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**ADAPTATION AND READAPTATION MEDICAL CONCERNS OF A MARS TRIP**

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**ABSTRACT**

This paper deals with the ability of the human body to adapt to microgravity environments and to later readapt to a gravity environment. Issues specifically relating to the effects of long-duration space flight on the adaptation/readaptation process are discussed. The need for better health prediction techniques is stressed in order to be able to better anticipate crew health problems and to perform corrective actions. Several specific examples are discussed of latent diseases which could occur during a long duration space mission, even after having subjected the crew to thorough pre-mission checkups.

The paper also discusses the need for learning how to prevent or ameliorate such problems as space adaptation syndrome, bone and muscle (and possibly tissue) atrophy, immune system atrophy, and heart arrhythmias. It briefly addresses the implications of the age of the crew, the influence of an on-board low level gravity field, and drugs as factors in the adaptation/readaptation process.

**INTRODUCTION**

Anticipating a trip to Mars will first engender excitement and then concern as the enormity of the task is realized. As this is written no human has lived in a microgravity environment for a period as long as it will take to reach and return from Earth's sister planet.

Before crews are selected for the historic event, Aerospace Medicine will need to develop much more skill in the art and science of predictive medicine. In no other situation has medicine been called upon to certify that an individual will be healthy enough to perform full duty for two years following the pre-flight examination. The annual physical examination is well ingrained in the practice of aerospace medicine and is used to certify pilots. But, it is not unknown for a seemingly healthy pilot to develop an incapacitating illness between examinations. Generally, illness presents itself with warning signs, often first realized on awaking in the morning so that the pilot can call in sick and in that way avoid illness during the trip. Most airplane flights are

relatively short so their duration often does not exceed the prodromal phase and minor symptoms of an illness. NASA and the USSR have had experience certifying astronauts and cosmonauts for mission periods up to eight months. In orbital space flights, any mistake could be rectified by having the crew return to Earth after the onset of symptoms from a dangerous illness or accident. On a Mars mission, the medical luxury of returning for hospitalization will not be possible. Therefore, a predictive system which will foretell illness two years in advance should be developed even though significant health maintenance capability should exist in-flight.

LONG TERM HEALTH PREDICTION TECHNIQUES MUST BE DEVELOPED USEFUL FOR A MISSION WHICH COULD LAST OVER A YEAR AND FOR WHICH EARLY RETURN TO EARTH IS NOT FEASIBLE

When the Mars craft launch acceleration slows, the crew will sense weightlessness (in reality, microgravity) which could continue until they begin the braking maneuvers needed to obtain a Mars orbit. The sudden unloading of the otolith as well as other physiological changes is followed by what is known as space adaptation syndrome (SAS). Crews report that the acute symptoms of SAS disappear in two to three days. Thus it will not be a major problem for a long duration Mars mission. However, long duration USSR crew members apparently report annoying returns at random times of the disorientation which they felt on entering weightlessness. It is probable that when NASA counters the acute symptoms, these later manifestations will be prevented. It is possible also that if the craft has some acceleration, none of the space adaptation syndrome symptoms will appear.(1)

SOLVING THE SPACE ADAPTATION SYNDROME IS NOT A PREREQUISITE TO A MANNED MARS MISSION

During a prolonged mission bone and muscle atrophy will occur if not prevented. In the case of muscles and bone, proper loading, stretching and use will prevent this problem. At present a low cost method to accomplish this has not been found. The USSR reportedly requires long duration crews to spend several hours each day in body conditioning maneuvers. We have no proof that these work or are even helpful. However, neither the U.S. nor the U.S.S.R. has flown people for long durations without the (presumed) countermeasures being taken.

Bed rest studies suggest that it takes four hours of vigorous walking each day to prevent negative calcium balance. Four hours daily is obviously too long a duration for a physical fitness program. Drugs are being looked at as a possible way to prevent bone atrophy. In microgravity, if a drug enhanced bone formation it could stimulate areas where increased calcium deposition is harmful, e.g. skull where calcium addition could cause damage to the cranial nerves. Nature relies on the stress and strain of everyday activity in gravity to signal the location of bone formation. Any failure to faithfully reproduce the gravity conditions could encourage bone formation in the wrong areas. Thus, development of a drug to correct this problem may be difficult. An ideal drug would keep the skeleton exactly as it was before the mission. This might interfere with the other major function of bone. Bone is used as a source of metabolic calcium for periods when calcium is not being added to the system from food. Additionally, the rate of calcium absorption is never ideal and calcium blood levels would go too high after a calcium containing meal if there were no way to rid the plasma of the calcium entering from the gastrointestinal tract. The kidney can do part of the job but its responses are relatively slow. The skeleton is used for this purpose. Any drug which hinders bone metabolic activity would likely result in hypercalcemia during the gastrointestinal absorptive periods and hypocalcemia when gastrointestinal calcium absorption ceases.(2)

NASA researchers are actively investigating the muscle and bone changes produced by microgravity. It can be anticipated that significant progress will be made before it is time for the Mars mission if a systematic investigative road-map is implemented. Unfortunately, these atrophies are best studied in microgravity and there is no plan for long duration U.S. missions until the Space Station. U.S. researchers are thus confined to ground based studies or experiments which look at the problem for periods of only about a week, the maximum planned duration of Shuttle flights. The USSR has longer missions. A cooperative program using the advanced technology and equipment of U.S. researchers during USSR Space Station missions would be mutually advantageous.

LEARNING HOW TO PREVENT OR AMELIORATE MICROGRAVITY INDUCED BONE AND MUSCLE ATROPHY IS AN IMPORTANT MEDICAL PREREQUISITE TO A MARS MISSION

NASA is just now learning the extent of the heart mass changes produced by the changed cardiac dynamics of microgravity living.(3) It is known that the microgravity cardiovascular adaptation causes undesirable symptoms on return to gravity. The cardiovascular changes are, in one sense, normal adaptation to the microgravity environment and, again a normal adaptation upon return to a gravity environment. NASA is beginning to learn also that the spontaneous adaptation to microgravity which causes changes in heart size may be associated with cellular changes in the heart which make the heart less stable electrically and thus more sensitive to arrhythmias. EVA crewmen who never before showed a tendency to develop cardiac arrhythmia can spontaneously develop them during or following an EVA. Whether this would be true also in the low G of Mars is unknown. This phenomena can be studied during the Shuttle era if plans are made to include regular cardiac monitoring during EVA.

LEARNING MORE ABOUT THE ELECTRICAL INSTABILITY OF THE HUMAN HEART ASSOCIATED WITH EVA ACTIVITIES IS AN IMPORTANT NASA GOAL

There are other atrophies associated with microgravity living. An interesting example is the decrease and leveling out in the number of circulating red blood cells which occurs early during a space flight and seems to continue throughout missions as long as six months(4). The reasons for this atrophy is unknown. The operational impact of a decrease in the circulating red blood cell mass is not very great, but unknown now is whether the bone marrow should respond normally if a crew member were to have a hemorrhage great enough to require a response in the bone marrow, although clearly the marrow is replenishing red cells once the lower level of red cell mass is reached. A large hemorrhage might come from the laceration of an accident or from a bleeding ulcer. Either way, the bone marrow would have to respond to prevent serious consequences. There are some who believe that the red cell decrease may be the most obvious example of a more extensive atrophy of body cells brought on by exposure to microgravity. Whether microgravity induced atrophy of other areas is of importance to the well being of a crew member is unknown at this time.

A GENERALIZED ATROPHY OF TISSUE CELLS MAY BE PRESENT DURING MICROGRAVITY LIVING. THE OPERATIONAL SIGNIFICANCE OF THIS NEEDS TO BE LEARNED FOR CONTINUED SUCCESS OF MANNED SPACE ACTIVITIES

Malignancies are another class of diseases for which medicine has yet to develop good predictive techniques, with the possible exception of cervical carcinoma. Certainly no one thinks it unusual when an individual develops clinical cancer a few months after being called physically fit by the examining physician. A single example makes this point. There existed an individual who as a research subject did much to enhance medical science. His esophagus was destroyed by lye ingestion during childhood. To allow him to eat, an accessible gastrostomy was placed on the abdomen. The physician/scientist caring for this patient used the gastrostomy for research studies several times each year. After a series of studies, the subject returned home for periods up to six months. Two months after a study series, the subject called the scientist to report bleeding that day from the exposed gastric mucosa. This had not previously happened. Brought immediately to the medical center, a small ulcer was visible. On biopsy it proved to be gastric cancer. Practicing physicians can document similar situations with cancer of the breast and lung appearing soon after negative chest x-rays and mammograms. Thus, it is desirable to have ways to predict cancer well before it is currently clinically recognizable. The potential for malignant change could be greater during a space flight because of increased exposure to radiation.

PREVIOUSLY UNDIAGNOSED MALIGNANT DISEASE HAS TIME TO BECOME CLINICALLY SIGNIFICANT DURING A MARS TRIP

The crew living in what amounts to an isolated state would have less problem with infectious disease except from those pathogens brought with them. The human adapts to isolation by a gradual decrease in the immune surveillance system since it is not called upon daily to respond to new disease threats. The immune system atrophies much as an unused muscle atrophies. It has been learned from the Antarctic isolations that symptomatic respiratory virus infections regularly appear among the station complement months after the start of the isolation.(5) It is generally believed that these viruses have been sequestered in one of the crew. This is similar to the reappearance of the chicken pox virus as herpes zoster years later. Some infectious diseases, for example acquired immune

deficiency syndrome, have incubation periods over one year in length and during the incubation period diagnosis is not now possible. It is possible also that illnesses appear because the virus has been present in food since its preparation. Presterilization of the food supplies has been part of the space program since the Mercury missions. An additional factor are aerosols and dust which in a weightless environment do not settle quickly to the floor and thus continue to be rebreathed unless the air is well filtered.

The same situation exists for bacteria and bacterial diseases. Most of these will be brought with the crew in the GI, GU and respiratory tracts. Depending upon the body area and severity of pathological changes, these bacteria may become important. As an example, poor drainage of the renal pelvis, made worse by weightlessness, might allow bacteria to produce a pyelonephritis. Similarly, trichomonas residing asymptotically in one female crew member might cause disease in a second. For most bacterial diseases there are easily administered antibiotics provided that resistant strains are not developed by transfer of plasmids.

Research must be done so that reappearance of infectious viruses from an unsuspecting crew member will not cause illness among the other crew members. Ways must be found to prevent adaptation of the immune system to an isolated environment. By the time of the Mars trips, immunization and/or effective antibiotics for virus infections should have been developed. An active reimmunization program might be useful.

THE CREW WILL NOT BE FREE OF INFECTIOUS DISEASES AND OPPORTUNISTIC INFECTIONS BUT IMMUNE SYSTEM ATROPHY MAY OCCUR

Unshielded radiation exposure is of great importance to the crew members; this topic is discussed elsewhere. Certain features of this exposure are important. First we might send a crew who no longer wish to produce children and in that way avoid concerns about genetic effects from the radiation. Crew members relatively advanced in age might be used and in that way these individuals would die of other natural causes before radiation induced malignancies become significant clinically.

On the other hand, NASA data indicate there are significant decreases in the response of the crew member's lymphocytes to stimulation by foreign proteins after a space flight and there is some evidence

from similar lymphocyte culture experiments on Spacelab #1 that gravity may be necessary for proper functioning of lymphocytes. If this is true, the combination of decreased lymphocyte function and increased radiation exposure would be predicted to increase the rate of clinically significant malignancies induced by the radiation exposure during the trip (6,7).

RADIATION EXPOSURE COMBINED WITH DECREASE FUNCTION OF THE SPACEFLIGHT ADAPTED IMMUNE SYSTEM MAY BE OF CRITICAL IMPORTANCE TO A MARS CREW SINCE THERE COULD BE AN ACCELERATION IN THE RATE OF FORMATION AND GROWTH OF MALIGNANCIES. NASA MUST VIGOROUSLY STUDY THIS FEATURE OF SPACE FLIGHT.

Some of the changes usually associated with aging may become more symptomatic in the spacecraft environment and the long duration of a Mars trip would allow these changes to become more symptomatic. A simple example makes the point. A crew member over 45 years of age could suddenly find that there is trouble with near vision due to symptomatic presbyopia which some crew members report is made more symptomatic in microgravity. Happily this is easily treated with glasses if these are available on board. Other aging symptoms might appear. This is particularly true of osteoarthritis of the spine which is made more symptomatic because of the changes in the spinal dynamics resulting from microgravity.

DISABILITIES OF AGING WILL HAVE TIME TO BECOME SYMPTOMATIC DURING THE TRIP. SOME OF THESE ARE MADE MORE SYMPTOMATIC BY MICROGRAVITY.

Gravity is required for physiologic processes to work efficiently. In microgravity, adaptations of physiology are required. Most of these adaptations are perceived as minor by the individual except during a short period following a sudden change from one gravitational state to the other. At the present time there is no information available which suggests that the adaptation process would be simplified or prevented by a gravity level somewhere between one G and zero G. Until this is known any attempt to design a spacecraft with partial gravity must rest on other than medical reasons.

AT THIS TIME IT IS NOT DETERMINED WHETHER PARTIAL ARTIFICIAL GRAVITY BUILT INTO THE MARS SPACECRAFT WOULD HAVE A POSITIVE EFFECT ON THE CREW'S HEALTH

#### SUMMARY

This has been a short review of some of the microgravity adaptation processes that Flight Medicine must take into account before NASA can

certify man for a trip to Mars. Certainly none of these are show stoppers and it is certainly possible to send a crew to Mars even if none of these physiologic adaptations and pathologic changes were prevented or solved. Happily, healthy middle aged humans tend to be relatively free of disease processes for long periods of time and the problems they do develop are usually not so severe that they can not continue to function for a period of time long enough to complete an important task.

Additional medical research is necessary to help man's adaptation to the flight environment and on return to the Earth environment after a Mars mission.

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