History of Nutrition in Space Flight: Overview

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Major accomplishments in nutritional sciences for support of human space travel have occurred over the past 40 y. This article reviews these accomplishments, beginning with the early Gemini program and continuing through the impressive results from the first space station Skylab program that focused on life sciences research, the Russian contributions through the Mir space station, the US Shuttle life sciences research, and the emerging International Space Station missions. Nutrition is affected by environmental conditions such as radiation, temperature, and atmospheric pressures, and these are reviewed. Nutrition with respect to space flight is closely interconnected with other life sciences research disciplines including the study of hematology, immunology, as well as neurosensory, cardiovascular, gastrointestinal, circadian rhythms, and musculoskeletal physiology. These relationships are reviewed in reference to the overall history of nutritional science in human space flight. Cumulative nutritional research over the past four decades has resulted in the current nutritional requirements for astronauts. Space-flight nutritional recommendations are presented along with the critical path road map that outlines the research needed for future development of nutritional requirements. *Nutrition* 2002;18:797–804. ©Elsevier Science Inc. 2002

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INTRODUCTION

The purpose of this introductory article is to review the historical efforts that resulted in our current knowledge of space flight nutrition and food science. Based on this knowledge, joint US–Russian nutritional recommendations (Table I) were developed and implemented.[1] Humans have adapted well to space flight, and over the past 40 y, we have substantially increased our understanding of the various physiologic changes that occur during and after space flight.[2] However, the underlying mechanisms for many of these alterations remain unclear. The articles in this special issue collectively describe prior and ongoing nutritional research undertaken with the goal of assuring human health and survival during space flight. Nutrition and food science research overlap with or are integral to many other aspects of space medicine and physiology including psychological health, sleep and circadian rhythmicity, taste and odor sensitivities, radiation exposure, body fluid shifts, and wound healing and to changes in the musculoskeletal, neurosensory, gastrointestinal, hematologic, and immunologic systems. Recent advances in genomics and proteomics are just beginning to be applied in space biomedical research, and it is likely that findings from such studies will be applicable to applied human nutritional science. The US space life sciences research community has developed a set of critical questions and a road map (Fig. 1) to clearly emphasize research efforts that ultimately will reduce to humans the risk associated with space travel and habitation.[3] Relevant research has been conducted in space and on the ground using animal models and human ground-based analogs.[4]

Throughout the four-decade history of human space flight, nutrition and food research have been an integral component of various missions (Table II). On October 4, 1957, the Soviet Union launched the first successful orbital satellite, Sputnik 1. Nearly 4 y later, on April 12, 1961, Soviet cosmonaut, Yuri Gagarin, orbited the Earth for 1 h 48 min in Vostok 1, becoming the first human to experience the sense of weightlessness technically termed *microgravity* or *hypogravity*. In the following month (May 5, 1961), the first US suborbital space flight by American astronaut, Alan Shepard, lasted about 15 min. A few months later (August 1961) in Vostok 2, Soviet cosmonaut, German Titov, became the first human to eat in space, an event that heralded the need for space flight nutrition support and research. The first American in orbital flight was John Glenn (February 20, 1962) in a Mercury capsule launched by an Atlas rocket. Glenn was the first American to consume food in the environment of space during this historical flight. Although seemingly insignificant now, at the time no consensus existed among American scientists concerning the ability of humans to eat, swallow, and process food normally in the microgravity of space and the prior experience of the Soviets was unknown to American specialists. Astronaut Glenn's meal included 80 kcal of applesauce, 130 kcal of beef and gravy, and 60 kcal of vegetables, all consumed at ambient temperatures with no utensils[5] and provided in aluminum tubes. The first woman to eat in space was Soviet cosmonaut, Valentina Tereshkova, aboard Vostok 6, a nearly 3-d flight during June 1963. From 1961 through 1963, during the Soviet Vostok and American Mercury programs, life science studies were primarily observations of physiologic effects such as postflight orthostatic intolerance (difficulty staying in an erect position). As missions were lengthened, life science studies became more important, and within this framework nutritional research has expanded in scope.[2] Human presence in space has been nearly continuous since these early flights. Missions have ranged from about 15 min to 14 mo, with goals varying from global environmental surveillance to lunar exploration. With each generation of spacecraft, the typical mission length progressively increased until the mid-1990s, when many human space missions lasted from 3 to 6 mo. Until the beginning of the International Space Station (ISS), all human habitable spacecrafts were built by the Soviet Union/Russia or the United States, and both countries have made enormous contributions to human space-flight capabilities, science, and technology. The ISS is a joint effort of interna-

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TABLE I.

DAILY NUTRITIONAL REQUIREMENTS FOR INTERNATIONAL SPACE STATION MISSIONS UP TO 360 D

Nutrient	Units	Requirement
Energy	KJ (kcal)	WHO* equation
Protein	%Total energy consumed	12–15
Carbohydrate	%Total energy consumed	50
Fat	%Total energy consumed	30–35
Fluid	mL/MJ consumed or mL/kcal	238–357 or 1.0–1.5 or 2000 mL/d
Vitamin A	μg retinal equivalent	1000
Vitamin D	μg	10
Vitamin E	mg α-tocopherol equivalent	20
Vitamin K	μg	80
Vitamin C	mg	100
Vitamin B12	μg	2
Vitamin B6	mg	2
Thiamin	mg	1.5
Riboflavin	mg	2
Folate	μg	400
Niacin	NE or mg	20
Biotin	μg	100
Pantothenic acid	mg	5
Calcium	mg	1000–1200
Phosphorus	mg	1000–1200 <1.5 times Ca intake
Magnesium	mg	350
Sodium	mg	1500–3500
Potassium	mg	3500
Iron	mg	10
Copper	mg	1.5–3.0
Manganese	mg	2.0–5.0
Fluoride	mg	4
Zinc	mg	15
Selenium	μg	70
Iodine	μg	150
Chromium	μg	100–200

* Individual energy requirements are calculated with the WHO equation, accounting for weight, age, sex, and moderate activity levels.
WHO, World Health Organization

tional partners including the European Space Agency, Japan, Russia, Canada, Brazil, and the United States.

US MISSIONS

Gemini missions, as implied by the name, were flown with two crew members.[2] Of the 10 missions, the shortest was about 4 h and the longest was nearly 14 d. The first space rendezvous and the first extravehicular activity were successfully completed, thus providing invaluable knowledge for future engineering and operational activities. The Gemini experience vastly increased our understanding of human performance in space and provided the basis for many improvements in extravehicular space suits. During the Gemini program, life sciences research was confined largely to medical examinations of astronauts before and after flight. These missions with their increased durations were the first to place emphasis on in-flight nutrition. They also helped define the critical issues related to the physiologic stresses of returning to Earth gravity.

The ambitious Apollo program had two primary goals: 1) to land humans on the Moon—a feat of both military and aerospace significance and a source of immense national pride, and 2) to return lunar geologic samples to Earth for intensive study. These studies provided an increased understanding of the origins of the universe.[6] Exposure to microgravity was short for the lunar astronauts—the journey to the Moon took 4 to 5 d one way—but these missions posed a potentially significant risk of radiation exposure through the combination of the flights to and from the Moon and time spent on the lunar surface without the protective shield of Earth's atmosphere. During some of the missions, physiologic studies were completed in the areas of endocrinology, clinical chemistry, hematology, immunology, cardiology, exercise, stress, nutrition, musculoskeletal, and neurovestibular research. Initial medical standards were established for in-flight care of crew members during the Apollo program.[7]

The Skylab program provided extensive data on human physiology during long-duration space flight. The three missions (Skylab 2, 3, and 4) with three male crew members each, lasted 28, 59, and 84 d, respectively.[8] Skylab missions provided an orbiting laboratory for life sciences research with the primary goal of investigating physiologic changes during exposure to the microgravity of space flight. Experiments were designed to study the cardiovascular and musculoskeletal systems, exercise physiology, clinical chemistry, hematology, neurophysiology (including sleep studies), radiation, and environmental monitoring. Essential to the success of many of these studies was the collection of excellent and detailed data on nutrition status and food intake. Thus, food (including frozen varieties) was provided as a metabolic diet, and metabolic balance studies for macronutrients were completed.

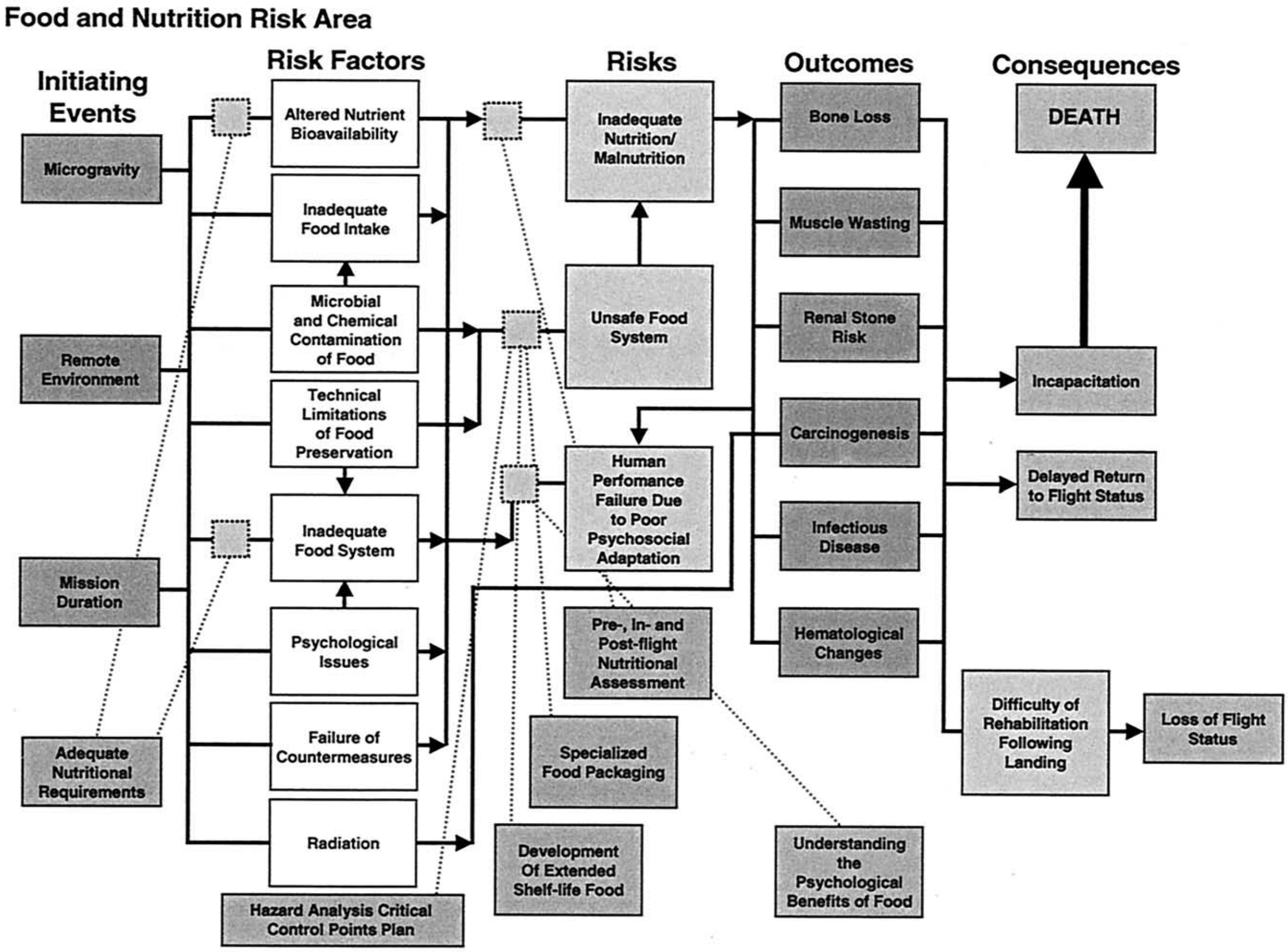

FIG. 1. Schematic detailing the effects of conditions, risks, and consequences of unmitigated risk associated with long-duration space missions on food and nutrition parameters. Interrelationships between different parameters are indicated. Shaded boxes represent intervention criteria that would mitigate the designated risks. The complete critical path road map for space life sciences is found at: http://criticalpath.jsc.nasa.gov.

Skylab was the only program to have a food system that met all nutritional requirements. During these three missions, the National Aeronautics and Space Administration (NASA) obtained the most complete set of space nutritional data,[9] and these data constitute the baseline for most of our understanding of nutritional requirements during spaceflight.[1,9–11]

The US Space Shuttle missions have focused on planetary and Earth science, on launching and repairing satellites, and on microgravity and gravitational biological research. The Shuttle program has comprised four dedicated life sciences missions: Space and Life Sciences 1 and 2 in 1991 and 1993, respectively, Life and Microgravity Sciences in 1994, and Neurolab in 1998. Research included studies on fluids and electrolytes, protein and calcium metabolism, hematology, the cardiovascular and musculoskeletal systems, and neurophysiology.[12] Studies conducted on three of the Spacelab missions provided major nutritional information for space research, second only to the data collected during the three Skylab missions.

SOVIET/RUSSIAN MISSIONS

The Soyuz missions brought dramatic changes in the Soviet Union's human space program. With crews of two or three cosmonauts, mission lengths were increased up to 237 d. Multiple Soyuz spacecraft designs were launched, with upgrades for each new model. The Soyuz missions conducted life sciences research that provided the foundation for the Salyut space station era. These flights had durations ranging from 8 to 326 d and provided important medical sciences research. Studies focused on the effects of weightlessness through extensive preflight and postflight examinations. Work–sleep schedules were normalized to Moscow time, and psychological support measures were developed. These experiences proved invaluable for maintaining a highly productive crew during exposure to microgravity in a closed system surrounded by the hostile space environment. The space diet subsequently used by the Russians during the Mir space station era was validated during the Soviet Soyuz/Salyut period. The diet was fed to ground-based subjects living in a closed chamber for long durations. During these long test periods, associated nutritional and palatability evaluations were completed.[13]

The launch of space station Mir by the Soviet Union in 1986 forever changed the reality of long-duration human space flight.[2] The Mir was designed for a crew of two to three, but during mission transition times, combined crews of five or six members remained aloft for several days to a few weeks. The Mir missions demonstrated that humans could tolerate microgravity for more than 1 y. Numerous onboard experiments were completed that included growing plants in space, nutrition studies, and other major life sciences research. Beginning in 1995, seven US astronauts participated in separate Mir missions lasting from 3 to 6 mo. The NASA–Mir program provided an opportunity to study crew members for longer periods with a limited set of experiments

TABLE II.

HISTORICAL SUMMARY OF HUMAN SPACE FLIGHT

Years	Program	Accomplishments related to life sciences
1961–1963	Vostok	First human to orbit the Earth (Gagarin), April 1961, 108 min
1961–1963	Mercury	First US astronaut in suborbital flight (Shepherd), May 1961, 15 min First US astronaut to orbit the Earth (Glenn), February 1962, 4 h 55 min
1964–1965	Voskhod	First shirt-sleeve environment; first life science activities
1965–1966	Gemini	Extended human stays in space Life science research performed during spaceflight
1968–1972	Apollo	Work on lunar surface by 12 US astronauts First human exposure to one-sixth gravitational field Life science research performed during space flight
1967–1985	Soyuz and Salyut	Life science research performed during space flight Russian space station, maximum time 188 d in space Life science research performed during space flight
1973	Skylab	First space station with life sciences as primary objective First metabolic studies completed in space
1975	Apollo–Soyuz test project	First joint Soviet/US program; first international orbital docking
1981–present	Space Shuttle	Deployment and retrieval of research satellites Observations of Earth and space targets Some life science research on most flights; four missions totally dedicated to life science research
1986–2000	Mir	Russian space station, maximum time >1 y for three cosmonauts Life science research performed during space flight
1994–1998	Shuttle/Mir	Joint Russian–US program Life science research, including skeletal muscle monitoring
1999–future	International Space Station	Will have international crews initially from US and Russia and then from Canada, Japan, and European countries; human research

(limited by the type of equipment available on orbit and by supply logistics). The Mir experience also provided an opportunity for the US to work with an international crew and to evaluate the psychological and social issues of diverse cultures in relation to long-duration space flight.

The NASA–Mir crew members shared US- and Russian-supplied foods. Both countries agreed to joint nutrition and food quality standards that included microbiologic and taste and palatability assessments. US and Russian crew members tasted the food before flight to determine acceptability, and menus were planned to include four meals per 24 h supplied as half Russian and half US. All food was stored without the benefit of refrigeration under ambient temperature and pressure. The water supply was limited to recycled condensate supplemented by the launch of potable water by other spacecraft such as Progress capsules and the Space Shuttle during docking; thus, the use of dehydrated foods was limited. The foods were primarily thermostabilized or of reduced moisture, and limited food warming capabilities were available. Information gained from these joint missions has enabled development of protocols that support human space flight and crew rehabilitation upon return to Earth. During its orbital life, the Mir space station hosted crew members from many nations and provided the international community with a preview of operations and human habitation on the ISS.[14]

INTERNATIONAL SPACE STATION

The ISS is providing another phase of human life in space flight. The collective extravehicular activity time scheduled will total about 500 h, more than the total extravehicular time logged by the Soviet/Russian and US space programs combined through 1998. Basic research will exploit microgravity as a laboratory tool to explore many facets of molecular biology and cell culture. Eventually all 16 international partners will provide crew members, making the station a space-borne international community. Crew diversity will provide challenges for nutritional scientists because international crews will have different food preferences and eating habits.[15]

ENVIRONMENTAL ASPECTS OF SPACE FLIGHT

Space flight exposes astronauts not only to microgravity and increased ionizing radiation levels but also to many potentially adverse factors associated with living in the confined volume of a spacecraft. These include changes in atmospheric pressure, temperature, and humidity; elevated levels of air contaminants and CO_2; and increased psychological stress.[16] Although microgravity itself is probably the driving force for many of the changes in skeletal muscle structure and function, cardiovascular performance, gastrointestinal and neurosensory effects, other environmental factors such as radiation and stress may affect numerous physiologic and metabolic processes that impinge on, or interact with, the crew member's nutrition status.

Environmental conditions in the enclosed pressurized spacecraft[16] are quite different from ambient Earth conditions (760 mmHg, 20% O_2, $< 0.1\%$ CO_2). Early US spacecrafts were pressurized at 258 mmHg (34.5 kPa), with a 100% oxygen atmosphere. In the Apollo spacecraft, CO_2 reached a maximum level of 7.6 mmHg. Atmospheric conditions on Skylab were 258 mmHg, with a gaseous mixture of 70% oxygen and 30% nitrogen. The Soviet/Russian program used an atmospheric pressure of 760 mmHg, with 19% to 30% oxygen, and the US Space Shuttle orbiter is maintained at 760 mmHg, with 21% oxygen and 79% nitrogen. ISS maintains atmospheric conditions similar to those of the Space Shuttle. However, due to engineering and structural design limitations, spacecraft for long trips outside low Earth orbit (exploration class missions) will probably have pressures near 362 to 414 mmHg (48 to 55 kPa), possibly with an elevated oxygen percentage and about 0.3% CO_2 concentrations. It is presumed that such missions will not have resupply capabilities. Currently, it is unknown how the lower pressure, higher oxygen percentage, and slightly elevated CO_2 levels will affect the physiologic or nutrition status of crew members.

Spacecraft require air handling systems capable of removing metabolic products like CO_2 and potentially toxic air contaminants.[16] In addition, all non-metabolic substances are controlled to ensure that neither flammable nor potentially harmful substances are present in the atmosphere.[17,18] Microgravity, however, introduces some unique problems to atmospheric control: skin shedding and other organic substances float in the spacecraft, providing excellent media for microorganism propagation. Hepafilters in the air recycling system help to control microbial growth, and chemical treatments and heat are used to remove compounds and metabolic products from the spacecraft atmosphere. For longer missions such as a trip to Mars or a return to the Moon, spacecraft environmental control will become even more complex. Current missions rely on basic provisions being launched initially with the spacecraft or resupplied, as is the case for ISS during docking of other vehicles. However, for exploration class missions, such a scenario becomes impractical because resupply is difficult to impossible due to logistics imposed by the distance from Earth. Biological and physical/chemical systems will be required for such missions to recycle air and water. Plants may be used in these systems, thus providing edible food for the crews.[19]

Availability of potable water affects the design of the food system and crew members' water intakes. The Shuttle systems produce water as a byproduct of power generation (fuel cells), so rehydratable foods can be used to reduce the required launch mass. For ISS, water is supplied through recycling of water condensate and transport of water up to the station by the Shuttle, Soyuz, or Progress spacecraft. Thus, the current ISS food system relies on foods as part of the water supply.

US water systems since Skylab have used iodine as the bactericidal agent, and this has complicated the interpretation of endocrine data. For most Shuttle flights and Skylab, reported thyroid stimulating hormone levels have been elevated after flight compared with preflight levels, but NASA has determined that the increase in thyroid stimulating hormone levels was due to the iodated water and not to a specific effect of microgravity on endocrine physiology.[20,21] There is no evidence to date showing that use of iodinated water has had a clinically significant effect on thyroid health.[20,21] However, the US space program now places limits on iodine concentration in the potable water supply by means of removing the iodine at the port that connects the water system to the food rehydration station (point of use).

Planning for long-term space flight also must include solutions to potential failures such as the loss of temperature and humidity control that occurred during the Apollo 13 mission.[6] Environmental system failures can affect all life support elements because of their interdependence. Examples can be found in the history of the Mir space station, which on occasion experienced prolonged periods of cold and warm temperatures with elevated humidity and CO_2 levels. During these periods there were constraints on water and power usage and on performance of exercise by the crew. All such failures have effects on food and fluid intakes. Water recycling constraints during a period of high ambient temperature have led to poor fluid consumption and power limitations have restricted astronauts to the consumption of cold foods. Periods of limited power or water and poor air quality always constitute a potential for serious problems. Thus, plans for nutritious food systems aloft must provide for possible emergencies.

Ionizing radiation has always been a space-flight concern.[22] Radiation exposures include acute, high-level exposures that may induce radiation sickness and chronic, low-level exposures that may increase cancer risk and immune dysfunction. At low Earth orbits (all US and Soviet/Russian human space programs to date except Apollo), acute radiation sickness has not been considered a high risk. Chronic exposures are limited to length of time allowed in low Earth orbit; usually missions are limited to 6 mo or less, although the Russian crew members have exceeded the 1-y mark on occasions. Radiation can damage cells, resulting in neoplastic and non-cancer pathologies. For example, Cucinotta and coworkers[23] recently reported an increased cataract incidence in US astronauts as compared with the incidence in the general population. For planetary travel, acute and chronic exposures are of concern. Galactic cosmic rays and solar particle events produce highly ionizing radiation including high energy protons and heavy ions. These types of radiation are potentially much more damaging than terrestrial radiation. Cucinotta et al.[24] reported chromosomal damage in lymphocytes taken from astronauts after space flight. The long-term significance of these chromosomal changes is not well understood, but biological monitoring of DNA damage is ongoing. Radioprotective interventions, including dietary components, may be needed for long-term space travel to reduce risks to crew members.

NUTRITION AND PHYSIOLOGIC CHANGES

Before the initial human flights into space, little was known about the physiologic aspects of space travel. For example, there were initial concerns about the ability to swallow, anorexia, and nausea in a microgravity environment, but it is now clear that cosmonauts and astronauts easily consume food and water.[9]

During various periods of their space programs and missions, the Soviet Union/Russia, the US, the European Space Agency, and Japan have focused on medical and life sciences research. Life sciences research from the early missions demonstrated decreased red blood cell mass,[25,26] altered immune function,[27] reduced appetite,[28,29] cephalad fluid shifts,[30] some neurosensory and cardiovascular changes,[31,32] and decreased body weight.[28,30] Despite the medical unknowns of early flight, cosmonauts and astronauts have performed well during space flight.[2] However, some of the original questions about physiologic mechanisms of adaptation to space are yet to be answered.

Psychological factors have important nutritional implications.[33,34] The isolated and unique environment of space presents additional stresses. In any intense, stressful situation with ample responsibilities and schedule pressures, nutrition status may be affected; space travel is no exception. For example, in space flight the most common response to schedule and time limitations is to skip meals and substitute with snacks. Current Russian and US biomedical programs include organized psychological support and training protocols to address the full spectrum of requirements from crew selection through postflight readaptation and rehabilitation. Training as a team is stressed, and family support during the mission is strongly encouraged. Food is an integral part of the celebration of family and holiday events, and special foods are provided to enhance the quality of daily life during space flight. These procedures appear to have been successful in maintaining high performance standards. Poor or inadequate sleep may affect eating and drinking behaviors, thus generating the potential for nutritional problems. Fatigue is a constant concern during preparation for and performance of a mission[31,32] and may reduce appetite and food consumption.

Some of the neurosensory effects of space flight include decreased ability of the subject to maintain a stable eye level (gaze) in microgravity; this can be mitigated in part by control of head movements.[31] These problems may lead to space motion sickness resulting in nausea that adversely affects the desire to eat. After launch and orbital injection, when crew members are free to move about the spacecraft, some 50% of crew members experience space motion sickness, with a reported 70% occurrence in rookie flyers.[35] Thus, food and fluid consumption may be low early in flight and during the first hours after return to Earth. This provides even more reason to launch well-nourished crews and to maintain a good nutrition status during flight.[36]

Gastrointestinal changes may affect the nutrition status through changes in appetite or absorption. Astronauts experience gastrointestinal changes early in flight. Gaseous stomach distention occurs due to the inability of gases to rise in microgravity. Chronic inactivity increases gastrointestinal transit time and potentially changes gastrointestinal microflora.[37] Further, the effects of microgravity are presumed to alter the physical contact between gastric contents and the gastrointestinal mucosal cells, thereby decreasing absorption. Anecdotal information suggests constipation is common in flight; however, this prevalence has not been well documented. Cephalad fluid shifts in combination with commonly observed dehydration may affect gastrointestinal motility, possibly through reduced splanchnic blood flow. Hepatic function in space has not been measured directly in humans. Comparison of some preflight and postflight indirect measures of liver function have shown a statistically significant change in serum γ-glutamyltranspeptidase activity, but the clinical significance of this finding is unclear.[37,38]

Crew members report changes in taste, particularly for specific foods. Two studies have examined changes in sensitivity to odors and tastes. Watt et al.[39] measured the detection and recognition threshold sensitivities of two astronauts to sweet, salty, sour, and bitter tastes and to lemon, mint, and vanilla odors. Although they found some shifts in the threshold levels for detection of some tastes and flavors, these shifts were highly individualized and were not statistically significant. In comparing flight data with preflight measurements, they found no impairment of astronauts' abilities to identify odors. A ground-based study[40] that simulated the nasal congestion of space flight by using an analog of space flight (6-degree head-down supine bedrest) also found no consistent changes in odor and taste perception. In this study, six subjects were maintained in a 6-degree head-down supine bedrest for 15 d. Their taste and odor sensitivities were determined before bedrest, during bedrest when there was nasal congestion, and after cessation of bedrest. Taste was measured using sucrose, sodium chloride, citric acid, quinine, monosodium glutamate, and capsaicin; odor was measured using the volatile compounds isoamylbutyrate and menthone. Neither bedrest per se nor nasal congestion affected these measures of taste and odor sensitivity. Anecdotal crew reports, however, suggest that there are changes in taste and odor sensitivities, both of which could affect appetite and eating habits.

Fluid status and changes in red blood cell mass have been some of the most extensively researched nutritional issues of space flight.[25,26,30] This research emphasis had its inception in the profound changes noted even in the initial flights of Gemini. During the early phases of human spaceflight (1 h to 1 d), plasma volume decreases. Without gravity to pull the blood toward the feet, there is fluid congestion in the chest and head.[30,36] The decreased plasma volume and lack of gravitational pull have immediate effects on the cardiovascular system. Catecholamine receptor and endocrine organ responses to shifts in fluid status are probably altered. The reduced plasma volume causes an increased concentration of red blood cells (hematocrit), which in turn decreases blood erythropoietin levels. Eventually a new set point of about 15% below Earth levels is achieved in both plasma volume and red blood cell mass. Return to Earth produces a relative space flight "anemia" because the plasma volume returns more quickly to preflight levels than does the red blood cell volume.[25,26,30]

Under current flight protocols, crew members consume the equivalent of approximately 1.0 L of saline solution immediately before the spacecraft leaves orbit to return to Earth. This is believed to replace about half of the plasma volume decrement.[30] Within a day or two after return to Earth, plasma volume returns to preflight levels. The percentage of red blood cells in venous samples (hematocrit) decreases with the restoration of the plasma volume, but red blood cell mass returns to preflight values over the next month or so, restoring the hematocrit to preflight levels. Nutritional requirements for fluids and iron are related to these physiologic changes.

Immune function has been studied rather extensively during the past 20 y of space flight. The initial studies showed depressed cellular immunity after space flight[27] and more recent research indicated latent virus reactivation[41] and a decreased ability of phagocytic cells to kill bacterial invaders.[42] Although there is considerable active research into the role of nutrition in immune system maintenance, very little has been completed with respect to the impact of nutrition on the immune system in space flight.

Microgravity significantly affects body composition, particularly the musculoskeletal system. Muscle and skeletal changes are caused by a combined lack of the Earth's gravitational field and normal ambulation.[43–45] Although some researchers have hypothesized that length of space flight would be the most important factor in muscle loss, decreases in muscle mass appear to occur primarily during the first month of flight. The rate of loss does not appear to increase with longer flights, but limited resistive exercise by crew members may have prevented continuous losses. Skeletal losses, unlike muscle losses, do appear to be related to length of flight.[43,45] Approximately 0.4% to 1.6% (depending on the bone measured) of bone mineral is lost per month during space flight. The role of nutrition in musculoskeletal losses during space flight has not been clearly defined, but data from Skylab missions demonstrated negative nitrogen and potassium balances despite supposedly adequate ingestion of energy and protein sources.[29] Return to Earth poses a major concern. The risk of stress fractures, muscle strains, and ligament stresses increases, and the ability to ambulate normally may take 2 to 8 wk after return to Earth. Muscle rehabilitation after long-term space flight is managed by traditional methods, with gradual increases in strength training and the use of swimming to restore aerobic capacity. The return of bone mass takes much longer—some investigators estimate two to three times as long as the time spent in space flight.[43]

Gender differences[46,47] and nutritional requirements have been reviewed, but no nutritionally relevant conclusions have been made except for the differences due to lean body mass and total mass. Of the 307 US astronauts, only 33 have been women and fewer than that have participated in life sciences research. With the completion of ISS Expedition 3 and STS-108, women flying with NASA accounted for a little more than 27,220 h in space flight compared with more than 185,777 h for men. As reported by Harm et al.,[46] the differences between individuals are larger than the known differences due to gender; however, women may have a lower risk for renal stones. Waters and coworkers[47] found that the incidence of presyncope (*syncope*, fainting due to cardiovascular changes) during standing immediately after space flight was greater in women than in men. Also, presyncopal female crew members showed a hypoadrenergic response during the immediate postflight period as compared with male crew members who had no presyncopal response. With continued research on women in space flight, gender differences may emerge, especially within the musculoskeletal, cardiovascular, endocrine, and reproductive systems.

Research on other micronutrients and physiologically active food components is incomplete. An example is the limited understanding of fiber needs during exposure to microgravity. During the Skylab missions, dietary total crude fiber levels were 5 to 10 g/d.[48] In 1991, NASA accepted the goal for dietary fiber as 10 to 15 g/d.[49] Due primarily to the Russian food system, the total calculated fiber per crew member on the ISS is 28.5 to 32.5 g/d. The only micronutrients studied during the NASA space program have been iron,[25] iodine,[21] folic acid,[50] and pyridoxine.[51]

Animal studies have evaluated the effect of space flight on physiology including investigations of the musculoskeletal, immunologic, and cardiovascular systems. However, with the exception of one energy expenditure study,[52] nutrition has not been the goal of these studies, although body mass and food intake have been measured incidentally. Animal housing and ambient conditions affect food intake, and these variables compound a nutritional assessment. Yet, given the limitations, there are a few studies with both monkeys and rodents reporting adequate food intake and maintenance of body mass.[53–56]

Although experience with long-term space flight has provided considerable confidence in the ability of the human body to recover from space flight and readapt to the Earth environment, effects observed on the long Skylab, Mir, and NASA–Mir missions have convinced flight physicians and scientists that countermeasures and monitoring are essential to the success of long-duration spaceflight. Countermeasures are methods used to limit the negative physical and psychological effects of the space environment on humans. Nutrition and foods are essential for maintenance of health and for enabling certain countermeasures such as exercise. Critical questions (http://criticalpath.jsc.nasa.gov) and a road map (Fig. 1) point to the important areas of nutrition and food science research needed in the future. These include development and use of genomic and proteomic research and development and use of other advanced technologies. There must be interactions between the various disciplines to determine the underlying mechanisms and to apply them to nutritional requirements to ensure a healthy and productive crew. However, due to limitations of spaceflight research opportunities, ground-based models are essential for understanding nutrition-related physiologic changes and their underlying mechanisms. Such models include traditional cell culture[57] including the NASA-invented bioreactors, animal studies, and human bedrest and other ground-based analog studies.[58] Recently, isolation environments such as wintering over in Antarctica or Devon Island Station, Canada, and closed-chamber studies[59] have provided good tools for nutrition research. Nutrition research efforts require a wide range of models and interdisciplinary approaches including contributions from physiology, biochemistry, psychology, food science and technology, horticulture, and advanced medical technologies.

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