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Nutritional Biochemistry of Spaceflight

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Introduction

Adequate nutrition is critical for crew health and safety during spaceflight. To ensure adequate nutrition, the nutrient requirements need to be both accurate and available from the spaceflight food system. The existing nutritional requirements for extended-duration spaceflight have been defined largely by extrapolation from ground-based research. However, nutritional requirements are influenced by most of the physiological consequences of spaceflight, including loss of lean, adipose, and bone tissue; changes in blood composition; and increased risk of renal stone formation. This review focuses on key areas where information has been gained in recent years: dietary intake and energy metabolism, bone health, fluid and electrolyte homeostasis, and hematological changes. Areas in which specific nutrients have the potential to serve as countermeasures to the negative effects of spaceflight are also reviewed.

Dietary Intake

Food and energy intake during flight are generally lower than preflight intake (**Figure 1**)(18-20, 35), despite data indicating that preflight and in-flight energy requirements are the same (18). Furthermore, increased exercise during flight can actually increase energy expenditure to above preflight levels (38). While it is evident from the Skylab missions that ingestion of the prescribed number of calories will not ensure maintenance of body mass (30), it is clear that reduced energy intake along with increased energy expenditure will ensure loss of body mass. This not only affects crew health, but also has a significant confounding effect on medical and research studies.

Recently, the assessment of crew nutritional status has been identified as a critical element for extended-duration missions. A comprehensive biochemical, anthropometric, and dietary intake assessment profile has been developed. Crew members are studied before flight to ensure optimal nutritional status. A limited in-flight protocol is performed to monitor dietary intake, body mass, and blood chemistry. Postflight studies are conducted to address any effects of the flight and to aid in rehabilitation.

A spaceflight food frequency questionnaire (FFQ) was developed to allow easy, yet reasonably accurate, in-flight dietary intake monitoring (32). The FFQ provides a reliable estimate of the intake of 6 key nutrients (water, calories, protein, iron, calcium, and sodium), as

validated in ground-based closed-system studies (32). The FFQ can be completed weekly in 10 to 15 minutes, and the information telemetered to the ground. The results are provided to the mission flight surgeons, allowing them to recommend in-flight (i.e., near real-time) alterations in dietary intake. Use of the FFQ was initiated at the end of the NASA Mir program, and is currently performed with International Space Station crews.

Bone

Bone loss during space flight is a critical issue, and calcium is obviously a key aspect of nutritional implications for bone. The movement of calcium through the body (**Figure 2**) is a complex phenomenon, and the changes during space flight must be understood before the bone loss can be countered. This understanding comes from studies of bone densitometry, coupled with measurements of indices of bone and calcium homeostasis. Calcium kinetic studies also provide detailed information about calcium movement in the body, as estimated using multicompartmental mathematical modeling techniques (**Figure 3**)(37, 44).

Spaceflight-induced bone loss (12, 26, 31, 43) increases urinary calcium excretion and the risk of renal-stone formation (37, 45, 46). In-flight and ground-based analog studies have shown that the loss of calcium from bones is variable between sites within a subject, and that the degree of loss varies between subjects (12, 26). The ability to understand and counteract weightlessness-induced bone loss remains a critical issue for astronaut health and safety during and after extended-duration exploration missions.

Despite the fact that rapid changes occur in bone and calcium homeostasis during spaceflight (36, 45), extended-duration flights are required for detection of measurable bone loss. The Mir space station has provided an excellent platform for this research, and the International Space Station, once it has been completed, can also be expected to provide such a platform.

Calcium balance studies estimate the rate of calcium loss to be about 200–250mg/d (12, 45). Similarly, calcium kinetic studies estimate bone calcium loss at approximately 250mg/d (37). On the basis of more limited studies, bone calcium recovery after extended-duration spaceflight is estimated to be about +100 mg/d (37). If these estimates are correct, recovery of lost bone mass will take approximately 2.5 times the duration of the mission. This prediction, if it is validated by additional data, has significant implications for long-duration missions.

Calcium absorption decreases during space flight, and appears to be related to decreased circulating 1,25-dihydroxyvitamin D (37), the active form of vitamin D. The decrease in circulating 1,25-dihydroxyvitamin D is likely related to decreased parathyroid hormone concentrations. Depleted body stores of vitamin D during long flights (37) are likely related to the lack of ultraviolet light in spacecraft; however, this does not appear to be related to changes in blood levels of 1,25-dihydroxyvitamin D. Despite daily supplementation of vitamin D (12.5 mg) on all 3 Skylab missions, plasma concentrations of 25-hydroxyvitamin D (the precursor of 1,25-dihydroxyvitamin D) were slightly lower after the 84-day Skylab 4 mission than before flight, but not after the 2 shorter missions (28 and 59 days). Further study is required to define the efficacy of vitamin D-fortified diets and supplemental vitamin D, and perhaps to investigate the use of in-flight ultraviolet light treatment.

Information about bone formation, as estimated from biochemical indices (e.g., bone-specific alkaline phosphatase and osteocalcin), is somewhat equivocal. Some investigators have found no change in bone formation during spaceflight (37); others have reported a decrease (6, 7). Ground-based studies with humans have provided similar results: either no change (27, 47) or a decrease (3) in bone formation during bed rest has been reported. Most of these studies, however, do show an increase in bone formation markers after flight or reambulation.

Bone resorption, as indicated by urinary hydroxyproline, increases during spaceflight and bed rest (24, 45). Urinary collagen crosslinks, also markers of bone resorption, are elevated by >100% during spaceflight (**Figure 2**)(6, 7, 36, 37). Calcium tracer kinetic data indicate that bone resorption increases about 50% (37).

For bone health, an obvious area of nutrition concern is that crew members consume adequate amounts of calcium and vitamin D. Recent preliminary information indicates that vitamin K nutriture may also have an impact on bone health during weightlessness (7,41), although more data are required to fully understand this relationship. Sodium intake is also a concern during spaceflight (4), as space diets tend to have relatively high amounts of sodium, and increased dietary sodium is typically associated with hypercalciuria (as reviewed in 13, 29). The potential effect of these, and other, nutrients on the maintenance of bone health during spaceflight highlight the importance of adequate dietary intake.

Fluid/electrolyte homeostasis

Fluid and electrolyte homeostasis is significantly altered during spaceflight (for reviews, see 25, 34). It was originally hypothesized that when humans entered weightlessness, a headward shift of fluids would occur, with subsequent diuresis and dehydration. While portions of this hypothesis are clearly supported by scientific data, other portions are not.

Within hours of the body's entering weightlessness, both plasma volume and extracellular fluid volume are reduced (**Figure 5**)(20) and the face typically becomes "puffy" (28). The decrement in plasma volume is larger than that in extracellular fluid volume, suggesting that interstitial fluid volume (the other four fifths of extracellular fluid) is initially conserved proportionately more than plasma volume. Decreases in total circulating protein, specifically albumin (20), also indicate that interstitial volume is conserved. This shift of protein, and associated oncotic pressure, from the intravascular to the extravascular space would facilitate the initial changes in plasma volume.

Following the initial adaptation to weightlessness, extracellular fluid volume remains decreased from the first days of flight through 8 to 12 days of flight, and during the same period, plasma volume is partly restored (although it is still well below preflight levels). It is hypothesized that the albumin that initially shifts from the intravascular to the extravascular space is metabolized during this period, and that the resulting loss of interstitial oncotic force results in the decreased extracellular fluid volume while normal synthesis of albumin partly restores plasma volume.

Total body water is slightly reduced or unchanged during Space Shuttle flights (**Figure 5**)(20, 21). The small changes in both water and total body mass were similar, suggesting that weight loss on short-duration flights represents primarily fluid and not lean tissue. However, the percent of body mass represented by total body water remained about the same before, during, and after the Spacelab Life Sciences flights (20). On a volume basis, the change in extracellular fluid volume was greater than the change (or lack of change) in total body water (**Figure 5**). Thus, by difference, intracellular fluid volume increased during spaceflight (20), as had been previously hypothesized from ground-based studies (11). The mechanism for this is unknown, and detailed study of this phenomenon to date has not been possible.

Thus, the most important shift of fluid during weightlessness appears to be an

extracellular to intracellular shift, or perhaps a vascular to extravascular shift, as opposed to the frequently cited headward shift. Clearly, a cephalad shift of fluid occurs, but from a physiological perspective, this is not as important as the shift between fluid compartments.

Rapid loss of body mass on the Skylab missions (which were at least 2 weeks longer than the Shuttle flights) was considered to be primarily due to fluid loss (39). Astronauts frequently have been thought to be dehydrated at landing because of their loss of body mass, reduced fluid intake during flight, and negative water balance (500 to 900 ml for the Skylab astronauts) (23). The hypothesis that diuresis and dehydration resulted from a headward fluid shift was consistent with these findings. However, a distinction must be made between dehydration due to inadequate fluid intake and a dehydrated state maintained by altered homeostatic mechanisms after adaptation to microgravity. The results obtained from recent flights (20) indicate that the hypothesized dehydration of spaceflight does not exist.

If negative water balance during spaceflight results mainly from inadequate fluid intake, as results indicate, it is not surprising that little evidence exists for the hypothesized diuresis. Diuresis has been observed to occur in weightlessness simulation studies (42), but only rarely has it been found to occur during spaceflight (5, 8, 10, 25, 34).

Hematology

Decreased red blood cell mass is a consistent finding after short- and long-term flights (2, 14, 15, 22, 40). This "spaceflight anemia" was observed as early as Gemini missions of the 1960s (9). Although the decrease in red blood cell mass is significant (reaching 10 to 15% below preflight levels within 10 to 14 days after launch), this appears to be an adaptation to spaceflight with no documented functional consequences. Several theories about the origin of this phenomenon have been advanced over the years: some have been eliminated, others expanded.

During the first several days of spaceflight, hematocrit is either unchanged (33) or slightly elevated (1, 22, 40). When hematocrit is elevated, it is not as great as would be predicted in relation to the decrease in plasma volume (20). The initial decrease in red blood cell mass occurs at the rate of slightly greater than 1% per day, with an eventual loss of 10 to 15% (1, 2, 22, 40). While removal of mature red cells from the circulation is unchanged during flight (2, 16, 17), the release of new red cells is halted upon entry into weightlessness (1, 2, 40).

Additionally, newly released red blood cells are selectively removed from the circulation (1). These nascent cells are larger than the more mature circulating red blood cells, allowing their selective destruction (1).

One consequence of the increased red blood cell destruction is that the iron released when they are destroyed is processed for storage. Increased serum ferritin concentrations during and after both short- and long-duration flights provides the evidence that this occurs. Serum iron concentrations are normal to elevated during and after flight (2, 40). Current space food systems provide excessive amounts of dietary iron (> 20 mg/d; 19), with the potential for deleterious effects during extended-duration space missions. Studies of dietary iron absorption have not been conducted, but could alleviate concern about iron overload during extended-duration spaceflight.

Summary

As we embark on missions to the International Space Station, and begin to plan for potential missions to Mars, the importance of nutrition is evident, as is the need for a better understanding of nutritional requirements for extended-duration spaceflight. The work completed through the 1990s on the Shuttle and Mir provided answers to some important basic questions, but we have only begun to scratch the surface of understanding the impact of weightlessness on the human body. A more complete understanding will not only enable the exploration of our universe, but will provide information we need for maintenance of human health and treatment of diseases here on Earth.

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Figure Legends

Figure 1. Dietary intake during space flight for four space programs. Data are expressed as a percentage of each individual subjects World Health Organization (WHO) predicted energy requirements. Data are mean ± SD, number of subjects (n) is indicated.

Figure 2. Diagram representing the movement of calcium in the body.

Figure 3. Multicompartmental model of calcium metabolism, as described in earlier reports (Smith et al., 1999 and Wastney et al., 1999). Arrows indicate site of tracer administration (i.e., oral and intravenous).

Figure 4. Urinary n-telopeptide excretion during the 84-day Skylab IV mission of the early 1970's. The data demonstrate the rapid and significant increase in bone resorption during space flight compared to preflight levels.

Figure 5. Fluid compartments during short-duration space flight. Data are adapted from a previous report (Leach et al., 1996).