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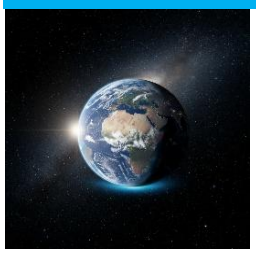

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Circadian Rhythm Disruption and Hypothalamic–Pituitary–Ovarian Axis Dysregulation Following Transmeridian Travel: A Narrative Review

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Abstract

Introduction and aim
Menstrual cycle irregularities are frequently reported by women exposed to circadian rhythm disruption, including frequent time-zone travelers and night/rotating shift workers. This narrative review evaluates evidence on how time zone change–related circadian misalignment may affect menstrual cycle regularity and female reproductive health.

Materials and methods
Literature was identified primarily in PubMed and supplemented by other accessible sources. We included randomized and crossover studies when available, and summarized epidemiological findings from questionnaire-based studies and selected systematic reviews.

Summary
Reported associations between circadian rhythm disruption and menstrual cycle irregularities appear to be modified by psychosocial stress, disrupted meal timing (chrononutrition), and endocrine disturbances such as hyperprolactinemia and altered diurnal cortisol rhythms. Mechanistically, the suprachiasmatic nucleus (SCN) and melatonin are key components linking circadian timing to reproductive regulation.

Conclusions
Circadian-related menstrual disturbances, including those after abrupt time-zone shifts, may be underrecognized by patients and clinicians. More studies are needed in high-risk groups such as flight attendants and frequent travelers. Clinical assessment should also consider comorbid endocrine and sleep disorders and disordered/restrictive eating.

Keywords
Circadian rhythm disruption; Hypothalamic–pituitary–ovarian axis; Female reproductive endocrinology; Menstrual irregularities; Chronobiology disorders; Melatonin; Neuroendocrine dysregulation.

Introduction

Circadian rhythms are generally viewed as the output of an internal timekeeping system that regulates numerous physiological processes in the human body, including aspects of the female reproductive system (Pines, 2016). Many physiological functions follow an approximately 24-hour cycle. Disruption of this cycle due to time zone changes or atypical working hours may affect the sleep–wake cycle and lead to hormonal dysregulation, insomnia, and stress (Shiml et al., 2024)

Jet lag is understood as a misalignment of the circadian rhythm after rapid transmeridian travel. This sleep–wake disorder presents with symptoms such as insomnia, impaired daytime functioning, general malaise, and other somatic complaints (Becker et al., 2015). Circadian rhythm disruption caused by time zone change–related jet lag may contribute to menstrual cycle changes (Wang et al., 2016).

Menstrual cycle regularity is considered one of the most important indicators of female reproductive health and is regulated by the hypothalamic–pituitary–ovarian axis (Wang et al., 2016). Problems with sleep onset and poorer sleep quality are more commonly reported in women than in men, particularly among those working in occupations that involve frequent circadian disruption, such as flight attendants or nurses. Evidence suggests the association between the sleep–wake rhythm and the endocrine secretion of hormones such as estrogen and progesterone, which play key roles in regulating the menstrual cycle (Peng et al., 2024).

Circadian Rhythms and the Biological Clock

The circadian clock comprises two principal components: the central clock located in the hypothalamic suprachiasmatic nucleus (SCN) and peripheral clocks present in most tissues and organ systems. The central clock is synchronized by light signals transmitted to the brain via retinal photoreceptors and then converted into chemical signals within the SCN. Peripheral clocks can be regulated by nonphotic cues, including feeding schedules and ambient temperature (Becker et al., 2015, Buhr et al., 2013).

It has been suggested that the SCN's ability to entrain peripheral clocks is linked to its capacity to regulate body temperature. Depending on the tissue, cellular clock gene cycles may be influenced by different external factors, including light and temperature. The neuronal rhythm of the SCN is reset primarily by the light–dark cycle, whereas tissue-specific clock gene rhythmicity in organs such as the lung, liver, kidney, and olfactory bulb can be modulated by temperature shifts, parasympathetic and sympathetic innervation, hormonal signals, and metabolic consequences of SCN-driven behaviors, including feeding and exercise (Saper, 2013). To maintain rhythmic clock-gene expression, peripheral oscillators must be sensitive to temperature variations within the physiological range (36°C–38.5°C in mice), whereas the SCN must remain resistant to such temperature changes (Buhr et al., 2013).
The SCN directly influences neurons that regulate melatonin secretion (Saper, 2013). Melatonin serves as an output signal of the SCN and can modulate circadian timing. Its secretion occurs predominantly during darkness and it modulates circadian timing via melatonin receptors MT1 and MT2 (Richards et al., 2013).

In mammals, the circadian clock operates in virtually every cell. At the molecular level, circadian rhythmicity is governed by the transcription–translation oscillation (TTO) loop. The core proteins CLOCK and BMAL1 initiate the cycle by driving the expression of Period (Per1, Per2) and Cryptochrome (Cry1, Cry2) genes. After PER and CRY proteins assemble into a functional complex, they translocate to the nucleus, where they interact with CLOCK and BMAL1 to inhibit transcription of their own genes. This cycle repeats approximately every 24 hours. Because PER and CRY proteins undergo ubiquitination, are recognized by E3 ubiquitin ligases, and are degraded in a time-dependent manner, the cell can track the time of day (Mohawk et al., 2012)

Zeitgebers are external cues that influence the circadian system and help synchronize biological rhythms. They include factors such as light exposure, food intake, and physical activity (Richards et al., 2013, Quante et al., 2018). Changes in meal timing may lead to alterations in circadian rhythm–related parameters, including body temperature, cortisol levels, and glucose tolerance (Quante et al., 2018).

Endogenous circadian mechanisms regulate major hormonal mediators of female reproductive physiology, including sex-steroid hormones, gonadotropins, and sex hormone–binding globulin (SHBG), in a menstrual phase–dependent manner. In the study *Endogenous Circadian Regulation of Female Reproductive Hormones*, Rahman and colleagues (2019) demonstrated significant phase-specific differences in circadian regulation of the reproductive endocrine system, with distinct patterns in the pre-ovulatory compared with the post-ovulatory phase. These findings suggest that circadian timing may influence ovulatory timing and function.

Time Zone Change-Related Jet Lag

Jet lag involves desynchronization between endogenous circadian rhythms and the external environment (Sack, 2009). It can be considered a form of acute circadian misalignment (Ahmed et al., 2024). Homeostatic sleep drive refers to the progressive accumulation of sleep pressure with prolonged wakefulness: the longer an organism remains awake, the stronger its physiological need for sleep becomes (Sack, 2009).

Time zone change–related jet lag is a well-recognized sleep–wake disorder that occurs when multiple time zones are crossed faster than the circadian system can adapt to the new local time (Becker et al., 2015, Sack, 2010). It is commonly described as a cluster of symptoms, including sleep disturbance, daytime fatigue, impaired performance, and increased irritability.

According to the *International Classification of Sleep Disorders, Third Edition* (ICSD-3), the diagnostic criteria for jet lag disorder include the following:
(1) Insomnia or sleepiness with impaired TST (total sleep time) after a minimum of two time zone crossings.
(2) Impairment of daytime function, general malaise or somatic symptoms within one or two days of travel.
(3) The absence of other causes of the above complaints (Becker et al., 2015).

Other manifestations of jet lag may include dysphoric mood, reduced physical performance, cognitive impairment, increased daytime fatigue, decreased motivation, and gastrointestinal disturbances (Becker et al., 2015, Sack, 2009). These symptoms may be exacerbated by misalignment between light exposure and the endogenous circadian schedule, prolonged immobility, altered melatonin timing and amplitude, disrupted sleep, and irregular eating schedules (chrononutrition disturbances), as well as dehydration and other conditions typical of long-distance flights, even in the absence of time-zone changes (Becker et al., 2015, Fowler et al., 2017). In addition, travel-related factors such as limited seat comfort, elevated noise levels, and inconvenient stopover times can further influence the severity of jet lag symptoms (Fowler et al., 2017).

Based on the assumption that delaying circadian rhythms is generally easier than advancing them, jet lag symptoms may be more pronounced after eastward than westward travel. It has been suggested that westward travel requires approximately half a day of adjustment for each hour of time-zone change, whereas eastward travel may require around one day per hour (Fowler et al., 2017).

The Menstrual Cycle: Regulation and Sensitivity to Circadian Disruption

The menstrual cycle is a key, readily observable indicator of female reproductive health. The normal physiological cycle length ranges from 24 to 38 days. A normal menstrual cycle is characterized by consistent frequency and regularity, with menses occurring every 24–38 days, and by a menstrual blood loss volume that does not exceed 80 mL per cycle (Thiyagarajan et al., 2024).

The menstrual cycle can be divided into three phases: the follicular phase (FP), the ovulatory phase (OP), and the luteal phase (LP). Each phase is characterized by a distinct pattern of sex hormone secretion (Tucker et al., 2025). Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are gonadotropins that act within the hypothalamic–pituitary–ovarian (HPO) axis, which regulates menstrual cycle timing. Both hormones are produced by the anterior pituitary and their secretion is driven by the pulsatile frequency of gonadotropin-releasing hormone (GnRH) release. GnRH is produced by the hypothalamus and released in a pulsatile manner. In general, lower-frequency GnRH pulses preferentially stimulate FSH secretion, whereas higher-frequency pulses favor LH secretion. In the late follicular phase, sustained high estradiol shifts feedback to positive, triggering the mid-cycle LH surge, which induces ovulation and luteinization and is followed by progesterone predominance in the luteal phase. During the luteal phase, progesterone (often in concert with estradiol) slows GnRH/LH pulse frequency; after luteolysis, the fall in ovarian steroids relieves negative feedback, allowing FSH to rise and initiate the next follicular wave (Holesh et al., 2023).

Phase 1 begins on day 1 of the cycle (the first day of menstrual bleeding) and ends with ovulation; it is referred to as the **follicular phase**. Early in the follicular phase, **FSH** stimulates follicular growth and promotes **estradiol (E2)** production. As follicular development progresses, granulosa cells increasingly sustain E2 synthesis as the dominant follicle becomes

more responsive to gonadotropin signaling, while **LH** stimulates **androgen production in theca cells**, providing substrates for aromatization to estrogens in granulosa cells. These coordinated processes support the selection and maturation of the **dominant follicle**, which secretes estradiol and **inhibin**, thereby reducing FSH secretion and limiting the recruitment of additional follicles. The onset of the follicular phase is characterized by relatively low E2 levels, which rise toward the end of the phase, while **progesterone (P4)** remains low (Holesh et al., 2023).
The **luteal phase** begins after ovulation, which typically occurs around the midpoint of the cycle.

Ovulation is preceded by changes in hypothalamic–pituitary signaling, including altered **GnRH pulsatility** and **upregulation of GnRH receptors** in the anterior pituitary under the influence of rising estradiol, which increases pituitary sensitivity to endocrine stimulation (Thiyagarajan et al., 2024, Holesh et al., 2023). During the follicular phase, factors such as **gonadotropin surge-attenuating factor (GnSAF)** have been proposed to modulate pituitary responsiveness and may contribute to preventing premature or excessive gonadotropin surges. Ultimately, these mechanisms culminate in the **LH surge**, which occurs approximately **36–44 hours before ovulation** and triggers follicular rupture and oocyte release. Progesterone, produced primarily by the corpus luteum under LH support, plays a central role in this phase. It prepares the endometrium for potential embryo implantation by promoting secretory transformation of the endometrial glands, increasing glycogen-rich secretions, and supporting remodeling and maturation of the spiral arterioles. A decline in progesterone levels (typically following corpus luteum regression in the absence of pregnancy) triggers endometrial breakdown and shedding, which clinically manifests as menstrual bleeding (Thiyagarajan et al., 2024).

The hypothalamic–pituitary–ovarian (HPO) axis is tightly interconnected with other endocrine systems. This is partly because GnRH neuronal activity is shaped by multiple hypothalamic networks and by upstream regulators (e.g., kisspeptin neurons) that integrate metabolic and stress-related signals, including glucocorticoids such as cortisol (Gombert-Labedens et al., 2024).

The circadian regulation of cortisol is well established: cortisol displays a pronounced daily rhythm that is coordinated by the suprachiasmatic nucleus (SCN) and conveyed through neuroendocrine pathways, linking circadian timing with reproductive regulation (Paragliola et al., 2025). Gifford et al. (2024) reported sex differences in stress responsivity at the neuroendocrine level, with women showing greater adrenal reactivity and higher cortisol output under sustained stress exposure. This heightened HPA-axis activation may plausibly contribute to menstrual cycle disturbances via downstream effects on the HPO axis. However, the evidence remains limited, and the proposed association requires further well-powered longitudinal and mechanistic studies (Gifford et al.,2024)

Circadian rhythm disruption may contribute to menstrual cycle irregularity. Several studies suggest that night shift work can induce circadian misalignment comparable to jet lag, thereby affecting menstrual regularity. Alemu et al. (2025) supported this association, reporting cohort-specific differences: women in the 1989–1995 cohort more frequently reported menstrual irregularities than those in the 1973–1978 cohort. Moreover, long-term longitudinal findings reported by Kim et al. (2024) demonstrated an association between night shift work and menstrual cycle irregularity. In a study by Peng and Chang (2024) examining sleep quality and

menstrual regularity among nurses, participants working night shifts had a higher risk of menstrual cycle irregularity than participants not working night shifts. Collectively, these findings support the notion that circadian misalignment is linked to irregular menstruation and may contribute to female reproductive dysfunction.

A range of mechanisms may underlie the association between circadian misalignment and menstrual cycle regulation. Melatonin, synthesized in the pineal gland, is a key circadian signal that synchronizes internal rhythms with the external light–dark cycle. Under typical conditions, melatonin concentrations peak during the biological night (often around 02:00–04:00), with reported nocturnal levels commonly in the tens of pg/mL range (Jia et al., 2025). Fazlali et al. (2025) reported that greater light exposure prior to laboratory assessment was associated with an earlier dim light melatonin onset (DLMO). In addition, the literature suggests that DLMO may vary across the menstrual cycle: the luteal phase has been associated with an earlier DLMO, whereas a later DLMO has been observed during the follicular phase (Fazlali et al., 2025; Kauppila et al., 1987). Taken together, these findings support the hypothesis that abrupt changes in the timing of light exposure could shift circadian phase and, through neuroendocrine pathways, contribute to alterations in menstrual cycle timing, although causal links require further confirmation (Fazlali et al., 2025; Kauppila et al., 1987).

Sleep quality and a stable sleep schedule influence endocrine homeostasis. Kauppila and colleagues illustrated this relationship by examining LH pulsatility across sleep and wake states: during sleep, LH pulses showed greater amplitude and longer interpulse intervals compared with wakefulness, and this pattern was observed irrespective of the timing of sleep (Hall et al., 2005). Collectively, these findings suggest that shifts in sleep timing can alter LH pulsatility and may contribute to changes in ovulatory timing, potentially leading to delayed or advanced ovulation.

Impact of Circadian Misalignment (Jet Lag and Shift Work) on Menstrual Function

Several studies report a higher prevalence of menstrual cycle irregularities among women who regularly travel across time zones. Flight crew members are repeatedly exposed to circadian misalignment (jet lag) together with occupational stressors, which may contribute to endocrine disturbances, including hyperprolactinemia (Radowicka et al., 2021). Elevated prolactin can inhibit reproductive function by suppressing hypothalamic GnRH pulsatility; mechanistically, prolactin can reduce GnRH drive via binding to the prolactin receptor (**PRLR**) expressed on Kiss1 (kisspeptin) neurons, thereby diminishing gonadotropin stimulation of the ovaries and potentially contributing to menstrual irregularity (Bocianska et al., 2025). Radowicka et al. (2021) reported a higher prevalence of hyperprolactinemia among female flight attendants than in a control group and observed an association with job tenure, with hyperprolactinemia occurring more frequently in women with more than 15 years of work experience. In contrast, the number of flying hours per month was not significantly associated with hyperprolactinemia in their analysis (Radowicka et al., 2021). In a subsequent study, the research group explored whether hyperprolactinemia in female flight attendants could be related to elevated thyroid autoantibodies (aTPO and/or aTG); however, the findings were not statistically significant (Radowicka et al., 2021). More broadly, recent evidence supports the view that frequent duty-related flights may adversely affect hormonal and reproductive health among flight crew, as

combined occupational exposures—including circadian rhythm disruption, cosmic ionizing radiation, and psychosocial stress—have been linked to an increased risk of reproductive complications (Stefańska et al., 2025). Consistent with this, Barraza-Ortega et al. (2025), as cited in Stefańska et al. (2025), highlight that women in flight crew may exhibit reduced reproductive potential, reflected by lower anti-Müllerian hormone (AMH) levels and diminished ovarian reserve.

Kim et al. (2024), in an 8-year follow-up cohort study, reported an association between the duration of night shift work and the risk of menstrual cycle irregularity. Compared with women with 0–3 years of night work, those with 3–6 years of night work showed a statistically higher risk of incident irregular cycles, with adjusted hazard ratios (AHRs; 95% CI) of 1.86 (1.71–2.03), 1.55 (1.42–1.70), and 1.54 (1.40–1.69) in Models 1, 2, and 3, respectively. In contrast, the corresponding AHRs for the 0–3-year group were 1.02 (0.92–1.12), 0.86 (0.77–0.95), and 0.85 (0.76–0.94) across Models 1–3.

In addition to menstrual cycle irregularities, the literature describes other female reproductive and menstrual-related complaints associated with circadian rhythm disruption, including dysmenorrhea (menstrual pain), increased fatigue, abdominal cramps, back pain, general somatic discomfort, and gastrointestinal symptoms such as diarrhea or constipation (Tsai, 2024). In a prospective longitudinal study of newly graduated nurses, PMS severity worsened six months after initiating shift work compared with pre-shift baseline and remained elevated at the 18-month follow-up ($p < .001$) (Huh et al., 2024).

Potential Mechanisms Linking Jet Lag to Menstrual Irregularities

Physiological alterations triggered by jet lag–related circadian misalignment may contribute to menstrual cycle irregularities. This effect may be mediated in part by dysregulation of the HPO axis together with disturbances in melatonin and cortisol secretion (Saadedine et al., 2023; Shufelt et al., 2017; Alhajeri et al., 2024; Brzezinski, 1997).
Sleep disruption is a plausible intermediary linking circadian misalignment to menstrual disturbances, as changes in sleep duration and timing often lead to irregular meal timing and shifts in energy intake patterns (Fujiwara et al., 2018; Alvero et al., 1998). Collectively, these abrupt changes in sleep–wake and feeding schedules may provoke endocrine perturbations that increase the likelihood of menstrual irregularities.

HPO-axis signaling and ovulatory function

Disruption of the HPO axis—manifested as altered GnRH pulsatility and dysregulated LH and FSH secretion—can impair follicular development and ovulation, ultimately contributing to menstrual cycle irregularities. Such neuroendocrine disturbances may be precipitated or exacerbated by psychological and social stressors, restrictive or otherwise dysregulated eating patterns, and excessive physical training/overtraining (Saadedine et al., 2023; Shufelt et al., 2017; Fujiwara et al., 2018; Alvero et al., 1998). Recent animal studies suggest a link between circadian disruption and reproductive neuroendocrine regulation, indicating that circadian

misalignment can modify GnRH/LH dynamics and ovarian steroidogenesis; however, extrapolation to human menstrual physiology should be made cautiously. In a rat study, Fujiwara et al. (2018) examined the effects of feeding time aligned versus misaligned with the animals' circadian activity phase. Daytime feeding (i.e., during the inactive phase in rats) was associated with fewer corpora lutea and a lower ovulation frequency compared with night-time feeding and time-unrestricted feeding (Fujiwara et al., 2018). Another study in lean women by Alvero and colleagues (1998) reported that a 72-hour fast was associated with altered LH pulsatility compared with a fed condition (12.9 ± 1.3 vs. 16.0 ± 1.9; $P < 0.05$), while mean LH and FSH concentrations did not differ significantly between conditions. The authors further emphasized that the frequency of LH pulses is important for ovulatory function, even when average LH levels remain unchanged (Alvero et al., 1998).

Melatonin and thermoregulation

The literature describes links between melatonin and sex steroid production, including intraovarian regulation of steroidogenesis. Accordingly, alterations in melatonin secretion caused by disrupted sleep schedules—such as those resulting from transmeridian air travel (time-zone changes) or irregular working hours—may adversely affect female reproductive health (Brzezinski, 1997). The circadian system, coordinated by the suprachiasmatic nucleus (SCN), drives the 24-hour oscillation of core body temperature (CBT), largely independent of ambient temperature (Krauchi and Deboer, 2010). Melatonin is closely related to CBT regulation: Krauchi et al. (1985) reported that higher evening melatonin levels (under SCN control) are accompanied by increased distal skin temperature (reflecting enhanced peripheral heat loss) and a concomitant decrease in CBT.

Cortisol rhythmicity and HPA-axis activation

Circadian misalignment is associated with impaired coordination between sleep timing and cortisol secretion. In a cross-sectional study, Burek and colleagues (2024) compared cortisol profiles in female hospital workers who performed night shift work with those of non-shift workers. Using cortisol curves, they showed that non-shift workers displayed a typical diurnal cortisol pattern, with a peak shortly after awakening followed by a progressive decline toward bedtime. In contrast, night-shift workers exhibited a **flattened** post-awakening decline, and their cortisol curve was described as **U-shaped** (Burek et al., 2024). In a study of flight attendants, Paragliola et al. (2021) reported an inversion of the normal circadian pattern of cortisol release and suggested that, after a west-to-east flight, cortisol secretion may remain aligned with the western time zone for at least 36 hours after arrival in the east. Together, these findings highlight the importance of circadian stability for normal cortisol rhythmicity.
A flattened circadian cortisol rhythm and dysregulated HPA-axis feedback control are biochemical hallmarks of Cushing's syndrome (Juszczak et al., 2024). Although Cushing's syndrome is a rare cause of hypogonadotropic hypogonadism, it illustrates how sustained hypercortisolism can disrupt reproductive function. Alhajeri and colleagues (2024) reported a case of hypogonadotropic hypogonadism secondary to Cushing's syndrome caused by a left adrenal cortical adenoma; menstrual regularity was restored within six months after laparoscopic adrenalectomy.

Menstrual cycle irregularities are frequently reported among women with Cushing's syndrome. Data from the European Registry on Cushing's syndrome (ERCUSYN) indicate that menstrual irregularities occurred in 56% of 390 women (Valassi et al., 2011). A population-wide survey conducted in New Zealand reported menstrual irregularities in 35.5% of women with Cushing's syndrome (Bolland et al., 2011). In addition, the studies summarized in a narrative review by Saei Ghare Naz et al. (2020) suggest that approximately 80% of patients experience menstrual cycle irregularities.

Clinical and Public Health Implications

Time zone change–related jet lag is an important yet often underestimated factor that may influence menstrual cycle regularity. Women at particularly high risk include flight attendants, frequent long-distance travelers, and night-shift workers (e.g., nurses). In practice, repeated time-zone crossings can be associated with greater variability in melatonin secretion, reflecting increased circadian disruption. Grajewski et al. (2023) reported that, compared with teachers, flight attendants showed significantly greater circadian rhythm disruption, indicated by higher adjusted melatonin rate variance values (2.8×10^5 versus 1.0×10^5 $(ng/h)^2$, respectively; $P = 0.04$). Such variability supports the plausibility of biological pathways linking circadian misalignment to menstrual cycle irregularities, supporting the biological plausibility (Grajewski et al., 2023).

However, the evidence on how circadian rhythm disruption affects fertility remains challenging to interpret. Freeman and colleagues reported that a sleep duration of ≥9 hours was associated with lower fecundability only among women who did not work night shifts (Freeman et al., 2023). One possible interpretation is that the relationship between sleep duration and fecundability may differ by work schedule and that individuals chronically exposed to circadian disruption could partially adapt over time. *Nevertheless, this finding does not rule out an effect of chronic circadian misalignment on fecundability; it may reflect exposure misclassification due to baseline self-reported measures, limited information on shift schedules, residual confounding, limited power in subgroup analyses, or chance findings from multiple comparisons* (Freeman et al., 2023).

In terms of miscarriage risk, Grajewski et al. (2015) reported that **≥15 hours of Standard Sleep Interval (SSI) travel** were associated with miscarriage in early pregnancy. In contrast, the number of time zones crossed was not a statistically significant predictor of miscarriage. Notably, flight attendants who did **not** fly during pregnancy reported miscarriages more frequently than those who continued working while pregnant. This pattern may reflect a "healthy worker effect," whereby women who remain flying during pregnancy constitute a healthier or lower-risk subgroup, while those experiencing complications are more likely to stop flying, which can bias comparisons.
The authors also reported evidence suggesting a potential association between higher absorbed cosmic radiation dose (≥0.1 mGy) and miscarriage occurring at 9–13 weeks' gestation (OR = 1.7; 95% CI: 0.95–3.2) (Grajewski et al., 2015).

To mitigate the adverse effects of time zone–related jet lag on well-being, the National Institute for Occupational Safety and Health (NIOSH) recommends maintaining a stable sleep–wake routine. Additional advice includes avoiding alcohol, caffeine, heavy or spicy meals, and screen exposure shortly before bedtime. For employees—particularly pregnant workers—NIOSH also recommends reducing physical workload when feasible (NIOSH, 2024). Furthermore, sleep-optimization training may support cabin crew in planning and protecting sleep both at home and during layovers, especially in preparation for ultra-long-haul (ULR) flights (Van den Berg et al., 2023).

Limitations of Current Evidence

This work has several limitations, including relatively small study cohorts and a limited number of randomized controlled trials. Moreover, there is still a shortage of studies focusing specifically on flight attendants and women who frequently travel across time zones, which restricts a more precise assessment of the impact of time zone change–related jet lag on menstrual cycle regularity. In addition, much of the available evidence is observational, which restricts causal inference.

It should also be noted that the concept of an "irregular menstrual cycle" is often interpreted differently by participants, which may introduce reporting bias. Women may not consistently track cycle patterns or may overlook important contributors to irregularity (e.g., recent weight change, sleep duration, stress intensity, or lifestyle changes). Conversely, some women may underreport irregular cycles by normalizing symptoms or attributing them to transient factors such as temporary sleep loss, rather than recognizing them as clinically relevant changes.

Conclusions

Circadian misalignment resulting from rapid time zone changes (jet lag) or night shift work is associated with menstrual cycle disturbances, more severe premenstrual symptoms, and adverse fertility-related outcomes. High-risk groups include women working in aviation (e.g., flight attendants and frequent flyers) as well as women employed in rotating or permanent night-shift schedules. Evidence points to several plausible biological pathways, involving alterations in melatonin signaling, disrupted cortisol rhythmicity, HPO-axis dysregulation, and changes in the timing of sleep and food intake. Practical measures aimed at minimizing jet lag—such as consistent meal timing, adequate hydration, and sleep-focused routines—may help reduce symptom burden. Clinically, when evaluating patients with menstrual irregularities, it is important to ask about circadian disruptors such as shift work patterns and recent or frequent long-distance travel, as these exposures may meaningfully affect female reproductive health. From a public health and occupational perspective, employers should support workers' well-being by monitoring cumulative night-work exposure, providing additional protection for pregnant employees, and implementing regular education on circadian rhythm disruption, its manifestations, and feasible mitigation strategies. Finally, emerging technologies that monitor

circadian rhythms alongside menstrual cycle parameters, as well as novel interventions to reduce jet lag, may offer additional preventive and therapeutic opportunities; however, further prospective and experimental studies are needed to clarify causality and identify effective interventions.

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