

Chapter 24

ENVIRONMENTAL EXTREMES: SPACE

RICHARD A. SCHEURING, DO, MS*; JOSEF F. SCHMID, MD[†]; AND J.D. POLK, DO[‡]

INTRODUCTION

DEFINITIONS

MILITARY HISTORY

MILITARY APPLIED PHYSIOLOGY

The Space Environment

Physiologic Effects

THE MILITARY MEDICAL OFFICER AND HUMAN PERFORMANCE

OPTIMIZATION IN SPACE

Role of the Military Medical Officer

Guidance to the Commanding Officer

SUMMARY

*Colonel, Medical Corps, US Army Reserve; Associate Professor, Military and Emergency Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland

[†]Major General, Medical Corps, US Air Force Reserve; NASA, Johnson Space Center, Houston, Texas

[‡]Chief Medical Officer, NASA Headquarters, Washington, DC

INTRODUCTION

The environment outside of Earth's atmosphere (space) is regarded by some as the future battlefield. Developed nations rely on space-based assets such as satellites to conduct day-to-day business, including communications, navigation, and financial transactions, to name a few. Military use of space for surveillance and reconnaissance has existed for decades. More recently the use of low Earth orbit (LEO) to conduct tactical operations has been proposed. Warfighters on this future battlefield will confront a variety of physiologic and environmental challenges. Knowledge of the challenges that confront service members, and

strategies to mitigate against stressors that impact optimal performance, are essential for the military medical officer (MMO). This chapter specifically addresses the environmental challenges of space flight as applied to today's warfighter, with a focus on enhancing performance in these settings. Specifically discussed are core definitions applied to these stressors, relevant military history and epidemiology, applicable applied physiology, and detailed prevention strategies. Specific guidance is provided to assist the MMO in the identification and prevention of environmental stress as applied to service members.

DEFINITIONS

Common terminology related to environmental challenges in space is shown in Tables 24-1 and 24-2. First, basic and specific applied physiologic definitions are provided to assist the MMO in interpreting relevant literature and established military guidance. Next are

terms associated with common medical conditions and injuries in this environment. The MMO must have a clear understanding of this terminology in the policy and literature to ultimately optimize service member performance.

MILITARY HISTORY

During World War II, Eugene Sanger of the German Herman Goring Institute developed a theoretical "space bomber" that would be capable of reaching suborbital altitudes to extend its range and deliver a weapons payload to New York City. Years later, the Soviet Union began testing the MiG-105, a military space plane that would make use of "skip-glide" suborbital flight to deliver a payload over long distances. The successful launch of the Soviet Sputnik on October 4, 1957, from the Baikonur Cosmodrome in Kazakhstan officially started the Soviet-US space race in public awareness.

The US military, with the help of German rocket scientists who came to America after World War II, most notably Wernher von Braun, had spent the previous decade developing intercontinental ballistic missile systems for weapons payloads. Von Braun and colleagues had also envisioned developing a manned space vehicle to support military operations. By late 1957, the US Air Force had incorporated their concepts into its program to develop a hypersonic "space plane" that would achieve speeds in excess of Mach 10 after being dropped from a heavy bomber and igniting rocket engines. The delta-winged Boeing X-20A Dyna-Soar would be capable of landing on a runway after carrying out suborbital military reconnaissance, satellite maintenance, and enemy satellite interdiction. However, it was canceled in 1963¹ when Congress deemed the project lacked a relevant

military mission and cost outweighed its benefits as a research platform. Several military space designs followed the Dyna-Soar program, but each failed to achieve its intended goal of supporting a manned space mission. The culmination of these efforts was the US Air Force Manned Orbital Laboratory (MOL) (Figure 24-1).

The MOL was announced to the public in 1963 as a general research program designed to "demonstrate the military value of a man in space."² Intended to be operational by the early 1970s, the program's actual purpose was reconnaissance of ground-based Soviet and Chinese military facilities. Astronauts would launch in a modified NASA Gemini spacecraft with the pressurized MOL attached as a single-use laboratory accessible through a hatch. Both would launch on a Titan IIIC booster rocket from Vandenberg Air Force Base in California to a polar orbital inclination (ie, flight orientation over the Earth) with a perigee of 89 nautical miles. Spending up to 40 days in space, astronauts would operate a sophisticated optical system capable of high-resolution still and video images of military targets on the ground, according to plans. During development, however, the MOL rapidly exceeded its budget. Analysis determined that unmanned spy satellites could match or surpass the capabilities of the MOL project. As the Vietnam War drained the nation's defense budget, the program was canceled in mid-1969.

TABLE 24-1
GENERAL APPLIED PHYSIOLOGY TERMINOLOGY

Term	Definition
Armstrong's line	Above an altitude of 18,900 m (63,000 ft) the total atmospheric pressure equals the vapor pressure of water at body temperature, ie, the ambient pressure is 5% that at sea level and the boiling point of water is now 98.6°F. Clinically, blood and body fluids will "boil."
Microgravity (μ g)	The result of balanced centrifugal and gravitational force vectors of an orbiting vehicle simulating the lack of true gravity. Not synonymous with zero-gravity.
Suborbital	Any flight outside Earth's atmosphere with a maximum flight speed below the orbital velocity, thereby preventing a vehicle from completing one orbit.
Low earth orbit (LEO)	An orbit around Earth with an altitude between 160 km (99 miles) (orbital period of about 88 minutes) and 2,000 km (1,200 miles) (orbital period of about 127 minutes).
Geosynchronous earth orbit	An Earth orbit located at 35,786 km (22,236 miles) above Earth's equator, which allows satellites to match Earth's rotation.
Solar particle event (SPE)	An injection of energetic electrons, protons, alpha particles, and heavier particles into interplanetary space following a highly concentrated, explosive release of energy from the sun.
Galactic cosmic radiation (GCR)	Energy that originates outside the solar system, consisting of ionized atoms ranging from a single proton up to a uranium nucleus.
Extravehicular activity (EVA)	Any activity done by an astronaut outside a spacecraft beyond the Earth's appreciable atmosphere.
Extravehicular mobility unit (EMU)	An independent anthropomorphic spacesuit that provides environmental protection, mobility, life support, and communications for astronauts performing extravehicular activity in Earth orbit.
High-performance jet aircraft	Jet planes capable of high-g acceleration, velocities approaching or surpassing the speed of sound, and operating altitudes above 9,144 m (30,000 ft) above sea level.
Hypercapnia	A condition of abnormally elevated carbon dioxide (CO_2) levels in the blood.
Hypobaric	Characterized by less than normal pressure or weight; applies to gases under less than sea level atmospheric pressure of 14.7 psi or 760 mm Hg.
Karman line	The boundary between Earth's atmosphere and the edge of outer space, generally 100 km (62.5 miles) above sea level. The atmosphere at this altitude is too rarified to support aeronautical flight thus vehicles require rocket propulsion for maneuverability.
Mean sea level barometric pressure	Measured as 1 atmosphere (atm), 760 mm Hg, 14.7 psi, or 101.3 kPa.
Perigee	Point in orbit nearest to the center of the Earth.

The military then shifted its interest to unmanned space capabilities with the development of robust satellite systems for reconnaissance and communications. The tactical military utility of these systems was virtually nonexistent, however; most were purely strategic assets. In early 1971, the US Navy Research Laboratory created the Timation (Time-Navigation) Development Plan, based on the Space Surveillance System technology developed earlier in the decade. This capability was the basis

for future highly classified navigation systems used in military operations, most notably the global positioning system (GPS).³

In contrast to the military efforts, civilian manned space missions dominated the late 1960s and early to mid-1970s. The six Apollo lunar surface missions fulfilled President John F. Kennedy's vision of landing a man on the moon and returning him safely to Earth. The Soviets abandoned lunar aspirations for establishing space "stations" capable of sustaining human

TABLE 24-2
SPACE ALTERATION/ILLNESS/INJURY TERMINOLOGY

Term	Definition
Circadian desynchronization	Disturbances in the normal sleep cycle that result when external environmental cues conflict with the internal clock.
Ebullism	Formation of water vapor bubbles in the tissues brought on by an extreme reduction in barometric pressure if the body is exposed to pressures above Armstrong’s line.
Space-adaptation back pain (SABP)	Musculoskeletal pain in the lumbar spine region that occurs after initial exposure to μg and persists for 48 to 72 hours.
Space motion sickness	A syndrome ranging in symptom severity that includes nausea, vomiting, global headache, anorexia, and fatigue after initial exposure to μg . A self-limited disorder, the symptoms typically resolve within the first 24 to 48 hours of space flight.

presence in space for extended periods of time. After the Apollo missions, the United States developed its own long-duration space station, Skylab, in 1973. The Skylab science missions ranged from 28 to 84 days and provided significant insight into the effects of microgravity (μg) on human physiology. The Apollo-Soyuz mission, the first joint US-Soviet mission in space, followed in 1975. This brief mission represented the beginning of an international collaboration in space that continues today.

In 1981 NASA began launching the Space Transportation System (STS), or space shuttle, missions. The STS, initially approved as a public space vehicle

by President Richard Nixon in 1972, was built with the understanding that military payloads and crew could be transported into space to support missions for the National Reconnaissance Office (NRO). The space shuttle provided crewed returns from LEO after launching from Kennedy Space Center in Florida. Beginning with the first classified Department of Defense (DoD) payload on STS-4 in 1982, the space shuttle flew nine classified missions for the DoD.⁴⁻⁶ Eight of these missions were considered “dedicated” military missions, flown by military astronauts.²⁻⁴ The NRO, in conjunction with the US Air Force, built a launch pad at Vandenberg Air Force Base with the intent that the space shuttle or other manned vehicles could be launched to polar orbits for high-orbital inclination, placing the spacecraft orbital path over Russia.⁶

The military had chosen its first group of space shuttle astronauts, known as manned spaceflight engineers (MSEs), in 1979. From the initial class of 13, only one MSE, Colonel Gary Payton, flew in space, on STS-51C in 1985. This mission deployed an Air Force inertial upper-stage spy satellite as a separate spacecraft from the shuttle payload bay. This permitted the payload to launch from the shuttle (in LEO) to a higher altitude geosynchronous orbit, enabling better visibility of the Earth. From 1985 to 1992, several classified DoD space shuttle missions deployed the Defense Satellite Systems, which included the ability to perform communications, surveillance, reconnaissance, weather and environmental monitoring, and nuclear missile launch detection.^{4,6} After the Space Shuttle *Challenger* accident in January 1986, however, the NRO and Air Force abandoned the manned military space program development at Vandenberg and returned to unmanned satellite deployment missions on Atlas and Titan launch vehicles.

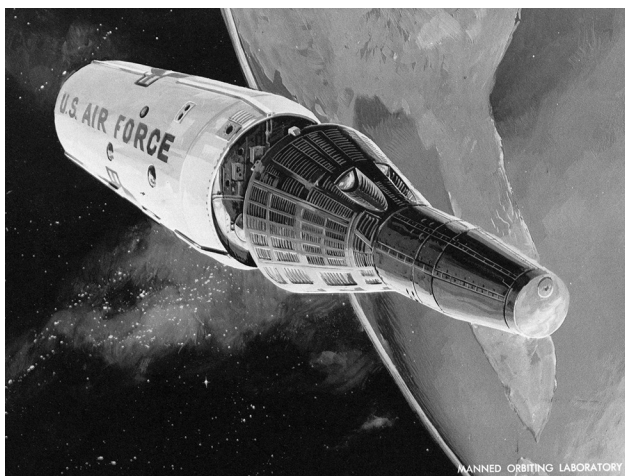


Figure 24-1. Manned Orbiting Laboratory (MOL), an evolution of the earlier “Blue Gemini” program, which was conceived to be an all-Air Force parallel of NASA’s Gemini efforts. US Air Force photo. Reproduced from: <http://www.nationalmuseum.af.mil/Visit/Museum-Exhibits/Fact-Sheets/Display/Article/195891/manned-orbiting-laboratory/>.

By the 1980s, space-based communications, weather satellites, and reconnaissance satellites had matured to add tactical utility to military operations in Central America. During the Persian Gulf War in 1991, GPS navigation satellites provided highly accurate navigation data aiding US and allied military forces in the region. Also, “smart weapons” began appearing in numbers that could make a measurable tactical impact. Cold War strategic systems were also modified to assist tactical forces, beginning a trend that continues today. These systems were refined during the bombing campaign in Kosovo in the late 1990s; in 5 short years the use of precision munitions led to highly accurate weapons that resulted in few nonmilitary casualties. The conflicts in the Middle East in the first decade of the 21st century made use of standardized space-based systems throughout the armed services, leading to unprecedented war-fighting capabilities in many theaters of operation.

In December 2006, *Popular Science* published an article called “Semper Fly: Marines in Space,” detail-

ing a plan to develop a vehicle that could transport up to 13 marines to a military objective anywhere in the world from the United States in 2 hours via suborbital spaceflight.⁷ The Marine Corps envisioned using suborbital space to develop a capability for greater operational speed and flexibility than conventional jets, called Small Unit Space Transport, or “Sustain.” Included in this vision was the ability to deploy forces outside the spacecraft at altitudes considerably above Armstrong’s line (see Table 24-1) to parachute to a ground-based objective. This goal was driven in part by expediency and to circumvent obtaining permission to use sovereign nation airspace, an issue between the United States and nations positioned along the space shuttles’ orbital track back in the early 1980s.⁸ While these technical and tactical benefits may be achievable in the near future, careful consideration of the space environment’s effect on human physiology and function must be considered to optimize human performance outside Earth’s atmosphere.

MILITARY APPLIED PHYSIOLOGY

Physiologic adaptation to μg and partial-gravity environments involves the following systems: neurovestibular, cardiovascular, musculoskeletal, immune, neuroophthalmological, hematologic, gynecologic, and behavioral/performance. First, a basic understanding of the space environment is necessary to understand its physiologic impacts on humans.

The Space Environment

A spacecraft orbiting the Earth requires adequate orbital velocity carrying it into space to overcome Earth’s gravitational pull. The resultant vector keeps the vehicle “falling” around the Earth as the planet surface is constantly curving underneath it. The acceleration forces cancel each other out, resulting in μg . Outer space, that is, the environment beyond the Karman line (see Table 24-1), is the most hostile environment humans have ever encountered (Figure 24-2). Outside a pressurized vessel, an unprotected person would suffer near instantaneous death from ebullism and anoxia. In the absence of Earth’s protective atmosphere, near +/- 250°F temperature extremes exist between darkness and sunlight. A near vacuum where only a few hydrogen molecules exist, the thermosphere has an ambient pressure of roughly 10^{-12} mm Hg / 3.2×10^{-2} Pa. Radiation (primarily charged alpha particles liberated by solar flares, ultraviolet radiation, and x-rays) and heavy charged particles from galactic sources are ubiquitous outside the protective layer of

the atmosphere and geomagnetosphere. Despite the harsh environment of space, humans have lived and thrived for over 5 decades outside of Earth’s protective shell. Today’s space vehicles orbiting in LEO are designed to maintain a habitable interior with sea-level ambient pressure and gas combinations, temperature and humidity at comfortable levels, and adequate lighting and protection from harmful solar radiation. In addition, nearly instant two-way audiovisual communications support communication with astronauts and ground command and control of the vehicle.

Physiologic Effects

Neurovestibular

Physiologically, balance and coordination are among the first systems affected in space. In μg , the otoliths are off-loaded, contributing to the temporary loss of spatial orientation and space motion sickness that astronauts experience early on in spaceflight.^{9,10} All humans are affected to some degree with mild loss of neuromuscular coordination, nausea, and vomiting soon after orbital insertion. Reaction times are initially slowed but quickly adapt to the novel μg environment.¹¹ Upon return to the 1-g environment, proprioceptive challenges and loss of visual depth perception from spaceflight deconditioning last 48 to 72 hours.

On the lunar surface following a 4.3-day transit from Earth, the Apollo astronauts generally felt “a little

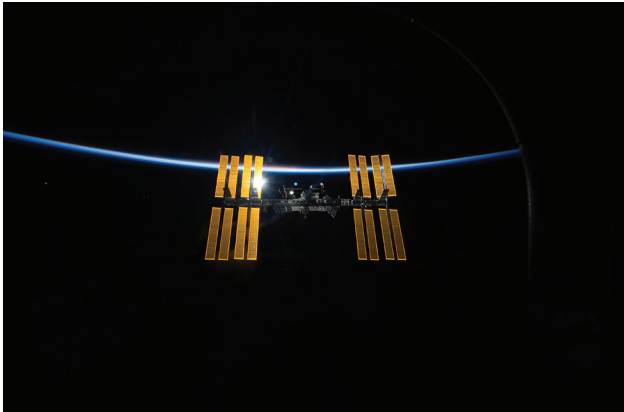


Figure 24-2. The edge of space. Fly-around view of the International Space Station (ISS) taken by an STS-119 crewmember after the undocking of the orbiter Discovery. NASA photo ID: S119E010500.

Reproduced from: <https://images.nasa.gov/details-s119e010500.html>.

wobbly” upon stepping on the moon. They attributed this sensation to the one-sixth Earth gravity environment and aft center of gravity of the lunar extravehicular mobility unit (EMU) rather than neurovestibular dysfunction (Figure 24-3).¹² Coordination seemed to improve steadily during the first couple of hours on the lunar surface. During three of the six lunar landings,

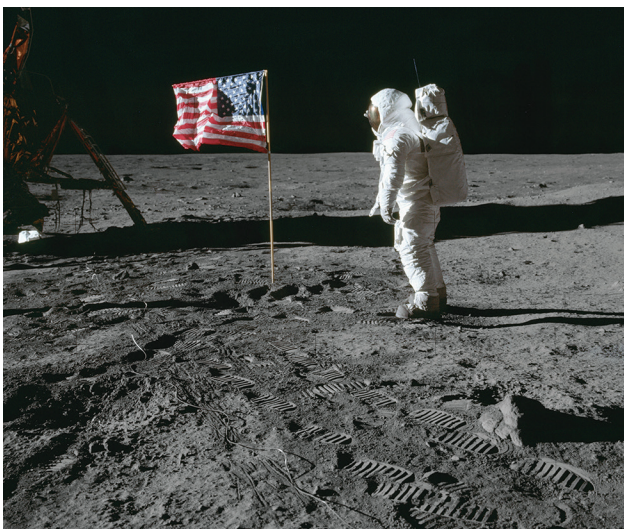


Figure 24-3. Apollo 11 crewmember Buzz Aldrin, Jr. Crew members countered the suit aft center of gravity by leaning forward. NASA photo ID: AS11-40-5874.

Reproduced from: <https://images.nasa.gov/details-as11-40-5874.html>.

blowing lunar dust caused loss of horizontal reference cues, complicating piloting during vehicle descent and resulting in longer descent times and deviation from the proposed landing site. Retrospectively, the Apollo crews stated that spatial disorientation did not play a factor in vehicle control. Whether environmental factors or loss of piloting proficiency played a role is unclear.

In LEO, correlations between mission length and landings outside (or nearly outside) planned parameters (landing too fast, too slow, or too hard) have been evaluated in operation and simulated environments.⁹⁻¹¹ In space missions lasting between 5 and 14 days, the commanders and pilots had minimal perturbation of neurovestibular function. Consequently, neuromuscular motor control to carry out complex landing operations was minimally impacted.⁹ Actual landing performance shows much greater variability than simulator performance parameters, but was within the margin of safety for short-duration missions. The implication is that short-duration spaceflight has a minor effect on pilot performance, but longer-duration μg exposures may complicate this dynamic phase of flight.

Cardiovascular

Cardiovascular changes that occur in space are most evident in cephalic fluid shift. On Earth, gravity exerts a downward force to keep blood flowing to the capacitance venous system in the lower body. Cephalad migration of nearly 2 L of intravascular volume occurs within hours of exposure to μg , when the lack of gravity causes blood and body fluid to be redistributed toward the chest and upper body. Astronauts experience nasal congestion, facial plethora, and a dull sense of taste.^{13,14} This “puffy face–bird leg” syndrome persists throughout the μg exposure to some degree. Initially the relative increase in cardiac pre-load results in diuresis, and the crew will urinate frequently for the first 24 to 36 hours of spaceflight. The crew then remains euvolemic in μg for the mission duration. As the lower extremities are minimally used for locomotion (the “arms become the legs” in space), there is consequent relative minor atrophy in cardiac muscle size and stroke volume. Heart rate does not change significantly, so cardiac output is naturally reduced up to 15% to 20%.

To determine the extent of cardiovascular deconditioning in μg and how it might potentially impact physical performance such as extravehicular activity (EVA), researchers have measured on-orbit maximum power outputs and oxygen uptake during exercise ($\dot{V}O_{2max}$) in astronauts relative to their preflight baseline measurements.¹⁵ Exercise performance, as measured

by $\dot{V}O_{2\max}$, is initially reduced in μg . Within the first 3 weeks of spaceflight, a pronounced deconditioning effect on aerobic capacity occurs without exercise countermeasures. The reduction in aerobic performance appears to peak at about 3 weeks in-flight, then slowly improves with use of a treadmill and cycle ergometer.

The cardiovascular adaptations to μg persist until reintroduction to the Earth's 1g environment. Changes in the heart muscle, vascular reflexes, and redistribution of body fluids during flight strongly predispose crew to orthostatic hypotension post-landing to varying degrees. Upon return to the 1g Earth environment, the reduced circulating blood volume experienced by the crew in space results in decreased standing blood pressure without adequate commensurate increase in heart rate to maintain cardiac output. This condition, known as orthostatic intolerance, varies in severity but is present to some degree in most returning astronauts. The incidence for short-duration (less than 30 days) and long-duration missions ranges from 20% to 67% of crewmembers. Symptoms range from dizziness and lightheadedness to transient syncope, but usually resolve in 18 to 24 hours after landing.¹⁶

Musculoskeletal

Physical performance in space after the initial adaptation period of 24 to 72 hours is minimally impaired from cardiovascular alterations. However, there is potential operational impact from the musculoskeletal changes that occur in μg . Astronauts experience decreased upper body strength and stamina for EVA to some degree, depending on preflight fitness level and in-flight training. Typical EVAs range in duration from 6 to 8 hours. During this time outside the spacecraft, astronauts manipulate equipment and move along the structure using mostly their hands, upper extremities, and core musculature. Crew members have described the upper body exertion during EVA as moderately physically demanding, depending on the task.

The musculoskeletal system undergoes significant adaptation in space in the form of bone and muscle loss due to the absence of gravitational loading. Prior to the use of the advanced resistive exercise device (ARED) on the International Space Station (ISS) in 2010, bone density losses of 1% to 2.4% per month in the lower extremities and spine were measured in astronauts.¹⁷ The skeletal changes and loss of total body calcium have been noted in both humans and animals exposed to μg from 7 to 237 days. Using dual absorptiometry x-ray to measure bone mineral density (BMD), LeBlanc et al determined that BMD losses were specific to weight-bearing bones. Specifically, monthly losses of 1% at the lumbar spine and 1.5%

at the femoral neck have been documented prior to the use of on-orbit resistive exercise training.¹⁸ Astronauts returning from long-duration space flight have also demonstrated persistent loss of trabecular bone, despite return of density to preflight baseline levels.¹⁹ Recently, finite element analysis and quantitative computed tomography have been used to assess bone architecture, in contrast to bone density measurements.²⁰ These methods may be more predictive of future fracture risk post-flight.

The potential clinical effects of long-duration space flight on calcium metabolism include the development of kidney stones due to increased urine and fecal calcium, as well as possible post-flight fractures. Fourteen post-flight kidney stones have been reported in short-duration space shuttle astronauts,²¹ although no in-flight episodes of renal lithiasis have occurred in US astronauts to date. There have been 54 post-flight fractures among US crew members, but aerospace medicine experts attribute none of them to in-flight bone loss. Research continues on the risk of post-flight fracture.

Consistent with the skeletal adaptations, muscle morphologic change and fiber loss are evident in space compared to baseline preflight levels. Atrophy of the antigravity muscles (thigh, calf) and decrease in leg strength (approximately 20%–30%), with extensor muscles more affected than flexor muscles, have been measured in short- and long-duration astronauts. Data from rats carried aboard spacecraft showed an increase in the number of type II (fast-twitch) muscle fibers (those that are useful for quick body movements but more prone to fatigue). This effect has been confirmed with muscle biopsy in US astronaut volunteers.²² Lower extremity muscle strength and size and overall decrease in leg volume and body mass were common prior to the current on-orbit exercise program using the ARED.

There are also significant changes to the axial skeleton in μg . Changes in the spine and antigravity muscles associated with μg exposure include lumbar back pain, fatigue, muscle stiffness and soreness, weakness, and atrophy in the core stabilizing muscles.^{23–27} Between 53% and 68% of astronauts experience some degree of lumbar back pain on orbit, known as space-adaptation back pain (SABP), ranging from mild to, in 10%, excruciating.²⁸ In-flight, there is dramatic postural change of the cervical and lumbar spine with loss of lordosis from lack of gravity and the stretching of tendons and ligaments. Consequently there is an average increase in on-orbit height by 2 to 6 cm. SABP etiology is unknown but may relate to intervertebral disk and vertebral end-plate changes, thoracolumbar myofascial changes, alterations in the facet joint, and

stretching of the anterior longitudinal ligament. SABP peaks in severity by 48 to 72 hours and subsides within the first week on orbit. Interestingly, the occurrence of SABP and post-flight herniated nucleus pulposus (HNP) appear to be inversely related.

As of this writing, post-flight HNP has occurred in 47 US astronauts, with 14 events occurring within the first year of return (Figure 24-4).^{26,28} The mechanism of the changes to the annular fibrosis that increases the risk of HNP is not well understood. The condition is equally common among short- and longer-duration crew, suggesting an unknown factor that injures the spine during μ g exposure.^{26,29} Spacecraft type at landing (eg, space shuttle, Apollo Command Module, Soyuz) does not appear to be a factor in post-landing HNP occurrence.^{26,28} Many experts speculate there may be a dynamic period of stabilization of the annulus in the first few hours of return to 1g. In space shuttle crew members who were not significantly orthostatic on landing and were able to stand and ambulate, the sudden axial loading may injure the annulus, causing annular tears that predispose the person to HNP. Deconditioned crew returning from long-duration missions on the ISS are generally unable to stand for a couple of hours and subsequently remain supine until their orthostasis subsides. Therefore, maintaining supine position post-flight for a brief period of time may reduce the risk of developing HNP. The possible contribution of loss of the spinal stabilizer muscles (eg, the multifidus) in long-duration astronauts, as assessed by pre- and post-flight magnetic resonance imaging and functional muscle testing, is also being considered in astronauts with clinical symptomatology.²⁹

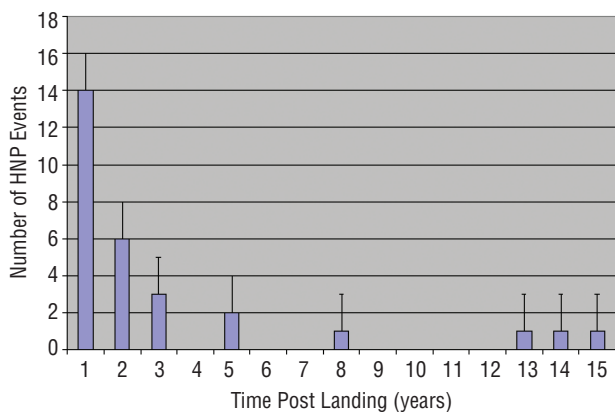


Figure 24-4. Number of herniated nucleus pulposus (HNP) events based upon the time following the mission in years. Data source: Johnston SL, Campbell M, Scheuring RA, Feiveson A. Increased incidence of herniated nucleus pulposus among US astronauts. *Aviat Space Environ Med.* 2012;81(6):566–574.

Immune System

The immune system has subtle responses to short- and long-duration μ g exposure. White blood cell function is impaired. Lymphocyte function is depressed in at least 50% of space crew members. Decreased lymphocyte response to mitogens in cosmonauts after space flight was reported for the first time in the early 1970s by Russian immunologists.³⁰ Among the possible causes of space flight-induced alterations in immune responses are exposure to μ g, physical and psychological stress, exposure to radiation, and potentially more as yet undetermined causes. Delayed wound healing has been reported anecdotally.³¹ Astronauts have described slowed healing of small skin wounds, up to a couple of weeks for paper cuts on their fingertips. There are also clinical implications from latent virus reactivation such as Epstein-Barr virus (EBV) and herpes simplex. Blood titers have confirmed elevations in EBV and cytomegalovirus in crew, with recrudescence of their lesions.

Neuroophthalmological

In the last decade, NASA has discovered many physiologic changes that have occurred in long-duration spaceflight that were unknown when spaceflight experience was limited to short-duration missions. Recently, changes in the neuroophthalmological system due to increased intracranial pressure (ICP) have been discovered in astronauts performing both short- and long-duration space missions.¹⁴ ICP changes on orbit appear to affect men more than women. It is unknown whether this effect is secondary to the fluid shift, vascular compliance within the cerebral vasculature, increased blood flow to the organs that make cerebral spinal fluid, hampered reabsorption and venous distribution of the cerebral spinal fluid by the arachnoid villi, or elevated ambient CO₂ levels. These factors combined may be the source of increased ICP. The recent discovery that lymphatics have a prominent role in cerebral fluid dynamics may clarify the etiology. Whatever the cause, there are differences between space-induced ICP and the terrestrial condition. Whereas patients with pseudotumor cerebri on Earth have headache and are typically female and often overweight, astronauts at risk do not exhibit any of these characteristics on orbit. Although the outcome or end state of vision change may be similar, the mechanism is not related to terrestrial ICP pathology.

Good vision is necessary for reading and operational assessment, and the eyes are also the primary organ for position sense on orbit. However, dynamic changes take place in vision over a period of time on orbit. Currently, low-grade papilledema or choroidal

foldes are the manifestation of increased ICP on orbit, leading to one or more diopters of shift in visual acuity, which may be partly secondary to changes in increased ICP and its subsequent impact of the optic nerves. There is also a visual change in smooth pursuit or tracking of an object, known as saccades, in which the eyes have a jerky pursuit of the object progressing through a field of view. This effect may be secondary to loss of practice in using the eyes in tracking in space while simultaneously receiving neurovestibular signals. Saccades may have implications for human factors designs for landing instruments on exploration missions, docking and range finding of vehicles after prolonged space exposure, or target tracking in the military context.

Hematologic

Hematologic changes after short-duration μg exposures were noted on routine blood analysis during space shuttle missions.^{32,33} A relative reduction in circulating red blood cell mass has been documented, reflected in a 7% to 14% decrease in hematocrit levels relative to preflight baselines. This so-called "space flight anemia" is thought to be due to a sequestration of young erythrocytes by the spleen in a process known as neocytolysis. Despite the reductions in red cell numbers, crew performance does not appear to have been impacted.

Gynecologic

The physiologic effects of short-duration μg exposure on gynecologic function have been documented during space shuttle missions. These reports have confirmed that menstrual efflux and required hygiene measures are similar to those experienced on Earth. Oral contraceptives use for short-duration missions has been encouraged because this method offers the opportunity to reduce the volume of menstrual efflux and the capability to shift the menstrual cycle to avoid menses on orbit, or to totally suppress menstruation. In addition, oral contraceptives can help maintain bone density, particularly in individuals who exercise to the point of reduced estrogen lev-

els and amenorrhea. Conception has apparently not been impaired in female astronauts following short- or long-duration μg exposures; several female astronauts have become pregnant and delivered healthy full-term babies post-flight.¹⁴

Behavioral

Psychological stress, as manifested in crew mood, morale, and circadian rhythm, has occurred to some degree during both short- and long-duration missions. On-orbit environmental factors that contribute to changes in crew morale include temperature, noise, odors, the relatively dry atmosphere, limited dietary choices in early space shuttle missions, and lack of family contact.²⁵ Symptoms of fatigue and irritability have been well documented, depending in part on the flight plan, including high work load and alterations in normal sleep patterns.

To maintain a stable altitude in LEO, a spacecraft needs to maintain a velocity of 17,500 mph. Consequently, "sunrise" and "sunset" occur every 90 minutes. The crew is subjected to fixed 6.5- to 8-hour sleep periods in an unusual sleep environment where loss of normal proprioceptive cues make falling asleep and maintaining sleep challenging. Head restraints are often needed to keep the head secured to a pillow, and loud background noise (ambient levels are 62–65 dB_A) requires noise-cancelling headsets. More recently, the ambient lighting frequencies (blue-green wavelength) and elevation in local CO₂ levels have been implicated in insomnia.

All these factors have resulted in poor sleep quality and reduced sleep duration.³⁴ Preliminary analyses indicate sleep on 2-week shuttle missions ($n = 44$) averages 6 hours per night, significantly less than the 8 hours recommended by the Institute of Medicine. Analyses of a small number of ISS participants ($n = 10$) further indicate that sleep continues to be reduced in space in duration similar to that found during shuttle missions. Also, crew members during ISS missions regularly have schedule shifts to their work/rest schedules to meet operational demands of the mission, such as visiting vehicle operations, EVA, or repair of hardware malfunctions. Taken together, these environmental stressors can lead to circadian desynchronization resulting in sleep loss and daytime fatigue.^{34,35}

THE MILITARY MEDICAL OFFICER AND HUMAN PERFORMANCE OPTIMIZATION IN SPACE

Role of the Military Medical Officer

The MMO supporting the space mission will be expected to have strong working knowledge of space physiology and operational space medicine. He or she will serve as subject matter expert providing recom-

mendations to the commander for prevention of space environmental illness or injuries, assist in the diagnosis and treatment of such injuries (utilizing telemedicine), and determine when crew return to duty is appropriate following any sick leave. As in most of military medicine, the best treatment strategy for all potential

environmental injuries/illness is primary prevention. Primary prevention is the cornerstone of optimizing human performance in extreme environments, and space operations are no different. Table 24-3 lists evidence-based strategies for specific risk factors or challenges to optimize warfighter performance in the extreme environment of space.

Human spaceflight provides unique challenges to human performance. Human physiology and function require significant support to adapt to the fluid shifts, neurovestibular dysfunction, musculoskeletal deconditioning, and circadian degradation associated with living in space. Radiation exposure, air quality, ambient pressure and gas component changes, toxicologic exposures, and loss of circadian rhythm control can affect every body system; these effects must be well understood by the MMO. In LEO, astronauts generally do not sustain radiation exposure levels that pose clinical risk for illness or injury. However, once missions extend beyond LEO and the protective shell of the geomagnetosphere and Van Allen belts, radiation effects on health become a major issue. The spacecraft must shield its inhabitants from radiation in these missions.³⁶

Astronauts engaged in EVAs must have medical oversight to prevent decompression sickness as well as monitor for thermal, ocular, and musculoskeletal injury. Isolation, interpersonal stress, and the real threat of death provide further impact to sleep patterns and immune systems. Basic human needs must be met within the constraints posed by living in a relatively small, confined environment, and the MMO will need to understand the effects of the habitable vehicle volume on crew health and performance.³⁷ Countermeasures include nutrition, exercise, medication, and psychological support, along with correction of environmental anomalies. It is therefore imperative that military space operations employ physicians and medics fully trained in space physiology, mission operations, and space biomedical engineering to ensure mission success.

Sleep and Rest

During the on-orbit phase of each mission, a large team of flight controllers—experts in individual engineering areas related to spacecraft control, environmental monitoring, power generation, attitude control, and EVA—will be supporting the crew and vehicle in space from the operations control center, also known as “mission control.”³⁸ Highly detailed and operationally exacting work are hallmarks of space operations both on and off the ground. The space MMO must be cognizant of the impact to operations presented by the mission on the crew in

space and the flight control team members on the ground. Physiologic and psychological effects of high work load, fatigue, and sleep deprivation often go unrecognized during mission operations but have the potential to affect crew and flight controller performance. Situational awareness of how medical issues could impact all phases of the space mission, and all operators, both on and above the Earth, should be the goal of the space MMO.

Preservation of optimal human performance in novel space environments will need to address changes to the circadian rhythm (or the “daily biological internal clock”), which regulates a circadian rhythm of 24.2 hours a day. Light serves as the strongest external stimulus for maintaining circadian alignment to Earth’s 24-hour day/night cycle. Melatonin, an endogenous hormone secreted by the pineal gland, serves as the biological “darkness” signal. When darkness occurs, melatonin is produced and released into the blood. Melatonin levels are high at night, resulting in decreased alertness and increased sleep inertia. Melatonin levels stay elevated through the night, then fall back to low daytime levels (which are barely detectable).

Bright light inhibits the release of melatonin. Even if the pineal gland is “switched on” by the circadian clock, it will not produce melatonin unless the person is in a dark or very dimly lit environment. Light therapy for circadian desynchrony has recently been implemented for astronauts on orbit and mission-control flight operators working the night shifts to maintain alertness.³⁴ Evidence shows that bright light hastens schedule shifting, improves circadian entrainment,



Figure 24-5. Extravehicular activity (EVA) on the International Space Station. S-116 MS Curbeam, Jr, and Fuglesang work on S1 Truss during EVA 1. NASA photo ID: STS116E05983. Reproduced from: <https://images.nasa.gov/details-s116e05982.html>.

TABLE 24-3

TARGETED RISK FACTOR/CHALLENGES AND EVIDENCE-BASED STRATEGIES TO OPTIMIZE PERFORMANCE IN SPACE

Performance Risk Factor or Challenge	Human Performance Optimization Strategy
Space motion sickness	Antiemetic medication; preflight adaptation training; work/rest/hydration
Circadian desynchrony	Light therapy; melatonin; short-acting nonbenzodiazepine hypnotics
Muscle and bone loss	Preflight exercise program and in-flight aerobic and resistive exercise
Cardiac deconditioning	Preflight exercise program and in-flight aerobic and resistive exercise
Space adaptation back pain	NSAIDs, short-acting muscle relaxants, and spinal mobilization/compression
Extravehicular activity (EVA)	Oxygen pre-breathe; aspirin therapy
On-orbit urinary retention	Judicious use of anticholinergics; frequent voiding early in mission; trained in self-catheterization
Increased intracranial pressure	Maintain cabin Pco ₂ below 3.00 mm Hg
Radiation exposure	Monitor daily radiation doses with active and passive dosimeters; high-density polyethylene shielding
Acute cabin decompression	Immediate isolation of leaking element; calculation of rate of leak and remaining time in orbit; oxygen supplementation
On-orbit visual changes	Have several diopter option eyewear available for each crew member
On-orbit headaches, congestion, confusion	NSAIDs, judicious use of oral/topical decongestants; monitor environmental CO ₂ levels, maintain pressure below 3.00 mm Hg
Post-flight orthostatic intolerance	Reentry g suit; fluid load prior to pre-deorbit burn; post-landing IV fluids and antiemetics
Post-flight deconditioning	Gradual reintroduction to balance, mobility, strength, and stamina conditioning program

IV: intravenous; NSAID: nonsteroidal antiinflammatory drug

and increases alertness and performance. Specific wavelengths optimize light as a countermeasure. Blue wavelengths (440–550 nm) mimic the morning light spectrum, hasten schedule shifting, and increase alertness, whereas red wavelengths (620–730 nm) simulate dusk and enable pre-sleep.

Pressure

EVAs during space missions require medical support (Figure 24-5). At altitudes above 15,240 m (50,000 ft), humans need either a pressure suit or enclosed pressurized cabin to prevent ebullism. For astronauts to operate in a space suit, the suit's engineers must balance life support requirements with mobility. Ambient pressures greater than 6.0 psi create a stiff, almost inflexible spacesuit or EMU. Therefore, lower pressures are required to improve mobility and reduce crew fatigue. The US EMU is pressurized to 4.3 psi. The hypobaric environment has the potential to create nitrogen bubbles in the blood and tissues, leading to decompression

sickness. To reduce this risk, astronauts perform “pre-breathe” of 100% oxygen for 2 to 4 hours to eliminate nitrogen gas from their tissues. They also take aspirin before beginning pre-breathe to reduce platelet adhesion and subsequent blood clot formation.^{13,14} The space MMO will also need to carefully monitor the spacecraft cabin's repressurization rate after EVA to prevent ear and sinus barotrauma. A generally acceptable repressurization rate is between 0.5 and 0.7 psi per minute.

Conditioning

During spaceflight, the main countermeasure for musculoskeletal and cardiovascular deconditioning is exercise. Astronauts on both short- and long-duration missions benefit from regular physical training. Fitness plans are created by NASA astronaut strength and conditioning rehabilitation specialists. These plans include the use of the CEVIS (cycle ergometer with vibration isolation system, Figure 24-6) and the T2 (Treadmill 2 with vibration isolation system, Figure 24-7) for aerobic



Figure 24-6. US Army astronaut Colonel (retired) Jeffrey N. Williams, Expedition 13 NASA space station science officer and flight engineer, exercises on the Cycle Ergometer with Vibration Isolation System (CEVIS) in the Destiny laboratory of the International Space Station. NASA photo ID: ISS013E17268. Reproduced from: <https://images.nasa.gov/details-iss013e17268.html>.



Figure 24-7. NASA astronaut Sunita Williams, Expedition 32 flight engineer, equipped with a bungee harness, exercises on the Combined Operational Load Bearing External Resistance Treadmill (COLBERT) in the Tranquility node of the International Space Station, 2012. NASA photo ID: ISS032E011701. Reproduced from: <https://images.nasa.gov/details-iss032e011700.html>.

endurance preservation, and the ARED for muscular strength (Figure 24-8). The ISS in-flight physical fitness plan consists of 2.5 hours per day of aerobic and resistive exercise, 6 days per week, for US astronauts. This aggressive on-orbit conditioning program has been shown to preserve aerobic performance within the range of individual baseline $\dot{V}O_{2max}$ levels and maintain moderate strength and stamina in most crew members. Flexibility in the extensor muscle groups and proprioception are still challenges faced by crew in space because of engineering constraints in exercise devices and vehicle limitations.

Medication

The MMO must ensure that crew ground-test all medications that could be used in space so that reactions and side effects are known. Of over 60 medications available for crew use in the on-orbit medical kit, the five most used are acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), nonbenzodiazepine



Figure 24-8. US astronaut Steve Swanson, commander of ISS Expedition 39, performs loading exercises on the Advanced Resistive Exercise Device (ARED) onboard the International Space Station 2014. NASA photo ID: ISS039E011261. Reproduced from: <https://images.nasa.gov/details-iss039e011261.html>.

hypnotics, antiemetics, and nasal decongestants. Of these, NSAIDs are the most commonly used.^{13,14} Conditions such as headache, low-back pain, and minor muscle aches warrant the use of NSAIDs. Melatonin and the newer generation nonbenzodiazepine hypnotics, such as zolpidem or zaleplon, are used to treat insomnia during the initial days of flight and during sleep shifting. These drugs have shorter half-lives than the older generation benzodiazepine hypnotics such as diazepam, temazepam, or triazolam. There has also been concern that the older drugs could sedate crew to a degree that wakefulness and clear cognition would be impaired during an emergency. Many crew members have prescription medications for benign medical conditions that do not preclude flying in space, such as hypertension, hyperlipidemia, hypothyroidism, or osteoarthritis, which require daily medication doses. Angiotensin-converting enzyme inhibitors, statin-class medication, thyroid replacement therapy, decongestants, and NSAIDs have been used for years in space and have been well tolerated.

On-Orbit Conditions

Several on-orbit medical conditions have occurred during NASA missions, and space MMOs must be familiar with them. Astronauts in the μg environment experience medical conditions similar to terrestrial experience, such as skin rashes, nasal congestion, dry eyes, ocular foreign bodies, serous otitis media, and constipation. Conditions that are rather unique to spaceflight include space adaptation syndrome (which includes nausea and vomiting, mild anorexia, fatigue, and insomnia), SABP, and urinary retention.^{21,23,39} Space motion sickness affects approximately 79% of all crewmembers, with 10% of cases felt to be severe. Approximately 70% of men and 50% of women have described symptoms ranging from a loss of appetite to nausea and vomiting. The time course is variable: onset occurs immediately post-insertion to 24 hours later, peak symptoms occur at 24 to 48 hours, and symptoms resolve at 72 to 96 hours, on average. Etiology is unclear, but contributing factors are thought to be a combination of entering a new motion environment; a sensory mismatch in which the inner ear and nervous system provide signals that do not make sense in μg ; and the approximately 2-L cephalad fluid shift that occurs in space. Flight surgeons have encouraged crew to maintain a 1g orientation despite the confusing visual cues created by the weightless environment. Medication has been moderately successful in reducing nausea and vomiting. The crew should be directed to use meclizine 25 mg orally or promethazine 25 mg intramuscularly every 6 to 8 hours as needed.

Inactivity or sleep, fluids, and gradual increase in activity over 24 to 48 hours restores crew members to preflight status in most cases, without recrudescence of symptoms.¹⁶

SABP peaks at 24 to 72 hour post-insertion and is treated with NSAIDs, short-acting muscle relaxers such as low-dose lorazepam, and assuming a fetal position to reduce pain. Urinary retention, although not unique to space flight, has been an issue due to medication side effects and mission activities that prevent bathroom breaks. Bladder distention and impaired detrusor muscle contraction has required in-flight catheterization to relieve symptoms or retention. Therefore, the MMO must ensure all crew members are trained in self-urinary-catheterization techniques for both short- and long-duration missions.

Vehicle launch and landing operations are also part of the MMO's responsibility as crew flight surgeon. Prior to launch, flight surgeons frequently premedicate non-pilot and commander astronauts with antiemetics to minimize the post-insertion nausea and vomiting associated with space adaptation syndrome. Crews are also advised to use enemas to minimize the need to defecate early on in the mission. Contingency launch operations during the space shuttle era included launch pad abort scenarios such as hypergolic fuel chemical leaks, fire, and explosion. Post-landing operations pose significant medical challenges to the flight surgeon due to the relative dehydration, muscle loss, and neurovestibular and cardiovascular deconditioning astronauts experience in space. Additionally, the potential operational implications of reduced muscle strength and endurance from μg exposure include decreased landing proficiency and impaired vehicle egress capability. The MMO will also need to consider the vehicle landing site characteristics (eg, water vs land), and prepare recovery operations accordingly.

Guidance to the Commanding Officer

Ultimately, the MMO is responsible for supporting the medical mission for the commander and crew. Being aware of individual crew member needs and identifying realistic countermeasures to prevent adverse health effects are essential for success. It is also important to identify resources for learning about new strategies, especially during contingency operations. In this role, the mission commander can expect the MMO to support the following duties:

- **Critical mission tasks**
 - Medical certification of astronauts for training and missions
 - Medical care of astronauts and their

- families
- Support during medical consultations
- Military astronaut selection exams
- **Operational mission tasks**
 - Medical support for space missions
 - Oversight of crew and flight controller medical training
 - Medical support to crew members prior to launch
 - Monitoring EVAs
 - Participation in contingency/rescue management during launch and landing.
 - Being part of the flight control team in the mission command center

SUMMARY

This chapter on environmental extremes has introduced the MMO to the basics of optimizing human performance in space. Specifically, it discussed the historical relevance of the environment to success in military space operations, the basic applied physiology relevant to understanding the warfighter in the μ g environment, and, finally, those evidence-based strategies demonstrated to preserve performance in

LEO and partial-gravity planetary environments. The space MMO operates in a unique setting with limited resources, where urgency and proper planning can make the difference between success and failure on the battlefield. It is important to remember that the MMO is present not just to treat the wounded, but also to critically optimize performance and ultimately strengthen the commander's hand for success.

REFERENCES

1. Dorr RF. X-20 Dyna-Soar Spaceplane was decades ahead of its time. Defense Media Network. <https://www.defensemedianetwork.com/stories/what-might-have-been-x-20-dyna-soar/>. Published September 3, 2011. Accessed July 18, 2018.
2. Air Force to develop Manned Orbiting Laboratory [press release]. Washington, DC: Department of Defense; December 10, 1963. <http://www.nro.gov/foia/declass/mol/6.pdf>. Accessed February 15, 2018.
3. Easton RD, Frazier EF. *GPS Declassified: From Smart Bombs to Smartphones*. Lincoln, NE: University of Nebraska Press; 2013.
4. Hale W. *Wings in Orbit: Scientific and Engineering Legacies of the Space Shuttle, 1971–2010*. Washington, DC: NASA; 2010.
5. Lane H, Lulla K, Miller J. *Select Astronaut Observations and Highlights of Space Shuttle Payloads and Experiments*. Washington, DC: NASA; 2011. NASA/TM-2011-216150.
6. Cassutt M. Secret space shuttles. *Air & Space Magazine*. 2009(Aug). <http://www.airspacemag.com/space/secret-space-shuttles-35318554/>. Accessed January 19, 2018.
7. Axe D. Semper fly: Marines in space. *Popular Sci*. 2006(Dec). <https://www.popsci.com/military-aviation-space/article/2006-12/semper-fly-marines-space>. Accessed January 19, 2018.
8. Reed WD, Norris RW. Military use of the space shuttle. *Akron Law Rev*. 1980;13(4):665–688.
9. Oman CM, Balkwill MD. Horizontal angular VOR, nystagmus dumping, and sensation duration in Spacelab SLS-1 crewmembers. *J Vestib Res*. 1993;3:315–330.
10. Young LR, Oman CM, Merfeld D, et al. Spatial orientation and posture during and following weightlessness: human experiments on Spacelab Life Sciences 1. *J Vest Res*. 1993;3:231–239.
11. Clement G, Moore ST, Rapha T, Cohen B. Perception of tilt (somatogravic illusion) in response to sustained linear acceleration during space flight. *Exp Brain Res*. 2001;138:410–418.
12. Scheuring RA, Davis JR, Polk JD, et al. The Apollo Medical Operations Project: recommendations to improve crew health and performance for future exploration missions and lunar surface operations. *Acta Astronaut*. 2008;63:980–987.

13. Davis JR, Johnson R, Stepanek J, Fogarty JA, eds. *Fundamentals of Aerospace Medicine*. 4th ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2008.
14. Barratt M. *Principles of Clinical Medicine for Space Flight*. New York, NY: Springer; 2008.
15. Moore AD Jr, Downs ME, Lee SM, Feiveson AH, Knudsen P, Ploutz-Snyder L. Peak exercise oxygen uptake during and following long-duration spaceflight. *J Appl Physiol*. 2014;117(3):231–238.
16. Meck JV, Reyes CJ, Perez SA, Goldberger AL, Ziegler MG. Marked exacerbation of orthostatic intolerance after long- vs. short-duration spaceflight in veteran astronauts. *Psychosom Med*. 2001;63:865–873.
17. Konieczynski DD, Truty MJ, Biewener AA. Evaluation of a bone's in vivo 24-hour loading history for physical exercise compared with background loading. *J Orthop Res*. 1998;16:29–37.
18. Leblanc AD, Schneider VS, Evans HJ, Engelbretson DA, Krebs JM. Bone mineral loss and recovery after 17 weeks of bed rest. *J Bone Miner Res*. 1990;5(8):843–850.
19. Carpenter RD, LeBlanc AD, Evans H, et al. Long-term changes in the density and structure of the human hip and spine after long-duration spaceflight. *Acta Astronaut*. 2010;76:71–81.
20. Zysset P, Qin L, Lang T, et al. Clinical use of quantitative computed tomography-based finite element analysis of the hip and spine in the management of osteoporosis in adults: the 2015 ISCD official positions, Part II. *J Clin Densitom*. 2015;18:359–392.
21. Pietrzyk RA, Jones JA, Sams CF, Whitson PA. Renal stone formation among astronauts. *Aviat Space Environ Med*. 2007;78(4 suppl):A9–13.
22. Baldwin KM, Herrick RE, McCue SA. Substrate oxidation capacity in rodent skeletal muscle: effects of exposure to zero gravity. *J Appl Physiol*. 1993;75(6):2466–2470.
23. Kertsman EL, Scheuring RA, Barnes MG, Dekorse TB, Saile LG. Space adaptation back pain: a retrospective study. *Aviat Space Environ Med*. 2012;83(1):1–6.
24. Ryder JW, Scheuring RA, Shackelford L. Musculoskeletal system: intervertebral discs disease. In: *Biomedical Results of the Space Shuttle Program*. Houston, TX: NASA, Lyndon B. Johnson Space Center; 2013: 257–292.
25. Scheuring RA, Moomaw RC, Johnston SL. Fatigue in US astronauts onboard the international space station: environmental factors, operational impacts and implementation of countermeasures. *Aviat Space Environ Med*. 2015;86(3):175.
26. Johnston SL, Campbell M, Scheuring RA, Feiveson A. Increased incidence of herniated nucleus pulposus among US astronauts. *Aviat Space Environ Med*. 2012;81(6):566–574.
27. Scheuring RA, Mathers CH, Jones JA, Wear ML. Musculoskeletal injuries and minor trauma in space: Incidence and injury mechanisms in US astronauts. *Aviat Space Environ Med*. 2009;80:117–124.
28. Feiveson AH, Mendez CM, Somers JT. *Assessing the Effect of Spaceflight on the Propensity for Astronauts to Develop Disk Herniation*. Houston, TX: NASA; 2015.
29. Bailey JF, Miller SL, Khieu K, et al. From the International Space Station to the clinic: how prolonged unloading may disrupt lumbar spine stability. *Spine J*. 2018;18:7–14.
30. Cogoli A. Space flight and the immune system. *Vaccine*. 1993;11(5):496–503.
31. Sonnenfeld G. The immune system in space and microgravity. *Med Sci Sports Exerc*. 2002;34(12):2021–2027.
32. Udden MM, Driscoll TB, Leach-Huntoon CS, Alfrey CP. Decreased production of red blood cells in man exposed to microgravity. *J Lab Clin Med*. 1995;125(4):442–449.

33. Rice L, Alfrey CP. Modulation of red cell mass by neocytolysis in space and on Earth. *Pflugers Arch.* 2000;441(2-3 Suppl):R91–R94.
34. Duffy JF, Czeisler CA. Effect of light on human circadian physiology. *Sleep Med Clin.* 2009;4(2):165–177.
35. Dawson D, Reid K. Fatigue, alcohol and performance impairment. *Nature.* 1977;388:235.
36. Epelman S, Hamilton DR. Medical mitigation strategies for acute radiation exposure during spaceflight. *Aviat Space Environ Med.* 2006;77(2):130–139.
37. Scheuring RA, Conkin J, Jones JA, Gernhardt ML. Risk assessment of physiological effects of atmospheric composition and pressure in Constellation vehicles. *Acta Astronaut.* 2008;63:727–739.
38. Murry M, Cox CB. *Apollo.* New York, NY: Simon and Schuster; 1989.
39. Thornton WE, Hedge V, Coleman E, Uri JJ, More TP. Changes in leg volume during microgravity simulation. *Aviat Space Environ Med.* 1992;63:789–794.