



RESEARCH ARTICLE

Female reproductive health in long-duration space missions: a narrative review of current challenges

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Abstract

Female reproductive health represents a critical dimension of long-duration spaceflight. This narrative review examined the impacts of space exposure, prolonged microgravity, cosmic radiation, and circadian rhythm disruption on female fertility and maternal–fetal health during space missions. A search was conducted in high-impact databases, and gray literature was also considered. The available evidence suggests that microgravity and radiation could suppress progesterone levels, reduce the ovarian reserve, or induce a nonreceptive endometrial phenotype. Furthermore, dysregulation of the hypothalamic–pituitary–gonadal (HPG) axis and gamete degradation could pose critical threats to conception and fetal development. Current mitigation strategies remain insufficient; hormonal contraception and assisted reproductive technologies have been explored, but they lack validation under real-world spaceflight conditions. These findings underscore the urgent need for biomedical protocols, regulatory frameworks, and ethical standards that enable safe and inclusive space missions.

Keywords: Cosmic radiation, female reproductive health, microgravity, spaceflight, space medicine

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1. Introduction

The advance towards longer-duration space missions and the eventual colonization of other planets position reproductive health as a fundamental pillar for the survival of humanity beyond our planet's atmosphere (Edelbroek, 2019; Sharma et al., 2024). However, current knowledge about the impact of the spatial environment on the reproductive system, especially the female reproductive system, is remarkably scarce.

Astronauts face the so-called "space exposome," a combination of unique risk factors that include ionizing radiation, alterations in gravitational forces, and changes in circadian rhythms (Williams et al., 2009) and temperature variation (Bailey et al., 2025; Williams et al., 2009), which are difficult to counteract with any conventional shielding model. These factors can cause physiological, genetic, and epigenetic alterations (Bonanni et al., 2023), potentially affecting every stage of reproduction, from gametogenesis to the moment of labor (Jain et al., 2023; Mathyk et al., 2024). In addition, effects such as gravity-induced muscle atrophy, bone loss, and longer healing times for wounds and fractures have been described, with repercussions on the human body's immune response, as well as anorexia and electrolyte imbalances (Bonanni et al., 2023; Da Silva et al., 2002; Laurens et al., 2019).

In female reproductive organs, ionizing radiation compromises the integrity of the endometrium and ovarian reserve, whereas microgravity alters the HPG axis, with consequences for folliculogenesis, ovulation and potentially early embryonic development described in animal models (Cutigni et al., 2025; Jain et al., 2023; Marin et al., 2025; Mathyk et al., 2024). These effects could not only compromise the individual fertility of astronauts but also raise questions about possible transgenerational risks not yet quantified in humans (Jain et al., 2023; Mathyk et al., 2024).

The lack of immediate access to specialized medical care, coupled with limitations in the supply of pharmaceuticals and biotechnology, necessitates the development of strategies capable of addressing reproductive health demands during long-duration space missions. Analysing these challenges is a crucial step toward ensuring that humanity can become a safe and sustainable interplanetary species (Edelbroek, 2019; Jain et al., 2023; Mathyk et al., 2024).

Likewise, despite the increasing participation of women in long-term missions, there is no up-to-date synthesis with methodological rigor that integrates, with solid statistical support, the physiological, technological, and ethical challenges of female reproductive health in deep space. This analysis aims to fill this knowledge gap and examine these challenges and the strategies available to address them.

2. Body

A narrative review was conducted via a structured search of the scientific and gray literature. Search terms in Spanish and English were used to identify scientific articles, reviews, and other relevant documents, including "female reproductive health," "spaceflight, microgravity," "cosmic radiation," "ovarian reserve," "fertility," "pregnancy in space," "menstrual suppression," and "space medicine." The search encompassed all literature published up to March 2026 in the following databases: Scopus, PubMed, and Web of Science. The gray literature was also identified via Google Scholar. Documents without an identified author or publication date, as well as articles that did not meet the search criteria, were excluded. No restrictions were applied on the basis of language or publication year.

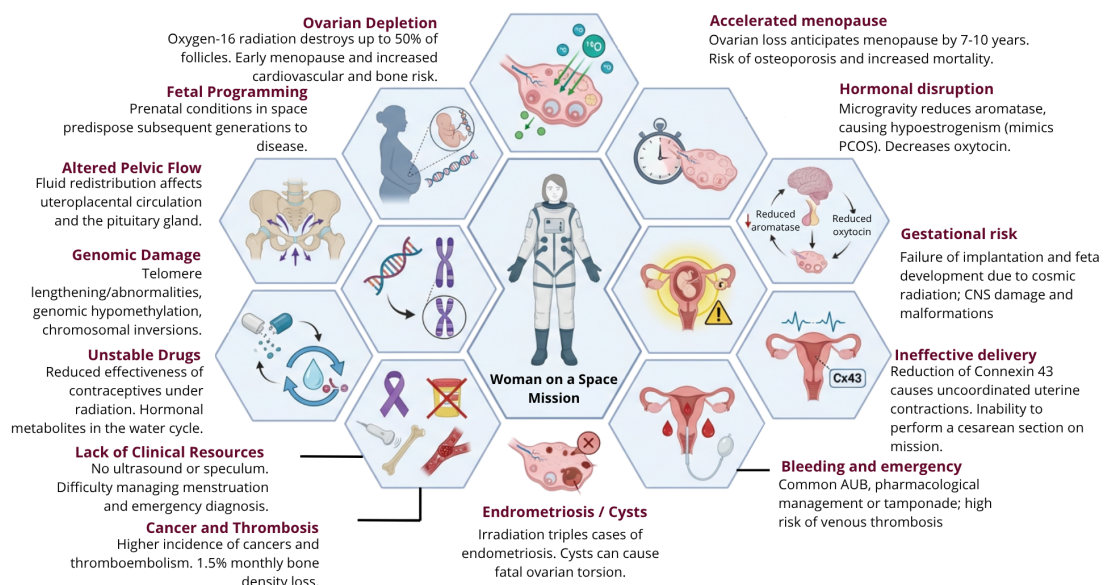
2.1. Effects of radiation and microgravity on the ovarian reserve and endometrium

Ovarian tissue is highly radiosensitive (Hughes-Fulford et al., 2024; Mathyk et al., 2024); a dose of approximately 2 Gy can destroy up to 50% of the primary follicular reserve, with primordial follicles being the most sensitive (Mishra et al., 2016, 2017). Studies in animal models have demonstrated that exposure to high-energy particles (HZE) and neutrons induces oxidative damage, double-strand DNA breaks, and apoptosis in oocytes and granulosa cells, resulting in dose-dependent depletion of the ovarian reserve, a greater incidence of ovarian tumors (Magni et al., 2025) and infertility (Mishra et al., 2017). These results should be interpreted with scientific caution, given that they come predominantly from murine models and in vitro platforms whose direct extrapolation to human reproductive physiology is limited (Hughes-Fulford et al., 2024; Marin et al., 2025; Mathyk et al., 2024).

It is postulated that, during long-term missions, the female ovarian reserve could be reduced by up to 50%, which would be associated with a greater risk of primary ovarian insufficiency and premature menopause (Gimunová et al., 2024; Rose, 2022). At the molecular level, a significant decrease in the proliferation and migration of uterine stromal cells is documented due to a reduction in the activity of the Akt pathway and the expression of FOXO3a, alterations that converge in a nonreceptive endometrial phenotype that could interfere with decidualization (Gimunová et al., 2024; Mathyk et al., 2024). This is compounded by a reduction in the blastocyst formation rate and quality, with DNA damage and alterations in epigenetic methylation profiles (Mathyk et al., 2024; Steller et al., 2020), as well as interference with meiotic spindle organization and oocyte maturation, which compromises chromosome segregation (Mathyk et al., 2024). In this context, space missions involve probable pathophysiological effects on women’s reproductive health, as described in (Figure 1).

Figure 1

Main risks to female reproductive health

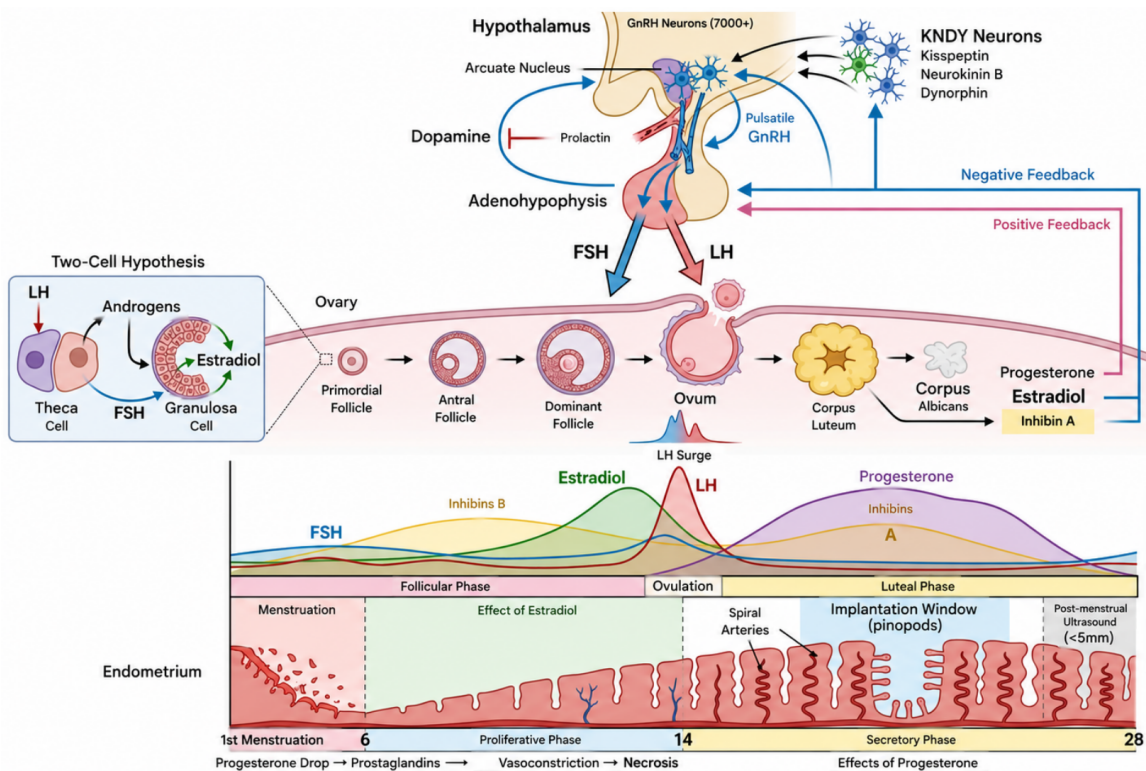


2.2. Hormonal changes and menstrual cycle alterations in extended missions

The reproductive capacity of females on Earth depends on finely coordinated neuroendocrine regulation via the hypothalamic–pituitary–gonadal axis (see Figure 2). However, a specific biological model has not been effectively described in humans; therefore, further in-depth studies and contributions are needed, as are potential synergies in the space exposome (Cutigni et al., 2025).

Figure 2

Physiology of the hypothalamic–pituitary–gonadal axis and normal menstrual cycle



It has been proposed that, under microgravity conditions, there is an approximately 12% decrease in luteinizing hormone (LH) levels, a 52% decrease in progesterone, and a reduction in the regulation of estrogen receptors in uterine tissue, compromising implantation and pregnancy viability in astronauts (Cutigni et al., 2025; Gimunová et al., 2024). The environmental stress caused by microgravity and/or ionizing radiation could substantially impact embryonic and fetal development (Cutigni et al., 2025; Demir et al., 2025; Holden, 2025). Taken together, these findings increase myometrial excitability and intrauterine growth restriction, the likelihood of preterm labor, pregnancy loss, potential transgenerational effects (Jain et al., 2023), and teratogenesis (Demir et al., 2025).

On the other hand, the reduction in pulsatile oxytocin waves associated with spaceflight (Ronca et al., 2014) is a physiological compensation in response to stress stimuli. Attempts have been made to link increased psychosocial stress resulting from isolation with circadian dysregulation, which affects menstrual cycle patterns (Chaloulakou et al., 2022; Cutigni

et al., 2025). Therefore, mental health assessments should not be limited to psychosocial stress or isolation: factors such as genetic predisposition, prior experience, and emotional capacity (Chaloulakou et al., 2022), as well as environmental interventions such as the use of natural landscapes and artificial windows to simulate the terrestrial environment (Sanchez Delgado et al., 2025), should be considered.

2.3. Assisted reproduction and reproductive control

Microgravity increases the risk of venous thromboembolism in astronauts undergoing menstrual suppression treatment with combined oral contraceptives (COCs), a common practice on space missions (Gimunová et al., 2024). This risk is exacerbated by changes in blood stasis and plasma viscosity, which are characteristic of spaceflight, and by space adaptation syndrome, which compromises gastrointestinal absorption, reducing the efficacy of oral contraceptives (Mathyk et al., 2024; Steller et al., 2020). Furthermore, the shift of fluids toward the head associated with microgravity increases the risk of potentially lethal clot formation (Steller et al., 2020). This scenario highlights an unresolved paradox: the only contraceptive methods with evidence of use in space inherently introduce cardiovascular risks that are amplified by microgravity.

In the field of assisted reproductive technology (ART), space embryo incubators designed to operate in low Earth orbit are already being developed, which integrate IVF/ART in an automated manner (Chaplia et al., 2024; Edelbroek, 2019). The use of artificial wombs would allow for more effective shielding of fetal development from ionizing radiation than the maternal body does, eliminating the complications of extreme gravitational transitions during launch and reentry (Edelbroek, 2019; Mathyk et al., 2024). However, the automation of IVF via microfluidics remains in the experimental phase, without optimized protocols for chronic exposure to galactic radiation (GCR) or solar particle events (SPE) (Chaplia et al., 2024; Wu et al., 2024). Spontaneous reproduction during active missions is considered contraindicated given the physiological stress generated by radiation, microgravity and pressure variations (Cole et al., 2025; Palmer et al., 2026; Reguera et al., 2023; Shahbazi, 2020), and space agencies have established operational policies to prevent mission pregnancy (Gimunová et al., 2024; Jennings & Santy, 1990).

2.4. Scientific and technological mitigation strategies

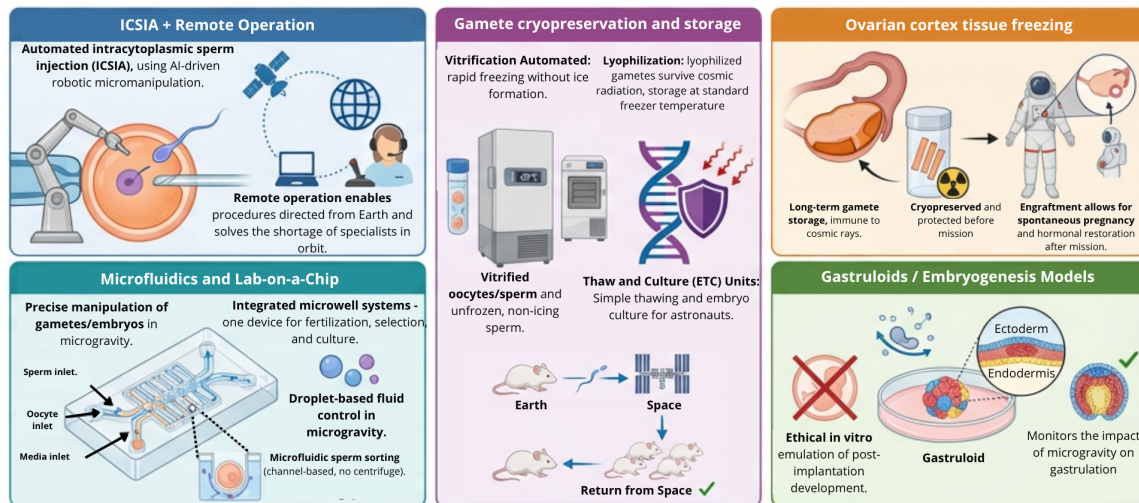
The most ambitious proposed mitigation strategies include habitats with artificial gravity created by rotation (Jones, 2023); radiation shields based on aluminum, water, or polyethylene (Steller et al., 2020); molecular-based radioprotectors with gene expression platforms (Chaplia et al., 2024); and AI-assisted real-time genetic monitoring systems (Rojas Barnett et al., 2024; Vilhekar et al., 2024). However, none have been validated in an integrated manner or under real microgravity conditions, which keeps them at the operational and implementable proposal stage.

In the field of in vitro experimental platforms, ovarian organoids and 3D follicular models have demonstrated the ability to reproduce cellular heterogeneity and basic endocrine function and have been proposed for studying radiation damage to human ovarian tissue (Del Valle & Chuva de Sousa Lopes, 2023; Francés-Herrero et al., 2022; Mathyk et al., 2024). Microfluidic organ-on-a-chip systems "manage to mimic" a complete 28-day menstrual cycle, allowing the study of endocrine cross-signalling (Francés-Herrero et al., 2022; Heidari-Khoei et al., 2020); bioprinted ovary-on-a-chip models using theca and

granulosa cells show sustained estradiol and progesterone production for nearly three weeks under perfusion, with cell viability exceeding 78% at 27 days (Healy et al., 2021). However, none of these platforms have been evaluated under actual microgravity or full-spectrum space radiation (see Figure 3).

Figure 3

Scientific and technological mitigation strategies



The immediate priority, consistently highlighted in peer reviews, is to transfer these platforms to simulated microgravity systems and, in a second phase, to the International Space Station to establish dose–response curves in human ovarian tissue (Gimunová et al., 2024; Marin et al., 2025; Mathyk et al., 2024). The absence of a longitudinal clinical-hormonal database of female astronauts prevents any in vitro model from being validated as representative of the real space environment (Gimunová et al., 2024; Mathyk et al., 2024).

2.5. Management of gynecological emergencies in long-duration missions

The management of acute gynecological emergencies—ovarian torsion, ectopic pregnancy and hemorrhage—represents the scenario of greatest immediate life risk in long-duration missions and the area where the gap between clinical need and technological capacity is most pronounced. Unlike missions in low Earth orbit, where medical evacuation can be carried out in hours, a mission to Mars imposes a structural impossibility of evacuation, with a communication latency of up to approximately 24 minutes per direction (Mathyk et al., 2024; Pantalone et al., 2021; Rajput, 2021). Robotic telesurgery, which is viable in terrestrial contexts (Macias et al., 2025; Rahmah et al., 2025), is technically unfeasible under that latency for direct control from Earth, which forces a rethinking of the paradigm toward surgical robots with partial autonomy assisted by AI, delayed teleassistance and reality (de’Angelis et al., 2022; Macias et al., 2025; Pantalone et al., 2021). Unresolved issues persist regarding volume, energy, reliability, and crew training, and there are few specific data on experimental and analogous surgeries (Mathyk et al., 2024; Pantalone et al., 2021; Rajput, 2021).

2.6. Ethical, social, and legal dimensions

The ethical, legal, and reproductive autonomy dimensions add a layer of complexity that cannot be resolved solely through technological advancements. Currently, there are no international treaties regulating human reproduction in space or the legal status of embryos conceived off-Earth (Balistreri & Umbrello, 2022; Kendal, 2021). Any assisted reproductive intervention in space requires the informed consent of the parties involved and a care infrastructure that includes equipment, trained personnel, and AI integration (Cole et al., 2025; Mathyk et al., 2024; Waisberg et al., 2023). The possibility of a pregnancy on mission, whether spontaneous or through ART, including ectogenesis, raises ethical, legal, and reproductive autonomy questions that remain unanswered (Cole et al., 2025; De Bie et al., 2023; Horn, 2021).

3. Conclusions

The reproductive health of females on long-duration space missions is a relatively unexplored and challenging field. The effects of the space exposome on the ovarian reserve, the hypothalamic–pituitary–gonadal axis, and human embryonic development are insufficiently documented, with evidence largely derived from animal models and in vitro platforms not validated under real-space conditions. The effects reported in this research not only compromise fertility viability but also raise questions about the feasibility and safety of human reproduction during long-duration space exploration. While mitigation strategies such as artificial gravity, radiation protection, robotic telesurgery, and organ-on-a-chip methods are plausible, none have achieved operational validation. Therefore, more methodologically rigorous research is needed, with a focus on longitudinal human evidence, experimental validation in real microgravity, emergency surgical protocols, and international legal regulation.

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