
- pharmacotherapy with a selective serotonin reuptake inhibitor (SSRI) or sedative/hypnotic.

## Sleep trouble during pregnancy

The prevalence of altered sleep during pregnancy ranges from 15% to 80% in the first trimester to 66% to 97% in the third trimester.<sup>17</sup> These changes include decreased total sleep time<sup>18</sup> and increased nocturnal awakenings.<sup>19</sup> Postpartum women have more awakenings, lower sleep efficiency and total sleep times, and increased REM latency.<sup>4</sup>

Factors that contribute to altered sleep in pregnancy and the postpartum period include:

- first-trimester nausea and vomiting
- second-trimester cramps, fatigue, and shortness of breath
- increased risk for sleep-disordered breathing (secondary to weight gain, increased snoring, mucosal edema, increased upper airway resistance [estrogen effect],

## Clinical Point

**A small study found increased sleep difficulties during the luteal phase; results from other trials were mixed**



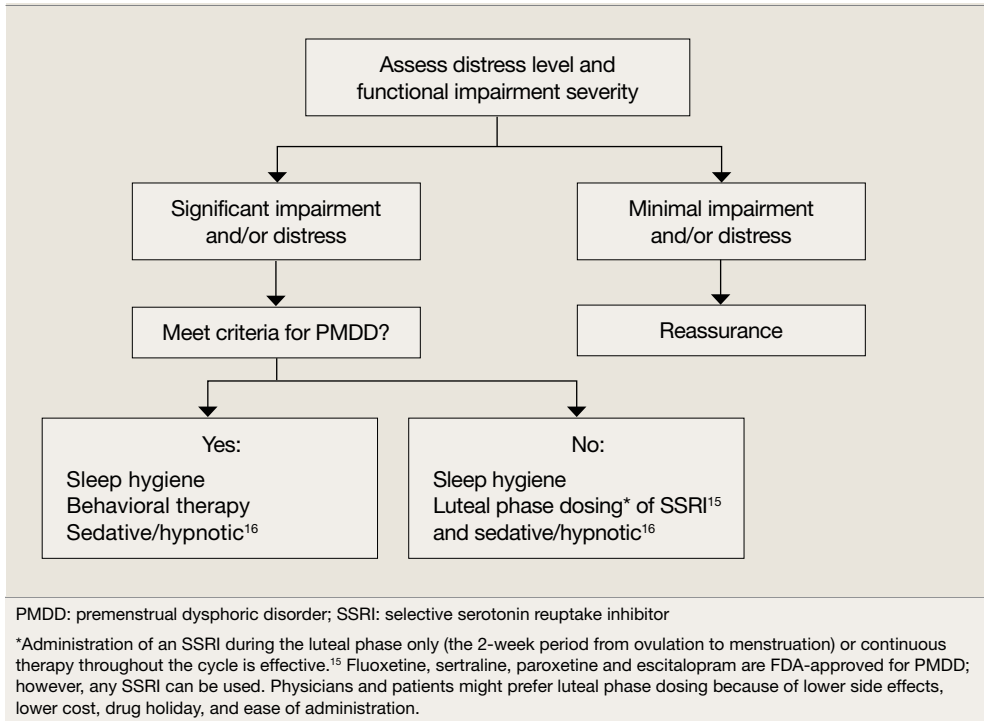
## Insomnia in women

### Clinical Point

Maintain a high index of suspicion for obstructive sleep apnea and restless legs syndrome

### Algorithm

## Perimenstrual insomnia: Distress, severity guide treatment



and changes in ventilator mechanics [progesterone effect])

- higher risk for restless legs syndrome (RLS) related to iron deficiency
- infant sleep and feeding schedule
- postpartum depression
- abrupt decline in estrogen and progesterone following childbirth.

**Treatment strategy.** Pay attention to pregnant women's sleep difficulties in the second and third trimesters because sleep deprivation may contribute to the development of "baby blues" and postpartum depression.<sup>20</sup>

Behavioral interventions such as CBT are first-line therapy for pregnant or postpartum women with insomnia. (For more on CBT for insomnia, see "Improve sleep with group CBT for insomnia," *CURRENT PSYCHIATRY*, April 2009, p. 70.) Pharmacotherapy during pregnancy and for breast-feeding mothers is guided by evaluating the risk/benefit ratio and safety considerations.

Maintain a high index of suspicion for breathing-related sleep disorders, such as OSA,<sup>21</sup> and RLS.<sup>22</sup> Atypical presentations

of OSA are common in pregnant or postpartum women; compared with men, women with OSA are more likely to report fatigue and less likely than to report sleepiness. Refer patients whom you think may have OSA for polysomnography.

If you suspect RLS, check for low ferritin and folate levels. Nutritional supplements may be necessary for women in high-risk groups, including those who are pregnant or have varicose veins, venous reflux, folate deficiency, uremia, diabetes, thyroid problems, peripheral neuropathy, Parkinson's disease, or certain autoimmune disorders, such as Sjögren's syndrome, celiac disease, and rheumatoid arthritis.<sup>23</sup> Advise these patients to avoid caffeine.

Although indicated for treating RLS, ropinirole and pramipexole are FDA Pregnancy Category C, which means animal studies have shown adverse effects on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite risks. Opioids, carbamazepine, or gabapentin may be safer for pregnant patients.<sup>24</sup>

Table 3

## Sleep difficulties during menopause: Differential diagnoses

Condition	Features	Findings	Other considerations
Hot flashes (prevalence: 75% to 85%) <sup>14</sup>	Vasomotor phenomenon characterized by feelings such as 'spreading warmth,' diaphoresis, palpitations, nausea, and insomnia  Mediated through the preoptic area of the anterior hypothalamus, which regulates temperature and sleep  Increased brain norepinephrine metabolism	Discrepancies between objective (PSG) and subjective measures (surveys) <sup>4</sup>  Discrepancies between self-reported and laboratory reported sleep data might be explained by thermoregulatory differences between NREM and REM sleep <sup>24</sup>	Nocturnal hot flashes trigger awakenings and insomnia <sup>14</sup>  Hot flashes can follow arousals and awakenings  HRT is highly effective in treating hot flashes; however, data on its direct effects on sleep complaints are inconsistent
Primary menopausal insomnia <sup>25</sup>	Menopausal symptoms (eg, hot flashes) trigger insomnia that persists secondary to behavioral conditioning	Increase in nocturnal skin temperature coincides with decrease in skin resistance and waking episodes in PSG	Behavioral insomnia therapies are useful adjuncts to treatment of menopause symptoms
Sleep-disordered breathing (OSA)	Menopause increases risk for OSA independent of body weight  Redistribution of body fat with an increase in the waist-to-hip circumference ratio occurs in menopause  Loss of ventilatory drive because of diminished progesterone levels	Sleep fragmentation and daytime sleepiness are common, as opposed to apneic episodes or oxygen desaturation in men	Maintain a high index of suspicion and promptly refer patients to a sleep center
Restless legs syndrome	Related to iron deficiency	Low ferritin and folate levels	Advise patients to avoid caffeine

HRT: hormone replacement therapy; NREM: non-rapid eye movement; OSA: obstructive sleep apnea; PSG: polysomnography; REM: rapid eye movement

### Clinical Point

Hot flashes and mood disturbances contribute to insomnia in postmenopausal women

### Insomnia during menopause

The prevalence of insomnia increases from 33% to 36% in premenopausal women to 44% to 61% in postmenopausal women.<sup>14</sup> Hot flashes, comorbid mood disturbances, sleep-disordered breathing, and RLS contribute to increased insomnia risk in postmenopausal women (*Table 3*).<sup>4,14,25,26</sup>

**Treatment strategy.** Always inquire about sleep in perimenopausal/postmenopausal women, even when her presenting complaint is related to menstrual cycle changes or vasomotor symptoms such as hot flashes.<sup>16</sup> Assess patients for OSA, RLS, and mood, anxiety, and cognitive symptoms.<sup>26</sup> In addition to pharmacotherapy and behavioral

therapy, treatment options include hormone replacement therapy (HRT) and herbal and dietary supplements (*Table 4, page 32*).<sup>27-32</sup>

### Comorbid psychiatric disorders

Women have a higher prevalence of psychiatric disorders such as major depressive disorder and anxiety disorders than men.<sup>1</sup> Women have a 10% to 25% lifetime risk of developing major depression. Three quarters of depressed patients experience insomnia.<sup>1</sup> Recent literature suggests insomnia is a risk factor for depression,<sup>33</sup> which emphasizes the need to screen women who present with sleep problems for depression and anxiety.

continued



## Insomnia in women

### Clinical Point

Postpartum depression and insomnia are correlated to estrogen and progesterone declines after delivery

**Table 4**

## Treating insomnia in menopausal women

Therapy	Comments
Hormone replacement therapy (HRT)	Effective for hot flashes, insomnia, <sup>26-28</sup> and sleep apnea <sup>29</sup> Long-term safety is questionable <sup>4</sup>
Behavioral therapy (cognitive-behavioral therapy, <sup>30</sup> stimulus control therapy, sleep restriction therapy, sleep hygiene, hypnotherapy, biofeedback)	Limited data in menopausal women
Sedatives/hypnotics/antidepressants (eg, zolpidem, 10 mg; eszopiclone, 3 mg; trazodone, 75 mg; ramelteon, 8 mg; SSRIs and SNRIs)	Benzodiazepines may be useful, although not specifically evaluated in menopausal women. Risk of tolerance, dependence, and psychomotor slowing
Herbal and dietary supplements (Cimicifuga racemosa [Black cohosh], <sup>31</sup> valerian)	Popular alternatives to HRT; however, evidence of efficacy as treatment for insomnia is inconclusive

SNRIs: serotonin-norepinephrine reuptake inhibitors; SSRIs: selective serotonin reuptake inhibitors

Five percent to 20% of women experience postpartum depression. Depression and insomnia are correlated to the rapid decline in estrogen and progesterone after delivery.<sup>34</sup>

**Treatment strategy.** Insomnia is a common presenting symptom in patients with psychiatric conditions such as mood and anxiety disorders. Treating the underlying psychiatric disorder often alleviates sleeping difficulties. However, if the insomnia is disabling, treat the psychiatric disorder and insomnia concurrently.

### CASE CONTINUED

#### Perimenopausal insomnia

Based on her history, you diagnose Ms. A with insomnia related to general medical condition (perimenopause). There are no indications to refer her for polysomnography. You educate Ms. A about sleep hygiene and recommend that she discuss her menstrual and physical complaints with her primary care physician or gynecologist. Ms. A is not interested in HRT because she has a strong family history of endometrial cancer. You reassure Ms. A and schedule a follow-up visit in 2 months to re-evaluate her insomnia.

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## Related Resource

• Krahn LE. Perimenopausal depression? Ask how she's sleeping. *Current Psychiatry*. 2005;4(6):39-53.

### Drug Brand Names

Carbamazepine • Carbatrol,	Paroxetine • Paxil
Tegretol, others	Pramipexole • Mirapex
Escitalopram • Lexapro	Ramelteon • Rozerem
Eszopiclone • Lunesta	Ropinirole • Requip
Fluoxetine • Prozac	Sertraline • Zoloft
Gabapentin • Neurontin,	Trazodone • Desyrel
Gabarone	Zolpidem • Ambien

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## Clinical Point

Treating an underlying psychiatric disorder often alleviates insomnia

## Bottom Line

Hormonal status and comorbid mood disturbances play a role in women's sleep complaints. Maintain a high index of suspicion for breathing-related sleep disorders and restless legs syndrome at any reproductive phase. Pharmacotherapy should be guided by insomnia severity, urgency for relief, comorbid medical and psychiatric conditions, safety issues, and patient preference. Although not systematically studied in women with insomnia, behavioral therapies should be an integral part of management because dysfunctional beliefs about sleep and poor sleep habits can intensify and prolong symptoms.