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COUNTERMEASURES TO MICROGRAVITY

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Many physiological systems sustain easily documented changes as a consequence of exposure to the space environment. Most often recorded in studies of astronauts, these changes are believed to be largely the effects of microgravity. Areas of physiological interest are summarized in Table 1. The problems may have rapid onset as common to the neurovestibular effects that cause space adaptation syndrome. Entry and exit to the microgravity environment are often highlighted by vertigo and gastric disturbances. Or, the problems may be protracted as in the case of bone deterioration that develops somewhat more slowly and that recovers slowly upon return to normal gravity. Unfortunately, the direct causes of these and the other alterations are poorly understood. Thus, direct countermeasures may be especially difficult to implement. Accordingly, I have attempted to provide a conceptual set of considerations for obviating the effects of micrgravity. The exercise may be whimsical but the thought it is meant to provoke may change the way we approach some microgravity problems.

Based upon observations of biological systems exposed to the space environment, it seems helpful to provide a structure within which to categorize classes of effects. Simply, some effects may be quite passive consequences of microgravity related to fluid redistributions or losses of mechanical loading. Others may signal an active cellular or tissue response to the altered environment in which they are immersed. Finally, some effects are reactive in that cells and tissues respond actively but inappropriately to the environment created by microgravity. Examples of such effects are provided later. However, it is crucial to recognize that such effects may have intracellular, membrane, immediate extracellular, tissue, organ or organism sites of action.

The passive consequences of microgravity translate into a variety of hydrostatic, mechanical and electrical effects. For example, fluid compartments change, loads on cells and tissues change and even a variety of piezoelectric changes may occur. Other alterations occur, as well. At the organism level, the consequences of fluid columns existing in the absence of loading and pressure changes promote passive, active and reactive effects, for example, in the cardiovascular and lymphatic systems. At the tissue level, these effects are reflected in cardiac, vascular and, perhaps, immune system changes. Mechanical and piezoelectric effects may be linked in regard to bone changes. But, it is critical to recognize that some of the known effects of microgravity on bone could result from passive microgravity influences on bone circulation or from the extracellular dynamics of bone formation and deterioration. Reactive changes are most evident in fluid shifts to the upper body that result in hormone messages that signal increased kidney function. Or, unweighted gravity sensors of the inner ear may produce spurious signals that produce disorientation in the central nervous system as well as altered neuromuscular-cerebellar communication to the peripheral nervous system. In the former, the system simply behaves in a normal way, ignorant of the microgravity. In the latter case, the system may be adapting to a point of accepting "noise" as a signal. In any event, candidates for microgravity influences are both numerous and complicated. As stated above, poor understanding of causal mechanism leads to limited and , perhaps, ineffective countermeasures; or worse, contra-indicated countermeasures.

The list in Table 1 summarizes physiological "problem areas" in regard to a few microgravity effects. Within each area effects are not well understood at any physiological level, and it is difficult to determine whether the effects arise from passive, active or reactive consequences of microgravity exposure. A sample of candidate causal factors is listed in Table 2. Taken together, the problems and their causes constitute an almost complete biomedical sciences research agenda, with or without the complications of the space environment exposure that may involved even more than microgravity and radiation exposures. However, Table 2 highlights several microgravity influences that have escaped serious research commitments. Direct mechanical effects on cells, tissues, organs and organisms have not received systematic attention except at high levels of exposure meant to simulate various traumatic insult circumstances. Direct tissue elasticity influences of mechanical loading have only recently received enhanced levels of research attention and, then, the attention is limited to cardiovascular studies. Yet, it is readily apparent that biological systems do function in the presence of nominal gravity and that such functioning may include a variety of dependencies on the presence of gravity-induced influences on the physiological environment. The problem may be that the gravity influences are so ubiquitous that they have escaped serious consideration. The space environment may make use rethink our present complacency regarding the importance of gravity in living organisms. The survival and function of biological systems in space may be a simple reflection of robustness and inadvertently produced protection protocols.

It is against this backdrop that we have begun to study ways to alleviate microgravity effects on biological systems And, it is from the above outlined "view" of the microgravity effects that we make some guarded recommendations. In several instances we have proposed remedies that appear facetious. This has been done to encourage a rather open-minded view of both the nature of the problems and possible countermeasures. It may be necessary to originate new methods or treatments. Modifications of existing treatments for use in space may be inadequate. And overall, we may need to institute some broad, novel concepts of space physiology.

Candidate Solutions

The items in Table 3 suggest several strategies for handling the microgravity problems. Such strategies, of course, are not particularly novel. The strategies range from replacement of nominal levels of gravity to broad pharmacological treatments. Again, we are reminded that we are speculating on therapies without much knowledge of the nature of a the problems. In some sense, replacements are the most innocuous treatments to attempt. We start there.

Perhaps the most common solution to microgravity problems is the simple replacement of what's missing -- gravity. A variety of rotating space habitats have been suggested including the now classic rotating torus concept circa 1950's. Realistically, we have very little data that focuses directly on the consequences of using centripetal forces as a substitute for gravity. Studies done with a variety of centrifugal methodologies have interpretation difficulties due to mixed centripetal-gravitational vectors, centripetal gradients and Coriolis effects. Thus, the simple replacement of a gravity vector may be much more difficult than expected. At this time, it would be difficult to envision relevant physiological studies unless they were actually conducted in the space environment.

Associated with the above biological interpretation difficulties are the implementation difficulties of creating a man-rated rotating space habitat. Structural problems would, at this time, be difficult to anticipate and center of mass asymmetries could contribute to much precession and wobble. These problems are additive to the problems of spin-up or spin-down and the problems of egress or safety.

It seems to follow from the above comments that evaluations in the 1.8 meter centrifuge planned for Space Station Freedom will provide the biological rationale either for undertaking or dismissing the possibilities for a rotating habitat. Even this capability will leave questions unanswered. So, a strong rationale for a rotating habitat may be quite far away.

The present approach to reduction of microgravity effects, of course, centers on exercise. The value of this approach and the limitations are already reasonably well documented in what might be considered preliminary demonstrations. The difficulty here is that exercises done in space have neither been done consistently nor done in a highly controlled fashion. Subject numbers have been small and subjects have varied considerably in a number of important ways; age, health, conditioning level, sex etc. It is yet to be determined whether or not we have identified and used the most effective exercise protocols. Nevertheless, the critical drawback of exercise is that (1) it does not seem to be a panacea for treatment of all microgravity effects and (2) it takes a significant toll on the length of time astronauts might otherwise have available for productive experiments, observations and maintenance. If exercise is to be the mainstay treatment for microgravity effects it must be made more effective and less time consuming. Ideally, it should be made recreational, as well. Such constraints, together, lead to a difficult challenge for medical practitioners and exercise physiologists.

For a number of tissues, it appears that some degree of healing and/or protection from deterioration might be afforded using either electrical or magnetic fields. At Bioserve we have pursued these possibilities for a rodent tail suspension model using changes in bone as the focal point of our analyses. Pulsed magnetic fields have prevented the bone deterioration usually seen in tail-suspended mice. Many variables, of course, are important. Field strength, pulse characteristics, field orientation, animal age and duration of daily treatment have been considered experimentally. Some of these results were reported at the annual ASGSB, 1988 meetings. Currently, effects of magnetic field treatments are being done for nervous system and muscular system tissues as well as bone. All of the experiments are promising but we are trying to (1) learn the limits of these treatments, (2) look for any evidence of side effecs and (3) sculpture the protocols for tests in the microgravity environment.

Our observations with these electromagnetic effects raised the possibility that rather ubiquitous force gradients (in the above case, magnetic fields) might substitute for some of the gravity forces experienced by organisms. The resulting "mixed gradients" could have desirable consequences at the organism, tissue and even cellular levels. We have begun to formalize this kind of hypothesis. It may not be unreasonble to assume that other ubiquitous variables could be found, as well. Again, however, the challenges and problems are significant in understanding and using such approaches to counteracting microgravity effects.

The next approach to devising countermeasures is the use of passively-induced gravity effects. This approach makes several assumptions about the causal factors, in microgravity deterioration or dysfunctions. Simply stated, the assumptions relate to some unquantified and uncharacterized need of organisms for gravity-promoted bulk fluid motions and mechanical force gradients. The effects might relate to modest mixing within cellular milieus, differential forces produced across a cell and/or cell membrane, organ distortions with allied mechanical and fluid forces generated asymmetrically within the organ, or to organism asymmetries, again, leading to a variety of different forcing functions. The linking of such forces is evident, for example, in the galloping horse that uses the various locomotive forces to aid in respiration. Evidence for the importance of such effects is just now arising from experimental literature. Nevertheless, some speculation on associated countermeasures to microgravity-induced losses of such factors seems warranted.

Assuming that fluidic mixing at a variety of tissue compartment levels is to be accomplished and that mechanical forces are to be generated across such tissue compartments, the replacement strategies appear quite clear. Direct acceleration and deceleration forces can be applied to the organism in microgravity. Or, direct mechanical forces can be applied. This treatment, I suppose, is tantamount to suggesting that astronauts be made to "bounce off the walls" in an almost literal sense. The resulting brief episodes and differing vectors for acceleration -- deceleration forces may provide fluid mixing and mechanical shear forces otherwise lost to the microgravity environment. Following some hypothetical biological need for gravity, it appears that a fair amount of direct mechanical stimulation should be provided. This could range from slow, broad coverage stimulation nearing whole body massage to rapid, narrowly directed stimulation such as focused ultrasound. With appropriate selection of acoustical wavelengths and intensities, it might be possible to effect virtually all tissue, organ and cellular compartments regardless of size and distance from the body surface. The beneficial effects might be reduced flow stagnation, reduced need for metabolic pumping across the cells and tissues in lieu of mechanical gradients, and enhanced tissue reactivity to stimuli like stretch stimuli used to maintain skeletal muscle tonus or stretch stimuli needed to elicit rather autonmous smooth muscle responses. Whether such approaches are likely to aid in the search for countermeasures remains to be seen. However, it seems equally important to evaluate the need of biological systems for such fluidic and mechanical stimuli. It may be important to separate the gratuitous production of these effects by exercise such that exercise can be supplanted, in duration, by more passive mechanical and fluidic stimulation. This approach allows more time for the simultaneous production of useful work in space by the astronauts.

For a number of biological effects produced in microgravity, it is tempting to employ directed pharmacological treatments. Thus, the microgravity dysfunctions are treated like any of a large number of other medical maladies. Many and more powerfu.l drugs are being developed. Some, like calcium loss inhibitors for bone, are at the threshold of FDA approval. Yet, at some point or another, it seems reasonable to question the use of drugs since already a major segment of American society is taking drugs to reduce the side effects of other drugs or is at risk in taking drugs with one another that don't mix either chemically or pharmacologically. The thing to be remembered here is that all drugs are "poisons." Unless a ubiquitous drug is found that is capable of treating most microgravity effects in different tissues at about the same time, drugs made for the variety of known physiological dysfunctions of microgravity would undoubtedly yield an unacceptably large number of side effects. Where possible to elicit general systemic effects, the drug would have to promote stasis or general anabolic biases --- this, of course, is a situation being pursued by world class athletes and the side-effects of these treatments are only too well known. As above, the implementation of pharmaceutical countermeasures to microgravity makes more assumptions about our information and therapeutics wizardry than we could reasonably live up to for several decades.

The other treatments mentioned as countermeasures simply reflect some current beliefs about nutrition and organism health. Even in the nominal gravity conditions of Earth it is difficult to reconcile the role of nutrition in health and disease states. The impact may be subtle and the required studies for corroboration must be, by nature, longitudinal. Only now are we beginning to grasp the significance of and the methodologies for longitudinal studies that may extend for 3 or 4 decades.

From each of the somewhat wistful comments regarding protection from microgravity effects in space, two things are abundantly clear. (1) We really don't know what the microgravity effects on biological organisms are! And, (2) we are not especially accomplished in instituting effective countermeasures for any of a wide variety of known medical dysfunctions. Yet, we are likely to have to control microgravity effects or minimize the influences of such effects on astronauts if Space Station Freedom is to become an effective reality. We must use this rather overwhelming challenge to learn what we can regarding biological system dependence on gravity, biological dysfunctions without gravity and biological independence from gravity. Only then, can long space missions become a reality and can man's future as a spacefarer be assured.

COUNTERMEASURES TO MICROGRAVITY

PROBLEM AREAS

MUSCULOSKELETAL
CARDIOVASCULAR
MICROBIOLOGICAL
RADIATION
FLUID/ELECTROLYTES
IMMUNOLOGICAL
PULMONARY
PHARMACOLOGICAL
BEHAVIORAL
TOXICOLOGICAL
NEUROVESTIBULAR

Table 1

COUNTERMEASURES TO MICROGRAVITY

CAUSAL FACTORS

WEIGHTLESSNESS
NO CONVECTION

Loss of shear stresses on cells and tissues
Loss of some fluid motion
Fluid redistributions
Altered tissue elasticity-fluid interactions
Reduced cell to cell communication

ALTERED INTERNAL MILIEU

Erroneous sensor function
Erroneous mechanical vectors
Altered hormonal states

Table 2

COUNTERMEASURES TO MICROGRAVITY

CANDIDATE SOLUTIONS

ARTIFICIAL GRAVITY
EXERCISE-INDUCED
MECHANICAL EFFECTS
ELECTROMAGNETIC
EFFECTS
PASSIVELY-INDUCED
GRAVITY EFFECTS
DISABLED SENSORS
NUTRITION
ARTIFICIAL CHANGES IN
CHEMICAL MILIEU

Table 3