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RESEARCH ARTICLE

REDUCING RISK OF NEIL ARMSTRONG SYNDROME.

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Abstract

Serum magnesium (Mg) invariably reduced in Space (S) ($p < .0001$), catecholamines elevated to twice Earth levels, conducive to catecholamine cardiomyopathy, exemplified by "Neil Armstrong Syndrome": severe (SE) dyspnea, SE thirst, SE tachycardia (up to 160) during lunar excursion before inhalation iron-laden dust. On Earth, to correct Mg deficits, shortening life, use Ca/ Mg intake ratio (R) not over 2:1; higher R reduces Mg absorption. In S, bone loss, increased Ca excretion; study young exercised female rats, correlating with WBC telomere length, telomerase to determine ideal ratio: 30 rats, 10 in each group: ? 2/1, 3/1, 4/1 R.

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The first published case of possible space flight - catecholamine cardiomyopathy (acute temporary heart failure) exemplified by Neil Armstrong, the first moon walker, occurred prior to exposure to a confounder i.e. highly toxic, iron-laden dust, with deadly hydroxyl radicals, brought into the lunar habitat on the space suit and conducive to oxidative stress. Since catecholamine levels are twice Earth levels when supine, clearly there will be many other cases until a way is found to correct invariable dehydration from plasma leaking, stemming from endothelial dysfunction and intensified by impairment in the thirst mechanism, magnesium (Mg) deficits, ischemia, catecholamine elevations and vicious cycles.(1-3)(Fig 1.) Furthermore, Mg deficits elevate circulating levels of inflammatory cytokines, also conducive to oxidative stress along with catecholamine auto-oxidation.(4,5).

The aging process is associated with progressive shortening of telomeres, repetitive DNA sequences and proteins that cap and protect the ends of chromosomes. Telomerase can elongate pre-existing telomeres to maintain length and chromosome stability. Low telomerase may be associated with increased catecholamines while the sensitivity of telomere synthesis to Mg ions is primarily seen with the longer elongation products (TTAGGG). Mg stabilizes DNA and promotes DNA replication and transcription, whereas low Mg might accelerate cellular senescence by reducing DNA stability, protein synthesis and mitochondrial function. Telomerase, in binding to short DNA's, is Mg dependent; over 300 enzymes are dependent upon Mg function. Correcting Mg deficiencies may prolong life. Since the telomere length is reduced with oxidative stress, the antioxidant effect of Mg provides a considerable advantage. (6).

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Mg is invariably reduced in Space; in 196 space shuttle crew members, serum Mg was significantly reduced ($p < .0001$) ---despite the poor sensitivity in the serum; similarly at the 11th Man In Space Symposium, Toulouse, France, this was shown in 143 Cosmonauts. Mg is both a powerful antioxidant and calcium (Ca) blocker. But with space flight, there is impairment in gastrointestinal absorption(7) necessitating parenteral administration; also, there is a progressive loss of skeletal muscle Mg storage sites beginning in a few days and in bones ---with 1-2 % loss of bone storage sites per month--- no matter how much one exercises; furthermore both too much and too little exercise will shorten the telomeres and in turn reduce the lifespan.(6) With the aging process accelerated by a factor of 10, research on the International Space Station with rats, provides the advantage of reduced time and cost.

Furthermore, NASA has encouraged such research and has emphasized its value in applying it to Earth. With catecholamine levels in Space twice Earth levels. (1) and invariable significant Mg ion deficits what measures can be taken to prevent heart failure exemplified by Neil Armstrong with severe dyspnea, severe thirst and severe tachycardia with the latter conducive to oxidative stress? (2) Because of very high carbon dioxide levels on the Russian satellite, Mir, for example, over 10 times higher than on Earth, it was postulated that there may be an intracellular shift of Ca. conducive to vasospasm and mitochondrial injuries; telomere dysfunction induces impairment in mitochondrial function which can contribute to cardiomyopathies with congestive failure. (2, 6).

A pioneer in magnesium research, Mildred Seelig M.D., emphasized decades ago, that an excessive intake of Ca will reduce the gastrointestinal absorption of Mg and that a low Mg/ Ca ratio increases release of catecholamines. (5) It is noteworthy that in the seventies, for example, Finland had the world's highest cardiovascular mortality rate and the highest Ca/ Mg intake ratio of 4:1. (8) Since a high Ca/ Mg intake ratio, was believed to be responsible for enhanced stress reactions, Durlach, published in the eighties, the importance of maintaining a Ca/ Mg intake close to 2: 1; (9) Regarding Ca, the requirements would be greater than on Earth with a progressive loss of bone; the longer the mission, the more Ca is lost with excretion; (10) this deficiency would be intensified by persistent malabsorption.(7)

A high Ca/ Mg intake ratio, was believed to be responsible for enhanced stress reactions. (5) Since space flight induces bone loss and subsequently Ca loss, progressively intensified with the duration of the mission, (10) how can a favorable Ca/ Mg intake ratio be established in space? It is unlikely that it will be 2/1 as on Earth; also, the ratio is likely to change as space missions increase in duration.

Since ground-based (head-down) studies have not shown the high space- catecholamine elevations and excessive loss of Ca, I propose the following 6 month Space study: Young Sprague-Dawley female rats would be used; it is note - worthy that bone formation is suppressed during space flight in young rats; (10) females would be more likely to survive because of estrogen's antioxidant effect. Also, when Mg levels are marginal, Seelig (5) has emphasized that females' Mg levels would be higher. Rats would be exercised on treadmills for a half hour every 12 hours with a gradual increase in the intensity of exercise as tolerated; 12 hour light/ dark cycles. Cooling would be required since in space, exercise intensifies renal Mg loss and in astronauts, Mg loss with sweating. Because of invariable malabsorption (7), subcutaneous Mg and Ca supplements would be required with close monitoring, particularly of serum Mg levels, since impairment in renal function is a contraindication to Mg supplements. (5)

To determine a favorable Ca/Mg intake ratio in microgravity: 30 rats with groups of 10 in each group using 2/1, 3/1, 4/1 Ca/Mg intake ratios; then determining which intake ratio is the most favorable regarding their life span, focusing on their leukocyte telomere lengths, and leukocyte telomerase; there would be age-matched controls on Earth. In those rats which do not survive 6 months, their organ blood vessel telomere lengths and telomerase levels would be determined. (Summary, Figure 1.) Using this plan, the hazards and complexity of pharmaceuticals are avoided, in the presence of potential progressive endothelial dysfunction with in turn, impaired hepatic and renal function in order to metabolize and excrete them.

This research method of utilizing telomere and telomerase levels is a new application in space medicine, to my knowledge; it opens the door for many other applications in addition to reducing the risk of worrisome space-cardiovascular complications. Readers must keep in mind that Mg may prolong life(6) and these Mg deficits invariably occur in space; but first, we must determine the ideal Ca/ Mg intake ratio which may be higher than the ideal level on Earth; it may be higher than 4:1 but this is unexplored territory.

Eventually, either exact Earth gravity must be duplicated in transit and while exploring further the moon and then on to Mars or an asteroid; this is a better option than the use of extremely complicated genetherapy (11) ; this proposed research concept is the first step. Recently, Professor Stephen Hawking emphasized that Man must eventually colonize in order to survive.

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