Nutritional challenges and countermeasures for space travel

T. Cahill* () and G. Hardiman*^{*†} ()

*Faculty of Medicine, Health and Life Sciences, School of Biological Sciences, Institute for Global Food Security (IGFS), Belfast, UK; [†]Department of Medicine, Medical University of South Carolina, Charleston, SC, USA

Abstract

There has been a reinvigoration of public interest in space exploration in what has been deemed the new space race, which aims to eventually take humans to Mars in the 2030s. This type of Earth-independent deep space mission presents a multitude of challenges for providing astronauts with adequate nutrition, which are not currently posed by our presence in low earth orbit. For example, there are technical challenges associated with providing enough food with sufficient nutrient content, bioavailability and increased shelf life. Environmental stressors may also impact physiology and in turn affect nutritional status. Increased exposure of radiation, for example, causes changes in the gut and liver that might facilitate nutrient deficiency. Current or potential countermeasures for these challenges are explored including the use of bio-regenerative systems such as growing crops or biomass, or inducing torpor to reduce nutritional needs. Additionally, the beneficial role of nutrients has also been explored for alleviating the harmful effects of spaceflight exposure. It is clear that such countermeasures will be necessary to maintain astronaut health during long-duration missions to potentially counteract physiological stresses and to allow us to continue pushing the boundaries of space exploration.

Keywords: astronaut nutrition, spaceflight, space food, space travel

Introduction

There has been a reinvigoration of public interest in space exploration in what has been deemed the new space race. This coincides with NASA's recent announcement of its Artemis programme, which aims to land the first woman on the moon by 2024, develop a sustainable human lunar presence by 2028 and test new technologies on the moon that will

E-mail: G.Hardiman@qub.ac.uk

98

eventually take humans to Mars in the 2030s (Dunbar 2019). It is estimated, depending on favourable alignments of Earth and Mars, that a manned mission to the red planet would involve around a 400-day transit there and back and a 500-day stay (Cucinotta *et al.* 2013). There are, however, a multitude of challenges involved in ensuring astronauts receive adequate nutrition during long-term space missions. This article discusses the technical challenges associated with supplying enough food of sufficient nutritional content on long-term space missions, the physiological stresses, such as microgravity and radiation exposure, that can be detrimental to the health of the astronauts and the nutritional measures that might counter them (Fitts *et al.* 2000; Fry 2002).

Correspondence: Prof Gary Hardiman, Institute for Global Food Security, Biological Sciences, 19 Chlorine Gardens, Belfast BT9 5DL, UK.

The provision of food in space

Current space food systems

Research and development on food in space has come a long way from the Mercury missions in the early 1960s, which had the objective to put humans into orbit. These short-duration missions, lasting up to 34 hours, provided little incentive to research and develop nutritional food or storage systems, and so used bite-sized cubes of a high-calorie mixture of protein, high-melting point fat, sugar and fruit or nuts. Longer missions, such as the Gemini missions lasting up to 14 days, led to the development of food packaging and testing procedures to ensure safety and that nutritional requirements were met. This ultimately led to the development of the Hazard Analysis Critical Point Control, a legal framework used to systematically identify hazards or risks in food operation procedures to eliminate or reduce food hazards to an acceptable level (Walker et al. 2003); a framework which is now widely adopted by the food industry. The Apollo missions in the late 1960s and early 1970s explored the use of dehydrated foods to decrease weight and volume, making use of the water generated as a by-product from the fuel cells on board to rehydrate the foods while in orbit. The Skylab missions made use of refrigerators, freezers and food warmers boasting a menu of 72 foods that cycled on a 6-day basis, on which NASA recorded metabolic studies (Lane & Schoeller 1999; Perchonok & Bourland 2002). The current menu on board the International Space Station (ISS), from the year 2000 onward, is comprised of a 50/50 American and Russian food system consisting of 200 foods and beverages, cycled on an 11-day basis (Clément 2011).

Although little research has been conducted on the optimum composition of dietary energy sources for spaceflight, a team of leading nutritionists developed recommended nutritional guidelines to insure adequate intake of nutrients for long-duration spaceflight of up to 360 days, which entail a reference intake of protein of 0.8 g per kilogram bodyweight, 350 g of carbohydrates and 70 g of fats per day (Churchill 1997; Heer et al. 2015). The total daily energy intake from the different macronutrients therefore translates to 12-15% total energy from protein, 50-55% from carbohydrates and 30-35% from fat (Lane & Schoeller 1999) which are largely similar to those on Earth (WHO 2018). Most of the crews' water supply is generated from the Water Recovery System which provides clean water by reclaiming cabin urine, sweat and condensation and passing it through a distillation and filtration system for reuse as potable water (Dunbar 2008). The recommended water consumption on ISS is 2000 ml/day, and while average intake is generally less than recommended, astronauts do not experience space-related dehydration (Smith *et al.* 2015).

Technical challenges and countermeasures for the provision of adequate nutrition in deep space

The latest space food system works well for our current presence in space, which involves inhabiting the ISS in low Earth orbit, situated at around 400 km above Earth's surface (Rola et al. 2005). In this regard, the ISS can be resupplied with food from Earth as needed (NASA 2015). However, for Mars missions a number of challenges arise that will require innovative solutions (summarised in Table 1). For example, orbital alignment between Earth and Mars can minimise costs of transit; however, their changing distances make relying on resupply missions to Mars inherently riskier. It is therefore important that a Mars mission reduces its dependency on Earth while maintaining its ability to provide nourishment to the crew over a longer period of time. This could be done by either providing sufficient food for the entire mission at the start or by developing systems to regenerate it along the way.

Provision of sufficient food from the start

Prior to a mission to Mars, innovation would be required to accommodate increasingly large supplies, creating the need for more powerful rockets with greater storage space. This would, however, equate to more fuel with consequent increases in mission cost. Food, in particular, is a commodity that increases with mission length and given that an astronaut consumes approximately 1.8 kg of food per day (Hanford 2006), it is estimated that as much as 24 000 pounds, or around 10 tonnes of food, would be needed for a 4-person crew on a round trip to Mars (Dunbar 2007). However, private companies such as SpaceX are breaking down these barriers to space travel by developing more powerful rockets that can be relanded and largely reused. These innovations increase the allowable payload, enabling more food supplies, and drive down the costs by a factor of 20 resulting in cost reductions from \$54 500/kg to around \$2720/kg for reaching low Earth orbit (Jones 2018).

Table I	Challenges	associated wi	th food	provision	on long-
duration	space travel	and potentia	l counte	ermeasures	5

Challenges	Countermeasures		
Providing enough food for long- duration missions without need for resupply	 More powerful rockets capable of increased food payload Innovative technology to decrease earth dependency including bio-regenerative systems to grow crops or phytobacteria biomass Suspended animation to reduce 		
Avoiding food spoilages and maintaining nutritional content	 nutritional needs Food with extended shelf life of 3-5 years Developing food processing techniques to maintain putrients 		
Ensuring nutritional status and health of astronauts	 Food with more bioavailable nutrients Sensing devices to assess food quality 		

While more powerful rockets may make it possible to send enough sustenance for a Mars mission, additional technical challenges exist in developing a varied and balanced diet for long-duration missions, with a shelf life of over 3 years required for the food sent [as discussed further by Cooper et al. (2011)]. A number of techniques for processing space food to increase shelf life have been extensively researched and employed by NASA, including thermostabilisation, irradiation and dehydration. However, it was found that some types of food processing designed to increase shelf life negatively impacted the nutritional content of the food (Evans et al. 1981). An analysis of the nutritional content of space menus indicated that potassium, calcium, vitamin D and vitamin K were lower than the recommended daily intake and that the content of vitamins A, C, B₁ and B₆, folic acid and pantothenic acid in most foods was observed to decrease considerably during storage by up to 40%. From a menu of 65 different items, most foods also experienced a decline in acceptability over a 5-year period based on appearance, flavour, texture and aroma (Cooper et al. 2011).

Given that the increased mission length would also increase the chance of food spoilages, which would pose a threat to crew health, it may be necessary to provide a way of assessing the food quality. It has been suggested this could be done using smartphonebased sensing devices that have the ability to screen for things like protein degradation or volatile amines that would indicate rot (Snyder *et al.* 2019). It is, however, evident that more research is needed into the development of processing techniques or storage systems that can maintain the nutritional content and the acceptability of space food prior to the mission to Mars. This must be done while also adhering to a number of other constraints such as minimising preparation time, volume, storage space and water usage (Perchonok & Bourland 2002; Smith *et al.* 2014).

Development of systems to generate food during the mission

Alternatively, a number of novel ideas have been proposed for providing enough sustenance in space travel. These include a closed bio-regenerative system that reduces dependency on Earth and involves growing crops such as wheat, potatoes and sweet potatoes to meet nutritional demands. This system is attractive as it removes the need for resupplies and would also regenerate oxygen and water in the process while removing carbon dioxide. A cost-effectiveness analysis based on mass provided evidence that this may be the most economical when it comes to long-duration missions to Mars. However, it was noted that these systems can take a long time to set up and fluctuations in crop yield risk exposing the crew to nutritional deficiencies (Drysdale *et al.* 2003).

The use of synthetic biology has also been proposed as a regenerative alternative for providing sustenance on long-term space missions. This would involve the growing of nutritionally rich photosynthetic bacteria such as Spirulina (Arthrospira platensis and Arthrospira maxima). Spirulina has been used in human health as a nutritional supplement and contains carbohydrates, lipids, proteins and essential amino acids, as well as a number of vitamins, minerals and phytonutrients (Gershwin & Belay 2007). Consuming the generated Spirulina biomass would overcome the need for extended shelf life foods, reduce the need for packaging and lead to a mass cost saving of around 38% based on a mixed menu of wet food for a long-duration mission to Mars. It has also been suggested that the flavour and nutritional content of the Spirulina can be manipulated with various taste-conferring molecules and genetic engineering, respectively, thus overcoming the challenges associated with loss of nutritional content and food acceptability (Menezes *et al.* 2015). Additionally, they may also be used for the synthesis of polymers for 3D printing and the synthesis of carbon-based fuels (Way *et al.* 2011).

Inducing suspended animation in the crew

A more counter-intuitive approach involves the use of suspended animation or induced torpor, which has been proposed for long-duration space missions as far back as the 1960s (Hock 1960), and was explored in a NASA-commissioned paper by SpaceWorks (Bradford et al. 2018) and is currently being explored by the European Space Agency (ESA 2019). This would most likely involve crew sedation along with reduction in body temperatures and lowered metabolism, which would consequently lower oxygen and nutrient requirements. Nutrition and hydration could be administered intravenously by total parenteral nutrition, which is routinely used in medical practice and is described as being more mass efficient. The solution usually contains dextrose, amino acids, electrolytes, lipids, vitamins, trace elements and glutamine, but could be modified based on the specific nutritional needs of the astronaut. Utilising this approach of inducing torpor would lead to an estimated reduction of 88% of total consumables. Additionally, a decrease in the need for power systems, life support, vehicle size and the need for consumable storage space would lead to a total mass reduction of the transit habitat by 68%, reducing fuel needs and overall mission cost (Bradford et al. 2018).

Physiological impact of spaceflight on nutritional status

In addition to the technical challenges of providing food for space travel, a multitude of environmental challenges unique to space travel arise posing a risk to astronaut health. The impact of exposure to radiation and the effects of microgravity on nutritional status are discussed below.

The effect of radiation on nutrient uptake and metabolism

The exposure to ionising radiation from solar particle events or galactic cosmic rays (GCR) increases beyond the protection of Earth's atmosphere and magnetosphere (Fry 2002). Ionising radiation can cause radiation sickness, damage to the central nervous system and direct damage to DNA leading to cancer. It may also result in the induction of other cancer progression-related cellular processes, such as oxidative stress, genomic instability, telomere shortening, extracellular-matrix remodelling and persistent inflammation, further establishing the high-risk nature of the radiation environment associated with space travel (Cucinotta & Durante 2006). The study of how radiation exposure affects organ functionality is important for ensuring astronauts receive adequate nutrition during space travel, particularly the effects on the gut and the liver that represent points of entry and metabolism for most nutrients. The epithelial cells of the gastrointestinal tract (GIT) are highly proliferative (Wong & Wright 1999), and as cell radiosensitivity is directly proportional to the rate of cell division, they are vulnerable to radiation injury (Rubin & Casarett 1968).

Radiation exposure to the GIT has been shown to elicit a number of different responses including immune dysfunction, nerve damage, inflammation and enterocyte cell death (Williams et al. 2010). Studies on patients with cancer show that receiving around 45-55 Gy of radiotherapy can induce fibrosis, stenosis, ulceration and ischaemia from blood vessel damage (Coia et al. 1995). This level of GIT injury can cause tissue remodelling, which alters the structure and motility of the gut, making it more rigid and susceptible to adhesions or perforations (Clément 2011). These changes are deleterious to the normal functioning of gut absorption and would have a severe impact on astronaut nutrition if sustained in space travel, increasing the possibility of developing deficiency-associated diseases (Rubin & Casarett 1968; Williams et al. 2010). These injuries are, however, associated with radiation doses much larger than those experienced in space, which, for a 3-year trip to Mars, would more likely be around 4 mGy (Cucinotta 2007). One study seeking to replicate lower levels of GCR space radiation used 0.5 cGy/min ⁵⁶Fe and ¹³⁷Cs to simulate high-linear energy transfer (LET) and low-LET radiation to observe the effects on mouse GIT. They found decreased epithelial cell migration, altered cytoskeleton remodelling and cell polarity, and increases in the senescence-associated inflammatory response genes, which have previously been shown to correlate with poorer overall survival in humans with colon cancer. More importantly, they found that lowdose radiation compromised various enzymes and intestinal transporters with important roles in digestion and absorption, respectively, occurring up to 12 months after exposure (Kumar et al. 2018). While this study indicates the later effects associated with acute radiation exposure, further research is needed on the effects of chronic exposures on these later effects.

Conversely, liver cells are less proliferative than those of the GIT and so are inherently less radiosensitive (Rubin & Casarett 1968). Nevertheless, the liver represents a central hub of metabolism and detoxification with a role in over 500 biochemical reactions. It is involved in the breakdown and synthesis of carbohydrates, proteins and lipid for energy supply and storage, as well as detoxification pathways, including phase I cytochrome P450 enzymes, highlighting its importance in maintaining nutritional status (Hodges & Minich 2015). Radiation-induced liver damage is reported as a complication to radiotherapy with symptoms including fatigue, jaundice, abdominal pain, increased abdominal girth, hepatomegaly, anicteric ascites and isolated elevation of alkaline phosphatase (Benson et al. 2016). Also, ionising radiation produces short-lived free radical-mediated events and production of reactive oxygen and nitrogen species, as well as changes in redox signalling linked to disruption of metabolic processes that persist long after radiation exposure, impacting the body's ability to utilise energy supplies (Spitz & Hauer-Jensen 2014). This oxidative stress and associated antioxidant response has been directly observed in mouse liver after whole-body lowdose radiation in the range of 0.05-0.2 Gy (Avti et al. 2005). Moreover, space flight studies conducted during shuttle and Mir missions observed depressed plasma protein synthesis and elevated levels of interleukin (IL)-6 in crew member urine that indicate abnormal liver function (Gridley et al. 2008). Therefore, emphasis should be put on understanding radiation damage to the liver in the context of spaceflight to discover novel therapeutic targets that help to circumvent liver damage especially, due to its importance in energy metabolism and detoxification.

The effect of microgravity on nutritional status

The physiological changes that occur in the body due to microgravity are well documented. Microgravity leads to a plethora of changes including bone demineralisation, muscle atrophy, disrupted calcium homeostasis, deconditioned cardiac function, circadian rhythm problems, fluid redistribution and immune-related problems and affects the neurovestibular system affecting balance and orientation (Williams *et al.* 2009). Unsurprisingly, such global changes in the body affect metabolic and hormonal pathways that disrupt homeostasis and lead to changes in metabolism and in the nutritional status of important micronutrients.

As astronauts first acclimatise to microgravity, a process which involves fluid redistribution and changes to their neurovestibular sensory systems, they can experience symptoms such as loss of appetite, nausea and motion sickness (Williams et al. 2009). Prior to ISS missions, and with the exception of Skylab, astronauts were observed to have a reduced dietary intake, averaging 70% of that required (Smith et al. 2014). This may have contributed to the loss in body mass frequently reported (Zwart et al. 2014). For example, a study of four astronauts on the space shuttle showed a decrease in dietary intake, which led to a reduction in body fat, indicating a state of negative energy balance and an inadequate nutritional status (Stein et al. 1999). It is also suggested that difficulty in consuming adequate dietary intake was caused by changes in food palatability caused by a change in smell and taste (Olabi et al. 2002). However, it is since reported that the ISS crew meet recommended intakes and maintain body mass (Smith et al. 2014).

In addition to the behavioural aspects of maintaining dietary intake, nutritional status is altered by changes in how the body utilises its energy sources under conditions of microgravity. Bed rest studies have consistently shown a change in glucose metabolism caused by alterations in insulin secretion, insulin sensitivity and glucose tolerance (Tobin *et al.* 2002). There is also evidence of increased lipid metabolism (Jonscher *et al.* 2016) and increased urinary excretion of amino acids, which is thought to occur as a consequence of increased protein catabolism in atrophying muscles (Stein & Schluter 1998). However, the evidence is currently insufficient to determine specific macronutrient requirements for astronauts experiencing microgravity.

In addition, many micronutrients also experience fluctuations due to spaceflight which can have negative health consequences, since they play an active role in many biochemical reactions (Shenkin 2006). For example, spaceflight considerably lowered urinary concentrations of magnesium, phosphorous and zinc (Smith *et al.* 2005), while iron stores are known to increase, as measured by serum ferritin (Zwart *et al.* 2013). Additionally, serum concentrations of vitamins B, D, E and K₁, and the antioxidant superoxide dismutase were lowered due to spaceflight (Leach & Rambaut 1977; Smith *et al.* 2005).

The effects on astronaut health by these changes can be detrimental, as some studies have linked changes in vitamin levels in astronauts to various health outcomes. For example, the development of arrhythmias by the Apollo crew was attributed to potassium deficiencies (Cooper *et al.* 2011). Likewise, spaceflight exposure has more recently been observed to lead to negative ophthalmic changes (Mader *et al.* 2011), which have been linked to changes in vitamin B_{12} levels and its associated metabolic pathways (Zwart *et al.* 2012). NASA's report *Risk Factor of Inadequate Nutrition* gives a fuller account of the risks associated with nutritional deficiencies (Smith *et al.* 2015).

Nutritional countermeasures to spaceflight exposure

There has been much research into methods of mitigating the harmful physiological effects of spaceflight, such as the use of exercise and testosterone to limit muscle atrophy due to microgravity (Dillon et al. 2018) or shielding from radiation (Hu et al. 2014). However, utilising food and nutrition to tackle detrimental physiological changes is an attractive approach that avoids the health impacts of some pharmaceuticals side effects. So much so that NASA, in partnership with AmeriSciences, has developed multivitamin regime, specialised dietary supplements and antioxidant formulas for astronauts (Lockney 2012) from the extensive literature linking some compounds with protective effects in animals.

Various studies have reported on the effects of certain vitamins and antioxidants to mitigate the DNA damage caused by oxidative stress initiated by radiation exposure. For example, research has shown increased 30-day survival in irradiated mice supplemented with a cocktail of antioxidants such as L-selenomethionine, vitamin C, vitamin E succinate, alpha-lipoic acid and N-acetyl cysteine, compared with controls (Wambi et al. 2009). Similarly, a longterm study replicating the effects of space radiation exposure in mice on cataract formation found that supplementation with antioxidants [L-selenomethionine (SeM), N-acetyl cysteine ascorbic acid, co-enzyme Q10, alpha-lipoic acid and vitamin E succinate] decreased cataract formation compared with controls (Davis et al. 2010).

While it may be helpful to pre-emptively incorporate such nutrients into the crew's diet, it could prove more beneficial to pro-actively measure crew health. This would enable a rapid response to the progression of nutrition-related conditions by altering nutritional intake or administering supplements during the mission. One example to which this could be applied relates to the accumulating effects that muscle atrophy due to microgravity can have on the body. The decreased protein synthesis can lead to hypercalciuria and metabolic acidosis, which then further promotes the breakdown of muscle protein (Straumann et al. 1992), increases bone resorption and consequently increases the risk of kidney stones (Dawson-Hughes 2003). Some studies have suggested that increasing the intake of an alkaline substance such as potassium can counteract the metabolic acidosis (Heer et al. 2015). The active detection of acidosis during spaceflight and treatment with potassium supplementation could mitigate its snowballing effect to other health issues (Thompson et al. 2000). The polyphenol resveratrol has also demonstrated protective affects against muscle atrophy in unloading experiments (Mortreux et al. 2019).

Similarly, the increase of bone resorption in spaceflight releases calcium, which in turn lowers vitamin D levels and consequently causes a decrease in calcium absorption through the intestinal tract (Smith *et al.* 2014). Both phosphate and calcium supplementation have proved ineffective at mitigating bone resorption, while omega-3 unsaturates from higher fish intake have been correlated with reduced bone loss (Zwart *et al.* 2010; Smith *et al.* 2014). Moreover, while magnesium levels are known to decrease during spaceflight, supplementation may prove beneficial for bone resorption and renal stone formation; however, more research is needed to determine the efficacy of magnesium supplementation in spaceflight (Zwart *et al.* 2013).

Conclusions

The technical and physiological problems associated with nutrition in the context of long-duration spaceflight are vast. Nutritional status is altered during and following long-duration spaceflight. Five decades of human spaceflight have demonstrated that human physiology is impacted by space travel, and this has many implications for adequate nutrition in space. The nutrients themselves may be impacted and this adds an additional challenge to exploiting them as countermeasures to the adverse effects of space travel. Additional research is needed to better comprehend the role of nutrition in bone health and changes in body composition. Maintaining and monitoring adequate nutritional status are critical for crew health during spaceflight and particularly in the context of longer duration exploration missions. This review has only addressed a small number of these problems. While much of the groundwork has been covered in researching and developing innovative countermeasures to the vast array of challenges, many obstacles remain. Nevertheless, human desire for exploration will one day overcome these obstacles and make long-duration interplanetary space travel a possibility.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

References

- Avti PK, Pathak CM, Kumar S *et al.* (2005) Low dose gamma-irradiation differentially modulates antioxidant defense in liver and lungs of Balb/c mice. *International Journal of Radiation Biology* **81**: 901–10.
- Benson R, Madan R, Kilambi R *et al.* (2016) Radiation induced liver disease: a clinical update. *Journal of the Egyptian National Cancer Institute* 28: 7–11.
- Bradford J, Schaffer M & Talk D (2018) Torpor inducing transfer habitat for human stasis to Mars. *Geology*.
- Churchill SE, ed (1997) *Fundamentals of Space Life Sciences*, Vol 2. Krieger Publishing Company: Malabar, FL.
- Clément G (2011) *Fundamentals of space medicine*. Springer Science & Business Media: Berlin, Germany.
- Coia LR, Myerson RJ & Tepper JE (1995) Late effects of radiation therapy on the gastrointestinal tract. *International Journal of Radiation Oncology, Biology, Physics* **31**: 1213–36.
- Cooper M, Douglas G & Perchonok M (2011) Developing the NASA Food System for Long-Duration Missions. *Journal of Food Science* 76: R40–R48.
- Cucinotta FA (2007) Space radiation organ doses for astronauts on past and future missions. NASA Johnson Space Center: Houston, TX.
- Cucinotta FA & Durante M (2006) Cancer risk from exposure to galactic cosmic rays: implications for space exploration by human beings. *Lancet Oncology* 7: 431–5.
- Cucinotta FA, Kim MHY, Chappell LJ *et al.* (2013) How safe is safe enough? Radiation risk for a human mission to Mars. *PLoS ONE* 8: e74988.
- Davis JG, Wan XS, Ware JH *et al.* (2010) Dietary supplements reduce the cataractogenic potential of proton and HZE-particle radiation in mice. *Radiation Research* **173**: 353–61.
- Dawson-Hughes B (2003) Interaction of dietary calcium and protein in bone health in humans. *The Journal of Nutrition* **133**: 852S– 54S.
- Dillon EL, Sheffield-Moore M, Durham WJ *et al.* (2018) Efficacy of testosterone plus NASA exercise countermeasures during headdown bed rest. *Medicine and Science in Sports and Exercise* **50**: 1929.
- Drysdale AE, Ewert MK & Hanford AJ (2003) Life support approaches for Mars missions. *Advances in Space Research* 31: 51–61.
- Dunbar B (2007) *Human Needs: Sustaining Life during Exploration.* Available at: https://www.nasa.gov/vision/earth/everydaylife/jame stown-needs-fs.html (accessed 30 October 2019).

- Dunbar B (2008) International Space Station Environmental Control and Life Support System. Available at: https://www.nasa.gov/cente rs/marshall/pdf/104840main_eclss.pdf (accessed 3 April 2019).
- Dunbar B (2019) *What is Artemis?* Available at: https://www.na sa.gov/what-is-artemis (accessed 3 April 2019).
- ESA (European Space Agency) (2019) *Hibernation*. Available at: https://www.esa.int/gsp/ACT/projects/hibernation.html (accessed 10 January 2019).
- Evans SR, Gregory JF III & Kirk JR (1981) Thermal degradation kinetics of pyridoxine hydrochloride in dehydrated model food systems. *Journal of Food Science* 46: 555–8.
- Fitts RH, Riley DR & Widrick JJ (2000) Physiology of a microgravity environment invited review: microgravity and skeletal muscle. *Journal of Applied Physiology* 89: 823–39.
- Fry RJ (2002) Radiations in space: risk estimates. Radiation Protection Dosimetry 100: 475–7.
- Gershwin ME & Belay A (2007) Spirulina in Human Nutrition and Health. CRC Press: Boca Raton, FL.
- Gridley DS, Coutrakon GB, Rizvi A *et al.* (2008) Low-dose photons modify liver response to simulated solar particle event protons. *Radiation Research* **169**: 280–7.
- Hanford AJ (2006) Advanced life support baseline values and assumptions document. Technical Reports 3. Available at: http://d ocs.lib.purdue.edu/nasatr/3 (accessed 30 October 2019).
- Heer M, Titze J, Smith SM et al. (2015) Nutrition Physiology and Metabolism in Spaceflight and Analog Studies. Springer: Berlin, Germany.
- Hock RJ (1960) The potential application of hibernation to space travel. Aerospace Medicine and Human Performance 31: 485-9.
- Hodges RE & Minich DM (2015) Modulation of metabolic detoxification pathways using foods and food-derived components: a scientific review with clinical application. *Journal of Nutrition and Metabolism* 2015: 1–23.
- Hu W, Pei H, Li H *et al.* (2014) Effects of shielding on the induction of 53BP1 foci and micronuclei after Fe ion exposures. *Journal* of *Radiation Research* 55: 10–16.
- Jones H (2018) The Recent Large Reduction in Space Launch Cost. 48th International Conference on Environmental Systems. *Computer Science*.
- Jonscher KR, Alfonso-Garcia A, Suhalim JL et al. (2016) Spaceflight activates lipotoxic pathways in mouse liver. PLoS ONE 11: e0152877.
- Kumar S, Suman S, Fornace AJ et al. (2018) Space radiation triggers persistent stress response, increases senescent signaling, and decreases cell migration in mouse intestine. Proceedings of the National Academy of Sciences 115: E9832–41.
- Lane HW & Schoeller DA (1999) Nutrition in Spaceflight and Weightlessness Models. CRC Press: Boca Raton, FL.
- Leach CS & Rambaut PC (1977) Biochemical responses of the Skylab crewmen: an overview. In: *Biomedical Results from Skylab* (RS Johnston & LF Dietlein eds), pp. 204–16. Washington, D.C.
- Lockney D (2012) Dietary Formulas Fortify Antioxidant Supplements. Available at: https://spinoff.nasa.gov/Spinoff2012/hm_2. html (accessed 10 January 2019).
- Mader TH, Gibson CR, Pass AF *et al.* (2011) Optic disc edema, globe flattening, choroidal folds, and hyperopic shifts observed in astronauts after long-duration space flight. *Ophthalmology* **118**: 2058–69.
- Menezes AA, Cumbers J, Hogan JA *et al.* (2015) Towards synthetic biological approaches to resource utilization on space missions. *Journal of The Royal Society Interface* 12: 20140715.

Mortreux M, Riveros D, Bouxsein ML *et al.* (2019) A moderate daily dose of resveratrol mitigates muscle deconditioning in a Martian gravity analog. *Frontiers in Physiology* **10**: 899.

NASA (2015) NASA's Journey to Mars: Pioneering Next Steps in Space Exploration. Available at: https://www.nasa.gov/sites/defa ult/files/atoms/files/journey-to-mars-next-steps-20151008_508.pdf (accessed 26 November 2019).

Olabi AA, Lawless HT, Hunter JB *et al.* (2002) The effect of microgravity and space flight on the chemical senses. *Journal of Food Science* 67: 468–78.

Perchonok M & Bourland C (2002) NASA food systems: Past, present, and future. *Nutrition* 18: 913–20.

Rola R, Sarkissian V, Obenaus A *et al.* (2005) High-LET radiation induces inflammation and persistent changes in markers of hippocampal neurogenesis. *Radiation Research* **164**: 556–60.

Rubin P & Casarett GW (1968) Clinical radiation pathology as applied to curative radiotherapy. *Cancer* 22: 767–78.

Shenkin A (2006) Micronutrients in health and disease. *Postgraduate Medical Journal* 82: 559–67.

Smith SM, Zwart SR, Block G et al. (2005) The nutritional status of astronauts is altered after long-term space flight aboard the International Space Station. *The Journal of Nutrition* 135: 437– 43.

Smith SM, Zwart SR & Heer M (2014) Human adaptation to space flight: The role of nutrition. National Aeronautics and Space Administration, Lyndon B. Johnson Space Center: Houston, TX.

Smith SM, Zwart SR & Heer M (2015) Risk Factor of Inadequate Nutrition Human Research Program. Human Health Countermeasures Element NASA.

Snyder JE, Walsh D, Carr PA *et al.* (2019) A makerspace for life support systems in space. *Trends in Biotechnology* 37: 1164–74.

Spitz DR & Hauer-Jensen M (2014) Ionizing radiation-induced responses: where free radical chemistry meets redox biology and medicine. *Antioxidants & Redox Signaling* **20**: 1407–9.

Stein TP & Schluter MD (1998) Excretion of amino acids by humans during space flight. Acta Astronautica 42: 205–14.

Stein T, Leskiw M, Schluter M et al. (1999) Energy expenditure and balance during spaceflight on the space shuttle. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology 276: R1739–48.

Straumann E, Keller U, Kury D *et al.* (1992) Effect of acute acidosis and alkalosis on leucine kinetics in man. *Clinical Physiology* 12: 39–51. Thompson A, Bailey MA, Michael AE *et al.* (2000) Effects of changes in dietary intake of sodium and potassium and of metabolic acidosis on 11β-hydroxysteroid dehydrogenase activities in rat kidney. *Nephron Experimental Nephrology* 8: 44–51.

Tobin BW, Uchakin PN & Leeper-Woodford SK (2002) Insulin secretion and sensitivity in space flight: Diabetogenic effects. *Nutrition* 18: 842–48.

Walker E, Pritchard C & Forsythe S (2003) Hazard analysis critical control point and prerequisite programme implementation in small and medium size food businesses. *Food Control* 14: 169–74.

Wambi CO, Sanzari JK, Sayers CM *et al.* (2009) Protective effects of dietary antioxidants on proton total-body irradiation-mediated hematopoietic cell and animal survival. *Radiation Research* **172**: 175–86.

Way JC, Silver PA & Howard RJ (2011) Sun-driven microbial synthesis of chemicals in space. *International Journal of Astrobiology* 10: 359–64.

WHO (World Health Organization) (2018) *Healthy Diet*. Available at: https://www.who.int/news-room/fact-sheets/detail/healthy-diet (accessed 17 January 2020).

Williams D, Kuipers A, Mukai C *et al.* (2009) Acclimation during space flight: effects on human physiology. *Canadian Medical Association Journal* **180**: 1317–23.

Williams JP, Brown SL, Georges GE et al. (2010) Animal models for medical countermeasures to radiation exposure. Radiation Research 173: 557–78.

Wong WM & Wright NA (1999) Cell proliferation in gastrointestinal mucosa. *Journal of Clinical Pathology* **52**: 321–33.

Zwart SR, Pierson D, Mehta S *et al.* (2010) Capacity of omega-3 fatty acids or eicosapentaenoic acid to counteract weightlessnessinduced bone loss by inhibiting NF-κB activation: From cells to bed rest to astronauts. *Journal of Bone and Mineral Research* 25: 1049–57.

Zwart SR, Gibson CR, Mader TH *et al.* (2012) Vision changes after spaceflight are related to alterations in folate–and vitamin B-12–dependent one-carbon metabolism. *The Journal of Nutrition* **142**: 427–31.

Zwart SR, Morgan JL & Smith SM (2013) Iron status and its relations with oxidative damage and bone loss during long-duration space flight on the International Space Station. *American Journal* of *Clinical Nutrition* **98**: 217–23.

Zwart SR, Launius RD, Coen GK et al. (2014) Body mass changes during long-duration spaceflight. Aviation, Space, and Environmental Medicine 85: 897–904.