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ORIGINAL CONTRIBUTION

Hellas Cena
Michele Sculati
Carla Roggi

Nutritional concerns and possible countermeasures to nutritional issues related to space flight

Summary The experience obtained in astronauts until now has revealed many nutritional problems during both short- and long-term missions that are still under investigation.

When the manned space program evolves to the point where it involves a considerable number of people operating at great distances from the Earth for long periods of time, continuous provision of food as well as physiopathological modifications partly related to nutrition will remain a challenge. Human space missions have outlined the importance of the diet on the quality of an astronaut's life, not only because an appropriate nutritional status can be maintained only through an adequate nutrient intake, but also because food plays an important socio-psychological role.

A great amount of research has been done both by the Russian and American teams in order to identify the nutritional requirements for humans during space flights. Crew members should be provided with nutritional adequate diets characterized by many different food items carefully selected according to technological techniques aimed to ensure long shelf-life periods, health, safety, satisfaction and convenience. An astronaut's nutritional status is greatly influenced by important weightlessness, environmental physiological adaptations.

Changes in muscle and bone mass, modifications of gastro-intestinal functions and immune alterations may be partly limited by adequate planned dietary countermeasures.

Key words spaceflight – nutrition – effects of microgravity – weightlessness – dietary countermeasures

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Dr. H. Cena · Dr. M. Sculati · Prof. C. Roggi
Department of Health Applied Sciences
Section of Human Nutrition
University of Pavia, Italy

Dr. Hellas Cena (✉)
Via Bassi 21
27100 Pavia, Italy
Tel.: +39-3 82/5 07-5 42
Fax: +39-3 82/5 07-5 70
E-Mail: hcena@unipv.it

Introduction

Manned space programs in the future will include extended missions to the moon, to Mars or beyond; as mission lengths continue to increase, nutrient imbalances due to alterations in dietary intake, bioavailability or excretion may become more important. Moreover the participation of international partners will provide crew members with different preferences and eating habits according to the different cultural background and country of origin; this will offer further challenges in the development of food systems and countermeasures necessary to preserve health. Considerable information has been collected on short-term missions regarding swallowing, symptoms like anorexia and nausea, food intake and nutritional status.

Factors such as limited food choices, preparation, and storage facilities on spacecraft may influence the astronaut's food intake. Voluntary dietary intake is reduced during spaceflight by about 20 % [1] leading to inadequate nutrition, a health-threatening condition in future long-term missions.

Many ground-based closed chamber studies have been conducted since then on the astronauts' diet adequacy provided by the spaceflight food systems outlining that the nutritional standard criteria chosen for subjects living on Earth, may be inadequate for extended missions [2].

Therefore, more emphasis has to be placed on inves-

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tigating the effects of dietary intake during long-term exposure to microgravity in astronauts [3]. As the understanding of how weightlessness affects physiology becomes more complete, new recommendations have been and will be set for all nutrients in order to enhance mission safety and crew well-being.

Protein and muscle homeostasis

One of the most consistent and physiologically important spaceflight findings is the loss of body protein. Studies on protein loss and its effect on the musculoskeletal system were conducted both on Skylab and Shuttle. Decrease in muscle mass occurs after both short and long missions, mainly in muscles with antigravity functions (Table 1) [4], despite attempts to ensure an adequate diet and a vigorous exercise regimen.

Magnetic resonance imaging analysis after a 115 day mission in 1995 revealed that protein loss from the various muscle groups ranged from 10 to 20 % [5]. On Skylab, most occurred in the first month, but continued up to the third month. Such losses are documented by nitrogen balance data, reported from data collected in various missions (Table 2) [6]. The deterioration of muscle mass caused by weightlessness is similar to that found with bed rest, characterized by protein loss while energy stores usually remain intact.

Table 1 Changes in muscle volume of four astronauts 1 and 15 days after an 8-day space shuttle mission

Muscle	% change	
	R + 1	R + 15
Calf		
Anterior	−3.9 ± 0.5	−3.3 ± 1.1
Soleus + gastroc.	−6.3 ± 0.6	4.4 ± 2.2
Thigh		
Quadriceps	−6.0 ± 1.7	−3.1 ± 2.3
Hamstrings	−8.0 ± 0.9	−4.8 ± 1.3
Lumbar		
Intrinsic	−10.3 ± 2.4	−5.9 ± 1.5
Psoas	−3.1 ± 1.5	−2.4 ± 1.6

From: Le Blanc et al, 1995
Data are ± SE. *R* Recovery day. *% change* flight vs. preflight

Since the first space missions, protein requirement, bioavailability, mechanism of action and supplementation have been considered. On most missions where protein intake has been measured or estimated, there is no evidence suggestive of inadequacy of the in-flight protein intake; except for particular phases of the mission, the in-flight amino-acid intake often exceeds requirements [5].

In fact, plasma levels of essential amino acids in short-term missions, in particular branched-chain amino acids, were increased even when there was a 20 % reduction in protein intake [7]. This event is explained to be a consequence of amino acid release from muscle.

After long duration flights, plasma amino acids may be reduced [7, 8] to support increased protein synthesis in the regenerating muscles. The increased muscle protein synthesis and the concomitant increase in acute-phase protein synthesis may become competitive; thus, leading scientists to hypothesize that there is some advantage in amino acid supplementation before landing and after long-term missions [1].

Research conducted until now does not entirely support the need for a constant in-flight supplementation; however, there is evidence in bed-rest studies for BCAA supplementation to counteract nitrogen loss [9].

In addition, it is well known that the role of these nutrients in a few conditions such as metabolic disorders, malnutrition or severe stress, becomes more and more important even with regard to the non-essential or "conditionally essential" ones, principally because their synthesis decreases [10].

Developing methods including nutritional support with amino acid supplementation that may counteract muscle atrophy would have great value not only for space flights but also within clinical medicine.

Further work is needed to determine optimal intakes of proteins for astronauts. In the weightlessness animal

Table 2 Summary of Shuttle (SLS-1 and SLS-2) and Skylab (Skylabs-2, -3 and -4) energy intake and estimated nitrogen balance data

	Shuttle SLS-1	Shuttle SLS-2	Skylab-2	Skylab-3	Skylab-4
Energy intake, Kcal · kg^{-1} · day^{-1}					
Preflight	44.5 ± 5.8 (3)	36.6 ± 2.4 (7)	39.2 ± 2.4 (3)	41.5 ± 2.1 (3)	42.6 ± 0.5 (3)
In flight	27.5 ± 1.1 (5)	32.9 ± 2.1 (7)	35.0 ± 2.0 (3)	34.2 ± 0.6 (3)	41.3 ± 1.1 (3)
Nitrogen balance, mg N · kg^{-1} · day^{-1}					
Preflight	66.1 ± 27.2 (3)	52.7 ± 6.3 (6)	81.3 ± 2.0 (3)	71.9 ± 10.2 (3)	68.7 ± 7.0 (3)
In flight	12.3 ± 5.0 (5)	19.6 ± 4.5 (6)	−1.2 ± 10.0 (3)	−35.8 ± 3.2 (3)	−18.5 ± 2.8 (3)

From: Stein TP, 1996
Data are means ± SE with no. of subjects in parentheses. Preflight data are for 10 days preflight; in-flight data are for 1st 12 days in-flight except for SLS-1 where only 9 days of data where available. Fecal nitrogen excretion was measured on Skylab but not on the Shuttle, assuming that daily fecal nitrogen excretion was 25 mg N · Kg^{-1} · day^{-1} for both Shuttle and Skylab, after adjustment for fecal nitrogen losses, the values are approximately –9 mg N · Kg^{-1} · day^{-1} for the Shuttle and –44 mg N · Kg^{-1} · day^{-1} for Skylab

model, high protein diets do not benefit the overall musculature [11]. In humans there is actually little evidence of benefit of increased intake of protein suggesting that current recommendations should not exceed the amount recommended for adults on Earth [12].

Besides the protein intake, the individual energy intake has to be taken into consideration, since much evidence has outlined that nitrogen balance improves as energy intake increases, suggesting that energy balance may be equally or even more important than nitrogen intake as a determinant of nitrogen balance [13, 14]. Supporting this, data available from a several-weeks' space mission reveal that loss of body mass during space flight is rather a consequence of under-nutrition and its accompanying effects [15]. Fairly accurate energy balance should be achieved taking in account individual estimated energy needs.

Exercise has been studied as a possible countermeasure but many related aspects have to be considered. Spaceflight suppresses exercise-induced release of bioassayable growth hormone [16]. Exercise must be done when the subjects are in energy balance [17]. Exercise generates waste products that cannot be disposed of rapidly: heat and CO_2; which may be one of the factors associated with depressed food intake [1].

Despite many attempts to counteract sarcopenia, there are still no fully effective measures for preventing muscle atrophy associated with spaceflight. Future researches should determine how much microgravity affects skeletal muscles during long missions in space and how long it takes for it to occur, so that predictions can be made regarding muscle changes, and thereby effective countermeasures can be developed to ensure health and performance during long crewed missions.

Bone mass

The reduction of bone mineral density (BMD) and the micro-structural changes of bone tissue, responsible for the increased risk of fractures and osteoporosis, are the major health concerns for manned spaceflight.

Losses in muscle strength, occurring in disuse and microgravity, decrease skeletal loading to the point where modeling is turned off and bone reabsorption exceeds formation [18]. This is followed by an increased plasma calcium concentration, a consequent down regulation of parathyroid hormone (PTH) and vitamin D [19], a reduction of active calcium absorption and an increase of urinary calcium excretion.

Bone mineral density reduction depends on the skeletal site, in particular: spine, femoral neck, trochanter, and pelvis (Table 3) [20–21], leading to a greater risk for earlier onset of osteoporosis of the astronauts returning to Earth.

Measurements during early space missions showed a wide variability in individual responses to microgravity on the calculated calcium balance value that was partly attributed to the different dietary calcium intake and partly to the different physical activity according to the mission.

Table 3 Bone loss during space flight on the Mir Space Station

	Mean loss (% per month)		
Variable	Mean	SE	n
Spine	1.07	0.15	18
Neck of femur	1.16	0.2	18
Trochanter	1.58	0.23	18
Total body	0.35	0.06	17
Pelvis	1.35	0.13	17
Arm	0.04	0.21	17
Leg	0.34	0.08	16

From : LeBlanc et al. (1996) and the National Research Council (1998).
Mean values with their standard error

Long-term effects from the Shuttle-Mir program supported earlier studies indicating that the rate of bone calcium loss is about 250 mg/d, that decreased calcium absorption is partly related to 1,25-dihydroxyvitamin D and PTH decreased concentrations, and that vitamin D body stores appear depleted because of the lack of ultraviolet light [22].

On the ground, it was shown that vitamin D supplementation increases bone calcium content [23], which is why astronauts are provided with oral vitamin supplementation that seems to be adequate for short-term missions [24], but maybe not for long missions [25]. Further studies are necessary to define the efficacy of vitamin D fortified diets, supplementation with vitamin D or even the use of ultraviolet light treatment in microgravity conditions, which works for post-menopausal women who often suffer bone loss in the form of osteoporosis, but may not work for astronauts in space.

It is possible that the extent to which dietary differences contribute to variability may be influenced by genetic variation [26]. Since diet and exercise were controlled in missions such as Skylab, genetic factors may be the dominant covariate, as they are for bone loss on the ground [27].

Recent studies provided interesting results on genes, such as the vitamin D receptor gene and polymorphisms of several other candidate genes, including those encoding for bone proteins, hormones and their receptors, cytokines, growth factors enzymes and transporting factors involved in mineral and bone metabolism. Yet the evidence provided until now indicates that 30–40 % of the variation in bone mineral mass is not accounted for by genetic factors. Nutrient-gene interactions have been observed on calcium absorption and calcium supplementation efficacy. Intestinal calcium absorption has been recently indicated to be reduced after only three weeks of microgravity exposure, in association with a severe suppression of circulating calcitriol levels, independent of the exogenous vitamin D supply and serum PTH levels [28]. Other nutrient-gene interactions have been observed, for example, in relation to the transport of vitamin K, an essential cofactor in the γ-carboxylation of osteocalcin, the increased intake of which has been indicated to counteract microgravity-induced bone loss [29, 30] associated with altered vitamin K metabolism and activity in cosmonauts [31]. In the 179-d Euro Mir 95 mission, investigators administered 10 mg of vitamin K from in-flight day 86 to day 136 in one astronaut. During and after supplementation, bone formation markers increased significantly during this part of the mission [32]. Therefore, vitamin K seems to play a significant role in bone turnover during space flight. However, the importance of such interactions is still under investigation.

The need to reduce bone loss has led to countermeasures that are studied mainly during bed rest experiments.

The past research programs on life sciences for spaceflight focussing on calcium balance and BMD took into consideration different potential countermeasures. Emphasis was principally on the following: exercise, especially high-load resistive exercise during bed rest [33–35] and immersion studies [36], vitamin D-fortified diets, supplemental vitamin D [37], the use of ultraviolet light treatment, and different biochemical regimens [18] such as bisphosphonates. Bisphosphonates are a class of antiosteoporosis drugs currently explored both in ground-based studies [38] and in hindlimb-unloaded animal model [39] that showed a protective effect, although the potentially adverse reactions and consequences during long-duration space flights are still unknown. The evaluation of the combined approach of using exercise and pharmacological interventions as well as vibration treatment [40, 41] may provide future synergistic benefits [1]. Although data from a recent study on three different strains of adult mice indicate that the sensitivity of trabecular tissue to both anabolic (low-level mechanical vibration) and catabolic (disuse) stimuli is influenced by the genome [42].

Evidence reported in a recent paper [32] suggests that in contrast to terrestrial conditions, high calcium intake, of at least 1000 mg/d, with vitamin D supplementation (650 IU/d of Ergocalciferol) during microgravity (data from the 21-d Mir 97 mission) do not efficiently counteract the development of space osteoporosis.

Diet alone is not likely to provide a direct remedy for weightlessness-induced bone loss; however it makes a sizeable contribution. It is essential that dietary calcium intake be adequate and at least brought up to the RDA level [1], since calcium and vitamin D intake is encouraged as a preventive and therapeutic measure on Earth [37]. The inability to check in-flight dietary intake or adherence to a dietary regimen leads to difficult interpretation of the results that on the recent shuttle-MIR missions show a 40 % reduction compared to preflight intakes [43]. Therefore it is obviously difficult to foresee how any countermeasure for bone loss may be helpful when intake is so low.

On the other hand, an excessive dietary calcium intake in flight may enhance the risk of renal stone formation which is already promoted by the hypercalciuria subsequent to the continuing loss of calcium from bones. The high Na content of space flight diets may also contribute, to a certain extent, to the promotion of urinary Ca loss as reported both in a spaceflight animal model [44] and in a recent five-year randomized trial study conducted on an outpatient population with recurrent calcium oxalate stones and hypercalciuria [45].

The high amount of sodium chloride in the diet, exceeding physiological requirements, typical of space flight diets, is also frequent in industrialized nations. The results of a study on postmenopausal women recently published propose that the addition of oral potassium citrate to a high salt diet prevents the increase excretion of urine calcium and the bone resorption marker caused by high salt intake [46]. Further research efforts in flight and on ground-based models for longer periods of time may elucidate the possible positive role of an increased consumption of dietary sources of potassium alkaline salts, namely fruit and vegetables.

In addition to the paper by Borghi et al. [45], significant observations are drawn on the influence of animal protein intake on calcium excretion. The reduced intake of protein, which may both affect tubular action [47] and lower the endogenous synthesis of oxalate [48], in association with a reduced salt intake and a normal-calcium intake, resulted in a reduction in calcium and urinary oxalate excretion.

Future studies on ground-based models should evaluate the evidence that diets with restricted intake of animal proteins and salt and a normal calcium intake provide greater protection from renal stone formation than the traditional low-calcium diet.

Other space-flight environmental factors and physiopathological modifications may contribute to increase renal stone risk such as urinary biochemistry changes, for instance super-saturation levels for calcium oxalate and phosphate, hypocitraturia, lower pH and lower urine volume compared with preflight values, promoting crystallization [49]. This suggests the importance not only of dietary factors (such as itamin B_6 deficiency associated with increased oxalate excretion [50] as well as calcium, protein, sodium previously reported) but also of fluid intake which tends to be reduced during space flight and which may in turn add the risk of urolithiasis.

The challenge for the research community is to optimize, using both ground-based models and in-flight studies, diet, exercise and anti-re-absorption drugs which remain, up until now, the most important factors to be modified. Bone research in space may add important insight into osteoporosis, which is a health problem facing society today.

Hormonal changes related to the nutritional status

The endocrine system appears to be sensitive to the conditions of space flight. Several hormones may increase in the circulation as part of the stress response to microgravity conditions, including epinephrine and norepinephrine, adrenocorticotropin, cortisol. These hormones play a role in the elevation of plasma glucose and fatty acids, in increased lipolytic activity in adipose tissue, in reducing lipogenesis and in raising glycogen content in the liver [51].

These hormones have been measured during and after space flight: data from Skylab show increases in catabolic hormones (cortisol, glucagone) and a prolonged elevation of 3-methylhistidine excretion, suggesting a chronic metabolic stress response that may be influenced not only by mission length but also by energy intake, exercise regimen and even gender [5, 52]. Such changes may indeed be involved in promoting muscle and bone loss, in impairing immune status, in the regulation of body fluids and electrolytes that affects the cardiovascular response to microgravity. Catecholamines as well as renin-aldosterone are also involved in fluid balance, being part of sodium-retaining endocrine systems; consistent observations in various missions (Mir 97, Spacelab mission D-2, Euromir 94) revealed an elevated activity that may lead to sodium storage without an accompanying fluid retention [53]. This may be part of the reason leading to an extravasation of fluid after an increase in vascular permeability. An enormous capacity for sodium in the extra vascular space and a mechanism that allows the dissociation between water and sodium handling may contribute to fluid balance adaptation in weightlessness [54].

Decreased plasma levels of anabolic hormones such as growth hormones and testosterone derivatives were found in cosmonauts after space flights exceeding 60 days; whereas the opposite was found after short duration space flights (3–10 days) [55]. The hypothalamic-pituitary-thyroid axis involves the thyroid hormones thyroxine and triiodothyronine, which are lowered in space, suggesting mild hypothyroidism [56].

Variations of growth hormone testosterone and thyroxin may contribute to the body's protein synthesis that is generally reduced in astronauts. The results of the observations on changes in endocrine functions of rats exposed to space flights for various periods show a decrease of testosterone and triiodothyronine plasma levels after space flight suggesting the suppression of thyroid and gonadal activity. Impairment in androgen production has been found in human subjects during space flight. The testosterone levels were decreased in various biological fluids in 7 astronauts during space flight, while a slight increase of LH values in plasma was noted as compared to pre-flight concentrations [57]. The cause for hypoandrogenism is unknown but it may depend on a fluid shift affecting testicular function or androgen distribution in various body compartments.

Despite having several women astronauts, no studies are available on their hypothalamic-pituitary-gonadal functions. Studies on the effect of spaceflight on women will be important as gender differences exist at various levels [56].

Many studies dealing with bed rest and head down tilt simulations showed a deterioration of the sensitivity to insulin over time, mainly considered one of the consequences of physical inactivity and subsequent sarcopenia. Humans in microgravity also show the same insulin sensitivity deterioration, as reflected by the excretion rate of the insulin precursor C-peptide [58].

The progressively increasing C-peptide excretion during a 9 d spaceflight is indicative of the development of insulin resistance in astronauts [59]. The negative nitrogen balance found towards the end of the mission in the Skylab astronauts correlates with the increased rate of C-peptide excretion, suggesting a role for the insulin resistance in the etiology of protein losses [60].

Of great importance is the finding that dietary factors can have a modulator action on insulin sensitivity. In animal experiments on earth, an increased intake of (saturated) fat and refined carbohydrates increased insulin resistance [61]. An extremely high carbohydrate to fat ratio improves insulin sensitivity, whereas more moderate changes produce less convincing results.

The available data support the idea that high carbohydrate diets do not adversely affect insulin sensitivity compared with high fat diets. In animals and in short-term human ground-based studies, a high intake of carbohydrates with a high glycemic index produced greater insulin resistance than did the intake of low-glycemic-index carbohydrates [62]. Epidemiological studies show that increased intake of dietary fiber appears to improve insulin action and may protect against the development of type II diabetes [62, 63]. In ground-based model studies, the response of humans and primates to a standard oral glucose tolerance test (OGTT) consists of an exaggerated hyperinsulinemia and hyperglycemia, sometimes referred to as bed-rest pseudodiabetes [64]. The mechanism for the intolerance is not only highly correlated with total daily energy expenditure, but is also associated with lack of intensive isotonic exercise. Blood glucose data collected on landing day and during short Space Shuttle flights have been studied. Smith et al. [65] found no changes in capillary glucose levels during space flight; yet data of several crew members, collected

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during longer flights, suggest slight ketosis and elevated landing-day blood glucose.

High-carbohydrate diets based on foods with a low glycemic index combined with high dietary fiber content should be evaluated on earth [66] and in microgravity conditions. The efficacy of the countermeasures applicable during space flight should be assessed taking into account the metabolic and functional modifications induced by changes of the hormonal pattern. A better understanding of these changes that partly resemble those observed during aging will contribute to physiological knowledge on senescence and counteractions of aging processes.

Gastrointestinal function

Astronauts experience gastrointestinal changes early in flight, gaseous stomach occurs due to the inability of gases to rise. Furthermore the effects of micro-gravity are presumed to alter the contact of the gastric contents with the gastrointestinal mucus. However, cephalic fluid shifts, in combination with commonly observed dehydration, could possibly affect gastrointestinal motility through reduced splanchnic flow.

The effect of chronic inactivity increases transit time and potentially changes gastrointestinal microflora [67]. Gastrointestinal integrity and bacterial balance may be improved by probiotics and prebiotics that should be studied for a possible inclusion in space foods.

Probiotics, defined as microbial food supplements that beneficially affect the host improving its intestinal microbial balance, have been studied to change the composition of colonic microbiota by increasing bacterial groups such as Bifidobacteria and Lactobacilli that are perceived as exerting health-promoting properties. However, these changes may be transient, and the implantation of exogenous bacteria becomes limited.

On the other hand, since astronauts do have an impaired immune function, as discussed in the next section, differences in the immunomodulatory effects of candidate probiotic bacteria should be taken into consideration and the positive effect should be studied in weightlessness models. The use of prebiotics partly overcomes the limitations of probiotics. Prebiotics are growth substrates and not viable entities, specifically directed toward potentially beneficial bacteria already growing in the colon [68].

Nondigestible oligosaccharides (NDOs) in general, fructooligosaccharides in particular, are the most investigated molecules with prebiotic activity. They have been shown to stimulate growth and or activity of one or a limited number of bacterial species already resident in the colon, thus, changing the composition of the microbiota, attempting to improve host health [69].

The effects of a prebiotic-containing food vs. placebo on the gut microflora of healthy human volunteers in a doubly blind crossover trial showed a significant increase of "beneficial" gut organisms (bifidobacteria) in the feces [70]. Evidence underlined that the response is not dose related but it depends on the gastrointestinal microflora composition prior to the intake.

Their functional effects beyond the colonic microflora are exerted on the gastrointestinal physiology, the immune functions, the bioavailability of minerals, and the metabolism of lipids. Potential health benefits may also concern reduction of the risk of some diseases like intestinal infections, constipation, non-insulin-dependent diabetes, obesity, osteoporosis or colon cancer [71].

Interesting results both from studies on animals and on humans on the Earth are those on mineral metabolism showing an increased absorption especially of magnesium and calcium, improving bioavailability of dietary calcium in humans [72, 73], and increasing bone mineral density in animal models [74–76]. However, in humans, long-term studies are required because it is impossible to extrapolate from short-term effects of NDOs on mineral absorption to effects on skeletal development or bone health [77]. Their positive role in reducing the risk of osteoporosis deserves further research in at-risk human populations including humans in microgravity conditions for long periods of time.

The range of foods into which they can be added is much wider than that for probiotics, where culture viability needs to be maintained. There are many potential applications for prebiotics as food ingredients to improve gastrointestinal health: virtually any carbohydrate containing food is susceptible to supplementation.

These fructooligosaccharides, such as oligofructose and inulin, can be combined with bifidobacteria to produce synbiotics which may have additive or even synergistic effects worthy of investigation [78]. In addition to their nutritional properties, they may also have technological advantages [79], improving the taste of food products which may counteract the decrease of palatability occurring in humans exposed to microgravity.

Gastrointestinal function plays an important role in the absorption and disposition of nutrients; thus, particular attention to specific nutrients which interact with the trophysm of enterocytes is required. There is increasing evidence that glutamine has a gut-protecting function; moreover the endogenous glutamine supply is insufficient in certain situations; factors contributing to a depletion of the glutamine pool include under-nutrition and metabolic stress. In the bowel, glutamine is the major fuel source, but it also acts as an essential substrate for the proliferating enterocytes [80, 81]. Thus, we suggest paying particular attention to the amino acid pool of diets and not only to the protein intake.

As far as hepatic function is concerned, studies on animal models provided evidence that space flight has pronounced and diverse effects on liver function [67]. Pre-flight and post-flight comparisons of some indirect measures of liver function in humans have shown a statistically significant change in serum γ glutamyl transpeptidase activity, while aspartate aminotransferase and alanine aminotransferase do not undergo a statistically significant change.

More research, by means of non-invasive measuring, is needed on gastrointestinal functions such as gastric and pancreatic functions, since the only ones reported are those by the Soviet scientists. They found evidence of gastric hypersecretion in rats and humans during space flight and in ground-based simulations, and an increase of pancreatic secretion [82, 83].

A deeper understanding of these factors could identify the interaction and countermeasures that an adequate nutrition may play on gastrointestinal changes that impact nutritional status, through changes in either appetite or absorption.

Immune changes

Exposure of animals and humans to space flight conditions has resulted in numerous alterations in immunological parameters, for instance, decreases in blast transformation of lymphocytes, cytokine production, and natural killer cell activity. After flight, alterations in leukocyte subset distribution have also been reported for humans and animals [84].

Findings of energy deficiency on long duration missions increase susceptibility to infections [85]. Studies on cosmonauts during space flight have shown that IgG levels were unchanged, whereas IgA and IgM levels were sometimes increased [86]. A decreased cytotoxicity in cosmonauts after space flight can be proposed, and this includes the defective function of NK cells and the reduced number of circulating effector cells [87]. Physical and psychological stress associated with space flight resulted in decreased virus-specific T-cell immunity and reactivation of EBV [88]; almost certainly immunity changes in space are similar to those occurring during acute stress conditions. Therefore, it is reasonable to consider stress-related immunotherapy approaches in the practice of space medicine mainly because concerns have been raised about the possible risks of post-flight infections. A decrease in the number of T-lymphocytes and impairment of their function is an important effect of weightlessness on the immune system. From a nutritional point of view, we have to consider that deficiency of zinc is associated with similar changes in T-lymphocytes.

Suggestions that modifications to the diet may have a beneficial effect on health are not new. Several micronutrients such as vitamin A, beta-carotene, folic acid, vitamin B12, vitamin C, riboflavin, iron, selenium, zinc have immunomodulating actions [89, 90]. Recent work demonstrates that some nutrients such as arginine, glutamine, nucleotides and omega-3 fatty acids may affect immune function [91].

The dietetic intake of these nutrients should be considered in order to recommend appropriate nutritional supplementation aimed at reducing immune changes due to sub-optimal nutrition that may eventually have negative consequences on immune status and susceptibility to a variety of pathogens.

Moreover, the latest data (from healthy subjects and patients with inflammatory diseases) show that probiotics can be used as innovative tools to improve the intestine's immunologic barrier and produce a gut-stabilizing effect. Many of the probiotic effects are mediated via immune regulation, in particular by control of the balance of proinflammatory and antiinflammatory cytokines [92].

Recent results demonstrate that dietary consumption of specific probiotics can enhance natural immunity in healthy elderly subjects [93]. This evidence suggests that the consumption of cultures of beneficial live microorganisms that act as probiotics should be evaluated in target specific populations, including astronauts.

Oxidative stress

During long space missions, crew members may receive significantly high radiation exposure, even with considerable shielding on the spacecraft. In the human body, solar radiation or low wavelength electromagnetic radiation (such as gamma rays) from the earth or space environment can split water to generate reactive free radicals. These reactive free radicals can react in the body leading to oxidative damage to lipids, proteins and DNA. Recent data on the oxidant damage have underlined its increase post-flight probably due to a combination of augmented metabolic activity and loss of some host antioxidant defences in-flight [94, 95].

The antioxidant defence system includes vitamins such as tocopherols and tocotrienols (vitamin E), ascorbate (vitamin C), vitamin A and its precursors beta-carotene and other carotenoids, trace elements and minerals such as copper, manganese, zinc, selenium and iron. Dietary and antioxidant defences appear to play a protective role in muscle cells by reducing associated oxidative damage to lipids, nucleic acids, and proteins [96]. However, iron supplementation in microgravity is not recommended because the reduction in red cell mass and the consequent increase in iron stores could augment free radical generation.

As far as the other nutrients mentioned above, ground-based studies with exercise suggest that giving supplemental dietary antioxidants such as vitamin C, vitamin E and β carotene may be of benefit [97–102].

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Furthermore, administration of pharmacologic doses of vitamin E is a possible method to improve insulin action in healthy subjects and non-insulin-dependent diabetic patients [103]. Those who benefit from antioxidant supplementation appear to be less fit individuals [104–105]; the combination of sarcopenia and nutritional depletion would place astronauts in this category.

Dietary intake and/or supplementation of particular nutrients showed an important prophylactic role against photo-oxidative damage to cell membranes. There is evidence of a potential protective effect by the macular pigments, in particular lutein (L) and zeaxanthin (Z), against light-induced retinal damage and age-related macular degeneration (AMD). Studies on humans reveal positive associations between dietary intake of L and Z and the serum concentration of L and Z, and between serum concentration of L and Z and macular pigment density [106]. Efforts have to be made to prove the reliability of the photo-protection hypothesis for the macular pigments and consequently recommend dietary intake of these nutrients in particular population targets such as the astronauts [107]. Indeed much of the evidence showed that in conditions associated with increased free radical production, such as inflammatory conditions, smoking habits, strenuous physical activity, there is an increased utilization of antioxidant vitamins. For these reasons actual recommendations of vitamin C intake have been raised from 60 to 100 mg per day, during space flights [12, 108]. Results on the vitamin-mineral supplementation benefits in humans with simulation radiation exposure as well as their absorption rate are lacking, making it difficult to draw up specific recommendations for humans in weightlessness conditions.

Nutritional countermeasures in space with antioxidant supplementation provide a great opportunity for research within space flight models, whereas the main concern is to counteract the potential for long-term oxidative damage in humans under these conditions.

Psychosocial role of nutrition

The psychological and behavioral changes that have been investigated until now are the following: disruption of cognitive and memory functions (especially in association with circadian rhythm variations), stress and anxiety states induced by concern for a successful mission, fear of the physical dangers encountered during space flight, social isolation, decreased personal space, interpersonal difficulties among crewmembers, depression that can be caused by any of the above mentioned factors and personality changes that may occur.

Diet may have a modulator effect on mood: several B vitamins may influence mood and/or the cognitive function; there is a high incidence of folate deficiency in depression, and there are indications in literature that folate-deficient depressed patients respond to folate administration [109].

Appropriate attention should also be given to carbohydrate intake: in stress-prone subjects there is a higher risk of serotonin deficiency in the brain and carbohydrates may prevent a functional shortage of central serotonin during acute stress, due to their strengthening effect on brain tryptophan [110]. In addition, there is evidence promoting a carbohydrate-rich diet as a cognitive performance improvement in stress-prone individuals [111]. Alterations in brain tryptophan levels cause changes in brain serotonin synthesis; low levels of serotonin may predispose subjects to mood and impulse control disorders [112].

Another important issue is that sensory responses to taste, smell, sight and texture of foods are a major influence on both food preferences and eating habits on earth [113]. During long missions, alterations in taste sensation, deficit in the palatability and attractiveness of the food are additional factors that have to be considered in order to contrast energy deficits and subsequent body mass losses by adequate and improved nutrition schemes [114].

Crew members may forego meals to ensure that their jobs are completed; such behavior could be accepted for mission success but, of course, it is not appropriate from a nutritional point of view.

It has to be considered that people construct their perceptions, beliefs, and attitudes about foods on the basis of cultural values, with psychosocial factors shaping their food choices [113].

Research clearly indicates that a social facilitation effect leads to lower levels of food consumption when people eat alone and to higher levels when eating occurs in a group setting [115]. Crew involvement in preparing and consuming meals should be pursued yet trans-cultural differences between dissimilar populations, with regard to cultural background and traditions, should be considered [116]. For human beings, food choices and intake contribute to the general feeling of wellness as a source of pleasure and as a source of diet-health link perception. Future investigations on the psychosocial role of nutrition in particular environments, such as microgravity, are recommended in order to better understand the critical influences on food choices and ascertain which of these are subject to modifications within the specific context.

Conclusions

It can be realistically predicted that nutritional balance and dietary adequacy will become increasingly important on future long-term space flights especially regarding future missions to the International Space Station and to Mars.

Diet will be important for the efficacy of the countermeasures and prevention of compounding problems. The frequent inability to match intake to expenditure on missions with high exercise requirement is a large concern. Although men adapt to chronic energy deficits, at some point, metabolic processes will become compromised and the under-nutrition consequences, such as decreased immunocompetence [117], and endogenous antioxidant defences, fall in protein synthesis [5], will become evident.

Nutrition is an essential part of maintaining the endocrine and immune system, skeletal and muscle integrity, and the hydration status of the space crew, all of which are important for extended-duration missions and in those where strenuous extravehicular activities are required.

In addition, the psychological aspects of individuals during space flights underline the role of the mealtime perceived as a welcome break from job-related activities as well as a chance to socialize.

Provision of a variety of available foods [118] with positive sensory characteristics [113], and adequate time for preparation and consumption of meals enhances food intake by the crew members.

The observed changes in food intake, hypothalamic monoamines, and peripheral hormones suggest that besides microgravity, continuous light exposure contributes to the observed anorexia, and its metabolic sequelae including bone loss [119]. Poor or inadequate sleep may affect eating and drinking behavior, thus, generating the potential for nutritional problems.

Ground models of microgravity and proper surveillance of crews on board will provide an approach to understanding psycho-physiological adaptation on healthy individuals undergoing unusual strain that are also observed in humans undergoing prolonged stress, physical immobilization or aging.

Further efforts are needed to ameliorate dietary adequacy and food safety in order to counteract deleterious physiological changes, psychosocial repercussions and microbiological hazards.

Finally, it is hoped that all space food systems will be designed to meet not only individual nutritional requirements but also different food preferences and eating habits, according to the different cultural background and country of origin of the crew members.

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