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Technological and Medical Human Health and Well-Being Options in Deep Space

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Introduction

The conditions in space are massively different than on Earth where we evolved. The environmental physical forces that shaped our life on Earth include a protective atmosphere that regulates temperatures, provides nutrition, shields us from lethal radiation, and provides a 1g gravitational force pointing toward the center of Earth. These major environment factors governed our biological evolution including from water to land. They determined the regulation and flow of our bodily fluids, our structural support, posture, mobility, metabolism, etc. Space travel beyond low Earth orbit exposes humans to environments with unique health hazards and challenges to the point where human health issues become major cost and mission issues. The environments of space and other plantetary bodies and moons are usually typified by low pressure, low temperatures, galactic cosmic radiation (up to some 50 GeV of iron nucleii particle radiation), and reduced to micro gravity [ref. 1]. These conditions, along with isolation and confinement, produce, and in major ways add to a plethora of concomitant and often interactive space faring "risks" to human health and safety in space that technology must seriously mitigate to enable human survival and effectiveness for deep space exploration, pioneering, colonization, industrial operations, and tourism. NASA has compiled a list of space risks and concerns, some 32 total, binned into the areas of altered gravity, radiation, impacts of distance from Earth, isolation, and a limited, closed environment [ref. 1].The latter two risk arenas are also present, at different scales and times and recovery conditions than in space going forward, during nuclear submarine patrols, and in Antarctica. The risks and concerns impact humans in space concomitantly. The effects of these risks and concerns have not been studied very much beyond the current operational conditions at ISS, which are 6 months of micro g and 45% full Galactic Cosmic Radiation (GCR), easily resupplied and within a day of arriving back to, and able to gaze out the window at, Earth. We have no experience with, and cannot simulate terrestrially, the concomitant in space conditions associated with deep space human operations of years duration such as humans-Mars travel and on Mars activities. The observed health impacts of crew's 6 month tenure at ISS conditions utilizing extant risk mitigation approaches is that most adverse health effects are recoverable over time once back on Earth. The NASA space health efforts, studies, and experiences have produced some 800 health standards thus far.

Zeroth order, maintenance of human health requires supportive protection from the hazards of space, including supplying breathable air, comfortable temperatures, a supportive diet/nutrition, radiation protection, and sufficient gravity to avoid the combinatorial impacts of such effecting human operability and health. Spacecraft operability must be "fail-safe" to ensure these basic human life support conditions are maintained throughout the mission and the mission(s) must be affordable. There are known effects and unknowns effects regarding aspects of human health for Mars duration missions. Mars has the order of a third g. We have no data regarding the health impacts of this on humans or the combinatorial effects associated with 45% GCR on the Martian surface over time. There is a suspicion that if humans survive such conditions over long times they will evolve to living at reduced g and become "Martians". Cascading failures and subcritical degradations in systems of systems causing an overall unrecoverable failure are a potential issue.

There are two exremely complex systems associated with humans-Mars missions: the technical, engineering, and architectural system of systems that enable the mission and the humans. Both need to be mutually configured and operated to mitigate the overall risks and hazards of the mission. Regarding the humans that mitigation includes both the mission risks and supporting-to-increasing the human immune and other concomitant physiological systems. This report will summarize the risks, current mitigation approaches, and putative approaches including lifestyle, nutrition, and "wellness" approaches to possibly improve the human capacity to withstand the large number of combinatorial human physiological rigors of the missions. The wellness observations also apply to and are derived from Earth terrestrial applicable research.

Human Health Impacts of Space Faring

Due to current lack of definitive information, the following is a worrisome but incomplete list of the human health issues and concerns for human missions to and from Mars [refs. 1 – 7]. The basic differences in health related parameters between the ISS in LEO and the missions to and from Mars includes a far longer time frame for the current 3 year roundtrip duration versus 6 months on ISS, spacecraft exposed to full GCR versus the 45% on ISS, and attendant increased time-related reliability, safety, psychological issues, and other health concerns. The detailed nature of the potential combinatorial clinical health impacts at Mars mission conditions and their potential synergistic effects are largely unknown. Where the impacts are known, they appear to scale in severity with the exposed time in space, to, and from Mars. The potential effects of the .38g on Mars are also unknown, but partial gravity is expected to relax the issues experienced on ISS during microgravity. The health and medical challenges expected in a human Mars mission are unlike any prior manned spacecraft/space faring experience. Determining the risk of unacceptable health and mission outcomes requires consideration of which medical scenarios are most likely to arise during a mission, as well as those presenting the highest risk. There are no analogs on Earth that can fully represent the combinatorial conditions for a human to Mars mission.

The identified, yet thus far unmitigated, human health issues associated with humans to Mars travel and onsite exploration include:

1. Mars dust that may contain hexavalent chromium which causes cancer; Perchlorates at 10,000 times higher than Earth levels that impact the thyroid; and small, sharp, and highly oxidative particles that affect respiratory and cardio-pulmonary systems [ref. 4].
2. Pathogens or in-space "bugs" which have been observed to become more virulent and which, in combination with immune system degradation, may result in "illnesses" for which extant medications may prove ineffective. Other adverse immune systems impacts are expected from weakened t-cell function and the combinatorial impacts of radiation, micro gravity, psychological, and other mission issues including sleep and nutrition factors.
3. Micro gravity allows fluid shifts that cause: Eye/vision changes that blur vision upon abrupt motions; motion sickness: affects balance and appetite, causes dizziness, and stuffiness; DNA damage such as double strand breaks, chromosome aberrations/mutations, and attenuated repair process; down regulation of P53;

weakened t-Cells; 1% per month bone mineral loss especially calcium and early onset osteoporosis plus kidney stone propensity; muscle atrophy: up to some 20% loss in 5-11 days; skin irritation; Cardiovascular deconditioning, cardio arrhythmia, and heart degeneration including 30% to 50% decrease in maximal O_2 uptake due to blood cell and capillary altered interactions and blood volume loss; Orthostatic Hypotension and low blood pressure; Neurologic, brain, cerebrovascular, neurovestibular changes and reduced release of neuro-transmitters; effects on spinal fluid; sensory changes and dysfunction; increased homocysteine; Liver damage including long term scarring and non-alcoholic fatty liver disease; and fibrosis.

4. Space radiation, especially high energy GCR particle radiation present both in space and on planet/body causes: radiation “sickness”; Degenerative tissue effects, DNA damage, DNA repair process alterations, and oxidative DNA damage; Immune system degradation including significant reduced ability to produce blood cells; Anemia; Carcinogenesis including leukemia, Tissue degeneration, Respiratory effects, cataracts, heart, cardiovascular, and digestive system impacts; Neurologic effects, central nervous system and cognitive impairment; Alzheimers (white matter hyperintensities of the brain) reduced length and area of dendrites, performance decrements, and memory deficits, loss of awareness, focus, and cognition. A recent study indicates that GCR (particle radiation) causes “collateral” tissue damage to adjacent cells (called bystander cell damage from heavy nuclei) and could increase the cancer risk by some factor.
5. Psychiatric effects due to combination of physiological effects already noted plus distance from Earth, diet changes, sleep deprivation, and proximity to other crew members.
6. Toxic chemical exposure from spacecraft components as well as the Martian dust.
7. Reliability/life support system failures, spacecraft/propulsion, and other “mechanical” failures including sensors.
8. The usual space conditions of cold, vacuum, and the presence of exhaled CO_2 which tends to stay near the face and be rebreathed.

Molecular changes that occur during spaceflight include DNA damage, oxidative stress, alterations of telemere length, shifts in the microbiome, mitochondrial dysfunction, and gene regulation with impacts observed on the cardiovascular system (CVS), central nervous system (CNS), musculoskeletal, immune, and gastrointestinal (GI) systems. Resultant health issues include muscle and bone loss, heart and liver problems, and immune dysfunction [ref. 2]. These observations are from the usual 6 months in LEO, with microG, but less than 50% of GCR. The impacts of years long deep space faring health issues is largely terra incognita.

Selected Pathophysiological Consequences

Cellular dysfunction: In the microgravity environment it has been demonstrated that human cells are influenced by converting mechanical inputs experienced in their environment into biochemical signals that initiate alterations in cell and tissue homeostasis by a processes known as mechanotransduction. The decrease in gravitational force reduces mechanical stress or unloading at the cellular level resulting in conditions that shifts the balance between physiology and pathophysiology, thereby accelerating the progression and development of some diseases. For example, kidney stone formation and osteoporosis is accelerated in a microgravity environment compared to a 1g environment [ref. 8].

Organ system dysfunction: There is a significant shift in body fluids peripherally to centrally in the process of adapting to a microgravity environment (e.g., lower peripheral pressure and higher central pressures). This results in adverse impacts on human physiology and metabolism (e.g., increased body temperature, dehydration, loss of body mass, decrease in renal perfusion, decreased GI absorption, decrease drug stability and availability, etc.). For example, medications used in space are based on the assumption they are stable, absorbable, and pharmacologically are as effective in microgravity as in the 1g environment. However, alterations in drug stability due to radiation exposure and absorption profiles are altered due to organ system dysfunction. Much more work needs to be done. This is particularly important on flights beyond low Earth orbit that prohibit crews from returning to Earth in an emergency [ref. 9].

Endocrine: The chronic psychological and physiological stressors encountered in long duration spaceflight induces changes in the endocrine system that adversely impacts kidney functions, bone resorption, muscle loss, immune system functions, glycemic control, etc. The cascade of hormonal dysfunctions includes the sympathetic nervous system, hypothalamic-pituitary adrenal axis system, the renin-angiotensin-aldosterone system, calcium-parathyroid hormone-vitamin D axis, glucagon bipolar axis increases serum glucose and insulin levels, elevated oxidative stress responses, etc. [ref. 10].

Genetic: Cellular reproduction dysfunctions experienced in the space environment undergirds every phase of human reproduction involving spermatogenesis, ovarian follicles, fertilization, implantation, and the gestational process. The qualitative and quantitative damage done on reproductive systems, at the cellular and organ system level, by long-term exposure to radiation and microgravity are largely undetermined. The potential for an increased risk of cancer and teratogenesis directly attributable to spaceflight environments is also unknown [ref. 11].

Immune System**:** The innate immune system comprises cellular and enzymes (chemical) components that are activated as the first line of defense against foreign body invasions (infections, cells, etc.). The adaptive immune system (immunologic memory) are composed of T and B lymphocytes that are the secondary line of defense that eliminate damaged and/or mutated cells due to viruses or cancer. Exposure to radiation in the space environment is the principle stressor on the immune system resulting in dysregulation, cellular dysfunction, cellular morphology, increased rate of cellular destruction, etc. In addition to the space flight environment suppressing immune responses, it also increases the infectivity of bacterial and funguses, the reactivation of latent viral infections, and antibiotic resistance [ref. 12] .

Blood: Red blood cells (RBC) are destroyed and replaced every 120 days. The human complement of RBC has been totally replaced four months after entering the space flight environment but at a lower level, resulting in a mild chronic anemia. The mechanism that results in a 10 to 12% reduction in RBC mass during spaceflight remains undetermined [ref. 13].

Skin: The most commonly reported medical events in space involve the epidermis, dermis, and skin microbiota. Dermatological conditions experienced in space flight include viral reactivations, contact dermatitis, eczematous patches, skin infections, radiation damage, and skin cancer. Diagnosis and treatment can be difficult given the lack of resources in space as well as the hazards and side effects of certain treatments.
The manifestations and management of dermatological diseases are varied and are important considerations for mitigation on missions to the Moon, Mars, and beyond [ref. 14].

Bone: Bone loss during space flight has multifactorial etiologies to include microgravity, radiation, and dietary deficiencies. Since the mid-seventies, space travelers have experienced bone loss at a rate of 1-1.5% per month. Bone loss in the lower extremities is progressive but diminishes with time during long duration flights. While exercise protocols only partially protect against bone loss and the increased risk of fractures upon return to Earth's 1g environment. it remains a significant unresolved health risk. Post-flight recovery of bone loss depends on the flight duration and is concentrated during a short period after flight when bone formation exceeds resorption [ref. 15].

Cardiovascular: Space travel negatively affects cardiovascular structure and function primarily because of microgravity and radiation exposure. In a microgravity environment there is approximately a 2 liter fluid shift centrally and towards the head resulting in neck vein congestion, puffy facies, nasal congestion, and thinner extremities. This predisposes crewmembers to spaceflight-associated neuro-ocular syndrome (SANS) or space blindness, neck vein thrombosis, and orthostatic intolerance upon return to Earth. The resulting cardiovascular unloading increases cardiovascular deconditioning (decrease in circulating blood volume by 10-15% with decreased blood pressure), atrophy (10% decreased in size after a 10-day flight), and changing its shape from elliptical to spherical. Cosmic radiation induces directed damage to heart and vascular structures with a higher lifetime risk of cardiovascular morbidity and mortality. The clinical relevance of these findings post-flight remain largely unknown [ref. 16].

Respiratory: Physiologically the lungs function well in microgravity with no significant structural or adaptive changes observed in space flight or upon return to Earth. There is no disruption in blood flow, the ventilation perfusion ratio, or gas exchange. There are potential sources of pulmonary damage during space flight due to radiation damage, toxic dust, and aerosol exposures [ref. 17].

Digestive System: Space flight affects the entire gastrointestinal (GI) system from the ability to chew and swallow to defecation. The GI system is highly sensitive to radiation with "acute radiation syndrome," resulting in self-limited vomiting by 75% of crew members in the early stages of flight. Additionally, there are a number of stressors that alter the composition of their intestinal microbiome as well as the skin, nose, and tongue. These alterations can adversely impact the health of space travelers, especially on long-duration missions. The liver, pancreas, and urological systems are also radiation and microgravity sensitive organs manifested by alterations in their biochemical pathways [refs. 18, 19].

Neurosensory: The absence of gravity unloads the neurosensory organ systems resulting in structural and functional changes spanning from hair cells in the otolith system to cerebral compensation. Neurosensory adaptation to the space flight environment involves the ocular system (cataracts, corneal abrasions, corneal foreign bodies, etc.), the olfactory/gustatory system (smell, taste), auditory/vestibular system (spatial orientation, balance, motion sickness, etc.), and sensory motor (balance, locomotion, fine motor control, etc.) systems [ref. 20].

Neuromuscular: In a microgravity environment, the antigravity muscle groups atrophy rapidly and progressively because they are not required (disuse atrophy, denervation atrophy, biochemical/nutritional requirements decline, etc.). Exercise countermeasures are limited to muscle groups that move limbs and the torso. Tendons and ligaments also weaken and are at risk for rupture or injury upon return to Earth [refs. 21, 22].

Neuropsychological: Adaptation of the central nervous system to ionizing radiation and microgravity impacts multiple regions resulting in structural, cellular, electrophysiological, behavioral/psychological, and functions during space flight. In the space environment, there is a diminution of sleep time (circadian dysrhythmia), cognitive dysfunction ("space fog"), psychological dysfunction (depression, anxiety, psychiatric disorders etc.), and psychosocial dysfunction among crewmembers and mission control. Even minor maladaptive neurological changes can impact performance and mission success of long-duration space flight [refs. 23, 24].

Then, there are the potential synergistic effects of all of these, which are an early stage work in progress. Thus far, only the Apollo crews have been subjected to micro g and full GCR and for only a few days. As stated, where examined, these health issues mostly tend to beome more worrisome with time in space. Some of the effects, to the extent currently known, appear to be more long lasting. Thus far, engineering system failure have been the major cause of human death in spaceflight. Additional concerns include radiation that causes a mutagen in a pathogen when the immune system is compromised, and the medication on board could become less effective because the human metabolism has shifted. Then there is the potential interaction of factors that nobody has considered, the interaction of "unknown unknowns". "Many of the risks associated with long duration space travel are not fully understood" [ref. 25]. " Given each crew member will experience multiple spaceflight hazards simultaneously, we need to identify and characterize the potential additive, antigonistic, or synergistic impacts of multiple stressors (e.g., space radiation, altered gravity, isolation, altered immune, and altered sleep) on crew health or CNS/cognitive functioning to develop threshold limits and validate countermeasures for any identified adverse crew health and/or operationally-relevant performance outcomes" [ref. 26].

Radiation, Safety, and Micro G Mitigation Approaches

Radiation Mitigation [ref. 27]- There are three fundamental approaches to radiation mitigation which can be employed combinatorially: Spend less time in space, shield or deflect the incident radiation, and biological/medical counter measures to mitigate the resultant health impacts. In general, shielding requires low Z materials to minimize worrisome secondary radiation. Protection approaches include magnetics, fast transits (less time in space), biological countermeasures (BCMs), three plus meters of regolith or ice igloos, and silicon crystals to divert the GCR away from humans. The latter may be able to provide protection while in space suits, albeit this may require an exoskeleton to carry the weight/handle the inertia, etc.

Overall, due to systems level and conceptual/technological breakthroughs, the outlook for GCR radiation mitigation has altered over these last years from problematical/unaffordable to a number of potentially viable solution spaces across the TRL spectrum. These breakthroughs include inexpensive space access via reusable rockets, a low kg/kW (Alpha) many MW class nuclear battery, high energy particle reflection via silicon crystals, and the synthetic biological/gene editing revolution as applied to biological/medical countermeasures.

In decreasing order of TRL:

For on Moon, planet, etc., ~ three meters of regolith

For in space

1. Fast transits (200-day round trips to Mars) via inexpensive chemical fuel
2. Three-meter reusable polyethylene spacecraft overcoat enabled by inexpensive chemical fuel
3. Biological/medical countermeasures, a partial solution for space faring thus far, effectiveness improving
4. Fast transits (200-day Mars round trip) via 6,000 sec. Isp VASIMR high thrust MHD propulsion powered by an alpha of order one nuclear battery
5. Magnetic redirection of GCR particles via superconductive (S-C) magnets located extended distances from the spacecraft
6. Silicon crystal reflection of GCR particles plus shielding for Gamma secondaries

All of these approaches require extensive research and optimization with subsequent triage and development to determine the most efficacious for development/utilization. The current unsatisfactory status of GCR mitigation makes such investment necessary due to GCR being the agreed upon most serious human health deep space exploration/colonization issue.

<u>Safety and Reliability Measures: Approaches</u> [ref. 27] - As in aviation, by far the most prevalent cause of accidents in space faring is human factors. Due to the IT/AI/Robotics technology revolutions, the major improvements in space safety and reliability (S&R) will probably develop as we increasingly utilize machines in lieu of humans for everything including design, manufacture, checkout, transportation, operations, etc. Compared to humans, machines have far less latency, know far more, are far less expensive, exclude operational human error (e.g., leaving rags in fuel lines, etc.), have a far longer duty cycle, are far faster, far more efficient, far more durable and patient, and operate where humans cannot. The major general categories of safety and reliability issues include human factors including errors, mechanical equipment functionality, cyber, and environmental effects, all of which need to be addressed. There are safety and reliability issues which are combinatorial, including cascading failures. Little of safety and reliability is simple and much is insidious. A sampling of cogent get-well approaches include redundancy/backup systems, certification/standards, inspections, margins, recovery designed in, emergency systems, reliability analyses, obviate single points of failure, fault tolerant systems, and graceful degradation. The NASA list of top technical risks include cyber security, shortfalls in ground and flight testing, and too heavy a reliance on analysis/modeling and simulation. The

major metrics for human space faring are cost/affordability and safety/health. Ref. 28 provides a multiplicity of approaches capable of significantly reducing the costs of humans-Mars missions which could/should increase/"free up" the resources to improve health and safety issues, including increasing redundancy and enabling fail safe-safe design.

MicroG mitigation [ref. 29] – There has been much experimentation over the decades of human spacefaring regarding exercise and medicine related mitigation of microG health impacts. Not all microG effects are addressed by exercise but several are; it is not a panacea for such. There have also been extensive studies of employing artificial gravity produced by spacecraft rotation. This is a potentially excellent microG mitigation approach, but thus far not yet employed although originally planned for ISS. The huge reductions in LEO access costs from such as reusable rockets and improvements in autonomy and manufacture should provide/"free up" sufficient resources for application of artificial gravity incorporation in spacecraft design to significiently reduce the major and wide band health impacts of microG for long space transits such as conventional humans-Mars missions. There is obviously, as with regard to GCR radiation mitigation, the option of spending less time in transit. Cheap chemical fuels enabled by cheap LEO access and the low Alpha NASA nuclear battery powering VASIMR could reduce the overall humans to Mars mission trip times and consequent exposure to microG by large factors.

Overall - Exercise places loads upon muscles and bones to counteract micro gravity effects mitigating musculature and skeletal issues. Such exercise helps maintain the immune system and cardiovascular fitness. Nutritional and Dietary supplements plus pharmaceuticals and anti-oxidants are also proving to be efficacious and are a work in progress. "Biological Countermeasure" research is upbeat with respect to several substances, but the research is in its early days yet. Still too early to determine implementation, there are long-term possibilities, currently glimmering for the future, of genomics and synthetic biology to solve catastrophic diseases and possibly someday "space harden humans". Conventional space radiation protection shielding using low molecular weight materials, required to mitigate radiation secondaries for high atomic number (Z) radiation, requires a sizable to large amount of additional spacecraft weight and cost. Reduced LEO access costs such as proffered by reusable rockets, would be enabling. Materials and their arrangements as components of spacecraft architecture are a contributor to radiation protection but additional measures are also required. As indicated herein, a reusable radiation protection overcoat that remains in orbit between missions and enabled by cheap space access, may be the better approach for minimizing dose over time. "Fast Transits" uniquely enabled by recent reductions in space access costs (provides cheap chemical fuel in orbit) and the new NASA low alpha nuclear battery to power VASIMIR would enable much shorter round trip durations to reduce human exposure time to space conditions, especially microG and GCR, that affect human health. Artificial gravity generally created by rotating portions of the in-space habitat is thought to be more efficacious than exercise per se in mitigating some health issues associated with micro gravity. Artificial gravity concepts pose additional requirements on the in-space architecture that are not easily accommodated. Space flight during solar maximum provides lower GCR levels. Then there is the application of partial vacuum to the lower body to pull fluid away from the head, eyes, upper body. This somewhat mimics the effects of gravity upon body fluid distribution. Also of interest for mitigation is hypnosis to induce sleep for alleviating many issues related to sleeplessness, electrical stimulation, and vibrating platforms for remediating bone/muscle issues and ever better virtual and robotic on spacecraft medical care including prevention, diagnosis, treatment, and robotic surgery. Recent research on utilization of small curved silicon crystals to divert incident GCR is promising.

Current and Experimental Space Faring Nutrition and Lifestyles

Human nutrition is perhaps the major determiner of our health. The common phraseology is “we are what we eat”. Given the many and serious combinatorial threats to human health associated with deep space faring, ensuring nutrition that goes beyond excellent in the terrestrial sense is highly efficious to ensure the health, well being, and functioning of the crew. This is also known as prevention. There are various adverse issues associated with medicine, treatment of health issues in deep space including possible new and more virulent ills, availability issues with effective and sufficient treatments, medicines, etc. and altered treatment impacts in space, along with the many and serious concomitant deep space faring health stressors which appear to require serious preventive health measures and approaches, the foremost of which is nutrition. There are foods, sometimes referred to as protective nutrition, that are considered effective preventatives or mitigators, such as anticarcinogenesis, antibacterial, anti-inflammatory, and antioxidation, which address a multitude of other health issues and boost the immune system and the gut microbiome. Nutritional supplements and various “wellness” activities and lifestyles as well as synthetic biology (SynBio) to block some proteins are also part of an augmented preventative regime to mitigate the combined additional rigors of space. Biological counter measures are not just for radiation; they can have efficacy with regard to the CNS, CVS, musculature, and other physiological systems. Conventionally, the field of medicine is focused on “fixing” things, but there is increasing awareness that prevention is also a powerful approach, which is more economical and reduces pain and mitigates human operability issues. From ref. 7, “Space food still does not meet basic nutritional guidelines”, so there appears to be opportunity to mitigate stressors via preventative nutrition. Conventionally, nutrition has been carried on board. Other food/nutrition options include agriculture via modifying soil on the Moon and Mars, closed soilless cultivation systems, (e.g., hydroponics, aquaponics, aeroponics, etc.), and precision nutrition based on an individual’s DNA, race, gender, health history, and lifestyle by using information derived from advances in genomics, metabolomics, transcriptomics, proteomics, and nutrigenomics. These differences can be amplified in extreme conditions, such as space flight and miniature hand-held and/or wearable health monitoring devices to assess health, nutritional status, and metabolism [refs. 30, 31, 32]

There are now increasing options for “dark” and other foods that can be produced on board readily on long trips which are nutritious. Due to technology advancements and the need to reduce climate change impacts, there is an ongoing near revolution in lab-grown foods, also termed cellular agriculture. The efforts were initially focused on meats and other proteins but are expanding across most foods. Using molecular biologics, tissue engineering, SynBio , bacteria, etc. foods could be manufactured on Mars with a smallish footprint and less resources and effort. Cyanobacteria, spirulina, mushrooms, duckweed, spirulina, and insects are a sampling of suggested deep space faring food sources/resources. Then there is dark food and other bioproducts not produced by photosynthesis but instead by chemotropic single-celled organisms. Projections indicate orders of magnitude reductions in the energy, water, and costs required to produce food by photosynthesis [ref. 33].

Adequate nutrition in human space flight is a mitigation strategy that can reduce the adverse physiological impacts of high metabolic rates, inefficient control of body heat, altered cardiovascular and immune system function, decrease muscle mass and strength, and loss of weight bearing muscles and bone. The body cannot store proteins resulting in potential protein insufficiency and therefore there is a need to consume adequate proteins to support metabolic requirements. Excess protein consumption adversely impacts kidney and bone chemistry. Vitamins are susceptible to degradation and inactivation during food preparation and exposure to radiation leading to vitamin deficiencies, especially vitamin D. Calcium is recruited from bones; poorly absorbed from the GI tract; and lost through urinary excretion [ref. 34].

Refs. 35 – 41 are representative of the sizable extant literature regarding nutrition in space, which mainly addresses the current situation but expresses the need for seriously improved nutrition as part of an overall health prevention campaign necessitated by the health issues of human deep space faring with longer, farther missions. Ref. 35 states that "astronauts in space are generally not optimally nourished", and that optimal nutrition varies with the individual, while ref. 36 opines that "the nutritional requirements of space travelers and the role of nutrition in human adaptation to microgravity are as critical to crew safety and mission success as any of the mechanical systems of the spacecraft itself." The historical and current space diet options are given in Ref. 38., Ref. 39, and 41, which discuss the increased nutritional needs of deep space, long trip human space faring, suggestions regarding nutritional and supplement approaches for mitigation of deep space physiological stressors and on-board food production.

In terms of lifestyles, provision of adaquate sleep, psychological training for dealing with populated closed spaces over long periods, and serious all body exercise are essential mitigators regarding space faring health stressors. Overall, current LEO space nutrition and lifestyles are avowedly less than what is needed and with the increasing prospects of humans to Mars and beyond there is the beginnings of consideration for super nutrition and lifestyles to help ensure crew health and operability.

Space Faring Impacts on and Remediation of the Immune System

The executive agent for human health is the immune system, which senses, interrogates, evaluates bodily functions and organs/piece parts, and dispatches threat mitigation agents as needed to maintain stasis [ref. 42]. This fundamental, essential functionality for human health in space is seriously affected by the adverse stressors of space faring [refs. 43- 46]. Such immune suppression is in the presence of extant spacecraft bacterial or viral agents which have been observed to become more virulent with in-space conditions. Results of this immune suppression include persistant inflammation, viral reactivation, upper respiratory conditions, neoplastic growth, altered wound healing, hypersensitivities, infections, and skin rashes. GCR heavily suppresses immune T-helper and T CytoToxic cell functions. Ref. 45 opines that for longer duration space missions the immune dysfunctionality is likely to be irreversible. Refs. 45 and 46 discuss immunonutritional mitigators for space related immune system suppression including dietary nucleotides and mushroom extracts. Other mitigators include crew isolation before flight, on vehicle/hab filtration, corrections to, and optimization of nutritional intake, whey protein for amino acid content, fruits and vegatables as foods, not piece part supplements, anti-oxidants, polyphenols, and omega-3 fatty acids. "The human immune system is fundamentally shaped by environmental exposures impacted by individual lifestyle choices (diet, exercise, social habits, etc.)" and "The benefits of exercise and nutritional countermeasues are striking" [ref. 46].

The human microbiome consists of trillions of microorganisms from thousands of species – bacteria, fungi, parasites, and viruses [ref. 47]. An individual's microbiome is determined by genetics, diet, and exposure. The microbiome is an important part of the immune system. It digests food and synthesizes vitamins, amino acids, and enzymes. Refs. 46 and 48 – 50 consider the potential impacts of the deep space environment and exposure duration upon the human microbiome along with some possible mitigation approaches. The current evidence regarding space faring effects on the human microbiome is mixed as is the situation regarding the efficacy of pre and probiotics in space.

Terrestrial Experience Regarding the Human Health Impacts of Lifestyle and Diet/Nutrition

There is extensive literature regarding the favorable health, immune system, and longevity impacts of a plethora of lifestyle changes including diet (e.g., refs. 51 – 61). The nominal "go-to" set of targets with favorable impacts include serious wide band exercise, a diet best currently nominally represented by a "Mediterranean" diet, minimal alcohol, smoking, and sugar, adequate sleep, social relationships, weight control, and stress reduction. Chronic and metabolic diseases, joint/structural problems, CV diseases, and hypertention, have been aggravated by less than healthy lifestyles. Studies [ref. 52] indicate exercise can reduce the incidence of demetia by 50%. It also reduces CV disease and high blood pressure. Diets rich in whole grains, vegetables, and fruits reduce breast cancer risk by 50% - 70% and alzheimers by 60% [ref. 53]. "Nearly half of all premature deaths may be due to unhealthy lifestyle choices." Lifestyle changes can lower heart disease risk by 50% [ref. 54] to 80% and obviate 50% of ischernic strokes [ref. 56]. Ref. 57 has an excellent summary of the relative effects of various foods upon both health and the climate/ecosystem. The spectrum of favorable impacts of targeted nutrition on the immune system are discussed in ref. 61. Overall, the terrestrial evidence is overwealming: nutritional optimization can boost the immune system, which would mitigate the health impacts of the many health stressors associated with deep space faring.

Space Medicine

The next line of deep space faring health defense after prevention and mitigation is space medicine (e.g., refs. 62 – 64]. Space medicine has been mentioned in connection with biological and medical countermeasures for radiation and microG, preflight preventive measures, and nutrition. Medical measures in deep space are subject to a plethora of issues including the inventory and amounts of medicines carried on the mission, the aging of these carryons and the possibilites associated with altered human physiology due to deep space faring and pathogens being altered due to in-space conditions. These issues involve knowns, known unknowns and, possibly, unknown unknowns. Ref. 62 provides an extensive overview of space medicine, which evidently involves 70 companies, 70 investors, and 60 R and D centers. This is a sizable endeavour instigated by governmental humans-space efforts and more recently by interest(s) in space tourism. Observations include a possible analogy regarding human aging and space health issue impacts indicating potential applications of human longevity research to deep space faring. Infection prevention and control in the confined interior spaces of deep space travel are discussed in ref. 64. This issue is adversely altered by crew impaired immune response, hightened virulence, air, and water recirculation, and microgravity alteration of droplet dynamics. Infection prevention and control measures, which are based upon terrestrial clinical practice, are extensive and include health histories, vaccinations, screening, isolation, testing, filters, coatings, food irridiation, prompt treatments, masks, and immune function support. As discussed in refs. 65 – 69, the several ongoing tech revolutions are altering the clinical practice of space medicine, including tele-medicine, robotic surgery, AI diagnostics and treatment, personalized medicine, human enhancement, frontier sensors for improved diagnosis and toxicology, synthetic biology for improved treatment, mitigation, and enhancement. There are synergistic interactions regarding terrestrial and space medicine with space requirements driving markets for monitoring, diagnostics, and therapeutics that are simple, safe, robust, and miniaturized [ref. 70]. These capability and attribute combinations are what are needed to develop further telemedicine, an increasingly "do it yourself" form of medicine which, along with AI, reduces the costs of terrestrial healthcare and broadens healthcare availability.

Synopsis – Options: Approaches to Improve Human Health in Deep Space (Arbitrary Order)

1. Reduce mission cost to increase resources for health and safety (ISRU, weak force new nuclear batteries, fast transits via cheap chemical in space or the new nuclear batteries, ditch and bury habs, cheap space access, AI, autonomous robotics, synthetic biology, rigidizable inflatables, dark foods)
2. Serious exercise and adaquate sleep
3. Training for living in confined spaces
4. Supportive nutrition beyond terrestrial precepts
5. Artificial gravity
6. Biological countermeasures, curved silicon crystals, ditch and bury for radiation
7. Effective dust protection
8. Engineering fail safe-safe design
9. Integrated vehicle health management
10. Immersive (VR/ Holographic) communications
11. TeleMed, sensors
12. Expect/intuit unknown unknowns

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