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# Overview of Sleep and the Lifecyle of a Woman's Life

## Childhood

- During the first months of life, sleep architecture is similar among males and females, but there are some differences in both quantity and quality of sleep, suggesting that CNS maturation is delayed in male vs female infants
- Sleep differences between men and women during childhood are difficult to capture at this age, potentially because "sleep-wake patterns are influenced by a complex interplay between biological processes and environmental, behavioral, and social factors; however, studies including a systematic review have not demonstrated significant sex differences in sleep among children
- Sex differences in sleep begin to emerge as children approach puberty
- With menarche, increased ovarian function and the cyclical release of estrogen and progesterone affect regulation of the sleep-wake cycle (among many other homeostatic functions, including metabolic systems, cardiovascular, and respiratory systems)
- Sex hormones play an important role in sleep regulation and arousals; they may also impact the outcomes of sleep conditions
- Interestingly, gonadectomy in female and male rats "eliminates all sex differences in the sleep-wake cycle; adding back physiological levels of sex-specific steroids restores these differences."
- Progesterone in particular improves sleep duration and quality, mainly by improving slow wave sleep (SWS) and slow wave activity; elevated prolactin levels seen in lactating women are also associated with increased slow wave sleep.
- Enhanced slow wave sleep due to prolactin, especially in the context of an abrupt withdrawal of estrogen and progesterone following parturition, presents "another important factor to support breastfeeding women in the postnatal period."
- Progesterone's impact on sleep goes beyond changes in sleep architecture: as a ventilatory drive stimulant, progesterone increases the activity of the genioglossus muscle involved in dilating the upper airway; one study in 11 healthy women lacking sleep disturbances demonstrated lower upper airway resistance during the luteal phase vs the follicular phase (recall: progesterone levels rise due to secretion by the corpus luteum during the luteal phase)

## Sleep at Menarche

- A National Comorbidity Survey indicated that women are twice as likely as men to have mood disorders with the onset of menarche
- A meta-analysis demonstrates that women between the ages of 15-30 have a 28% higher risk of reporting insomnia than men; interestingly, poorer sleep quality has not

manifested on polysomnographic measures: a 2018 review by Pengo et al states, "although young women report significantly more sleep problems than men, this perception of a poorer sleep quality in women is not reflected in objective polysomnographic measures, suggesting that other non-sleep-related conditions such as mood disorders play an important role."

- The most significant change in sleep across the menstrual cycle occurs during the luteal phase when progesterone and estradiol levels are high: studies have shown increased EEG activity in sleep spindle frequency range (12-16 Hz) during non-rapid eye movement (NREM) sleep

**Fertility**

Sleep plays an integral and complex role in women's health and well-being throughout the lifecycle, with pronounced changes in sleep architecture occurring with changes in the menstrual cycle, during pregnancy, and menopause. The role of sleep in fertility is not clearly understood, yet some have postulated that stress and circadian rhythm dysregulation may play a role in fertility challenges. Despite the prevalence of infertility in our general population, compounded by the prevalence of disordered sleep, there is a scarcity of research focusing on the interplay of sleep and fertility. While researchers acknowledge that a relationship between disordered sleep and reproductive health exists, the exact mechanisms and mediating pathways remain unknown. Researchers acknowledge that infertility can be associated with significant stress; and that stress alone may lead to sleep disturbances. Normal versus disordered sleep is a factor that predicts reproductive function in isolation, however, has not been deeply examined. We do understand, however, that the hypothalamic-pituitary-adrenal (HPA) axis plays a clear and important role in both infertility as well as sleep dysregulation. Although many hypotheses attempt to clarify the relationship between sleep and human fertility, researchers continue to point out the paucity of properly designed trials to elucidate the exact mechanisms involved, and the potential for medical intervention

Some facts that we do know:

- Sleep plays an integral and complex role in women's health and well-being throughout the life cycle with pronounced changes in sleep architecture occurring during the menstrual cycle, pregnancy, and perimenopausal period.

- Infertility may be attributed to myriad factors, including congenital, iatrogenic (for eg, chemotherapy or radiation), and environmental / behavioral (for eg, exposure to endocrine disrupting chemicals; substance use; nutrition balance–being underweight or overweight can negatively impact fertility)

- We know that an association between sleep and reproductive hormones exists, as physiologic and hormonal changes occurring during pregnancy, lactation and menopause–or those seen in pathological conditions such as polycystic ovary syndrome (PCOS)–are tied to sleep disturbances; and evidence demonstrates that sleep disorders in women lead to menstrual abnormalities

- Infertility itself can be associated with significant stress; and it's important to recognize that stress alone may lead to sleep disturbances

- A healthy lifestyle may be one of the first interventions recommended to improve fertility among women struggling to conceive.

    - The American College of Lifestyle Medicine's "6 Pillars of Lifestyle Medicine" describe the crucial factors for achieving wellness, which are important for everyone but may be particularly impactful for those affected by infertility:
        - Nutrition: a predominantly whole food plant-based diet
        - Physical activity: consistent cardio and weight training
        - Stress management: negative stress impacts one's risk of anxiety, depression and immune dysregulation

- Restorative sleep: improving sleep quantity and quality

    - Social connection: positive social connection may improve physical, mental and emotional health
    - Avoidance of risk substances: excessive alcohol and tobacco use increase our risk of chronic diseases

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- Normal versus disordered sleep as a factor that predicts reproductive function in isolation, however, has not been deeply examined. We do understand that the hypothalamic-pituitary-adrenal (HPA) axis plays a clear and important role in both infertility as well as sleep dysregulation.

- Given the prevalence of infertility in our general population, compounded by the prevalence of disordered sleep, we need to continue to advocate for research exploring the interplay of sleep and fertility so that intervention may aid those whose fertility may be impacted by sleep disturbances

**Pregnancy**

- Pregnancy is associated with changes in sleep architecture as well as changes in sleep quality and duration due to various physiological and anatomic changes, including:
    - Increased nocturnal micturition due to an increase in overnight sodium excretion
    - Changes to the musculoskeletal system in preparation for the growing uterus
    - Nocturnal uterine contractions due to a nocturnal oxytocin peak
    - Secretion of steroid hormones (estrogen and progesterone), which affect the circadian and homeostatic regulation of sleep
- A table from "Sleep in Women Across the Lifespan" by Pengo et al (2018) demonstrates changes occurring by trimester. Pregnant women often present with complaints of sleep

disturbance to their physicians. During the first trimester, frequent urination and sleep interruption may contribute to decreased overall sleep quality. As the pregnancy progresses, musculoskeletal changes leading to cramping and pain, fetal movements, contractions, and gastrointestinal issues (eg, heartburn and constipation) may contribute to decreased quality and quantity of sleep.

- One study suggests that insomnia risk may approximately double during the third trimester as compared with the first and second trimesters.
- Although sleep complaints during pregnancy are common, severe disturbances in sleep during pregnancy may require medical intervention, as there may be associated risks for both the mother as well as the baby:
    - One study demonstrates that poor sleep quality, even after adjusting for depression, is associated with antepartum suicidal ideation
    - In another study, researchers identified a potential association between poor duration and quality of sleep with an increased risk of preterm birth as well as giving birth to a baby that is small for gestational age (SMA)

- Low quality sleep or sleep of short duration during pregnancy is associated with a number of adverse perinatal outcomes, including:
    - Risk of gestational diabetes
    - Higher risk of hypertensive disorders of pregnancy
    - Higher risk of cesarean delivery
    - Longer duration of labor

**Postpartum**

- Although sleep deprivation is common for the postpartum period, one study demonstrated that sleep *quality* may be a risk factor for negative maternal affect in the postpartum period, prompting a need for more research considering how maternal sleep hygiene may affect a woman's risk for postpartum anxiety and depression.

**Menopause:**

- The complex interaction between menopausal changes and sleep disturbance account for a marked increase in sleep complaints in women approaching midlife. In fact, sleep disturbances are very common in older women, affecting >40-60% of peri- or post-menopausal women.
- Data suggest that:
    - Women had a 41% greater risk for developing insomnia than men
    - 25% of women between 50 and 64 years of age report sleep problems, and 15% of those report severe sleep disturbance significantly affecting their quality of life
    - 31-42% of women may develop chronic insomnia by the end of their transition into menopause
- The factors that affect sleep at a woman's perimenopausal transition include changing hormone levels–decreased estrogen and increased follicle-stimulating hormone (FSH), progesterone and testosterone– as well as physiological and mental health changes

occurring as a consequence of the shifting hormonal milieu. Women are at increased risk for sleep disturbances–insomnia, poor sleep quality and sleep deprivation, obstructive sleep apnea, restless legs syndrome–during times of hormonal change. Both aging and hormonal changes independently influence sleep architecture.

- Nocturnal melatonin secretion decreases with age, but also specifically decreases with the onset of menopause
- Women may experience vasomotor symptoms such as skin and temperature changes, in addition to mood disorders, circadian rhythm abnormalities, and altered lifestyle and metabolic factors that play a role in disordered sleep.
- These changes and conditions that occur as a consequence of, or in concert with menopause may exacerbate age-related sleep architectural changes that may be due to the decline in melatonin that accompanies aging and menopause onset
- In addition, mood symptoms such as depression and anxiety occur more frequently in women than men, and often occur in concert with sleep problems in peri- and postmenopausal women.
- Finally, there are many medical disorders that may cause or exacerbate sleep difficulties.
- Chronic pain conditions and other chronic conditions, as well as physical disorders such as restless legs syndrome (RLS) or periodic limb movement disorder (PLMD) may coincide with menopause and can aggravate preexisting sleep problems associated with these conditions.
- Randomized controlled trials examining the impact of hormone therapy (HT) on sleep demonstrate improved sleep quality and quantity with improved total sleep time and REM sleep, as well as decreased wakefulness
- The National Institute on Aging suggests the following lifestyle changes to improve sleep in perimenopausal women:
    - Adopt a regular sleep schedule and regular bedtime routine
    - Avoid napping, especially in the late afternoon / evening
    - Maintain a comfortable bedroom temperature
    - Exercise regularly, but not close to bedtime
    - Avoid caffeine and large meals close to bedtime