REVIEW ARTICLE

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Fundamentals of Anesthesiology for Spaceflight

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SPACE EXPLORATION BEYOND low Earth orbit has been termed as "exploration class space missions."[1,2] Such future missions may involve extended flights to the Moon, asteroids, or Mars and will most likely engage not only governmental space agencies but also the private sector, in what some have termed "the new space race."

During those missions, the risk for a crew member to require advanced medical care, including anesthesia and surgery, is significant.[3-5] In the first section of this review, human adaptation to the space environment is detailed, with a focus on the cardiovascular system, along with a discussion regarding which medical conditions may arise. The second part of the review focuses on discussing the extensive list of challenges associated with delivering an anesthetic procedure in space or on a foreign planetary surface. The challenge of providing advanced critical care in these settings encompasses many other issues that are beyond the scope of this review, which primarily focuses on anesthetic techniques.

THE SPACE ENVIRONMENT AND EXPECTED MEDICAL CONDITONS

Pathogenesis in the Space Environment

The boundary of space, according to the official definition of the International Aeronautics Federation, sits at an altitude of 100 km above sea level,[6] although the transition to space actually involves a series of boundaries progressively more hostile to human existence.[7] The space stations in low Earth orbit travel at an altitude of 220 to 280 miles (350 to 450 km) and a speed of 17,500 mph (28,000 km/h). This velocity generates a centrifugal force capable of compensating Earth's gravity, which at this altitude is still 88% of sea level's gravity. Both forces counterbalance each other, leading to the state of weightlessness, or microgravity.

In addition to the "conventional" medical conditions that threaten every human being, the unique environment of spaceflight, and in particular the loss of gravity, may predispose a person to the onset of a number of specific illnesses unique to space travel and especially prolonged weightlessness. Both types of conditions are summarized in Table 1.[8] The majority of this list overlaps with the risks identified by the National Aeronautics and Space Administration (NASA) Human Research Roadmap.[9]

The phases of launch and landing are extremely critical due to the stress put on the vehicles (and, subsequently, the crew within) by tremendous changes in velocity (accelerations and decelerations), and indeed, all human losses during spaceflight have occurred during those transition phases (Challenger, Columbia, Soyuz 1, and T11).[10]

The latest NASA Mars mission design concept corresponds to a 6-person crew conducting a 900-day mission.[11] Recently, a NASA report outlined "deep space" cislunar missions for the 2020s followed by a Mars mission in the 2030s for "at least 4 crew" for "up to 1,100 days."[12] In deep space, the vast distances involved imply that real-time communications will not remain possible, with delays between Earth and Mars, for example, reaching 4 to 20 minutes in each direction. An unprecedented level of crew autonomy will be necessary, including for medical care. With electronic transmissions limited by the speed of light, telemedicine, telementoring, and telesurgery all become impractical options. The exact crew composition has not been decided, but could be limited to a crew medical officer who is not necessarily a physician.[13] An astronaut survey argued against this and recommended having a medical doctor with broad medical skills on board.[13]

Inside any spacecraft, astronauts absolutely rely on the Environmental Control and Life Support Systems (ECLSS) to maintain an atmosphere that can sustain human life that is steady, normoxic, and normobaric, with neutral temperatures. Inside the cabin, the carbon dioxide concentration is on average 10 times higher than on the ground (0.3%-0.5%). An extremely hostile environment lies outside the vessel, marked by a nil barometric pressure, high levels of radiation, and extreme temperatures (-150° to +120°C).[14] Living in a closed environment involves an immediate vital risk in the possible loss of cabin pressure (eg, if a meteorite or satellite debris were to hit the station), fire, release of toxic substance, or malfunction of the ECLSS.[5,15]

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Table 1. Earth-like and Space-specific Medical Conditions in Space

Earth-Like Conditions	Space-Specific Conditions
Trauma	Cardiovascular deconditioning
Infections	Radiation exposure
Cardiovascular diseases: arrhythmias, myocardial ischemic events, stroke	Vision impairment and intracranial pressure syndrome
Renal stone	Hypobaric decompression sickness
Psychiatric disorders	Exposure to a toxic atmosphere
Cataract	Hypothermia/heat stroke
Cancer	Exposure to planetary dust

(Adapted from Komorowski M, Neuhaus C, Hinkelbein PDJ: Emergency medicine in space. Notfall Rettungsmed 18:268-273, 2015.[8])

When astronauts perform spacewalks (extravehicular activities [EVAs]), they transition into a hypobaric (300 to 400 hPa), pure oxygen environment inside an EVA suit.[16] Reproducing such a decompression profile in a hypobaric chamber results in a 50% to 80% occurrence of venous bubbles or decompression sickness (DCS) symptoms.[16] Very few actual cases in space have been reported, possibly because microgravity and the EVA suit provide protection against DCS, but also because astronauts likely underreport the issue.[17,18] There also is a theoretical risk of barotrauma and subsequent pneumothorax with such activities.[19] Suits pressurized at 565 hPa (tissue ratio of 1.4) and running 34% oxygen (normoxic mixture) are envisioned by NASA for Mars exploration EVAs and would eliminate the need for denitrogenation and drastically limit the risk of DCS altogether.[12,17]

Living in an enclosed and isolated environment has profound physiologic and psychologic effects, such as immunodepression, sleep and mood disturbances, and decrease in cognitive performance.[20]

The astronauts in low Earth orbit are somewhat protected from radiation by the Van Allen magnetosphere belts.[21] Beyond those, no effective shielding technology currently exists, and the exposure to solar particle events could have dramatic consequences such as acute radiation sickness.[22] Radiation in space also seems to increase the risk of cancer, infertility, and cataract.[21] The NASA Longitudinal Study of Astronaut Health identified an increase in mortality from cancer, which fortunately has been below the significance level.[23]

Concerns related to the potential health effects of inhalation of planetary dust have been raised since irritation symptoms of the skin and airway were described by Apollo astronauts.[24]

The conditions of highest concern include major trauma and hemorrhagic shock[3,5]; orthostatic intolerance upon re-exposure to gravity and reduction of aerobic capacity[25]; ionizing radiation[21,22]; the psychologic effect of isolation and chronic stress[20]; and challenges regarding the delivery of surgery, anesthesia, and subsequent critical care.[26-28] Realistically, the human management of severe trauma and surgical conditions implies the capability to provide anesthesia.[3,5,29]

Experts have estimated the risk of a serious medical event during a mission to be around 0.06 per person-year of flight, which corresponds to 1 event per 2.8 years for a crew of 6 (ie, 1 emergency during a 900-day mission to Mars).[4,30-32]

The individual risk of death from illness or trauma during an exploration mission to Mars has been estimated to be 0.24% per year.[4] In comparison, the observed mortality risk on Earth in high income countries and in the age range of 30 to 59 years, is 0.39% per year.[33] To put these numbers in perspective, the safety objective for the individual risk of death from spacecraft failure is 3% per year, or 12 times higher than death of medical origin.[4] However, regardless of population statistics, planning for medical care in expeditionary spaceflight involves hard decisions regarding whether capabilities to attempt treatment of catastrophic illness will be provided or whether realities of the mission will mandate that such catastrophes are simply palliated, and if so, whether the remains will be preserved or "buried in space."[28]

Human Adaptation to Space

More than 50 years of space medicine research has provided a reasonably good picture of how human physiology is affected by spaceflight.[10] The human body has evolved millions of years under gravity and is thus adapted for this environment. Weightlessness fundamentally affects most, if not all, physiologic systems (Fig 1).[34] Of greatest concern, these effects of microgravity on several systems (eg, bone demineralization) do not reach a plateau, with deadaptation seemingly continuing relentlessly as long as weightlessness persists.

Cardiovascular System

From the point of view of the anesthesiologist and when considering urgent medical care during or immediately after spaceflight, the cardiovascular system is undoubtedly one of the most critical to consider. Weightlessness induces profound cardiovascular changes, which are summarized in Table 2.[35-50]

In the human body, the equilibrium among the different functional fluid compartments of the vascular system, most notably the venous capacitance vessels, is largely under the control of gravity.[35,51] When entering weightlessness, fluid is redistributed toward the upper body, a phenomenon referred to

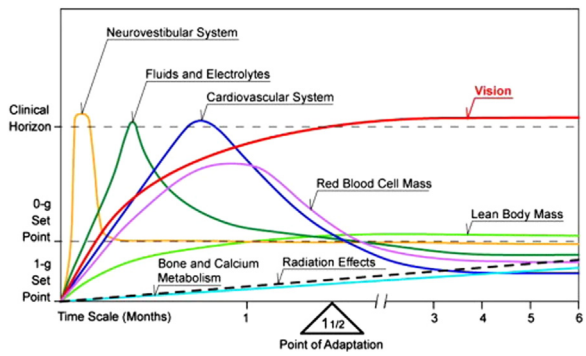


Fig 1. Timescale of the deadaptation of human systems to weightlessness. (Reproduced with permission from Nicogossian AE, Parker J, et al: Space physiology and medicine. CreateSpace Independent Publishing Platform, 2012.)[34]

Table 2. Main Cardiovascular Changes Occurring in Weightlessness

Parameter	Change in Weightlessness
Heart rate	Initially ▼, then ►[10]
Blood pressure	Initially ▼, then ▼ or ►[10,35]
Central venous pressure	Paradoxically ► or ▼[36-39]
Blood volume	▼ 9% to 17%[36,40-43]
Intracellular fluid	▲[40,43]
Cardiac systolic function	►[25]
Cardiac diastolic function	▼[25]
Systemic vascular resistances	▼ 14% ± 9%[44]; ▼39%[35]
Cardiac output	Initially ▲, then ▼ 17% to 20%[10] or ▲ 41%[35]
Baroreflex	▼ 50%[36,45,46]
Aerobic capacity: VO_2 max	▼ 22%[10]
Red blood cell mass	▼ 10%[41,47,48]
Endothelial function	Deficit in vasoconstriction[49,50]

NOTE. ▼ Reduction, ▲ Increase, ► No change.

as the "fluid shift."[10,35,43,51] Clinically, the astronauts display facial edema and the so-called "chicken legs."[10]

Leach et al have shown that in response to early weightlessness, there is a profound diuresis, presumably from the physiologic response to perceived hypervolemia, as the large intravascular fluid volumes previously localized to the venous capacitance vessels are released to the central circulation.[40,43] Subsequently, the plasma volume is reduced from 3.5 to 3.1 L after 1 week in space, whereas the intracellular volume increases from 23.9 to 26.3 L.[40,43] Similar results have been obtained using a dilution technique of radioisotopes.[47] Blood volume has been shown to decrease by 9% to 17% as early as day 1, which represents up to 1 L for a 70-kg man.[36,40-42] Multiple mechanisms are involved in the reduction of the plasma volume, including a decrease in oral intake (even in the absence of space motion sickness) and fluid shifts toward interstitial and intracellular spaces.[36] Diuresis does not seem to be increased.[36]

The red blood cell mass drops significantly by about 10% after 1 week in weightlessness.[41,47,48] A possible explanation for this "space anemia" lies in the inhibition of erythropoiesis in space, secondary to the increase in kidney tissue oxygen partial pressure. Indeed, the fluid shift toward the upper body is associated with an increase in oxygen transport in this area.[52] Another hypothesis could be hemolysis, as suggested by the increase in ferritine (+35 to 46%) that has been measured.[42,52]

Heart rate and blood pressure are affected little by weightlessness, but some authors have suggested that they may decrease marginally.[10,35,53]

Initially, because of the headward fluid shift, stroke volume and cardiac output are increased (+20 to 50%).[10] After a few days of adaptation, mostly as a result of hypovolemia but also cardiac atrophy, the ejection fraction increases and the stroke volume decreases (only possible if the decrease in end-diastolic volume exceeds the reduction in stroke volume).[25,54,55] At this point, the drop in cardiac output can reach 17% to 20%.[10,25] A reduction in left ventricle mass of 8% to 14% has been reported.[41,56] Even though diastolic dysfunction clearly has been identified in astronauts and prolonged bed rest studies, the left ventricular systolic function seems to be little affected, if at all (Fig 2).[25]

The risk of arrhythmias is increased in space, particularly during EVAs, due to catecholamine discharge.[24,25,57] In 1987, a cosmonaut was evacuated from MIR after a 14-beat run of ventricular tachycardia.[10]

It has been estimated that the baroreflex response was blunted by 50% after only 1 day in space.[45] Some suggest that short-term spaceflight does not alter the baroreflex,[58] but all agree that it is inhibited after long-duration spaceflight and that those changes can last for up to 2 weeks after returning to Earth.[36,46]

Systemic vascular resistances are decreased by 14% ± 9% after 1 week of weightlessness as a result of systemic arterial vasodilatation.[35,44] Paradoxically, given the headward fluid shift, the central venous pressure is not increased and may even decrease.[36] Of note, central venous pressure has been

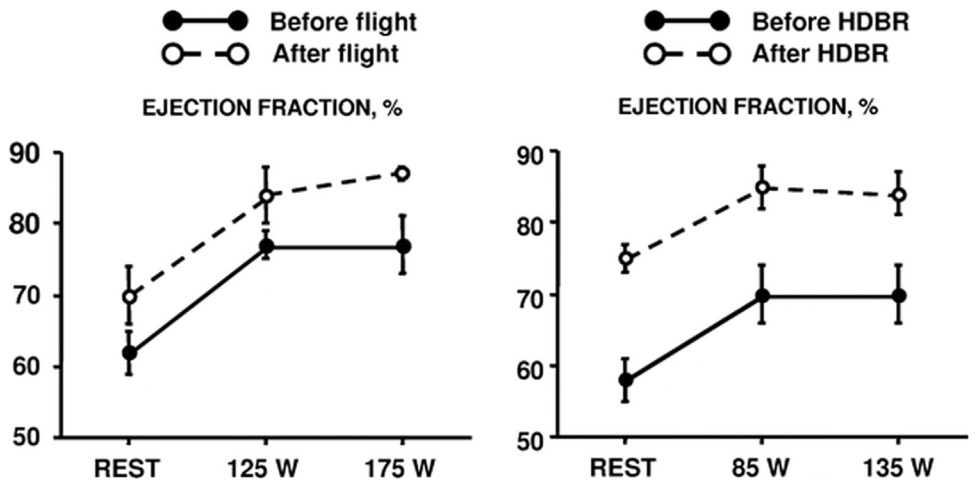


Fig 2. Cardiac ejection fraction (%) at rest and at exercise before and after spaceflight (*left panel*) and bed rest study (*right panel*). Abbreviation: HDBR, head-down bed rest. (Adapted with permission from Convertino VA, Cooke WH: Evaluation of cardiovascular risks of spaceflight does not support the NASA Bioastronautics Critical Path Roadmap. Aviat Space Environ Med 76:869-876, 2005.[25])

recorded historically in NASA astronauts using a 4-French catheter inserted through an arm vein![37,38] Among the hypotheses, some have suggested the reduction in intrathoracic pressure or the loss of gravitational force on the cardiac muscle.[39] The systemic vasodilatation and lower blood pressure might be beneficial during long-duration missions.[35,44]

Weightlessness induces endothelial changes.[49,50,53,59] The loss of gravitational constraint and the important reduction of motor activity alter regional blood flow and vascular transmural pressure,[60] which induce an adaptation of vasomotor tone, and in the long term vascular remodeling. The structural changes involve all layers of blood vessels but predominate in the endothelium and the smooth muscular cells.[59] Release of proinflammatory molecules could contribute to the endothelial changes.[53] Animal studies in the rat have identified similar endothelial changes after experimental endotoxinemia and antiorthostatic hypokinesia (hindlimb unloading by tail suspension, a model of weightlessness), suggesting that the endothelial dysfunction after spaceflight could be linked to an increase in endotoxin translocation from the gut.[61] Finally, weightlessness could alter cellular survival mechanisms and induce signals causing apoptosis.[62] The changes lead to endothelial dysfunction with a deficit of vasoconstriction that contributes to the orthostatic intolerance after landing.[49,50]

Changes in adrenergic-receptor sensitivity have been identified and contribute to a syndrome sometimes referred to as "syndrome of inadequate sympathetic response after exposure to microgravity."[63] Most agree that the sensitivity of beta-adrenergic receptors is increased, and the sensitivity of alpha-adrenergic receptors is decreased.[36,64] Agnew et al suggested that these changes have therapeutic consequences and recommended limiting the use of adrenergic antagonists and potentially increasing the dosing of alpha-agonist agents.[36,64]

Other Systems

In weightlessness, the gravitational stimuli disappear, which leads to conflicts between the sensory organs and alters, in particular, spatial orientation, balance, gaze control, and autonomous vestibular function.[65] These disturbances induce a form of space-specific motion sickness in about two-thirds of astronauts.[66] It can last up to a few days and frequently reappears after landing.[66] The international space medicine community has expressed growing concerns regarding changes in visual acuity after spaceflight. This syndrome appears to be related to an increase in intracranial pressure and is now referred to as "vision impairment and intracranial pressure" syndrome.[67,68] The constant exposure to artificial light affects sleep and circadian rhythms aboard spacecrafts, and lighting is now provided on the International Space Station (ISS) by specific solid-state lights developed to provide a more appropriate spectrum.[69] Maintaining crew mental health, cohesion, and performance during a several-year mission will be essential and highly dependent on the success of the crew selection process.[20]

The loss of physical stimulus on the skeleton leads to a 1% loss of bone mineral density per month on average and can exceed 2% per month in the pelvic area.[10,64] The heavy-resistive exercise regimen followed by current astronauts on the ISS is able to counterbalance bone loss by increasing bone formation, resulting in an overall maintained bone mineral density compared with earlier space programs.[70] The quality of the bone nevertheless remains doubtful, and the risk of fracture (in particular at the hip level) might be increased despite a maintained bone mineral density.[4,70] Increase in urinary calcium due to bone resorption and a reduction in diuresis significantly amplify the risk of kidney stones.[70,71] A few cases have occurred in the past.[3,72] Underused groups of muscles (back, abdominal wall, lower limbs) show a decrease in peak strength and endurance of up to 25%.[73] The diaphragm most likely is not affected.

Compared with preflight measurements, the respiratory rate is increased in space (+9%) and the tidal volume is reduced (-15%), leading to an overall unchanged alveolar ventilation.[74] The functional residual capacity is increased, which could in theory reduce the risk of atelectasis during mechanical ventilation.[74,75] In the absence of gravity, the ventilation:perfusion ratio becomes homogenous, which could improve hematosis. The total alveolocapillary surface may be increased and thus improve the lung diffusing capacity.[74,76] Initial studies in parabolic flight demonstrated that spontaneous changes in thoracoabdominal compliance fundamentally were beneficial to pulmonary function.[77] The impairment of pulmonary mechanics due to intraabdominal pathology and subsequent intraabdominal hypertension is a critical factor in the provision of life support and ventilatory management in particular.[78,79] Fortunately, it has been determined that the relative impairment in pulmonary function typically created by intraabdominal hypertension and intraabdominal gas insufflation (in the case of laparoscopy) is ameliorated by weightlessness.[77]

Immune system dysregulation in space has been confirmed.[80] The incidence of infectious disorders during spaceflight is increased, affecting, for example, 50% to 60% of Apollo crew members.[24,80] The likelihood of infections may be further increased by changes in bacterial virulence in space.[64,81]

Gastrointestinal motility is significantly slower in space, at least during the first 72 hours of the flight.[32] A rise in gastric content acidity has been reported.[82] Astronauts generally exhibit a loss of body weight, proportional to the duration of the flight, which reaches, for example, 5% on average after 6 months on the ISS[83] and is attributed to an imbalance between caloric intake and expenditures.[84]

The readaptation of human physiology in space is only one of the factors that complicate medical care during space missions. The second section of this review recapitulates those factors, with a particular focus on anesthesia.

CHALLENGES FOR THE DELIVERY OF ANESTHESIA

The delivery of advance medical care such as anesthetic procedures is complicated in the space environment by many factors that schematically fall into the following 2 categories: lack of technologies to actually perform the procedure and lack of knowledge about which protocol to choose (Table 3).

Table 3. Summary of Missing Technologies and Knowledge for the Provision of Anesthesia During Space Exploration Missions

Missing Technologies	Missing Knowledge
Intravenous (IV) fluid and vascular access • IV fluid generation • IV fluid handling • Lack of rapid vascular access capability	Physiology • Cardiovascular physiology in microgravity and partial gravity • Prevention and mitigation of orthostatic intolerance and loss of aerobic capacity
Medical equipment • Complete set of medical equipment fulfilling spaceflight standards and restrictions • Prevention of oxygen buildup in the cabin • Design of medical kits	Pharmacology • Pharmacokinetics and pharmacodynamics of drugs • Safety and dosing of vasopressors and inotropes
Drugs conservation	Anesthetic technique • Best general anesthesia protocol • Role of regional and perimedullary techniques
Lack of onboard expertise • Expert medical decision support systems • No telemedical link for distant missions	Medical training • Profile of crew medical doctor • Preflight and inflight training

Challenges Due to Missing Technologies

Fluid Generation and Handling

Shipping and storing intravenous (IV) fluids in a spacecraft is expensive and uses precious stowage volume. IV fluids are unlikely to be used and have a limited shelf-life. The capacity to generate onsite and on-demand IV fluid from drinking water is highly desirable. A demonstration prototype was tested successfully on the ISS (project IVGEN).[85] Fluid handling and drug preparation are complicated in space because fluids and gas do not separate spontaneously (Fig 3).[29] NASA experts are confident that this is not a major issue and that efficient techniques of air bubble removal exist.[86]

Medical Equipment

Advanced medical care typically requires a set of specific equipment such as a monitor, ventilator, suction equipment, and oxygen concentrator. Spaceflight imposes a number of restrictions in terms of weight, size, and power consumption in addition to compliance with specific spaceflight standards. The NASA Human Research Roadmap-Exploration Medical Capability group has demonstrated a concept of an integrated platform, inspired by military equipment and requirements.[87]

Any medical procedure involving the administration of supplemental oxygen to a crewmember implies the risk of oxygen buildup in the closed cabin environment, with major risks of explosion and fire.[29] This will have to be addressed by either limiting the dumping of oxygen in the cabin (closed ventilation circuit) or effective oxygen removal by the ECLSS. The use of volatile anesthetics will be prohibited, therefore any general anesthetic will have to be administered exclusively via the IV route.[26]

Vascular access might be difficult to obtain in a medical contingency. An intraosseous access kit has been integrated into the ISS medical gear. The use of ultrasound, potentially operating autonomously or robotically, to obtain central vascular access is another option, with such development ongoing.[88] In general, ultrasound has been shown to be a very useful and practical tool for use in spaceflight.[19,89,90]

Related Risks and Gaps

Many other factors, not directly related to the provision of anesthesia, will complicate the provision of advanced medical care. For example, most current blood products are of human origin and have a limited shelf-life. The availability of blood substitutes (eg, synthetic hemoglobin) would drastically improve the survivability after severe trauma.[5] Current shock resuscitation strategies emphasize earlier use of blood products and colloids, with dramatically less crystalloid fluids administered.[91]

Several other limitations of missing knowledge or equipment have been identified in the following fields: on-board medical expertise, adapted medical protocols for resource-poor settings, telemedicine (especially for distant missions), noninvasive medical imaging, minimally invasive laboratory testing, bone fracture stabilization and wound healing, medical equipment sterilization, body sounds auscultation, medical data management, medical supplies inventory management, and risk of ineffective or toxic medications after long-term storage.[92]

Challenges Due to Missing or Incomplete Knowledge

Incomplete Knowledge About Human Physiology in Partial Gravity

Gravity on the Moon and Mars is about one-sixth and one-third of Earth's, respectively. Precise knowledge about human adaptation to partial gravity levels is required and will affect mission planning and medical preparation.[64] Artificial gravity could provide an effective global countermeasure against bone,

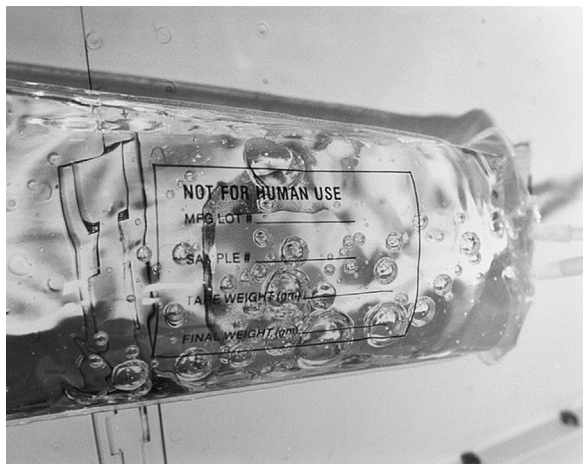


Fig 3. Behavior of intravenous fluids in space. (Reproduced with permission from Norfleet W: Anesthetic concerns of spaceflight. Anesthesiology 98:1219, 2000.)[29]

muscle, and cardiovascular deconditioning.[93] Unfortunately, very little is known about human physiology in partial gravity.[14,94] The Apollo moon missions did not include extensive physiologic experiments.[24]

The only available data, obtained in parabolic flight, head-up tilt and lower body unweighting experiments, provided answers to short-term changes from transitioning from 1G to partial gravity levels.[94-96] It is critical to understand the physiologic impact of prolonged stays (days to weeks) in reduced gravity levels. What is the minimum level of gravity required to maintain fitness and prevent deconditioning? An important consideration for mission planning is determining whether daily physical exercise is necessary in reduced gravity.

One way to address questions such as these with current technologies would be to install a short-arm centrifuge on the ISS and test the physiologic responses to various levels of gravity (project currently on hold). The ground research on the question is active, a recent study on a short-arm centrifuge suggesting that 0.75G at the heart level (2G at feet level) produces similar cardiovascular stimulus to standing.[97]

Challenges Related to Cardiovascular Changes in Space

A reduced aerobic capacity historically has been measured during spaceflight.[10] Thanks to the intense countermeasure regimen, many are nowadays able to maintain or even improve their aerobic capacity.[41,64] Cardiovascular changes and hypovolemia lead to orthostatic intolerance on return to gravity in about 80% of astronauts after 6 months on the ISS.[51] This condition has, in some cases, required administration of IV drugs and fluid.[64] Immediately after landing, the aerobic capacity is impaired because of hypovolemia, anemia, and orthostatic intolerance.[25,43,63] This, along with the space motion sickness, may compromise astronauts' ability to perform critical tasks directly after a landing on a foreign body surface.[25]

For many experts, the new cardiovascular status reached after equilibration does not correspond to a pathologic state, but simply to a new physiologic equilibrium in weightlessness, tailored to reduced loading conditions.[25] This equilibrium nevertheless is delicate and the tolerance to any additional event (such as blood loss, anaphylaxis, or further reduction in cardiac function) or interventional procedure (general anesthesia, mechanical ventilation) may be compromised.[26]

A few precautions could reduce the risk of severe cardiovascular collapse in these situations. Vasopressors, in particular alpha-agonists (phenylephrine, metaraminol, midodrine, norepinephrine), should be readily available, including for continuous infusion.[36,64] Higher-than-usual doses could be required.[36] Beta-agonists and beta-antagonists should be used with caution.[36] Any clinically significant relative or absolute hypovolemia should be treated concomitantly with IV fluids and vasopressors. An IV fluid loading procedure should be carried out before the induction of general anesthesia.[26] The volemic status should be monitored during resuscitation using objective parameters (eg, response to fluid challenge on the stroke volume or cardiac index).[98] Electrolytes (potassium, magnesium) should be maintained within normal ranges to limit the risk of arrhythmias.

Pharmacology in the Space Environment

Many factors may alter the pharmacokinetics and pharmacodynamics of drugs in weightlessness; eg, weight changes, redistribution of body fluids, changes in renal perfusion, among many others.[99,100] Drugs may become ineffective or even toxic after long-term storage.[92] The clinical relevance of these changes is unclear. Of interest for the anesthesiologist, the use of depolarizing muscle blockers (succinylcholine) is contraindicated after prolonged exposure to microgravity due to changes in the neuromuscular junction and risk of hyperkalemia.[29,36] Rocuronium represents a valid alternative.[101,102]

Choice of Anesthetic Techniques

Given the specificities and challenges associated with spaceflight, the choice of the most appropriate anesthetic technique is not straightforward.

The experience of invasive medical procedures in microgravity-exposed patients is very limited.[3] To what extent cardiovascular deconditioning will complicate the management of a general anesthetic is unknown. Anesthesia has been induced in animals in space and immediately after spaceflight.[103] In 2002, a NASA working group concluded that the safe delivery of anesthesia could be achievable with enough understanding of the human physiology in space, as detailed by McSwain, MD, et al in written communication. In the absence of strong evidence, it appears sensible to formulate choices based on a worst-case scenario approach and consider that astronauts in this setting will be severely deconditioned, hypovolemic, at risk for arrhythmias, difficult to intubate, intolerant to succinylcholine, have a full stomach, and be managed by nonmedical personnel with limited training, if the crew medical doctor is incapacitated or dead.

Perhaps the most stringent limiting factor is that anesthesia protocols should be achievable in a safe manner by a limited crew of nonphysicians. In low-income countries, nonmedical personnel regularly carry out anesthetic procedures with a relatively low complication rate.[104-106] Simplified protocols could be carried out safely by nonphysicians.[107] In addition to physicians, astronauts, with their comprehensive skillset, are ideal candidates to perform lifesaving medical procedures.

The extended discussion regarding regional anesthesia, general anesthesia (GA), and conscious sedation has been laid out previously.[26,108,109] To summarize, the risks associated with regional anesthesia are rather limited, but it requires extensive training, whereas the situation is diametrically the opposite for GA.[26,109,110]

The wide adoption of ultrasound techniques in anesthesia has greatly simplified the execution of regional blocks and increased their safety and success rate.[111,112] With only 3 techniques (axillary brachial, femoral, and subgluteal sciatic blocks), most surgeries of the upper and lower limbs are possible. An axillary brachial block allows operating on the arm below the shoulder level, and anesthesia of the entire leg below mid-thigh can be achieved with a combined sciatic and femoral nerve block.[113] Using ultrasound-guided techniques, as few as 10 procedures per block can be necessary to reach a

90% success rate.[114] These techniques can be combined with IV sedation if necessary.

The relevance of including perimedullary techniques (spinal and epidural) can be discussed. The effect and safety of spinal anesthesia are most likely unpredictable in microgravity because heavy local anesthetic solutions rely on gravity.[108] Epidural techniques might be usable, but they require extensive training and asepsis and carry significant risks.[108]

GA would be suitable for any surgical condition.[26] The consequences of the fluid shift and facial edema on the risk of difficult intubation are not documented, but could be of concern. Intubation conditions in general are much more favorable with muscle paralysis, which should therefore be recommended.[101,102] Astronauts should be tested for allergy before flight. The intubation success rate also is higher with video laryngoscopes, especially for novice operators.[115,116] Finally, gastric motility has been demonstrated to be slower in space.[32]

Altogether, the safest procedure for GA appears to be a rapid-sequence induction after IV fluid loading, using drugs that respect hemodynamic stability (most likely ketamine) and orotracheal intubation with a video laryngoscope.[26,107] For limb or superficial surgery, simple ultrasound-guided regional blocks or local infiltration could be proposed, alone or in combination with conscious sedation.[3,109,110] Fracture blocks are safe and efficient for pain relief and mobilization.[109] Minor surgery can be performed after local infiltration.[31]

CONCLUSION

Future space exploration missions will push beyond the current limits of human experience in maintaining health and performance of crew members in extreme settings. After more than 5 decades of human presence in space, the understanding of the space environment and human physiology in weightlessness is advanced. Despite many challenges, the safe delivery of an anesthetic procedure on previously healthy individuals, given the current knowledge and technologies, could be possible, even by nonanesthesiologists. There always will be risks in exploration, with deep space being an extreme case of this, and these risks should not constitute a block for future space exploration missions if the crew are volunteers fully understanding and accepting of the risks. Medical care for any individual with significant medical history (eg, "space tourist") in the space environment would, however, require physician-level expertise.

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