Chapter 34

MILITARY SPACEFLIGHT

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INTRODUCTION

Support of life in space is surely the most demanding technical challenge undertaken by humankind, and requires close collaboration among physicians, physiologists, engineers, and professionals with a variety of other skills. This chapter is designed to help the reader develop a basic understanding not only of the challenges of life support in the space environment but also of the medical issues related to health maintenance in physiological readaptation on return to the planetary surface. The topics should be of interest to all military physicians as well as to those specializing in aerospace and occupational medicine.

Long before human spaceflight was technically possible, aeromedical physicians were considering its possibilities and discussing the problems that humans would face when leaving Earth. Probably the best early discussion of aeromedical problems of space travel occurred at a symposium sponsored by the US Air Force and the National Research Council of the National Academy of Sciences in the late 1940s.[1] The authors of the report of that symposium, who included General Harry Armstrong, Dr Heinz Haber, and Dr Hubertus Strughold, noted that human physiological responses "will play a more decisive role in the initial stages of space travel than it did during the early stages of aviation."[1] These prescient scientists identified potential problems with acceleration, radiation, rapid decompression from collisions with orbital debris, temperature extremes, sensorimotor and neurological changes, psychological stresses, and the dangers of fire with hyperoxic environments. They actually divided these problems into two phases: (1) adaptation to microgravity and (2) readaptation on return to Earth or another celestial body's gravity field. Their discussion concluded with the telling observation that "We can only guess the facts here: experiments must be the final answer."[1]

More than 1 decade later (12 Apr 1961 and 20 Feb 1962, respectively), the brief orbital flights of Yuri Gagarin (1 h, 48 min) and John Glenn (4 h, 55 min) showed that human orbital flight was indeed possible. The close confinement and short duration of early flights limited the development of medical data; several more decades were required to acquire precise data regarding specific physiological changes associated with acute and chronic exposure to microgravity.

The early astronauts and cosmonauts were recruited from military flying programs. Military physicians provided a substantial component of the medical expertise for developing and supporting human spaceflight, and much of the medical and physiological testing of early astronaut candidates took place at the US Air Force School of Aerospace Medicine, Brooks Air Force Base, San Antonio, Texas. Military facilities have continued to provide research and testing support to the US space program, and resources from all of the uniformed services have been used to support launch, recovery, and contingency planning for piloted orbital flight. Although the US Air Force Space Command does not now have a defined role for humans in orbit, this is almost certain to change with the continuing evolution of sophisticated orbital reconnaissance capabilities and single-stage–to–orbit spacecraft.

ORBITAL MECHANICS AND FREE FALL

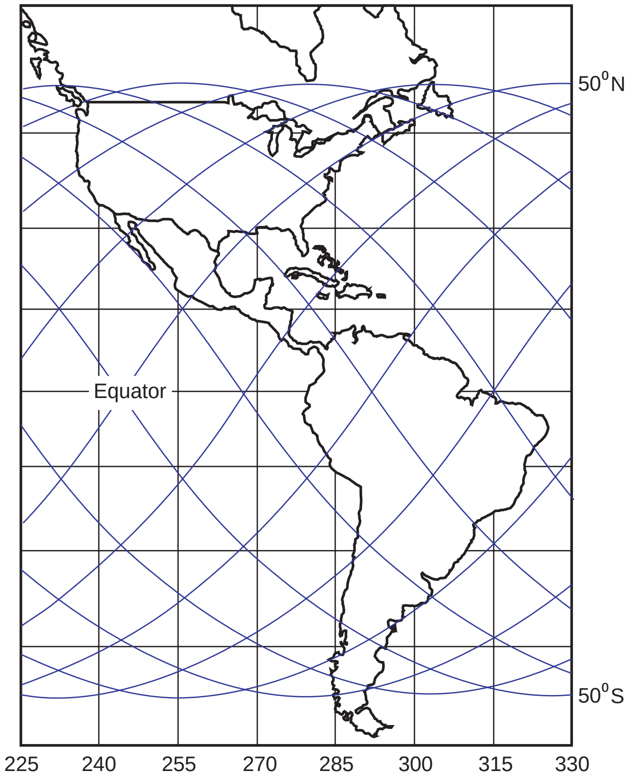
How do spacecraft remain in orbit and why do astronauts find themselves "weightless"?[2] It is a popular misconception that microgravity is caused by the spacecraft's distance from Earth. In fact, if a spacecraft were simply lifted into space, it would fall back to Earth as a ball dropped from the hand would, owing to the pull of gravity. Orbital flight occurs when the pull due to gravity ($A_{gravity}$) equals the centripetal acceleration that is related to the object's tangential velocity ($V_{tangent}$) as described in Equation 1, where the radius of the orbit (r_{orbit}) is measured from the center of Earth (Equation 1):

1. $$A_{gravity} = (V^2_{tangent}) \, / \, r_{orbit}$$

A typical low-Earth orbit of 170 miles' altitude requires a speed of approximately 17,400 mph (25,520 fps) and yields an orbit with approximately a 90-minute period. As in any orbital condition, the spacecraft is in "free fall" on a curved path that continuously misses Earth. Although this condition is often called "zero G" (0*g*) because astronauts do not feel the pull of gravity, the subtleties of orbital mechanics actually impose *microgravity* on the order of a few millionths of a *g* (the Systéme International d'Unités symbol representing units of gravity and acceleration).

Because orbital flight involves a balance of forces, returning from orbit is a matter of decelerating the spacecraft to destroy this equilibrium and allowing gravity to alter the orbital altitude. A small decrease in tangential velocity causes a reduction in the craft's orbital altitude; drag from the upper atmosphere further decelerates the craft, which con-

Fig. 34-1. A diagram of the orbital path of the Skylab space station. Note that the craft crosses the Equator at approximately 50°; this results in a groundtrack extending from 50°N to 50°S in latitude. Higher orbital inclinations provide overflight of a larger portion of Earth's surface but substantially increase the energy required to reach orbit. Photograph: Courtesy of National Aeronautics and Space Administration, Washington, DC.



tinues to reduce its speed (and therefore its altitude) until it eventually lands on Earth's surface.

All known human spaceflight missions have utilized equatorial low-Earth orbits. These launches point toward the east to take advantage of the tangential velocity provided by Earth's spin, reducing the energy, and more importantly, the fuel and mass needed to achieve orbit. The closer the launch site is to the equator, the greater this effect. The precise direction of launch sets the orbital inclination, which is the angle at which the orbital plane crosses the equator (Figure 34-1). A large angle is desirable for Earth observation flights because it increases the maximal northern and southern latitudes of the track over the ground and allows direct observation of a large percentage of Earth's land mass. However, available inclinations have been limited by considerations of safety of people and objects on the ground under the launch track. Shuttle launches from the Kennedy Space Center in Cape Canaveral, Florida, are generally restricted to a band between 28.5°N and 62°N. Russian crewed flights launched from Kazakhstan are 51.6°N. Shuttle launches from Vandenberg Air Force Base in southern California would have permitted polar orbits overflying 100% of the planetary surface, but the required launch facilities were never completed.

LIVING IN SPACE

Living and working in space poses a number of medical and physiological challenges. These stem from conditions created by the microgravity environment as well as other factors that are created by the technical details of the methods used to deal with the hostile physical environment. The following section provides a brief overview of the unique medical-support requirements associated with spaceflight operations and identifies some directions for aerospace medicine in the 21st century.

Life Support

Space is a near-vacuum with temperatures ranging from –156°C (–250°F) in shade to +120°C (+250°F) in direct sunlight. Humans must be protected from this hostile environment by means of sophisticated spacecraft or suits for extravehicular activity (EVA) (Figure 34-2). Both use insulation and reflective materials to minimize direct heat gain and loss and have thermal control systems to properly compensate for the radiative heat gain and loss, as well as heat generated by the people and/or the equipment onboard the spacecraft.

Early US spacecraft utilized a cabin atmosphere of 100% oxygen at 5.0 psi. This low-pressure, high-oxygen system permitted lighter weight spacecraft that were within the lift capabilities of existing US ballistic missiles.[3] However, the elevated partial pressure of oxygen (PO_2) presented significant risk due to flammability and contributed to the Apollo 1 fire, which took the lives of three astronauts. The atmosphere was subsequently changed to a sea-level composition for launch, then depressurized to 5.0 psi, and gradually increased to 100% oxygen once in space. Skylab was the first US spacecraft to use a two-gas, hyperoxic, hypobaric system. A molecular sieve was utilized for removal of carbon dioxide, replacing the CO_2 absorption canisters that had been used in previous spacecraft.

Fig. 34-2. Astronaut Edward White II performing the United States's first extravehicular activity during the Gemini IV mission, 3–7 June 1965. Photograph: Courtesy of National Aeronautics and Space Administration, Washington, DC. Photograph S65-30427.

The US Shuttle and current Russian spacecraft use an atmosphere similar to air at sea level. A simple sensing system controls inflow of nitrogen and oxygen, the former to maintain barometric pressure and the latter, the vessel's PO_2. Carbon dioxide is removed from the Shuttle with lithium hydroxide canisters, while the Russians utilize both absorption compounds and a molecular sieve system.

Initial EVA suits were air-cooled but this proved inadequate, and water-cooled suits were quickly developed to provide adequate heat transport. Current US and Russian EVA suits are constructed with multiple layers of fabric, which provide pressure retention, thermal insulation, and some degree of protection from penetration by sharp edges and micrometeoroids. A water-cooled undergarment is used to reject excess body heat to the exterior through the backpack. Suit pressure is reduced below that in the spacecraft because a higher level of inflation would make movement difficult or impossible, but pressure reduction is limited by the requirement to maintain an adequate inspired pressure of oxygen and the need to prevent decompression sickness. The current US suit, the Extravehicular Maneuvering Unit (EMU), utilizes 100% oxygen at 4.3 psi, while the Russian suit (Orlan-DMA) operates at 4.0 to 5.88 psi; the lower pressure is intended for use during periods when enhanced manual dexterity is required. The reduced pressure option is not being incorporated in the design of the next version of Russian suit (Orlan-M).[4]

EVA imposes increased physical demands on astronauts, especially of their upper extremities and hands, because the inflated suit resists movement and requires the use of awkward gloves. Heart rates were measured during the United States's first EVA mission, in 1965 on Gemini IV (see Figure 34-2). This and subsequent Skylab data showed pulse rates averaged 110 to 155, with peak rates up to 180 beats per minute.[5,6] No oxygen utilization data were obtained from those flights. Apollo lunar surface EVAs (1969–1972) were associated with an average energy consumption of 185 W (159 kcal/h). Energy levels during orbital EVAs ranged from 175 to 585 W (151–504 kcal/h) in the Apollo flights, while those of the 3 Skylab missions averaged 267 W (230 kcal/h).

Development of New Space Suits

One of the principal challenges of constructing the space station will be the necessity for routine, prolonged EVAs. The current space suits are extremely complex and require extensive maintenance on the ground between uses. In addition, the combination of reduced pressure and hard exercise during EVA dictates that astronauts spend hours "prebreathing" 100% oxygen to minimize the risk of decompression sickness (see Chapter 32, Pressure Changes and Hypoxia in Aviation). Engineers and scientists are working to develop suits that do not require prebreathing, can be repaired and refurbished aboard the spacecraft, and require only occasional major maintenance on Earth.

Spacecraft Contamination

Contamination of the spacecraft environment (by normal activity and by accident) is another problem that deserves attention. Spacecraft contamination may come from a broad range of sources, including metabolic waste products from the astronauts, off-gassing of materials, products of air and water reclamation systems, and chemicals used in onboard experiments. Unrecognized effects of contamination on astronaut performance or behavior could have catastrophic consequences, with loss of life and equipment costing billions of dollars. Because astronauts live continuously in their working environment, threshold limit values for inhaled or contacted substances aboard the spacecraft are generally far more conservative than Earth-based occupational safety limits, which assume exposures of a few hours per day. The effects of common environmental contaminants in such chronic settings are not known, and in most cases there are insufficient data on which to base recommendations. A method for determining spacecraft environmental guidelines has been developed by the National Research Council's Committee on Toxicology[7]; this monograph also contains an extensive discussion of terms, relevant compounds, and an excellent bibliography.

Physiological Adaptation to Microgravity

Concerns about the possible rigors of space travel produced an extensive (and in retrospect, perhaps excessive) screening program for early astronauts. Although the US and Soviet space programs had accomplished experimental flights with both dogs and monkeys, the absence of human data dictated extreme caution in planning the initial orbital flights. Substantial emphasis was placed on tolerance to the hypergravitational, thermal, vestibular, and psychological stresses thought to characterize spaceflight.[8] As Patricia A. Santy notes in her comprehensive description of early astronaut selection, it was difficult to develop specific astronaut screening criteria because there had been no experience with humans in space.[8] This concern for crew health and safety and its resultant batteries of medical testing did little to improve the relationship between flight medicine physicians and astronauts, but it did lead to the development of space-age telemetry. Electrocardiographic telemetry and extensive postflight medical examinations and debriefings documented only minimal physiological effects of short orbital flights and reassured program managers that longer orbital and lunar flights were medically feasible. The lack of physiological "showstoppers" contributed to the operational focus that characterized the Mercury, Gemini, and Apollo programs (1961–1972).[9–11]

Skylab, the world's first space station, followed the lunar Apollo program and provided a magnificent microgravity laboratory, with an extensive array of medical experiments examining the physiological effects of long-duration flights lasting up to 84 days in duration.[12,13] Blood, urine, and stool specimens were collected in flight, and onboard medical equipment included a multilead electrocardiograph system, an automated sphygmomanometer, an exercise bicycle, a lower-body negative pressure (LBNP) device for studying cardiovascular deconditioning, a rotating chair for vestibular experiments, an electroencephalography system, and a mass spectrometer for respiratory gas analysis. Findings from the Skylab II, III, and IV missions, which lasted 28, 59, and 84 days, respectively, became the basis for long-duration missions conducted over the next decade. Those results and data from a series of Spacelab missions, especially Spacelab Life Sciences (SLS) 1 and 2 and NeuroLab, conducted almost 2 decades later, have provided a detailed characterization of microgravity-induced physiological changes and their underlying mechanisms.

Physiological adaptation to microgravity can be characterized by three principal physical effects: a redistribution of fluids toward the head (cephalad), an unloading of the musculoskeletal system, and a dramatic alteration of somatosensory and vestibular inputs. Several major reviews have been published,[14–16] so only a brief summary will be provided here. The actual adaptive processes are complex, and the affected organ systems appear to change over different time courses. Vestibular symptoms[17] and cardiopulmonary changes appear within minutes after reaching orbit, but may stabilize after a few days or within 1 to 2 weeks, respectively, whereas changes in the musculoskeletal system may take days to weeks to become manifest and continue for months to years, if not the entire time the astronaut remains in orbit.[18]

Fluid Redistribution

On a typical US Space Shuttle flight in low-Earth orbit, the time from lift-off to orbit is approximately 8 minutes, with maximal acceleration of 3*g*. This acceleration is almost all +Gx in direction, although a small component of –Gz is present. (The positive and negative acceleration vectors are Gx, front to back; Gy, left side to right side; and Gz, head to foot; see Figure 33-1 in Chapter 33, Acceleration Effects on Fighter Pilots.) The change from 3*g* to microgravity at main-engine cutoff (MECO) is virtually instantaneous, with facial edema and engorged neck veins observable within minutes of reaching orbit. These fluid shifts last the entire flight, regardless of its duration. Leg volume, measured as early as 2 to 3 hours in space, is significantly decreased and has a downward trend. Initially, losses in leg volume are due to fluid loss from interstitial tissues, but this stabilizes after a few days. Subsequent decrease in leg volume is caused by muscle atrophy.[19–21] Surprisingly, central venous pressure (CVP) does not appear to be elevated despite the obvious clinical signs documenting major cephalad fluid shifts and increased jugular venous distention.[22–24] Cardiac chamber dimensions and ventricular function have been assessed by several investigators[22–24]:

- M-mode echocardiographic measurements made by Atkov[25] on 15 cosmonauts during 7- to 237-day flights on a series of Salyut missions demonstrated an absence of change in myocardial contractility. No consistent alterations of resting ventricular volume were noted.
- Two-dimensionally guided M-mode measurements from Shuttle astronauts, reported by Bungo and colleagues,[26] showed a decrease in ventricular volumes and a slight increase in heart rates, compared with supine, 1*g* control values. Cardiac dimensions, estimated from two-dimensional echocardiographic measurements on the SLS-1 and SLS-2 flights, showed significant increases in left atrial and left ventricular diastolic dimensions and stroke volumes when measured early in flight. This combination—of a low, near-zero CVP and increased cardiac dimensions and stroke volume—was surprising, given that these normally change in parallel. This finding, confirmed on three separate Spacelab Shuttle flights (SLS-1, SLS-2, and D-2) in four astronauts, suggests that intrapleural pressure decreased, or cardiac compliance increased, or both. Although it is theoretically possible that intrapleural pressure falls in space, there are no data to suggest that it is does. It is more likely that (1) redistribution of pulmonary blood volume away from the lungs' bases and the heart and (2) the absence of myocardial muscle and blood weight in microgravity are the basis for the paradoxically low CVP with increased left ventricular volume.

Carotid baroreflex function, assessed by measuring heart rate changes caused by mechanically altered carotid sinus transmural pressures, is depressed by spaceflight (as it also is during periods of prolonged bedrest).[27,28] The onset of change in space seems to be more rapid than is seen during the bedrest studies. It is not known how or why microgravity produces baroreflex dysfunction or the extent to which the dysfunction contributes to cardiovascular deconditioning following spaceflight.

The cephalad fluid shift that occurs with microgravity does not seem to decrease total body water, although a major redistribution of fluids within the body's various compartments does occur.[29] Plasma volume decreases approximately 17% within the first 24 hours of flight and remains approximately 10% below preflight values for at least 1 to 2 weeks on orbit (Figure 34-3). Plasma volumes measured after landing following flights of short or long duration show similar reductions, suggesting that this probably represents a stable, adapted volume state. Transient increases in plasma proteins

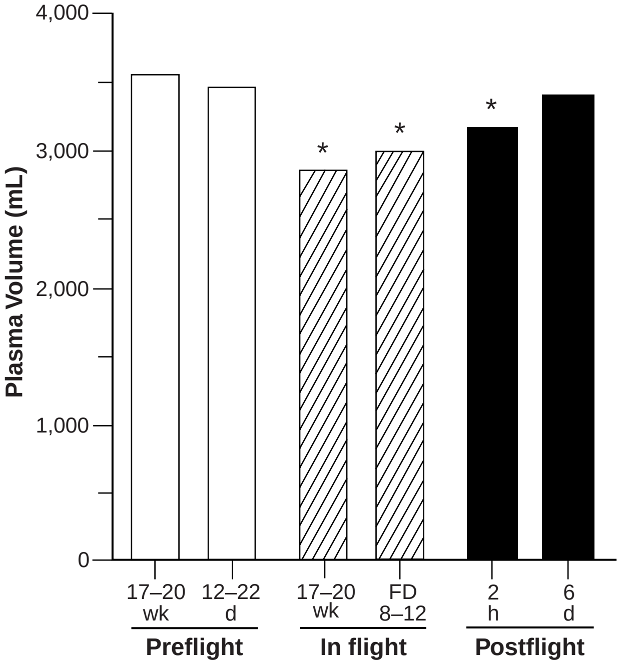


Fig. 34-3. Plasma volume was measured in six Spacelab Life Sciences 1 (SLS-1) and SLS-2 astronauts with injection of iodine 125–labeled serum albumin. Values before, during, and after flight are shown. Plasma volume is significantly reduced during flight. The decrease in plasma (and blood) volume contributes to the postflight orthostatic hypotension seen after essentially all orbital flights. Reproduced with permission from Alfrey CP, Udden MM, Leach-Huntoon CS, Driscoll T, Pickett MH. Control of red blood cell mass in space flight. *J Appl Physiol.* 1996;81:99.
*Significantly less than both preflight and 6-d postflight mean values
FD: Flight day

early in the flight probably reflect hemoconcentration, while subsequent decreases suggest increased vascular permeability with migration of plasma proteins out of the vascular compartment. The extravasated fluids seem to move into the extravascular and intracellular compartment. No diuresis occurs early in flight.

Much of the initial intravascular volume loss is probably caused by decreases due to immediate prelaunch intake restriction, along with associated nausea, vomiting, and space motion sickness. Renal function has been studied with intravenous injections of inulin and *para*-aminohippuric acid (PAH).[29] Glomerular filtration increases early in flight, while effective renal plasma flow appears to be unchanged throughout the flight. Urinary antidiuretic hormone increases early in flight but quickly normalizes. Aldosterone and plasma renin activity both decrease early in flight but normalize as the flight continues.

Spaceflight anemia was identified as a problem in the earliest days of the space program. In-flight studies published in 1975[30] and 1996[31] utilizing chromium 51–tagged red blood cells (RBCs) and iron 59 injections have provided a clear understanding of RBC production and destruction in space and have shown the anemia to be a physiological response to cephalad fluid shifts.[30,31] RBC mass in space decreases approximately 10%. The cephalad fluid shift and hemoconcentration early in flight cause an increase in central blood volume and effective increase in RBC mass sensed by the body. This increase, in turn, produces an almost immediate decrease of erythropoietin to levels associated clinically with little or no RBC production (Figure 34-4). Thus, there is a significant depression in RBC production and an inhibited maturation of newly formed RBCs prior to their release from the bone marrow. RBC production appears to normalize once a new equilibrium is established with a "normal" hematocrit associated with a significantly reduced plasma volume. The reduced RBC mass, appropriate for microgravity, persists until the astronaut returns to Earth. Subsequent gravitationally driven redistribution of blood and fluids within the various body compartments and increased fluid retention lead to hemodilution and anemia. This anemia then contributes to the orthostatic hypotension seen in astronauts after spaceflight. Erythropoietin is again stimulated and the anemia is resolved without medical intervention.

Pulmonary function on Earth is influenced, to a major extent, by gravity-dependent inequalities of ratio between ventilation and perfusion ($\dot{V}/\dot{Q}$). These $\dot{V}/\dot{Q}$ variations account for commonly observed clinical findings such as tuberculosis affecting the oxygen-rich apices of the lungs and atelectasis occurring in the relatively less-well-ventilated basal regions. Thus, microgravity would be expected to produce substantial changes in pulmonary gas exchange and spirometry. Vital capacity decreased approximately 10% in Skylab astronauts, but there was concern that Skylab's hyperoxic, hypobaric atmosphere could have caused this change.[32] More extensive studies subsequently confirmed these early observations and extended the range of tests performed.[33] Expiratory flow rates also decrease approximately 10% in the first week of flight but seem to normalize after that. Diffusing capacity, as estimated by uptake of carbon monoxide, increases approximately 28% (Figure 34-5).[34] Although the in-

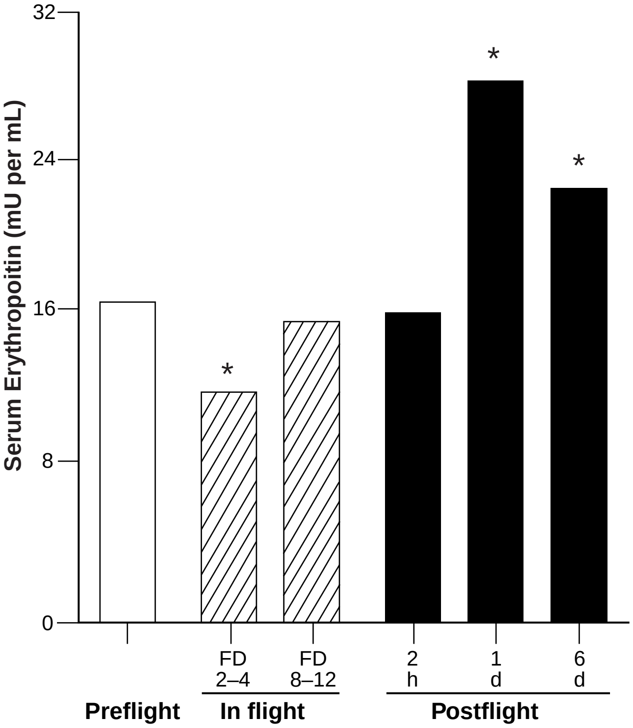


Fig. 34-4. Serum erythropoietin levels were measured in six Spacelab Life Sciences 1 (SLS-1) and SLS-2 astronauts. The initial decrease in plasma volume is associated with a transient hemoconcentration, which leads to depressed serum erythropoietin levels. Values rebound briskly as intravascular volume is restored after the flight to preflight levels. Reproduced with permission from Alfrey CP, Udden MM, Leach-Huntoon CS, Driscoll T, Pickett MH. Control of red blood cell mass in space flight. *J Appl Physiol.* 1996;81:101.

*Significantly different from preflight mean

FD: Flight day

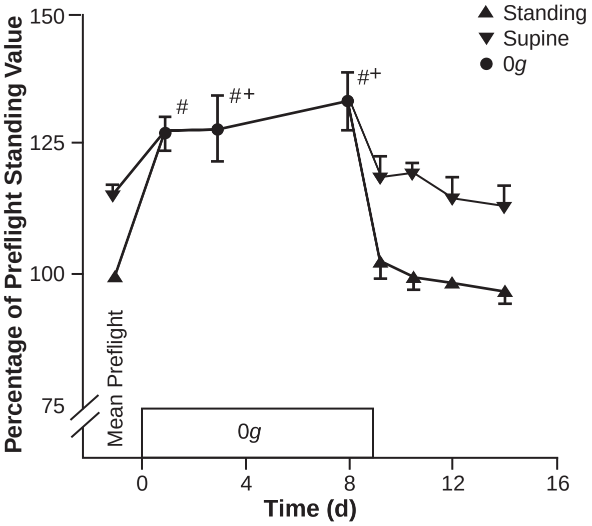


Fig. 34-5. The diffusing capacity of lung for carbon monoxide (DLCO), a simple test of alveolar–capillary lung function, was measured before, during, and after spaceflight. The in-flight values were significantly higher than those measured either standing or supine in 1*g*. Changes in pulmonary capillary blood volume were not sufficient to explain such a large increase in DLCO. The investigators postulated that a substantial increase in alveolar–capillary surface area occurs in space. Reproduced with permission from Prisk GK, Guy HJB, Elliott AR, Deutschman RA III, West JB. Pulmonary diffusing capacity, capillary blood volume and cardiac output during sustained microgravity. *J Appl Physiol.* 1993;75:19.
#:Significant difference ($P < .05$) between preflight standing average and average data from individual days in-flight and standing postflight
+:Significant difference ($P < .05$) between preflight supine average and average data from individual days in-flight and supine postflight.

crease in diffusion capacity correlates significantly with an increase in pulmonary capillary blood volume, the change is not sufficient to explain the improved gas exchange as measured by the diffusing capacity of lung for carbon monoxide (DLCO). It appears that a substantially larger effective capillary surface area is available in microgravity because more capillaries are perfused in the absence of gravity gradients in the pulmonary arterial circulation (Figure 34-6). It was expected that microgravity would eliminate all $\dot{V}/\dot{Q}$ inequalities, but tracings of expired carbon dioxide concentrations continue to demonstrate evidence of inhomogeneities within lung, even in the absence of gravity.[35] Studies comparing the pulmonary distribution of inhaled helium and sulfur hexafluoride also documented the persistence of what were previously thought to be gravity-dependent inhomogeneities in pulmonary ventilation.[36] These pulmonary function data from space demonstrate that a component of the $\dot{V}/\dot{Q}$ mismatch always seen on Earth is anatomically determined and+ not solely due to gravity. Airway closing volumes were not altered by microgravity, although residual volume decreased almost 18%.[37] Table 34-1 provides a summary of microgravity-induced changes in lung function.

Vestibular Inputs and the Space Adaptation Syndrome

Because of extensive linkages between gravity and otolith stimulation, significant alterations in vestibular function during and after spaceflight could be expected (see Chapter 35, Motion Sickness). Neurovestibular symptoms are most notable in the first few days of flight. These symptoms are called the space adaptation syndrome (SAS) and are clinically similar but not identical to ordinary motion sickness. Extensive in-flight testing was first conducted on the Skylab missions.[38] These investigators utilized a rotating chair and programmed head movements during rotation to test the Skylab astronauts' susceptibility to motion sickness following their adaptation to microgravity. A remarkable decrease in sensitivity was documented both inflight and immediately after the flight. The investigators also noted that the greater freedom of movement possible in the spacious workshop of the Skylab was more likely to produce vestibular symptoms than had been seen in earlier flights in more confined spacecraft, and they suggested that prevention of symptoms would require both drugs and adaptive training.

Further testing in cosmonauts and astronauts from Salyut, Mir, and Shuttle missions has documented major changes in otolith function and oculovestibular responses.[39–43] It appears that astronauts in space initially increase their dependence on visual and tactile stimuli. As the flight continues, however, they appear to "internalize" the reference system for determining up–down orientation and decrease their dependence on visual cues. There also appears to be significant reinterpretation of linear acceleration–induced otolithic input in the absence of the otoliths receiving head-tilt stimuli in space.[44] However, the character, magnitude, and time course of postflight perceptual responses are not fully consistent with the "central otolith reinterpretation" theory. Other mechanisms, such as central and peripheral nervous system changes, probably play a significant role as well.

SAS remains a problem in human spaceflight.[17]

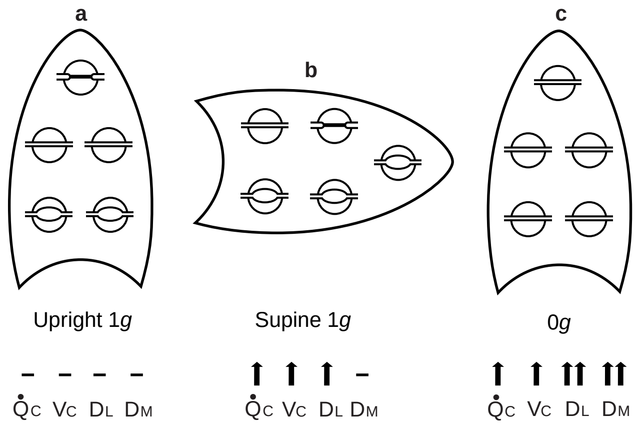


Fig. 34-6. A simple cartoon showing human alveolar–capillary relationships in (**a**) upright (1*g*) and (**b**) supine (1*g*) positions on Earth and (**c**) in microgravity (0*g*). On Earth, hydrostatic gradients alter pulmonary perfusion, and the superior regions of the lung in standing and supine subjects are relatively underperfused, as represented by the collapsed capillaries. In microgravity, all capillaries are well perfused and the effective capillary–alveolar surface area is greatly increased, leading to an augmented diffusing capacity of the lung. Pulmonary capillary blood flow ($\dot{Q}_C$), pulmonary capillary blood volume (V_C), lung diffusing capacity (D_L), and alveolar membrane diffusing capacity (D_M) are reflected by the arrows showing relative changes (bars represent no change) in each experimental condition. Reproduced with permission from Prisk GK, Guy HJB, Elliott AR, Deutschman RA III, and West JB. Pulmonary diffusing capacity, capillary blood volume and cardiac output during sustained microgravity. *J Appl Physiol.* 1993;75:24.

A majority of astronauts experience symptoms that may include nausea, malaise, anorexia, and headaches in the first hours of spaceflight. About three

TABLE 34-1

CHANGES IN PULMONARY FUNCTION IN SPACE

Physiological Responses to Microgravity	No. of Subjects	Changes in Microgravity (In-Flight vs Preflight Standing Measurements)
Pulmonary Blood Flow		
Total pulmonary blood flow (cardiac output)	4	18% increase
Cardiac stroke volume	4	4% increase
Diffusing capacity (carbon monoxide)	4	28% increase
Pulmonary capillary blood volume	4	28% increase
Diffusing capacity of alveolar membrane	4	27% increase
Pulmonary blood flow distribution	7	More uniform but some inequality remained
Pulmonary Ventilation		
Respiration frequency	8	9% increase
Tidal volume	8	15% decrease
Alveolar ventilation	8	Unchanged
Total ventilation	8	Small decrease
Ventilatory distribution	7	More uniform but some inequality remained
Maximal peak expiratory flow rate	7	Decreased by 12.5% early in flight but then returned to normal
Pulmonary Gas Exchange		
O_2 uptake	8	Unchanged
CO_2 output	8	Unchanged
End-tidal Po_2	8	Unchanged
End-tidal Po_2	8	Small increase when [CO_2] in spacecraft increased
Lung Volumes		
Functional residual capacity	4	15% decrease
Residual volume	4	18% decrease
Closing volume	7	Unchanged as measured by argon bolus

Adapted with permission from West JB, Elliott AR, Guy HJ, Prisk GK. Pulmonary function in space. *JAMA.* 1997;277(24):1959.

fourths will experience mild symptoms, whereas one fourth will experience more-severe symptoms, such as one or more episodes of vomiting, especially in the first day of flight. The symptoms generally subside within the first 24 to 72 hours on orbit, but they can be prolonged. Efforts to predict which astronauts will be affected by SAS have not succeeded. Age, gender, aerobic fitness level, prior aviation experience, and response to multiaxis, ground-based trainers (human centrifuges) are not accurate predictors.[45]

The etiology of SAS is not known, but the main theories are "sensory conflicts" and "fluid shifts." The former hypothesis states that discordant signals arising from visual, proprioceptive, and otolithic inputs produce the syndrome; the latter states that increased cerebral and otolithic perfusion and fluid content (ie, edema) cause the syndrome. Analogues such as "simulator" motion sickness show that neurovestibular sensory conflicts can produce symptoms similar to SAS. Direct evidence of cerebral edema in spaceflight is lacking, but intraocular pressures rise significantly in microgravity.[46] Also, many of the features of SAS, including headache, fatigue, nausea and vomiting, malaise, and slowed cognition, are consistent with the symptoms of cerebral edema. Our own unpublished transcranial doppler studies also lend support to changes in the intracerebral circulation. Neither hypothesis excludes the other and both mechanisms may play a role.

Treatment for SAS has been difficult, but since 1989, intramuscular promethazine has been the drug of choice in the Shuttle program.[47] Sedation on orbit has not been a problem despite intramuscular doses of 25 to 50 mg promethazine, and the drug has provided better relief than any previously tested drugs, including oral promethazine, scopolamine, dextroamphetamine, methylphenidate, and metochlopramide. Treatment with promethazine has minimized the operational impact of SAS. Testing on short parabolic flights suggests that astemizole will not be effective.[48] Potent, nonsedating, newer drugs such as ondansetron or granisetron have not yet been tested in spaceflight.

Musculoskeletal Unloading

Musculoskeletal changes are relatively minor during short-duration flights, but they represent a major challenge for missions of longer duration. Data from the National Aeronautics and Space Administration's (NASA's) Skylab flights suggest significant losses of bone and muscle mass despite aggressive exercise countermeasures.[49,50] Additional evidence of major decrements in both bone and muscle mass from the weight-bearing structures during long-duration MIR missions was published in 1996.[51] These data, gathered as part of a joint US–Russian study using computed tomography and and dual-energy X ray absorbancy (DEXA) scans, show continued tissue losses as the mission duration increases. No asymptote was reached for missions as long as 14.4 months (Table 34-2). These changes occurred despite extensive in-flight exercise programs of 1 to 2 hours daily, utilizing powered and unpowered treadmill and bicycle ergometers. Current exercise programs will probably not be sufficient to prevent significant, progressive bone loss during interplanetary travel. It remains to be determined whether high impact or pharmacological interventions or different exercise programs, including those focusing more on resistive than aerobic exercise, will suffice on future, long-duration missions.

Space Radiation

Radiation exposure for astronauts was reviewed by the National Academy of Sciences in 1993,[52] 1996,[53] and 1998.[54] These works provide in-depth discussion and extensive references, so only a brief overview will be provided here. Space radiation comes from three principal sources: galactic cosmic rays (approximately 87% protons, 12% helium ions, and 1% heavy ions)[55]; protons trapped in Earth's magnetosphere; and solar particle events (which are also composed of protons, but of much greater fluence than is found in galactic cosmic radiation).[56] Exposure in low-Earth orbit depends on orbital altitude, the magnitude and direction of Earth's magnetic field, solar flare activity, and shielding provided by the spacecraft. Substantial variation exists for each of these factors. Peaks in solar flare activity may occur at any time, but tend to follow approximately 11-year cycles. Increased solar flare activity can raise spacecraft radiation over 10-fold within a few hours. The most recent *solar maximum* occurred in the year 2000. Conversely, higher-energy particles increase during *solar minima*.

The physics of shielding is extremely complex and must take into account the types of incident radiation as well as the type and density of material of the shield. Gamma ray and proton shielding are relatively well understood and account for almost 2-fold changes in dosage at different locations in the International Space Station (ISS). High-energy particles, which are commonly found in interplanetary travel, remain highly problematic. Collisions of these high-energy particles with cells in the retina are responsible for the bright flashes (Cherenkov flashes) first reported by early astronauts and cosmonauts.[57] These particles also easily pass through traditional shield-

TABLE 34-2

MIR SPACE STATION: CHANGES* IN BONE MINERAL DENSITY AND LEAN BODY MASS

Body Region	Crew Members Studied	Mean	SD
Bone Mass Density			
Spine	18	–1.07†	0.63
Neck	18	–1.16†	0.85
Trochanter	18	–1.58†	0.98
Total	17	–0.35†	0.25
Pelvis	17	–1.35†	0.54
Arm	17	–0.04†	0.88
Leg	16	–0.34†	0.33
Lean Mass			
Leg	16	–1.00†	0.73
Arm	17	0.00	0.77
Total Lean	17	–0.57†	0.62
Total Fat	17	1.79	4.66

*Percentage per month, compared with baseline (preflight) measurements
†$P < .01$
SD: standard deviation
Adapted with permission from LeBlanc A, Schneider V, Shackelford L, et al. Bone mineral and lean tissue loss after long duration spaceflight [abstract]. *J Bone Miner Res*. 1996;11(suppl 1):S323.

ing materials such as aluminum and lead, producing a large range of secondary fragments including other nuclei, heavy fragments, and both protons and neutrons. In that setting, both primary and secondary radiation effects are important but poorly understood. The relative biological effects for such high-energy particles may be as much as 40-fold greater than for protons. The differential effects of acute versus chronic exposure and possible interactions of radiation with microgravity itself are likewise poorly understood.

Some evidence for spaceflight-induced chromosomal and cellular damage in humans has been reported.[58] The frequency of cellular changes is used to calculate bio-doses and seems to be in general agreement with other dosimetry methods. White blood cells from seven MIR cosmonauts were cultured after their flights. The X-ray equivalent dose was found to be below the cytogenetic detection level of 20 mGy in samples studied after flights of 2 to 3 weeks. After flights of 6 months' duration, the biological dose varied greatly among the cosmonauts, from 95 to 455 mGy equivalent dose (1 Gy ≈ 100 rad).

Spaceflight radiation dosage standards have been recommended, but the associated uncertainties are large.[59–61] The new recommendations for career dose limits, based on lifetime excess risk of cancer mortality, take into account age at first exposure and gender. The career limits range from 1.0 Sv (100 roentgen equivalents for man [rem]) for a 24-year-old woman to 4.0 Sv (400 rem) for a 55-year-old man, compared with the previous single limit of 4.0 Sv (400 rem). To decrease cataractogenesis, the career limit for the lens of the eye has been reduced from 6.0 Sv (600 rem) to 4.0 Sv (400 rem). Most astronauts can complete their careers without exceeding these recommended occupational exposure limits, but longer-duration flights and interplanetary travel will likely produce excessive exposures and could lead to fatalities if adequate shielding and effective radioprotectants are not developed. This remains an important area for aerospace medical research.

RETURN TO GRAVITY

Although it is generally agreed that physiological adaptation to microgravity is rapid and effective for full function in space, readaptation to Earth's gravity on return from space remains problematic and of major operational significance. The major problems associated with re-entry following orbital flights of up to 14 months are muscle weakness, vestibular disturbances, and orthostatic hypotension. A variety of

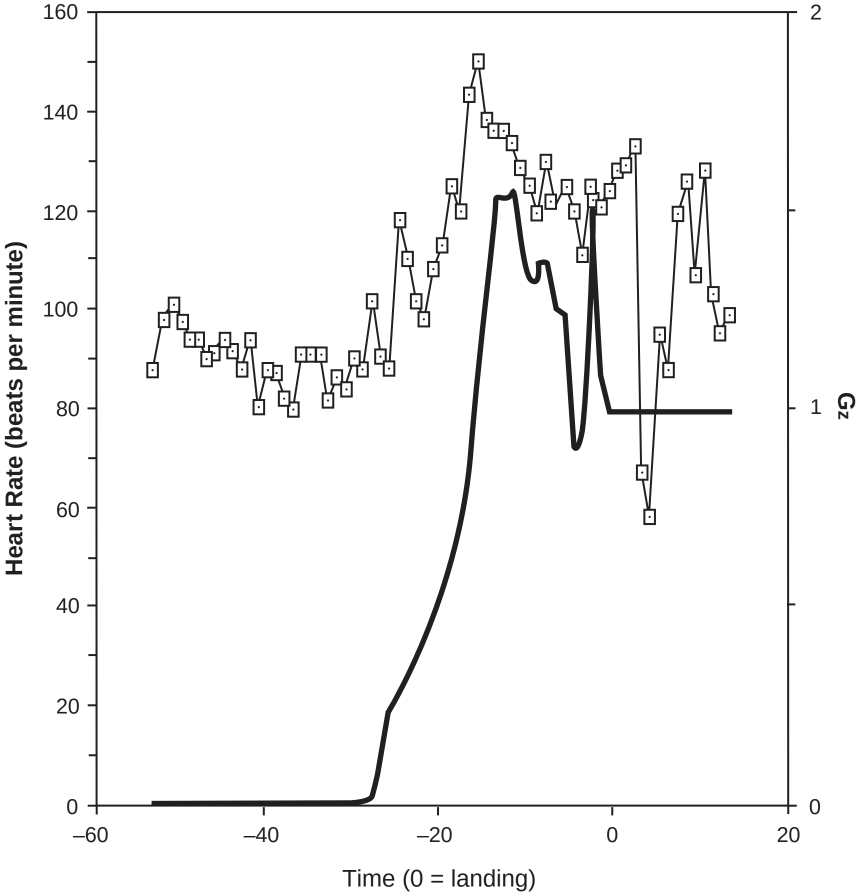


Fig. 34-7. An astronaut's heart rate (—⊡—), measured via continuous electrocardiographic recording, and acceleration (Gz; ▬) are shown for a typical Shuttle re-entry period. A significant tachycardia is observed. Vasovagal episodes occurred just before, and more prominently, just after landing (time 0 = landing). Re-entry is characterized by hypovolemia, depressed baroreflexes, vestibular disturbances, and a significant heat load associated with both the launch-and-entry suits and a warm (35°C–36°C) cabin temperature. Reproduced with permission from Buckey JC Jr, Lane LD, Levine BD, et al. Orthostatic intolerance after space flight. *J Appl Physiol*. 1996;81:16.

visual and vestibular disturbances have been reported by returning astronauts and documented with detailed postflight testing.[62,63]

Bone and muscle wasting in-flight have already been described. Although there have been no postflight fractures associated with loss of bone mass in humans, substantial muscle weakness and incoordination have been noted. It is likely that this results from simple muscle atrophy as well as neuromuscular changes postflight. Skylab leg volume data showed rapid reconstitution, from 10% below preflight volume to approximately 5% below within 5 days of landing; but by 10 days after the flight, however, volumes were still below preflight levels.[50(p195)]

The absence of biopsy data precludes determination of the time course and extent of recovery of bone mass. Also, it is completely unknown whether normalized bone and muscle mass also indicates normal structure. Differences in trabecular structure and myoneural junction numbers could persist despite normalized masses of bone and muscle.

Decreased orthostatic tolerance is a universal finding in astronauts exposed to microgravity for longer than a few days, although its magnitude has considerable interindividual variation. Skylab crews underwent serial orthostatic challenges with LBNP and showed decreased tolerance within 4 to 6 days on orbit.[64] The greatest decrements were during the first 3 weeks of flight, with stability at a reduced level reached by 5 to 7 weeks in-flight. In-flight tolerance to LBNP seemed to be predictive of postflight tolerance as well. More-recent data from the Spacelab Life Sciences missions show that after landing, almost two thirds of astronauts experience clinically significant orthostatic intolerance with 5 to 10 minutes of quiet standing.[65] Excessive lower extremity venous pooling does not appear to play a role, although excessive pooling in the abdomen and pelvis could be present. As noted previously, spaceflight produces hypovolemia, anemia, and baroreflex dysfunction, which contribute to significant orthostatic intolerance during re-entry and after landing (Figure 34-7). Extensive hemodynamic measurements during postflight orthostatic stress document a failure to increase total peripheral resistance appropriately. It is unknown whether this inadequate vasoconstriction is related to impaired baroreflex function, defective end-organ responsiveness, or both.

Aerobic exercise capacity appears to be well preserved in-flight, but there is a substantial decrease when it is measured immediately after the flight.[66–68] Elements of both muscle atrophy and poor neuromuscular coordination are undoubtedly present in this postflight deconditioning, but the main disability seems to stem from the cardiovascular dysfunction. Maximal heart rate is maintained, but stroke volume is reduced by almost 23%. Recovery is relatively rapid but varies with the length of the time on orbit.

Attempts to correct in-flight hypovolemia with saline ingestion immediately prior to re-entry have had limited success.[69] Despite careful hemodynamic measurements, no difference was found between those who did and those who did not undergo saline fluid loading prior to re-entry. The Russian space program uses in-flight LBNP and a high-salt diet prior to re-entry to retrain baroreflexes and volume load, but conclusive proof of efficacy in ameliorating orthostatic hypotension is lacking. A few attempts to use fludrocortisone to enhance volume replacement have likewise proven ineffective. The main countermeasure against orthostatic intolerance remains an abdominal or a lower-extremity pressure garment, or both. US astronauts use an anti-G suit (paradoxically, modified from the standard US Air Force G-suit) as part of the standard launch and entry suit (LES), and Russian cosmonauts utilize tight leg wrappings (called *Karkas)* to prevent lower-extremity venous pooling.

FUTURE MILITARY SPACE MISSIONS AND INTERPLANETARY EXPLORATION

At the present time, there is no official military role for humans in space, and most of the Department of Defense–supported Shuttle flights in the 1980s were for the launching of unmanned spacecraft. However, with improved launch capability, we can envision a number of types of future crewed missions that currently do not exist, the most obvious of which is reconnaissance. Both US and Russian flight experiments have examined observational abilities of humans in space, and claims have been made regarding abilities to detect subtle contrast changes over land and, perhaps even more so, over water.[70] Claims have also been made that the dynamic range of human vision and the ability to process unexpected information provide a significant advantage over the limited sensing spectra of many satellite systems, as was demonstrated during the Skylab missions. However, the broad geographical range of threat areas and the difficulties associated with keeping humans in the desired orbits appear to limit this application's military value. Most experts believe that for routine, anticipated, observation conditions, available technical means of data gathering offer adequate resolution at far less cost than human observation flights. In-flight repair of expensive sensing devices has already required human involvement, and the increasing costs and complexity of spacecraft make future repair missions likely. Current launch costs and the Shuttle's range, which is limited to low, equatorial Earth orbit, make repair by humans of most space systems—those in geostationary or polar orbits—impossible. However, newer launch systems and enormously expensive satellites could easily change the cost–benefit ratio in favor of more human repair missions, as has been done twice for the Hubble Space Telescope.

Development of an operational aerospace plane with appropriate lift vehicles would make short-notice "pop-up" (short-term, low-Earth-orbital) missions possible.[71] Crewed, transatmospheric vehicle flights could include emergency repairs of militarily important space assets, highly specialized reconnaissance missions, or even "insertion" flights that transport personnel to any spot on Earth within an hour or so. Rapid, relatively low-cost launch capability would almost certainly lead to a military role for humans in space but would simultaneously create significant physiological problems. The severe cardiovascular deconditioning associated with spaceflight would prevent the on-orbit stationing of specialists who could be returned to desired locations on Earth on short notice and be expected to function soon after landing. Likewise, brief orbital or suborbital pop-up missions might be complicated by vestibular symptoms associated with SAS. Our current knowledge of countermeasures for these basic problems remains suboptimal. Unless effective interventions are developed, future mission planners will continue to be limited in their ability to fully utilize the first few hours on orbit or on return to Earth immediately following spaceflight.

Spaceflights of long duration will be necessary if humans are to explore other planets. By the end of 1996, there had been 190 successful spaceflights (and 3 failed attempts) with 221 US astronauts, 83 Soviet or Russian cosmonauts, and 48 fliers from other countries.[72] Thirty-one of the 352 were women. The total days in space for humans was slightly over 17,000; Valery Polyakov, a Russian physician-cosmonaut holds the records for the longest flight, 437 days, as well as the most days in space, 678. These milestones will easily be surpassed when the ISS, now under construction, is used in part for systematic investigation of the biomedical challenges of exploration-class missions such as a proposed expedition to Mars, which might involve 6 to 12 months in transit each way and a stay of 1 to 2 years on the Red Planet. Such a voyage raises critical questions regarding human health and medical care in prolonged spaceflight and on return to planetary gravity. NASA's National Space Biomedical Research Institute (NSBRI) is charged with developing countermeasures against the deleterious effects of spaceflight, including problems observed in orbit and new difficulties associated with the remote, isolated conditions of an exploration-class mission. Validating the countermeasures is a formidable task, since even ISS will provide scientists with access to only limited numbers of subjects exposed to 0*g* for months rather than years.

Related issues include the willingness of astronauts to volunteer as subjects of medical studies and difficulties with protocol compliance in a remote operational setting. On the positive side, some of the research may find application to problems on Earth, including medical screening, training techniques, telemedicine, and rehabilitation. NSBRI has articulated 10 investigative themes, briefly summarized here[73]:

1. *Cardiovascular Alterations*
   Although spaceflight of any duration is known to produce orthostatic intolerance, neurovestibular readaptation-related problems, and an altered response to physical exertion, prolonged residence in 0*g* may lead to reduction of cardiac mass, increased susceptibility to arrhythmias, and possible unmasking of previously asymptomatic cardiovascular disease. Areas of investigation include identification and characterization of operationally significant medical problems as well as development of techniques for preflight screening, noninvasive onboard monitoring, and rehabilitation after landing.

2. *Muscle Changes*
   The muscle atrophy associated with spaceflight is viewed as a major threat to an exploration-class mission because the crew may be unable to deal with an emergency requiring muscular strength and may be prone to exertional muscle injury. Research will address mechanisms of muscle atrophy, response to muscle loading, and neuromuscular changes in 0*g*.

3. *Nutrition, Physical Fitness, and Rehabilitation*
   Astronauts in orbit lose muscle mass and strength, show significantly reduced aerobic capacity, and eat less than they do on Earth. Research in this area seeks an integrated approach to minimizing these changes during space missions and techniques for rehabilitation on return to Earth.

4. *Neurovestibular Adaptation*
   Research during the Shuttle era focused on problems associated with arrival in orbit due to changes in otolith function and the vestibulo-ocular reflex, as well as prediction of space sickness. Expedition-oriented research turns toward methods of preadaptation, improved drug countermeasures, the use of artificial gravity, and especially neurovestibular impairment and rehabilitation on return to a 1*g* field.

5. *Hematology, Immunology, and Infective Processes*
   In addition to the self-limited 10% reduction in plasma volume and RBC mass known to develop in orbit, interplanetary crews may be predisposed to secondary immunodeficiency due to a combination of stress, isolation, microbial contamination, nutritional deficit, and radiation exposure. Scientists seek to develop countermeasures for possible altered immune response, viral reactivation, and radiation-induced microbial mutation in flight.
6. *Bone Loss*
   Because bone loss in 0*g* progresses at a rate

of 1% to 2% per month indefinitely, astronauts could return from Mars with a 20% deficit. Major concerns include progressive osteoporosis and the associated problems of increased fracture risk and delayed bone healing, soft-tissue injury, and renal calculus formation. Research goals include screening out candidates at increased risk and optimizing environmental, nutritional, and hormonal conditions to minimize loss. Furthermore, astronauts must be given some assurance that recovery will occur following their retmastonurn to Earth.

7. *Radiation Effects*
   Astronauts en route to Mars risk clinically significant exposure to radiation from galactic cosmic rays and high-energy solar particle showers. These types of radiation have not posed a major problem in low Earth orbit, and their bioeffects are not well understood. Studies with animals indicate that disruption of the function of the central nervous system is a possibility; other concerns are accumulating cellular pathology and carcinogenesis. Research in this area includes improved prediction of space radiation effects on human health, identification of appropriate biomarkers, and provision of effective shielding and pharmacological countermeasures.

8. *Human Performance, Sleep, and Chronobiology*
   Crews in orbit have experienced chronic sleep disturbances due to stress and the artificial environment in which they live. Research focuses on methods of minimizing these effects as well as techniques for monitoring sleep and performance.

9. *Neurobehavioral and Psychosocial Factors*
   Crew composition, leadership style, and communication with Earth posed significant difficulties aboard Russia's Mir space station but are only now receiving serious research attention. The prolonged isolation and close confinement of a mission to Mars will place extreme stress on individual function and group effectiveness; breakdown at either level could threaten crew performance and productivity and the safety of the mission. Research areas include crew selection, preflight training, and support mechanisms in flight.

10. *In-Flight Medical Care*
    Medical emergencies and traumatic injury to crew members are real possibilities in the course of a long mission that offers no possibility of medical evacuation. Although the crew will likely include a physician, he or she cannot be expected to provide specialist knowledge in all areas. NSBRI is therefore investigating "smart medical systems," such as

    - onboard computer systems for monitoring the crew, diagnosing problems, and assisting with surgical procedures, and
    - communications systems designed to work within the effects of bandwidth limitations and the delay of up to 40 minutes between transmission of information from the spacecraft and the receipt of answers from Earth.

Many of the problems described by NSBRI relate to the absence of gravitational stress during spaceflight; experience aboard Russia's Mir space station shows that even vigorous exercise programs fail to prevent debility. Although artificial gravity on the scale seen in the motion picture *2001: A Space Odyssey*,[74] is unlikely to be provided by spacecraft in deep space, a more realistic possibility is development of a short-arm centrifuge combined with a cycle or other exercise device that would provide a Gz acceleration gradient sufficient to maintain at least partial adaptation to gravity. Such a device could be tested aboard the space station to optimize required workout schedules.

SUMMARY

Despite the relatively small number of flight opportunities, much has been learned about living and working in space. The knowledge gained has contributed to improved safety and performance on space missions and to a better understanding of human physiology on Earth. However, much work remains for the aeromedical military physicians of the future. We hope that readers will find aerospace physiology and medicine exciting and challenging as they provide support for flyers in this most unusual operational environment.

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