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Overview on Space Medicine and Human Spaceflight

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ABSTRACT

A thorough grasp of the physiological and psychological difficulties present in alien habitats is essential to humanity's continued quest for space travel. An integral component of human space exploration is space medicine. It promotes performance, function, and survival in this harsh and sometimes fatal environment. It operates at the intersection of exploration, science, technology, and medicine and is global, multicultural, and interdisciplinary. Numerous challenges associated with space travel jeopardize astronauts' survival in the intensely radiative environment by negatively impacting physiological processes like cardiovascular adaptation, infection, bone loss, kidney stones, muscle deterioration, and genetic disorders. Preventing rapid drug degradation, loss of active medication potency, and time-dependent changes in pharmacokinetic and pharmacodynamic studies due to various physiological changes under microgravity all depend on maintaining pharmaceutical stability. The stability studies and the intended long shelf-life of pharmaceuticals cannot be entirely based on guidelines for the terrestrial environment; instead, they must take into account particular spaceflight conditions such as microgravity, high radiation levels, particularly from galactic cosmic rays and solar particle events, vacuum, and changes in relative humidity. The primary focus of this review paper is on the causes and consequences of instability-causing variables such as temperature, humidity, radiation, and microgravity, along with state-of-the-art approaches to deal with such issues utilizing both established practices and promising new developments in the future.

Keywords: Space Medicine, Medicines Used In Space, Spaceflight, And The Immune System, Medical Standards For Spaceflight, Space Nutrition

INTRODUCTION

Future orbital and interplanetary return space flights will benefit from space medicine, which also helps to advance Earth medicine, which has evolved through the discovery of new technologies on Earth but has been fueled by the harsh environment and scarce resources of space, and the development of new technologies to deal with these circumstances. Any technology about space travel or exploration is collectively referred to as space technology [1]. A turning point in human history, the onset of the space era in the middle of the 20th century drastically changed how we view our role in the universe. What started as a daring scientific and technological venture has quickly developed into a long-term human presence in Earth's orbit, with plans to visit the Moon, Mars, and other planets. But there are significant physical and mental obstacles for the human body as a result of this extension into the alien world. The core mission of space medicine, a rapidly developing interdisciplinary field essential to enabling sustainable human spaceflight, is to understand and mitigate the impact of these stressors on human health and performance. In contrast to the familiar environment of Earth, space presents a unique and hostile confluence of stressors, including microgravity, altered radiation environments, extreme temperatures, and psychological isolation. It is now more feasible than ever to explore space because of advancements in technology and sophisticated materials. This drive is driving scientists to push the limits of science and technology to explore space.

Numerous studies have been carried out on space stations like Mir and the International Space Station (ISS) since the groundbreaking flights of Yuri Gagarin and Alan Shepard. These studies have provided previously unheard-of chances to monitor and investigate how humans react to extended space exposure. These studies have uncovered a wide range of adaptations, from advantageous physiological modifications to potentially harmful health hazards. For example, fluid changes, cardiovascular deconditioning, and neurovestibular abnormalities are among the acute impacts of microgravity. For longer periods, issues include immune system changes, muscular atrophy, bone demineralization, and vision impairment. At the same time, there are serious long-term dangers associated with exposure to solar particle events and galactic cosmic rays, including heightened vulnerability to cancer and potential central nervous system damage.

In order to research the many fundamental aspects involved in human acclimation in space, space medicine focuses on the long-term safety and health of astronauts in the constantly discordant environment of space. People on Earth have been fighting diseases for generations to find better medical cures, and the space station, which conducts research in long-term microgravity circumstances, offers a viable tool to provide a new dimension for that fight [2]. The unique and harsh environmental aspects of space, including microgravity, radiation, artificial light, onboard noise, acceleration pressures, isolation, confinement, poor sanitation, and a hard workload, provide a number of difficulties for the spaceflight crew at the space station [3-5].

Astronauts' physiological systems are significantly impacted by spaceflight conditions, which can result in common and expected side effects such as fluid redistribution from the lower to the upper body, which causes head congestion, face edema [6], leg shrinkage [7], 10% to 15% loss of plasma volume due to increased capillary permeability of intravascular fluids into the extracellular space in hypovolemia [8], decreased baroreflex sensitivity [9], and orthostatic intolerance [10]. Additionally, spaceflight-associated neuro-ocular syndrome [11], transient anemia, bone loss, calf and quadricep muscle atrophy, increased kidney filtration rate, kidney stones as a result of bone loss, immunosuppression, neurological changes with altered sensory inputs that cause occasional disorientation [12], visual impairment (due to intracranial hypertension), insomnia, corneal irritation, ulcer, infection and abrasion, nosebleeds, and constipation [13] are all symptoms of the space environment.

Medicines Used in Space

According to the general population, astronauts may encounter a variety of medical problems, ranging from minor illnesses to more severe disorders. For each human spaceflight mission, a complete medical package with a range of drugs is therefore necessary, particularly for extended stays on the International Space Station (ISS) or upcoming deep-space expeditions. Common drugs that relieve the effects of spaceflight on the human body include those for space motion sickness, sleep deprivation, circadian rhythm abnormalities, headaches, muscle and joint pain, bone resorption, congestion, nutritional deficiencies, respiratory infections, cardiac conditions, and hypersensitivity reactions [14].

New medical developments in diagnostic and therapeutic equipment [15] and a wide range of supplies, including convenience medication packs, medical supply packs, emergency medical treatment packs, physician equipment packs, medical diagnostic packs, minor treatment packs, topical and injectable medication packs, oral medication packs, intravenous supply packs, respiratory support packs, crew medical restraint systems, and crew contamination protection kits [16, 17], are part of the ISS's health maintenance system.

Like everyone else, astronauts can suffer from a variety of illnesses, ranging from minor maladies to more severe disorders. Therefore, any human spaceflight mission must have a complete medical package with a range of drugs, particularly for extended stays on the International Space Station (ISS) or upcoming deep-space adventures.
The following lists the common medications used in space, along with the particular difficulties and factors to be taken into account:

TYPICAL TYPES OF MEDICINES

- **Pain Relievers**: For headaches, muscle aches, minor injuries, and other unpleasant conditions, acetaminophen (Tylenol), ibuprofen (Advil, Motrin), and stronger analgesics are essential.
- **Motion Sickness Drugs**: During the early days of spaceflight, "space sickness," also known as space adaptation syndrome, was prevalent. Commonly used medications include scopolamine and promethazine, which are usually administered by injection.
- **Medications for allergies and congestion**: Astronauts frequently suffer from "puffy face" and nasal congestion as a result of fluid changes in microgravity. Decongestants and antihistamines are frequently utilized.
- **Sleep Aids**: Because of noise, cramped quarters, and altered circadian rhythms (the Earth's 24-hour day/night cycle is disturbed), sleep difficulties are prevalent in space. Non-benzodiazepine hypnotics (often known as "Z-drugs" like zolpidem) and melatonin are employed. Although they are also accessible, benzodiazepines like temazepam are used less commonly because of their longer half-lives.
- **Antibiotics**: Since the immune system functions differently in microgravity, broad-spectrum antibiotics (such as ciprofloxacin, amoxicillin/clavulanate, and azithromycin) are essential because infections can happen in space just like on Earth.
- **Antifungals**: For infections caused by fungi.
- **Antivirals**: For viral infections, antivirals are used (e.g., acyclovir for herpes viruses).
- **Gastrointestinal Medications:** The basic package includes antacids, laxatives, and anti-diarrheals (such as loperamide).
- **Drops for the eyes and ears:** For small infections or discomfort.
- **Corticosteroids:** For allergic responses or inflammation.
- **Topical medications** include antiseptic wipes, skin irritant creams, and wound care products.
- **Emergency Medications**: Injectables for severe allergic reactions (like epinephrine), cardiac problems (like lidocaine or atropine), or extreme pain are examples of emergency medications.

Spaceflight and Immune System

Spaceflight is a special environment where physiology is impacted by unique and severe stimuli, some of which are impossible to precisely duplicate on Earth. Increased radiation exposure, microgravity, and continuous fluid shifts, extended seclusion and confinement, difficult-to-re-entrain circadian shifts, and challenging job demands and timetables are all hazards faced by astronauts. It has recently been established that immunological system dysregulation happens during flight and lasts for the duration of a 6-month orbital mission [18–22].

The occurrence usually happens at the same time as latent herpesviruses continue to reactivate and shed.

The reactivation of these latent herpesviruses may be a "biomarker" of impaired adaptive immune function, specifically cytotoxic T lymphocyte activity, since a functional immune system is required to prevent latent virus reactivation. Investigations are presently underway to determine the specific type of immunological dysregulation that occurs during spaceflight; nevertheless, research has shown that the distribution of peripheral leukocytes has changed, and that certain leukocytes no longer operate as well as subpopulations, and many astronauts have distorted cytokine profiles.

The human immune system is significantly impacted by spaceflight, frequently resulting in immunosuppression or immunological dysregulation. This raises the danger of infections, allergic responses, and the reactivation of dormant viruses, which is a serious health concern for astronauts, particularly on extended flights. These alterations are caused by several interrelated factors:

Microgravity

Modified Immune Cell Function: Different immune cells' behavior and functionality are directly impacted by microgravity.

T-cells are essential for adaptive immunity; however, in microgravity, they exhibit decreased activation, proliferation, and cytokine synthesis (signalling molecules). According to studies, T-cells become less reactive to infections or “naive” as a result of changes in gene expression.

Neutrophils and macrophages: These cells can produce fewer reactive oxygen species (ROS) and engage in phagocytic activity, which involves engulfing pathogens.

Fluid Shifts: Immune cell circulation and localization may be impacted by the redistribution of body fluids towards the upper body under microgravity, which may make it more difficult for the cells to reach infection sites.

Cytoskeletal Changes: Immune cells' cytoskeleton, which is essential for their adherence, signalling, and mobility, can change under microgravity.

The innate immune system's natural killer (NK) cells are less able to eliminate malignant or infected cells, a process known as cytotoxicity.

Immunological weariness and chronic low-grade inflammation (also known as "inflammaging") are two characteristics of immunological aging (immunosenescence) that are strikingly similar to many of the immune alterations seen in microgravity. This implies that spaceflight may hasten some immune system aging processes.

Radiation from Space:

DNA Damage: Two extremely powerful radiation types that can directly harm immune cells' DNA are Galactic Cosmic Rays (GCRs) and Solar Particle Events (SPEs).

Radiation can cause immune cells, especially lymphocytes (T and B cells), to die off, which lowers the total amount of immune cells. The body's capacity to develop a successful immunological response may be jeopardized.

Long-Term Effects: Although research on radiation's long-term effects on the immune system is ongoing, it raises questions regarding heightened vulnerability to chronic illnesses like cancer.

Psychological Stress

Isolation and Confinement: Prolonged seclusion, cramped quarters, and being away from loved ones are all major psychological stressors for astronauts.

Disruption of Circadian Rhythms: Immune function is tightly tied to circadian rhythms, which can be disturbed by irregular sleep-wake cycles brought on by particular lighting conditions and mission schedules.

Stress Hormones: Prolonged stress raises levels of stress hormones, such as cortisol, which have been shown to inhibit the body's immune system. It is thought that similar mechanisms function in space.

Modified Microbiome:

The microbiome—the community of microorganisms that live in and on the body—of astronauts may alter as a result of the enclosed spacecraft environment. These changes may also affect immune function and infection susceptibility, as may possible exposure to new microbial strains.

Medical Standards for Spaceflight

Medical care is heavily constrained by factors including power, weight, and volume, as well as the crew's skill set. Human space flight occurs in a harsh, isolated, and physiologically taxing environment. It also symbolizes a setting where the health and safety of the entire crew could be in jeopardy if a person who plays a crucial part in a mission is incapacitated.

The extremely strict medical requirements for spaceflight are intended to minimize the danger of in-flight medical emergencies while also ensuring that astronauts can endure the harsh demands of space travel and carry out their responsibilities efficiently. Both individual space organizations (such as NASA, ESA, and Roscosmos) and multilateral agreements are used to create these requirements for international missions like the ISS.

Adequate prophylaxis through screening is the most effective way to mitigate against the substantial physiological risks associated with spaceflight [24, 25]. Thus, medical requirements for spaceflight have historically been crucial, with the goal being to weed out any pre-existing medical issues that could jeopardize the mission's objectives or the crew's safety.

The desired sortie profile and the individual's position within the larger crew must be taken into account while evaluating medical criteria for spaceflight.

General Health and Fitness:
Overall Excellent Health: Astronaut candidates must be in peak physical and mental condition, free from any chronic diseases or conditions that could be exacerbated by the space environment or require significant medical intervention during a mission.

Low Risk of Incapacitation: A primary goal is to select individuals with a very low risk of sudden or subtle incapacitation (e.g., heart attack, stroke, seizure) that could jeopardize the mission or crew.

Low Risk of Developing Medical Conditions: Candidates are screened for conditions that might develop over time in space and negatively impact performance or strain limited medical resources.

Age: While there isn't a strict upper age limit, younger candidates often have an advantage due to the physical demands of training and the potential for a longer career. However, increasingly, older individuals with specific skills are also being considered, especially for short-duration or commercial flights.

SPECIFIC PHYSIOLOGICAL SYSTEMS

Cardiovascular System:
Blood Pressure: Typically, blood pressure must not exceed a certain limit (e.g., 140/90 mmHg for NASA, measured in a sitting position).

Heart Health: No history of significant heart disease, arrhythmias (irregular heartbeats), or other cardiac abnormalities. Extensive cardiac evaluations (ECGs, echocardiograms, stress tests) are performed.

Vision:
Correctable to 20/20: Visual acuity must be correctable to 20/20 in each eye for both distant and near vision.

Refractive Surgery: While previously disqualifying, procedures like LASIK and PRK are now generally allowed, provided sufficient time has passed (e.g., one year for NASA) without adverse effects.

Color Perception & 3-D Vision: Good color vision and depth perception are essential.

Ocular Health: Comprehensive eye exams to rule out any pre-existing conditions that could worsen in space (e.g., the Spaceflight-Associated Neuro-ocular Syndrome, SANS, which causes vision changes in some astronauts).

Auditory System (Hearing):
Specific audiometric standards are in place to ensure adequate hearing for communication and situational awareness.

Musculoskeletal System:
Bone and Muscle Health: No significant bone density issues (osteoporosis) or muscle weakness that could be exacerbated by microgravity. Full range of motion in all joints is typically required.

Height and Weight: There are often height and weight restrictions to ensure compatibility with spacecraft and equipment (e.g., NASA: 62 to 75 inches standing height; Roscosmos: 1.50m to 1.90m height, 50kg to 95kg weight).

Neurological System:
No history of seizures, severe headaches, or other neurological disorders.

Good balance and vestibular function (crucial for adapting to microgravity).

Gastrointestinal System:
No chronic digestive disorders that could pose problems in space.

Immune System:
While specific tests vary, overall robust immune health is desired, given the documented immune dysregulation in space. No chronic infections or autoimmune diseases.

Dental Health:
Excellent dental health is crucial to avoid in-flight dental emergencies.

Psychological and Psychiatric Stability:
Sound Mental Health: Candidates must be free from any psychiatric disorders (e.g., psychosis, bipolar disorder, severe personality disorders).

Stress Management: Ability to cope with extreme stress, isolation, confinement, and high-pressure situations.

Teamwork and Communication: Strong interpersonal skills, emotional stability, and the ability to work effectively in a small, diverse team for extended periods.

Motivation and Resilience: High levels of motivation, adaptability, and resilience are essential.
No Substance Dependence: Freedom from any dependency on drugs, alcohol, or tobacco.

Other Considerations
Medical History: A thorough review of an applicant's complete medical history is conducted, including past illnesses, surgeries, and medications.

Vaccinations: Up-to-date vaccinations are critical.
Emergency Response: Candidates undergo training to act as Crew Medical Officers (CMOs) to provide basic medical support in space.

Annual Recertification: Even after selection, astronauts undergo annual comprehensive medical examinations to ensure continued fitness for duty.

Waiver Process: For experienced astronauts who develop a medical condition, there may be a waiver process if the condition can be effectively treated, mitigated, and does not interfere with mission duties. However, for initial selection, waivers are generally not considered for disqualifying conditions.

Mission-Specific Standards: Medical standards can be further tailored based on the specific mission profile (e.g., short-duration orbital flight vs. multi-year deep-space exploration). Deep-space missions to the Moon or Mars will likely require even more rigorous screening due to prolonged radiation exposure, greater isolation, and limited rescue/resupply options.

Commercial Spaceflight: As commercial spaceflight grows, the medical standards for "space tourists" or "private astronauts" without critical duties may be less stringent than for career astronauts, focusing more on immediate safety risks rather than long-term health implications [26-30].

Space Nutrition

Inadequate dietary supply and nutritional imbalance can impact immune function. It is commonly known that immune function can be significantly impacted by shortages in macronutrients and/or micronutrients [31]. The average calorie intake has increased dramatically in recent years, even though crew members on board the ISS are not provided with an optimal diet [32, 33]. Increased oxidative stress and inflammation are linked to hypocaloric diet, which was frequently seen during previous space missions [34, 35]. Protein is the most limiting element when the body is denied energy [36].

Damage brought on by oxidative stress triggers inflammatory and immunological responses. Ionizing radiation and other variables may intensify oxidative stress, change the rate of DNA damage and the efficiency of DNA repair systems, and worsen inflammation and DNA damage on deep space missions outside of low Earth orbit (LEO). Oxidative stress is exacerbated by increased DNA damage, creating a vicious cycle that eventually results in chronic inflammation and immune system failure.

Providing astronauts with the nutrients they need to maintain their best possible health, performance, and well-being while in space is the focus of the specialized and vital discipline of space nutrition. It covers the logistical difficulties of food preparation, storage, and consumption in microgravity as well as the particular physiological difficulties brought on by the space environment.

Nutritional Requirements in Space

Caloric Intake: Depending on personal characteristics such as age, gender, metabolism, and degree of activity, astronauts usually need a daily caloric intake that is comparable to or slightly higher than that of active people on Earth. This range is usually between 2,500 and 3,800 calories (e.g., during extravehicular activities, caloric needs increase). It's critical to maintain a sufficient energy intake to avoid unintended body mass loss.

The Macronutrients

Protein: To prevent muscle atrophy, or the loss of muscle mass that happens in microgravity, a high protein intake (1.2–1.8 g/kg body weight) is essential.

Primary energy is provided by carbohydrates. For a longer-lasting energy release, complex carbs are recommended.

Fats are necessary for a variety of body processes and energy production.

Micronutrients (Vitamins and minerals)

These are especially important because of certain physiological changes that occur in space.

Astronauts frequently suffer from severe bone demineralization (loss of bone density) in microgravity, even with proper nutrition of calcium and vitamin D. Even with calcium and vitamin D supplements, bone loss cannot be completely avoided, which emphasizes the necessity for combination countermeasures like intense exercise. Space might cause a decrease in calcium absorption.

Vitamins C, E, and beta-carotene are examples of antioxidants that are crucial for reducing oxidative stress brought on by exposure to space radiation.

Energy metabolism and brain function depend on B vitamins.

Iron: Tracked to prevent excess and insufficiency.

Sodium: Considering its possible effects on fluid balance and cardiovascular health in microgravity, sodium intake is carefully controlled.

Fluids

Considering the fluid shifts and the possibility of increased insensible water loss in space, maintaining hydration requires an adequate fluid intake of at least 32 mL/kg body weight, or $\ge$2,500 mL/day.

CONCLUSION

Protecting human health and facilitating our expansion into space depend heavily on the vital and ever-evolving area of space medicine. Future long-duration trips to the Moon and Mars will require even more sophisticated medical countermeasures, in-situ resource utilization, and autonomous healthcare systems, despite the fact that tremendous progress has been made in comprehending and addressing the physiological and psychological difficulties associated with microgravity, radiation, and isolation during orbital missions. The safety and success of humanity's ambitious deep-space projects ultimately depend on sustained investment in space biomedical research, which also yields priceless insights that improve healthcare and human well-being on Earth. Numerous cutting-edge demands in personalized medicine, telemedicine, diagnostics, artificial intelligence, regenerative medicine, bioprinting, and biomanufacturing have been impacted by space medicine, underscoring the significance of space research.

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