

Sleep and Sleep Disorders in Pregnancy

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Sleep problems are common in pregnant women. This review examines sleep in normal pregnancy; discusses the physiologic bases for alterations in sleep, including hormonal and mechanical factors; and correlates these factors with changes in sleep of pregnant women, as determined subjectively by surveys and objectively by polysomnographic studies. The changes in respiratory physiology during pregnancy, the possible predisposition of the pregnant woman to sleep-disordered breathing because of these changes, and results of published studies of sleep-disordered breathing in pregnancy are discussed. Finally, the effect of preg-

nancy on other sleep disorders and the management of these sleep disorders during pregnancy are outlined, including changes in management necessitated by this state. The paucity of available data and the need for further studies of incidence and outcomes of sleep disorders in the pregnant woman are emphasized.

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For a glossary of terms, see end of text.

That sleep can be disturbed in pregnancy has been known for some time. Hippocrates' pregnancy test consisted of giving a suspected woman hydromel at sleep initiation; arousal due to abdominal discomfort indicated a positive result (1). The sleeplessness that accompanies labor led to prolonged disagreement in the 18th century over whether to promote or prevent sleep in the postpartum period (2). The concern was that a sleeping woman would miss the occurrence of "uterine flooding" and die of postpartum hemorrhage. Smellie (2) recognized the restorative effect of sleep and suggested promoting it with "comfortable beds and clean linen," noting that patients generally do not fall asleep while actively bleeding. It has been noted that thalidomide's teratogenic effect would not have been quickly discovered had not many sleepless pregnant women asked their obstetricians for sleeping pills (3). These and other sleep-related problems have prompted the American Sleep Disorders Association to propose the existence of "pregnancy-associated sleep disorder" (4).

In this review, we discuss sleep changes in normal pregnancy and sleep disorders occurring in the pregnant woman. We also propose the possibility that the descriptive term "pregnancy-associated sleep disorder" might cause attribution of undiagnosed sleep disorders in the pregnant woman to presumed physiologic mechanisms unique to pregnancy.

METHODS

We searched the MEDLINE database for relevant studies by using the term *pregnancy* combined with each of the following terms: *sleep, wakefulness, sleeping, in-*

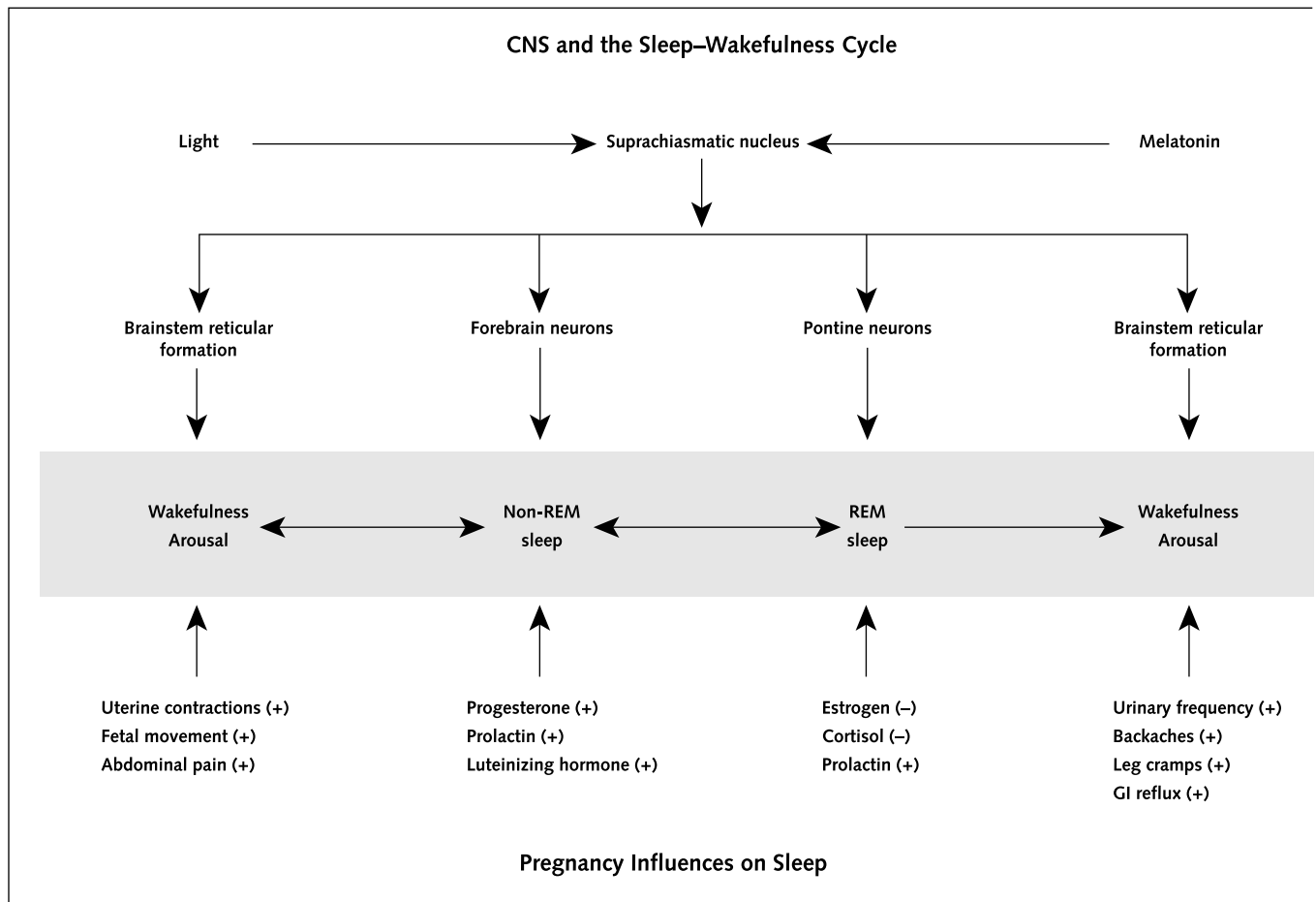
somnia, parasomnia, hypersomnia, pulmonary, lung, circadian rhythms, REM, NREM, polysomnogram, apnea, OSA, narcolepsy, snoring, desaturation, sleepwalking, CPAP, movement disorders, restless legs, and PLMS. Only English-language articles and selected cross-references were considered for inclusion. Conference proceedings, bibliographies of review articles, and book chapters were also searched for appropriate articles. Articles were screened for relevance on the basis of information in the title and abstract. The main criterion for inclusion of articles was relevance to the physician caring for pregnant patients with sleep-related problems and sleep disorders, as determined by the authors.

NORMAL SLEEP IN PREGNANCY

Physiologic Basis for Sleep Changes

The sleep-wakefulness cycle follows a circadian rhythm that is controlled primarily by the suprachiasmatic nucleus of the hypothalamus (5). This structure, which is sensitive to both the light-dark cycle (6) and the pineal hormone melatonin (7), promotes wakefulness by influencing neuronal activity in the brainstem reticular formation (8). Aided by decreases in sensory input, this structure helps regulate sleep-inducing neurons, thereby promoting non-rapid eye movement (non-REM) sleep and cortical slow-wave activity (9). Forebrain structures, especially in the preoptic area, seem to be important in causing non-REM sleep (10, 11), and γ -aminobutyric acid neurons located in the cortex contribute to the generation of slow-wave activity (9). Rapid eye movement sleep and its accompanying neurophysiologic phenomena are generated by cholinergic

Figure. Central nervous system (CNS) structures involved in the sleep–wakefulness cycle and pregnancy influences on the cycle.



The biological clock (the suprachiasmatic nucleus), influenced by light and melatonin, interacts with brain neurons to generate a circadian timing for wakefulness and arousal and for rapid eye movement (REM) and non-REM sleep. Bidirectional changes in physiologic states can occur, with the exception of REM sleep and wakefulness. Physiologic and hormonal events in pregnancy promote (+) or reduce (–) time spent in each state through as yet unclear neural mechanisms. GI = gastrointestinal.

neurons in the pons (12). The onset of REM sleep is accompanied by cessation of activity in brainstem noradrenergic and serotonergic neurons (13). The near 24-hour oscillation generated in the suprachiasmatic nucleus and the alteration of sleep and wake states influence the hypothalamic structures responsible for the pulsatile release of hormones that stimulate or inhibit secretion of other hormones (14). Thus, several hormones exhibit 24-hour rhythms, some of which have been described in pregnancy. They include growth hormone (15); prolactin (16–18); melatonin (19); cortisol (17, 20); thyroid-stimulating hormone (17); oxytocin (21); and placental hormones, including chorionic go-

nadotropin, progesterone, estriol, and dihydroepiandrosterone (15). Several hormonal rhythms, some of which affect sleep, are altered by pregnancy. The relationship between sex steroids and sleep has been recently reviewed (22). Hormonal influences and mechanical and somatic factors that affect the sleep–wakefulness cycle during pregnancy are shown in the **Figure**.

Two hormones that progressively increase in pregnancy and affect sleep are estrogen and progesterone. Ample evidence indicates that estrogen decreases REM sleep (23–25). Ovariectomy enhances REM sleep in rats (26), and subsequent estrogen administration reduces REM sleep (23). Rapid eye movement sleep also de-

creases during proestrus, when plasma concentrations of β -estradiol are approaching their maximal values (24, 25). One study (27) suggested that estrogen exerts this influence by increasing turnover of brainstem noradrenaline. In contrast, progesterone applied directly to the preoptic area of the forebrain induces sleep (28). Furthermore, exogenously administered progesterone has a sedating effect in both men (29) and women (30) and has been shown to increase non-REM sleep (31). This effect may be mediated by progesterone (or its precursors) acting as γ -aminobutyric acid_A-receptor agonists (32). In pregnant rats, non-REM and REM sleep significantly decreased 24 hours before parturition, a phenomenon attributed to the concomitant increase in estrogen and decrease in progesterone during this period (33). It therefore appears likely that these two hormones influence sleep during pregnancy, although their combined effects may depend on their relative concentrations.

In the nonpregnant woman, the cortisol level peaks in the early morning and at noon. Although the latter peak is abolished by placental adrenocorticotropic hormone in pregnancy, cortisol concentrations increase twofold in late pregnancy and fourfold during labor (20). Cortisol infusions in men that increase plasma levels to 3.6 times the normal value reduce REM sleep (34). Progesterone shares binding sites on corticosteroid-binding globulin; hence, increased levels of progesterone also elevate free cortisol levels (15). Pregnant patients who are sleeping poorly in the third trimester have been found to have lower cortisol–melatonin ratios than good sleepers because of a lower early morning peak in cortisol level and a relatively higher concentration of melatonin (35). Previous studies have demonstrated elevated cortisol levels in depressed patients compared with controls, and cortisol levels are lower in the same patient during depression-free intervals (36). This finding has led to the hypothesis that the pituitary–adrenal axis contributes to the genesis of depression. This idea remains to be proved; however, it is of interest that the cortisol–melatonin ratio may help differentiate between a primary sleep disturbance, in which the ratio is low, and psychiatric depression causing disturbed sleep, in which the ratio is high (37).

Since melatonin modulates the circadian pacemaker, it has been extensively studied during pregnancy. Several studies in ewes tracked levels of melatonin in a given day and throughout pregnancy and concluded

that melatonin secretion is unchanged from the non-pregnant state (38–40). Concentrations of melatonin in the serum and amniotic fluid of pregnant women in labor have been found to follow a diurnal rhythm similar to that in nonpregnant women (19). Induction of labor or operative delivery had no effect on melatonin levels (19). Thus, circadian pacemaker disturbances secondary to melatonin do not appear to contribute to the changes in sleep seen in pregnancy.

Prolactin secretion during sleep is maintained at a higher set-point in pregnancy (18, 41). Prolactin injections promote REM sleep in rabbits (42) and may be responsible for the increase in REM sleep in early pregnancy in rats (28). Prolactin together with luteinizing hormone may also contribute to the increase in non-REM sleep seen throughout pregnancy in rats (28).

Uterine activity behaviorally affects sleep and is linked to rhythms in maternal secretion of steroid, melatonin, and oxytocin (15). Oxytocin peaks at night coincident with the peak of uterine activity (43). This probably contributes to insomnia during the third trimester of pregnancy and may explain the increased incidence of labor and delivery during the evening hours (15). Of note, phase-shifting the light–dark cycle results in a parallel shift in uterine activity (44).

The rhythm of nocturnal uterine activity carries implications for maternal and fetal oxygenation. In pregnant ewes, uteroplacental blood flow and oxygen delivery decrease by about 19% during active (REM) sleep in the presence of myometrial activity (45). This reduction may cause fetal problems during maternal hypoxemia or when uteroplacental blood flow is decreased, such as in preeclampsia.

Finally, other hormones and growth factors, including human chorionic gonadotropin (46), renin (28), nitric oxide (47), interleukin-1 (28), tumor necrosis factor (28), and interferon (28), may be somnogenic in pregnancy and deserve further study.

In summary, during pregnancy, various hormonal and mechanical influences promote insomnia and several hormonal factors promote hypersomnia.

Sleep Surveys and Polysomnographic Data

Sleep in women of childbearing age has been investigated by various authors. Total sleep time ranges from 7 to 9 hours between the ages of 18 and 45 years (48, 49). Of this time, about 80% is spent in non-REM sleep

Table 1. Characteristics of Sleep in Pregnancy*

Stage of Pregnancy	Subjective (Surveys and Sleep Logs)	Objective (Polysomnography)
First trimester	Increased total sleep time due to naps (3, 51) Increased daytime sleepiness (3, 51) Increased nocturnal insomnia (3, 51)	Increased total sleep time (56) Decreased stage 3 and 4 non-REM sleep (56)
Second trimester	Normalization of total sleep time (51) Increased awakening (3)	Normal total sleep time (56) Decreased stage 3 and 4 non-REM sleep (56) Decreased REM sleep (56)
Third trimester	Decreased total sleep time (3, 51) Increased insomnia (3, 51) Increased nocturnal awakening (53, 54) Increased daytime sleepiness (3, 51)	Decreased total sleep time (52, 56) Increased waking after sleep onset (55, 58) Increased stage 1 non-REM sleep (55) Decreased stage 3 and 4 non-REM sleep (53, 56) Decreased REM sleep (52, 55, 56, 58)

* Numbers in parentheses are reference citations. REM = rapid eye movement.

and about 20% in REM sleep (50). Several studies have been performed in normal pregnancy by using questionnaires, sleep logs, and polysomnographic studies (3, 51–60). A summary of subjective and objective changes in sleep in the pregnant woman is shown in **Table 1**.

Most pregnant women (66% to 94%) report alterations in sleep (3, 51). During the first trimester, total sleep time, daytime sleepiness, insomnia, and nocturnal awakenings increase and overall sleep quality decreases (3, 51). Sleep appears to normalize in the second trimester (51), although sleep disturbances continue in about 19% of patients (3). In the third trimester, women awaken three to five times per night (53, 54), nap daily for an average of 65 minutes, and experience worsening insomnia and diminished daytime alertness (3, 51). The most common reasons given for third-trimester sleep disturbances are urinary frequency, backache, fetal movement, general abdominal discomfort, leg cramps, and heartburn (3, 51, 55).

Because it is a complex procedure, polysomnography has been less often performed in pregnant women who are not suspected of having sleep disorders. Studies in which polysomnography was used to characterize sleep during normal pregnancy reached somewhat similar conclusions and are in close concordance with subjective perceptions.

Both longitudinal and single-trimester studies have been done. A prospective study of 33 pregnant women followed before conception and during pregnancy noted an increase in total sleep time in the first trimester, normalization by the second trimester, and a decrease in the third trimester (56). Sleep stage distribution showed de-

creased stage 3 and 4 non-REM sleep in the first trimester and throughout pregnancy (56). Other longitudinal studies (52, 58–60) showed decreased sleep efficiency and increased awake time after sleep onset with advancing pregnancy, as well as decreased REM sleep, especially in the third trimester. Third-trimester studies of 7 and 12 women confirmed these findings (53, 55). Primiparous women experienced more sleep disturbances than multiparous women (56). During the postpartum phase, the amount of non-REM and REM sleep recovered to near baseline levels, but reduced sleep efficiency and increased wakefulness persisted up to 3 months after delivery (53, 55). However, the latter finding is difficult to interpret because of the role of environmental factors (for example, a crying baby).

No polysomnographic studies detailing sleep alterations have been performed in pathologic states, such as preeclampsia or pregnancy-induced hypertension. By using questionnaires and a static charge-sensitive bed, sleep quality was studied in nine patients with preeclampsia and compared with that in eight women with uncomplicated pregnancies (59). Patients with preeclampsia had poorer sleep quality and increased sleep fragmentation with increases in total nocturnal movements, total frequency of body movements, and time spent out of bed.

The American Sleep Disorders Association has proposed the existence of “pregnancy-associated sleep disorder.” Consensus is that this disorder begins with excessive sleepiness and progresses to severe insomnia (4). The excessive sleepiness is attributed to somnogenic hormones and the insomnia, to abdominal discomfort from

Table 2. Drug Therapy for Sleep Disorders*

Drug	Pregnancy Category†
Sedatives and hypnotics	
Alprazolam	D
Diazepam	D
Lorazepam	D
Midazolam	D
Temazepam	X
Clonazepam	C
Diphenhydramine	B
Secobarbital	D
Zolpidem	B
Zaleplon	C
Stimulants	
Dextroamphetamine	C
Methamphetamine	C
Pemoline	B
Mazindol	C
Methylphenidate	C
Modafinil	C
Antidepressants	
Fluoxetine	B
Paroxetine	B
Amitriptyline	D
Other	
Carbamazepine	C
Carbidopa	C
Levodopa	C
Codeine	C

* Adapted from reference 64, except for information on zaleplon and modafinil.
 † The U.S. Food and Drug Administration assigned five categories of labeling for drug use in pregnancy:

- A: Controlled studies in women have failed to demonstrate a risk to the fetus in the first trimester, and the possibility of fetal harm appears remote.
- B: Animal studies do not indicate a risk to the fetus; no controlled human studies have been published, or animal studies show an adverse effect on the fetus but well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus.
- C: Studies have shown teratogenic or embryocidal effects in animals, but no controlled studies are available in women or no studies are available in either animals or women.
- D: Positive evidence of human fetal risk exists, but benefits from use in pregnant women may be acceptable despite this risk (for example, when the life of the mother is in danger or she risks serious disease for which safer drugs are ineffective or cannot be used).
- X: Studies in animals or humans have demonstrated fetal abnormalities or evidence of fetal risk exists on the basis of experience in humans (or both) and the risk of use clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

increased size, fetal movement, and bladder distention. Other factors, including urinary frequency, backache, and heartburn, also contribute (3, 51, 55). However, since primary sleep disorders also present with hypersomnia or insomnia, ready attribution of these symptoms to pregnancy-related mechanisms could lead to nonrecognition of sleep disorders in pregnancy.

Despite the significant sleep disruption that occurs in pregnancy, particularly during the third trimester, most women do not ask for assistance in improving sleep (51). This is perhaps because pharmacologic ther-

apy is often the first option offered to treat insomnia, and pregnant women may be reluctant to take medications. However, if a detailed sleep history reveals no other cause of insomnia (such as depression, witnessed apneas, restless legs, or periodic leg movements) and if the insomnia manifests during the third trimester when it is physiologically expected to occur, nonpharmacologic interventions are frequently effective and should be the initial therapy. Such interventions include improving sleep hygiene (establishing regular sleep-wake hours, limiting naps, and avoiding caffeine); practicing relaxation techniques; minimizing intrusive bedroom noises; limiting fluid intake after 6 p.m. to reduce nocturnal urinary frequency; and managing low back pain with massage, local heat, and pillow support (61, 62). Stimulus-control techniques, such as going to bed only when sleepy, using the bed only for sleep, and getting out of bed in the event of prolonged awakenings, might also be tried (63). If these conservative measures fail, the pharmacologic agents of choice are diphenhydramine or zolpidem, both of which are category B agents in pregnancy (64) (Table 2). Experience with zolpidem in pregnant women is still limited.

SLEEP AND BREATHING IN PREGNANCY

Physiologic Changes

Pregnancy induces changes in the respiratory system through mechanical and biochemical mechanisms. Changes in the airway mucosa consisting of hyperemia, hypersecretion, and mucosal edema occur, especially in the third trimester (65); these may predispose to snoring and upper-airway obstructive events.

Large-airway function is preserved (66, 67), but a high incidence of small-airway closure at lung volumes greater than functional residual capacity occurs during the last month of pregnancy (68). Functional residual capacity itself decreases because of a reduction in expiratory reserve volume (66, 69). A reduced functional residual capacity reduces oxygen stores and makes changes in arterial oxygen more likely to accompany respiratory disturbances, such as those that may occur during sleep.

Another factor that both protects against and is conducive to sleep-disordered breathing is the hyperventilation that occurs during pregnancy. The increase in ventilation at term is greater than the increase in basal

metabolic rate and is attributed to the sixfold increase in circulating progesterone, which enhances respiratory center sensitivity to CO_2 (70, 71). This hyperventilation reduces arterial PCO_2 to a nadir of about 30 mm Hg, but blood pH remains normal (69). The heightened respiratory drive protects against upper-airway occlusion by enhancing responsiveness of upper-airway dilator muscles to chemical stimuli during sleep (72, 73); progesterone itself has been shown to increase upper-airway dilator muscle (genioglossal) electromyographic activity (74).

However, this heightened respiratory drive may induce obstructive sleep-disordered breathing by increasing suction pressure on hyperemic upper-airway structures (75). Furthermore, studies have shown that enhanced sensitivity of the respiratory center to CO_2 , which occurs in pregnancy, also predisposes to central sleep apnea (76). Modeling of the respiratory control system predicts that increased gain of the respiratory controller will predispose to cyclic breathing (77). A low PCO_2 , which may result from increased respiratory drive and is present in pregnancy, is also conducive to cyclic breathing because it removes the stabilizing influence of the central chemoreceptors on respiration during sleep, making it more dependent on the nonlinear responses of the peripheral (hypoxic) chemoreceptors (78). However, patients with increased respiratory drive may exhibit cyclic breathing in the absence of a low PCO_2 (79).

Taken together, these physiologic changes may predispose a pregnant woman to respiratory irregularities during sleep. Maternal oxygen tension decreases in the supine position near term (80); up to 25% of pregnant women exhibit a PaO_2 less than 90 mm Hg while supine and awake (81). Thus, even mild respiratory irregularities during sleep may have significant consequences for fetal oxygenation.

Sleep-Disordered Breathing in Pregnancy

The prevalence of sleep-disordered breathing during pregnancy is unknown. It is clear that fetal growth and development may be impaired by maternal hypoxemia, whether it occurs as a primary obstetric event or as a consequence of respiratory abnormalities, such as sleep apnea (82) or poorly controlled asthma (83).

Several investigators have performed polysomnography with respiratory monitoring in small groups of patients with normal or complicated pregnancy. One

study found that nocturnal arterial oxygen saturation (SaO_2) was preserved during the third trimester and the frequency of apneas and hypopneas (predominantly central events) was decreased compared with the postpartum period (84). In third-trimester multiple pregnancy, sleep quality was worsened but apneas and episodes of desaturation were rare (85).

In contrast, polysomnography in 12 healthy women near term revealed a small but significant decrease in basal SaO_2 during sleep compared with 10 age-matched controls (82). The pregnant women also experienced more nocturnal desaturations greater than 4%. In a more recent study, SaO_2 was monitored overnight in 13 nonpregnant women, 13 pregnant normotensive women, and 15 patients with pregnancy-induced hypertension (86). Mean SaO_2 was lower in both near-term pregnant groups (>35 weeks' gestation) than nonpregnant controls; 7 pregnant patients (4 of whom had pregnancy-induced hypertension) had an SaO_2 less than 90% for more than 20% of the recording time.

Reported cases of obstructive sleep apnea in pregnancy are shown in Table 3 (87–97). Two series from the same group reported a total of 11 primiparas with this diagnosis (87, 88). The women were obese and experienced snoring, multiple arousals, and witnessed apneas. Nine of these patients delivered babies with intrauterine growth restriction. Two of 7 babies delivered to the women in other series had intrauterine growth restriction. Three of four treated mothers delivered babies of normal birth weight. Four patients had preeclampsia and obstructive sleep apnea, 1 had hypothyroidism, and 3 had diabetes mellitus. The effects of apnea and hypoxemia on fetal heart rate are unclear; one study reported significant acidosis and heart rate alterations during apneic spells (87), and another reported normal fetal heart rate reactivity to fetal movements during these periods (89).

In summary, evidence suggests that pregnant women may experience sleep-disordered breathing, and the accompanying hypoxemia and hypertension may result in intrauterine growth restriction. An association between maternal hypoxemia and intrauterine growth restriction has been noted in women living at high altitude or those with parenchymal lung disease (98). Furthermore, some patients with hypertension have lower-than-expected blood volume expansion during pregnancy; this factor has also been associated with intrauterine growth restriction (98). Sleep-disordered breathing is commonly asso-

Table 3. Sleep-Disordered Breathing in Pregnancy*

Study	Patients, n	Pregnancy Complication	Method of Diagnosis	Apneas and Hypopneas per Hour, n	Treatment	Birth Outcome
Joel-Cohen and Schoenfeld (87)	3	None	Clinical examination	NA	None	1 infant had intrauterine growth restriction; information on remaining births not available
Schoenfeld et al. (88)	8	None	Clinical examination	NA	None	All 8 infants had intrauterine growth restriction
Conti et al. (89)	1	Preeclampsia	Clinical examination	NA	None	Normal-birthweight infant
Kowall et al. (90)	1	Preeclampsia	Polysomnography	78.6	Continuous positive airway pressure	NA
Hastie et al. (91)	1	Gestational diabetes mellitus	Polysomnography	42.5	Tracheostomy	Normal-birthweight infant
Charbonneau et al. (92)	1	Gestational diabetes mellitus	Polysomnography	159	Continuous positive airway pressure	Intrauterine growth restriction
Sherer et al. (93)	1	Diabetes mellitus, preeclampsia	Polysomnography	144 (postpartum)	None	Normal-birthweight infant
Lefcourt et al. (94)	1	Preeclampsia	Clinical examination	NA	None	Intrauterine growth restriction
Lewis et al. (95)	1	Pulmonary hypertension	Clinical examination	NA	Continuous positive airway pressure	Normal-birthweight infant
Taibah et al. (96)	1	Hypothyroidism	Polysomnography†	128	Thyroid replacement	NA
Pieters et al. (97)	1	None	Polysomnography‡	0	Nocturnal ventilation	Normal-birthweight infant

* NA = not available.
 † Central and obstructive apneas.
 ‡ Central alveolar hypoventilation.

ciated with hypoxemia and both acute and sustained hypertension; a causal relationship between these factors may involve increased sympathetic tone (99). However, since development of hypertension during pregnancy is a hallmark of preeclampsia (100), sleep-disordered breathing that develops or worsens in pregnant women might predispose to this complication by induction of repetitive acute hypertension during disordered breathing events (101).

Are pregnant women at higher risk for sleep-disordered breathing? Snoring, a marker for upper-airway obstruction, is more prevalent in pregnant women (102, 103). A study of 11 preeclamptic women documented a 100% incidence of upper-airway flow limitation and further increases in blood pressure, which were most apparent during stage 3 and 4 non-REM sleep (104). A recent study of 502 women reported that snoring pregnant women had a twofold greater incidence of hypertension, preeclampsia, and intrauterine growth restriction than did nonsnorers (103). In some women, preexistent obstructive sleep apnea was worsened by pregnancy (90, 91). The number of women with sleep apnea may be substantial: 7.6% of women 30 to 49 years of age experience more than five apnea–hypopnea episodes per hour (105), and some premenopausal nonpregnant women without sleep-disordered breathing by current

definitions exhibit excessive daytime sleepiness and abnormal respiratory effort during sleep (106). However, at present, obstructive sleep apnea in pregnant women is likely to go undiagnosed unless apneas are witnessed (107–109). The reasons for this include the idea that sleep-disordered breathing is rare in premenopausal women (110). Furthermore, women are less likely than men to report symptoms of apnea—snorting and gasping (111, 112). Finally, patients with clinically significant sleep-disordered breathing experience daytime sleepiness, or less commonly, nocturnal insomnia, symptoms that are assumed to be less discriminatory for obstructive sleep apnea in pregnant women (113). Not surprisingly, a recent report estimated that sleep apnea goes undiagnosed in 93% of middle-aged women with the condition (114). Until the incidence of sleep-disordered breathing in normal and complicated pregnancy is defined, the indications for polysomnography in pregnant patients should probably be expanded to include those with hypertension, previous babies with unexplained intrauterine growth restriction, and persistent sleep-related symptoms (hypersomnia or insomnia) associated with snoring or obesity.

Once obstructive sleep apnea is diagnosed in a pregnant woman, treatment is indicated, especially in the presence of maternal hypoxemia. Conservative measures

are avoidance of excessive weight gain; use of position monitors and alarms to minimize time spent in the supine position; elevation of the head of the bed by about 30 degrees; and avoidance of central nervous system depressants, such as ethanol and sedatives (82, 92, 94). Nasal continuous positive airway pressure (CPAP) is the therapy of choice for obstructive sleep apnea (115, 116). Although this therapy carries theoretical concerns about diminished cardiac output and placental blood flow, it is safe in pregnancy for both mother and fetus (90, 92). The level of nasal CPAP should be titrated during polysomnography.

If the patient cannot tolerate nasal CPAP, an oropharyngeal appliance can be used (94). Upper-airway surgery (uvulopalatopharyngoplasty) is less effective and carries additional surgical risks from upper-airway hyperemia; it is thus not recommended in the pregnant woman (82). Tracheostomy has been performed to treat severe obstructive sleep apnea in pregnancy (91), but this procedure is clearly unnecessary in most cases. The balance of evidence indicates that nocturnal oxygen can be used safely in sleep apnea (117). Although administration of oxygen has been reported to prolong the duration of apnea, even patients with sleep apnea have higher end-apneic SaO_2 while breathing oxygen (118). Furthermore, other investigators have found that in eupneic patients, the frequency of apnea is reduced and overall oxygenation during sleep is improved by long-term nocturnal administration of oxygen (119, 120). In pregnant patients, inhalation of oxygen in theory could also minimize the tendency to cyclic breathing by lessening the influence of the nonlinear responding peripheral (hypoxic) chemoreceptors. Since minimizing maternal and fetal hypoxemia is of paramount importance in obstetric care, the risk-to-benefit ratio favors administration of oxygen in pregnant patients (81).

OTHER SLEEP DISORDERS IN PREGNANCY

Other sleep disorders that have been reported to occur and in some cases were triggered or worsened by pregnancy are periodic leg movements (85), sleepwalking (121), night terror (122), and narcolepsy.

Pregnancy appears to be associated with increased neural reactivity, as evidenced by the common occurrence of hyperreflexia during normal pregnancy (123). Among pregnant patients with preeclampsia and eclampsia,

30% and 80%, respectively, exhibit hyperreflexia (123, 124). Periodic leg movements and the restless legs syndrome may represent another manifestation of this tendency.

Although the true incidence of periodic leg movements during sleep and the restless legs syndrome is unknown, they are acknowledged to be the most common movement disorders during pregnancy (125). In one study, all 10 mothers with multiple pregnancy had periodic leg movements during sleep, and 4 mothers developed the restless legs syndrome during pregnancy (85). Questionnaire surveys cite leg cramps as a primary reason for sleep disruption during pregnancy (3, 55). Thus, the possibility that periodic leg movements cause insomnia in pregnancy must be considered.

Treatment of periodic leg movements should be considered when they significantly disrupt sleep. Conservative measures include avoidance of caffeinated beverages, correction of electrolyte abnormalities, use of an electric vibrator to the calves, and administration of folate supplements if folate deficiency is present (125). If these treatments fail, effective medications in the non-pregnant state include a benzodiazepine (clonazepam), a dopaminergic agent such as L-dopa or carbidopa, or codeine (126, 127), all of which are classified as category C in pregnancy (64). Since the effects of persistent insomnia on pregnancy are currently unknown, it is difficult to balance the risks of taking these drugs on a prolonged basis. Current consensus favors avoidance of benzodiazepines and narcotics during pregnancy (128); therefore, therapy for periodic leg movement during pregnancy should be limited to the conservative measures listed above.

Sleepwalking (somnambulism) and night terrors occurring during pregnancy and exacerbated by the condition have also been reported. Sleepwalking and night terrors are complex behaviors occurring in stage 3 and 4 non-REM sleep. Their occurrence is facilitated either by an increase in time spent in these sleep stages or by forced arousals from them (129). Pregnancy, especially in the third trimester, could predispose to these sleep disorders by the latter mechanism. This is probably exemplified by a woman with a childhood history of sleepwalking who had recurrence during her two pregnancies (121). She received no treatment, and in both instances, sleepwalking ceased after delivery. Another report concerned a woman with sleep terror who experienced

worsening during the third week of pregnancy, necessitating the use of diazepam and imipramine (122). She experienced a spontaneous abortion, after which her sleep terror ceased.

Published reports of narcolepsy during pregnancy are rare, probably because narcolepsy is common in women of childbearing age (130). Interactions between pregnancy and narcolepsy in which one condition influences the course of the other have not been reported, although in theory the REM-inhibiting effects of estrogen and, to a lesser extent, cortisol should be beneficial. Narcolepsy is primarily treated with stimulants and REM-sleep suppressants (130–133). If a pregnant patient requires pharmacologic treatment for narcolepsy, the drug of choice is pemoline, which is a category B agent in pregnancy (64). No well-controlled studies of pregnant women who are using stimulants have been done, but current recommendations are to discontinue treatment with dextroamphetamine sulfate or methamphetamine hydrochloride (134). No studies have evaluated methylphenidate or modafinil (which are both category C agents) in pregnancy (132, 134). Good sleep hygiene and daily scheduled naps are helpful adjuncts to pharmacologic therapy. Suppressants of REM sleep (such as paroxetine and fluoxetine, which are category B agents in pregnancy) are useful for control of cataplexy.

MANAGEMENT OF THE PREGNANT WOMAN WITH PREVIOUSLY DIAGNOSED SLEEP DISORDERS

Not infrequently, physicians will have to counsel and care for women with previously diagnosed sleep disorders who are contemplating pregnancy or who have become pregnant. Patients with insomnia should be counseled to adhere to regular sleep schedules; practice good sleep hygiene; and continue conservative therapy, such as stimulus control or relaxation techniques. If discontinuation of therapy with a hypnotic drug is not possible, zolpidem or diphenhydramine should be prescribed. Patients with narcolepsy will have to accept less stringent control of their daytime sleepiness both because of the somnogenic effects of early pregnancy and the advisability of using weaker but safer stimulants. If possible, women who are employed should consider taking disability or maternity leave earlier or requesting that their employers allow more daytime naps. Treatment with benzodiazepine or other pharmacotherapy for periodic leg movements or somnambulism should ideally

be discontinued. Patients with known sleep-disordered breathing will probably experience no greater risks during pregnancy if they are receiving nasal CPAP therapy. In all patients, conservative measures, such as avoiding excessive weight gain and sleeping in a lateral position instead of a supine one, will help control sleep-disordered breathing. For reasons given earlier, patients who cannot tolerate nasal CPAP should be given nasal oxygen (up to 2 L/min) during sleep in addition to conservative measures. Until more data are available, polysomnography should be done in pregnant patients who are known to snore before pregnancy and who develop hypersomnolence, insomnia, or hypertension.

CONCLUSIONS

Pregnancy induces physiologic alterations that result in changes to sleep and respiration. Sleep disorders occur during pregnancy and may be modified by this state. However, our knowledge base is limited and further investigation appears warranted. Future studies appear to be most needed in the areas of monitoring respiration and sleep in pregnancy complicated by hypertension, such as preeclampsia and pregnancy-induced hypertension; in overweight pregnant women who snore; and in women who have delivered infants with unexplained intrauterine growth restriction. It has been noted that previous birth of a growth-restricted infant is the obstetric factor most strongly associated with subsequent birth of a growth-restricted infant (135). Studies also appear to be indicated in women with significant insomnia and leg cramps or witnessed apneas. The effects of sleep-disordered breathing, chronic insomnia, and, perhaps, narcolepsy on fetal outcomes need to be determined. Finally, clinical predictors of sleep-disordered breathing need to be established in pregnant women. To assume that snoring, insomnia, and daytime somnolence are expected events in pregnancy may well be a self-fulfilling fallacy. As has been pointed out, most of our knowledge base in sleep has been obtained primarily in men (136). The case to correct this imbalance appears to be strong for the pregnant woman.

GLOSSARY

Apnea: Cessation of airflow at the mouth and nose lasting at least 10 seconds. There are three varieties: obstructive, which is due to upper airway obstruction; central, which is due to cessation of respiratory effort, and mixed, which is a combination of central and obstructive apnea.

Central chemoreceptors: Sensors for carbon dioxide and acid located in the ventral surface of the medulla.

Circadian rhythm: An endogenous fluctuation of physiologic or behavioral functions occurring at approximately 24-hour intervals.

Eclampsia: The occurrence of convulsions that are precipitated by pregnancy-induced hypertension and not attributable to other causes.

Expiratory reserve volume: The maximal volume of air that can be expired beyond the functional residual capacity.

Functional residual capacity: The amount of air in the lungs and airways at the end of a spontaneous expiration: that is, the resting volume of the lungs.

Intrauterine growth restriction: Failure of the fetus to reach growth potential; it is associated with increased perinatal morbidity and mortality.

Narcolepsy: A syndrome characterized by excessive sleepiness and pathologic manifestations of REM sleep, including loss of muscle tone (cataplexy), dreams at sleep onset (hypnagogic hallucinations), and sleep paralysis.

Non-rapid eye movement sleep: A major sleep state comprising 75% to 80% of total sleep time; it is composed of sleep stages 1 through 4, which are characterized by specific electrometric changes.

Periodic leg movements: Repetitive leg movements occurring during sleep, characterized by rapid partial flexion of the foot at the ankle, extension of the big toe, and partial flexion of the knee and hip.

Peripheral chemoreceptors: Sensors for hypoxia located in the carotid bifurcation and aortic arch (carotid and aortic bodies).

Polysomnography: Continuous and simultaneous recording, during sleep, of multiple physiologic variables, including electroencephalographic changes, eye movements by electrooculography, muscle tone by electromyography, respiration, electrocardiographic changes, and leg movements.

Preeclampsia: A hypertensive disorder of pregnancy consisting of hypertension plus proteinuria, nondependent generalized edema, or both.

Pregnancy-induced hypertension: Hypertension that develops as a consequence of pregnancy and regresses after delivery; it includes hypertension alone, preeclampsia, and eclampsia.

Rapid eye movement sleep: A major sleep state comprising 20% to 25% of total sleep time; it is characterized by dreaming, suppression of resting muscle activity, spontaneous rapid eye movements, and specific electrometric changes.

Restless legs syndrome: A disagreeable, deep creeping or crawling sensation in the calves that occurs during sitting or in a recumbent position.

Sleep log: A daily written record of a person's sleep-wake pattern, including time in bed, estimated total sleep time, num-

ber of arousals, number and duration of naps, quality of sleep, and use of medications.

Slow-wave sleep: Stage 3 and 4 non-REM sleep, characterized by electroencephalographic waves with a frequency of less than 4 Hz and peak-to-peak amplitude of 75 μ V.

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