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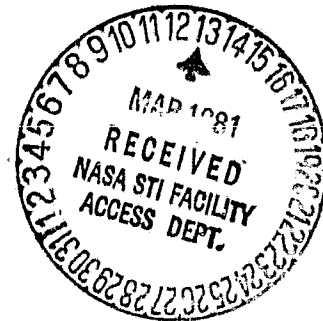
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BIOMEDICAL CONSIDERATIONS
FOR
FUTURE MANNED SPACE FLIGHTS

by

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BIOMEDICAL CONSIDERATIONS FOR FUTURE MANNED SPACE FLIGHTS

The intent of this chapter is to provide an overview of biological and medical factors pertinent to space flights of varying durations. While the overall goal of our effort is devoted to the behavioral, psychological, and sociological aspects of space travel, particularly with emphasis on longer duration missions, it is important to briefly discuss the biomedical aspects of space flight. Certainly, these factors may strongly interact with the various psycho-social factors to be detailed in this volume and as such they stand as an immensely important area of concern in and of themselves. It is hoped that this chapter will provide a suitable foundation for understanding weightlessness related medical problems through a discussion of the history of symptoms reported, specific details on the major areas of concern, and approaches to their investigation. Also, discussion is given to the possibility of various countermeasures. Some indication of the effects of various biomedical changes in performance will also be covered in this chapter although the majority of this discussion will be reserved for a later chapter.

HISTORICAL DEVELOPMENT

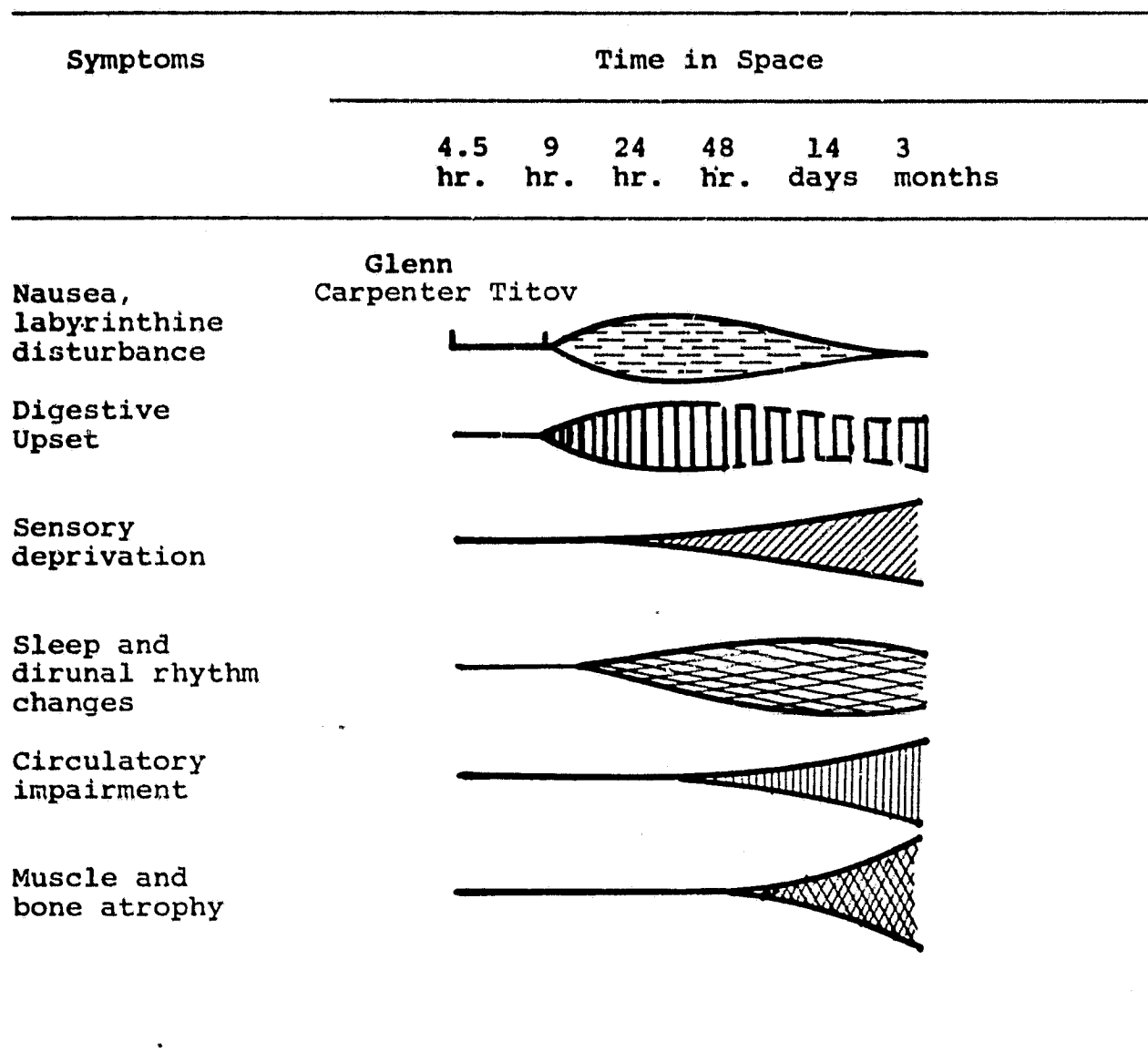
During the Mercury Program, NASA scientists offered some tentative predictions regarding the time course of certain symptoms that were expected to occur during weightless flight (1).

Figure 1 provides a convenient starting point for discussing biomedical performance aspects of flight related to the null gravity conditions since these predictions have generally proved valid (with the exception of sensory deprivation and sleep changes to be discussed in later chapters).

The first series of manned space flights (Mercury Program, 1961-63) were quite brief in duration (range of 5 minutes to 34 hours). Even so, indications of cardiovascular or circulatory impairment were observed following the 9 hour MA-8 flight of Schirra (2) and again following the 34 hour MA-9 flight of Cooper (2). Schirra exhibited orthostatic intolerance and hemoconcentration as well as weight loss (dehydration) and dizziness on standing. These biomedical findings set the stage for the heavy emphasis placed upon evaluation of the cardiovascular system during the Gemini missions (1965-66). Three flights of the Gemini Program were of particular biomedical concern. Gemini 4, 5, and 7 lasting 4, 8, and 14 days respectively confirmed the postflight orthostatic intolerance observed during the Mercury Phase (3, 4). Moderate decreases in red blood cell mass were also reported. Table 1 outlines the major medical findings from the Gemini Program. Note that the Gemini flights were the first to produce problems related to the musculoskeletal system including loss of bone calcium and muscle nitrogen, and moderately decreased postflight exercise capacity. Also, it was noted that extravehicular activity resulted in high metabolic costs.

During the Apollo Program (5) when flight duration ranged from 6 to 12.5 days, vestibular disturbances began to plague

Figure 1. Predicted Time Course of Biomedical Symptoms Anticipated During Mercury Program.



Dietlein (2)

Table 1. Significant Biomedical Findings in the Gemini Program.

Moderate loss of red cell mass
Moderate postflight orthostatic intolerance
Moderate postflight loss of exercise capacity
Minimal loss of bone density
Minimal loss of bone calcium and muscle nitrogen
. High metabolic cost of extravehicular activity

Dietlein (2)

crews. Previous Soviet flights had produced motion sickness problems even during 1 day flights (6). Cosmonauts reported some type of motion sickness symptom in nearly every Vostok and Voskhod mission (7, 8), but none had been reported among American astronauts prior to the Apollo Program. Apollo missions 8 and 9 were particularly significant in illustrating the problems of space sickness (2). All three Apollo 8 crew members reported some degree of motion sickness as did the crewmen of Apollo 9. Overall, 9 of the 25 astronauts involved in the Apollo program displayed some type of space sickness symptoms (9). These and other significant biomedical findings of the Apollo Program are shown in Table 2. Note that cardiac arrhythmia was observed during Apollo 15. The same crewmember experiencing this problem in space suffered a myocardial infarction some 21 months after flight. This suggests that coronary atherosclerosis was the principle factor and that the incident may not have been directly related to flight.

The longest American flights to date have been the 28, 59, and 84 day missions of the Skylab Program (1973-74). Table 3 outlines some of the problems encountered during these flights. Note that no new symptoms were encountered; indeed, many positive findings were obtained as summarized in Table 4.

Results similar to those observed during American flights have been reported by the Soviet Union. However, the Soviets experienced greater problems with space motion sickness earlier in the history of their manned space program than did the astronauts of the United States. This interesting difference is discussed more fully later. Other differences in the findings and

Table 2. Significant Biomedical Findings in the Apollo Program

Vestibular disturbances

Adequate diet; less than optimal food consumption

Postflight dehydration and weight loss

Decreased postflight orthostatic tolerance

Reduced postflight exercise tolerance

· Apollo 15 cardiac arrhythmia

Decreased red cell mass and plasma volume

Dietlein (2)

Table 3. Significant Biomedical Findings in the Skylab Program.

Cardiovascular deconditioning inflight

Skylab 2 cardiac arrhythmia

Postflight decrease in work capacity

Postflight orthostatic intolerance

Moderate losses of calcium, phosphorus, and nitrogen

Loss of red blood cell mass

Space motion sickness symptoms

Adapted from Dietlein (2)

Table 4. Skylab General Summation

Biomedical results show that man can adapt and function effectively in weightless environment for extended periods.

Daily in-flight personal exercise regimens coupled with appropriate dietary intake and programmed adequate sleep, work, and recreation periods essential for maintaining crew health and well-being.

No untoward physiological changes noted that would preclude longer duration manned space flights; however, research required to understand the mechanisms responsible for many observed changes.

Remedial or preventive measures may be required for mission durations in excess of 9 to 12 months (e.g., bone demineralization countermeasures).

Ideally, further observations of man in Earth-orbit for an uninterrupted period of 6 months should precede a Mars-type mission.

Deitlein (2)

research approaches of the two countries will be described in appropriate sections within this chapter. The reader is referred to references 10 and 11 for a comparative overview of the biomedical results reported by the U.S. and the Soviet Union. Also the results of the 9 day joint American-Soviet Apollo-Soyuz Test Project of 1975 may be of interest to readers (12).

It is clear from this brief discussion that several major areas of biomedical problems have been and will continue to be of concern to the health status of space flight crew members. This is particularly true with regard to the prospect of future space travel of durations considerably longer than previously achieved. These problems focus around two important issues. Some biomedical alterations have their greatest effect during transition periods, that is during insertion into weightless orbital or during reentry to earth's atmosphere. Under these circumstances the greater the duration of flight the more severe are the reentry effects. During flight the appropriate systems change to adapt to accommodate the new demands of weightlessness. Problems occur, then, primarily when the conditions of weightlessness are reversed and the human once again is subject to the conditions of earth's atmosphere. For other systems the actual changes produced by weightlessness are the major focus of problems with possible hazardous consequences resulting during the flight itself. The following sections provide more detail on the nature of these difficulties.

CARDIOVASCULAR SYSTEM

Berry (13) has succinctly summarized the cardiovascular-hemodynamic responses of man in space. This is illustrated in Table 5. The reaction of the cardiovascular system to the conditions of spaceflight are varied, complex, and only partially understood at present. To a great extent, cardiovascular deconditioning in weightlessness is due to a lack of hydrostatic pressure. On earth, a hydrostatic pressure head exists which is equal to the length of a column of liquid. The heart must operate against this gravitational pressure to sustain blood flow and proper functioning of the cardiovascular system. However, under zero gravity conditions no such hydrostatic pressure gradients exist; only vascular pressure from the myocardial and skeletal muscle, and from elastic tissues are produced. As a result, deconditioning may result as the heart lessens its pace and achieves an equilibrium appropriate to the decreased demands placed upon the system. In addition, it is probable that the action of mechanoreceptors in the walls of the blood vessels and in the cardiopulmonary reflexes are significantly altered by the lack of gravity. These changes affect the tone of the system and output of the heart. Blood volume regulation is affected as well.

While in-flight decrements in the effectiveness of the cardiovascular system obtained to date have not been particularly severe, the question of how this system will respond to more long term weightlessness is certainly crucial. As the heart adapts to the lowered demands placed upon it deconditioning occurs, but fortunately appears to stabilize after 4 to 6 weeks (2). Most of the

Table 5. Cardiovascular-Hemodynamic Responses to Weightlessness.

Measure	Finding
Heart rate	Stabilized at lower levels in zero g
Electrical activity	Normal except for bigeminis, PAC's, PVC's in Apollo 15
Cardiac silhouette	Decrease in size postflight
Blood pressure	Normal in flight--Labile postflight
Orthostatic tolerance	Decreased postflight

Berry (22)

questions associated with long duration travel center more on the re-adaptation of the system following flight than they do on actual changes during flight. For example, following the Apollo 16 and 17 flights, crews demonstrated decreased cardiac size (14). Exercise tolerance was reduced and blood pressure did not immediately stabilize. This appears to result because the heart adapts to the lowered demands of zero gravity and is therefore unprepared to deal with the increased stress of earth's atmosphere immediately following flight. A critical issue here is the possibility that the longer the space flight, the more stressful is this re-adaptation process. This supposition has been at least partially supported by the results of space flights of increasing duration (15). However, discrepancies are prevalent indicating the necessity of more extensive and duration-related research.

In brief, we can state that the major cardiovascular problems related to weightlessness include altered blood circulation due to the absence of hydrostatic pressure. This encourages increased filling of vessels with blood which can lead to arteriole spasms, increased pulmonary artery pressure (Ketayev reflex), and increased load on the right ventricle. The possible consequences of these circulatory changes must be evaluated and effective preventative measures sought.

MUSCULOSKELETAL SYSTEM

Insufficient loading of the musculoskeletal system is a significant effect of weightlessness. Reduced weight bearing in

space leads to "disuse" symptoms including loss of calcium, nitrogen, and phosphorus, muscle atrophy and weakness of limbs, decreased bone size and volume, and formation of urinary stones (16, 17, 18, 19).

The effects of weightlessness on this system during long duration flight are particularly difficult to predict. While the symptoms outlined above have occurred during flights of up to three months in duration, the severity of the problems have been minimal. It is unclear whether longer exposures will intensify the symptoms to dangerous levels or whether these changes will increase to some adaptive asymptotic level and establish a new homeostasis. Decalcification of bones, as a characteristic finding in spaceflight averaged .3 to .4 percent per month during the 59 day Skylab mission (2). Since mineral loss is differentially greater in trabecular areas of bone, the possibility exists that during very long exposures to weightlessness local area losses of mineral to a degree equivalent to osteoporosis could occur, endangering the strength of critical bones. If this .3 to .4 percent decalcification continued unaborted severe problems could develop including increased susceptibility to fracture, ectopic calcification, and nephrocalcinosis. These problems would certainly pose a severe health hazard to the crew during the actual flight. Furthermore, decalcification might continue beyond the point at which return to earth could reverse the cycle. It is not entirely certain at what time point, if any, the demineralization process might reach homeostasis. However, Donaldson, Hulley, and associates (20) showed that under bedrest conditions

simulating weightlessness calcium levels in the urine indicative of decreased reabsorption remained significantly higher than controls for as long as bedrest was continued (7 months). Hattner and McMillan's (18) review of the effects of weightlessness on the skeleton predicts calcium losses of 1-2 percent each month for a year to several years. While this monthly loss figure has proved somewhat high, based on Skylab results, the possible tendency for decalcification to continue unremitting at any rate for such long periods is alarming for reasons of safety during actual flight as well as re-adaptation.

The long time course of these problems is a particularly limiting factor in assessing whether asymptote may be reached at some period prior to the point of no return. Although flight related bone losses have been reversible following return to normal gravity, there is no available estimate on the magnitude of loss at which restoration is impossible.

As the degree of decalcification continues, another problem of potential danger arises: free-circulating calcium. Excess urinary calcium has been a consistent finding of exposure to weightlessness. While so far observed in tolerable amounts, continued accumulation could result in calcification of tissues and formation of kidney and other stones. Unfortunately, because of the long time course involved in studies of this problem, it is not entirely clear whether this effect is progressive.

The lack of mechanical stress of the muscle system during sustained weightlessness is another source of concern. Postflight analyses have demonstrated increased urea content in the blood,

increased creatinine excretion in the urine, and decreased total potassium content indicating a degradation of muscle proteins. Negative nitrogen balance has also been noted. Weightlessness leads to decreases in muscle tone and strength, decreases in tolerance and physical work capacities. There may also be some motor coordination disturbances postflight as reported by the Russians (21). Fortunately, most of these problems were demonstrably minimized during the longer Skylab missions through a specific exercise regime. However, it is not entirely certain that such exercises will provide complete compensation during longer-term missions.

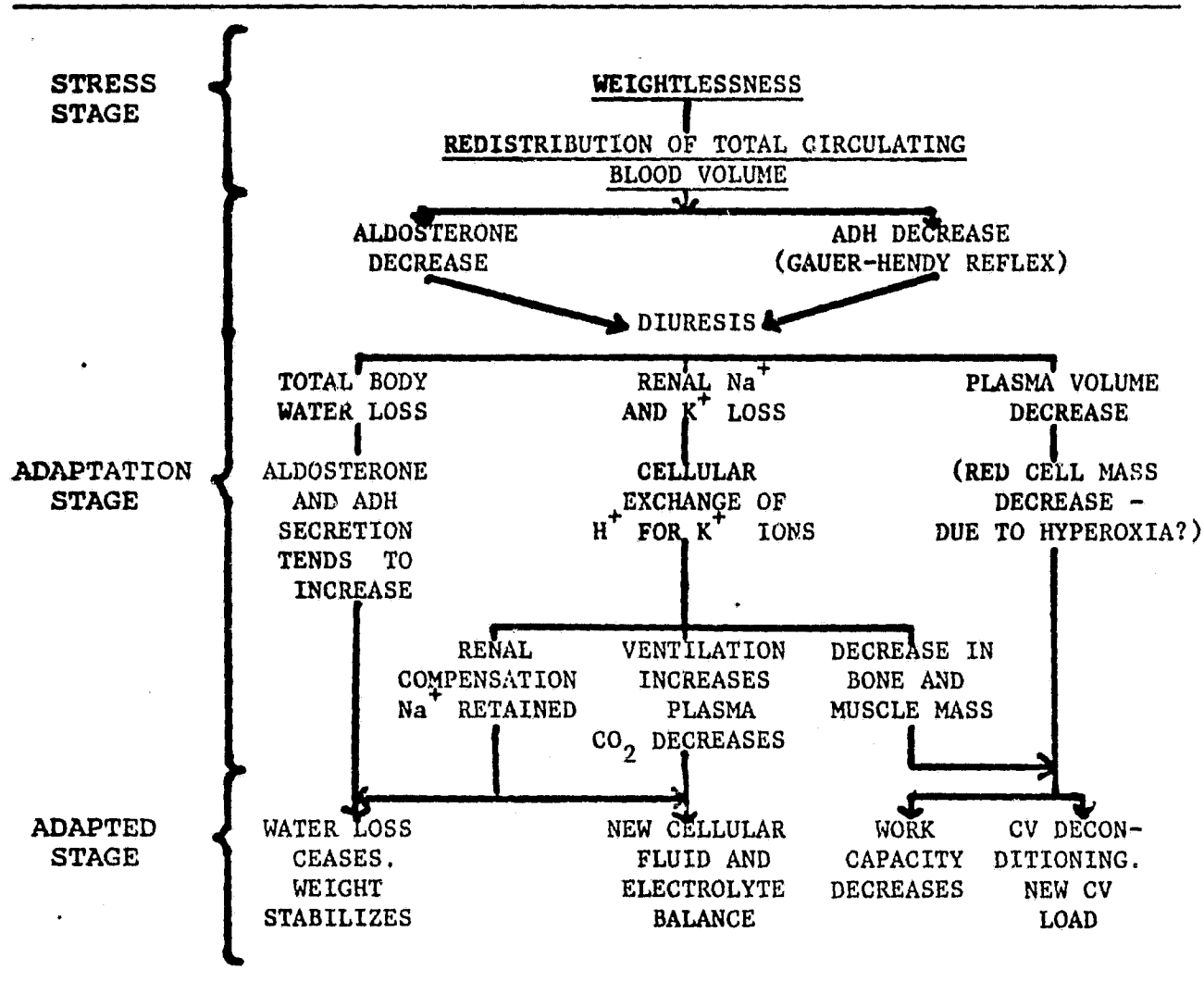
ELECTROLYTIC AND FLUID BALANCE CHANGES

The changes in potassium, nitrogen, creatinine, etc. discussed in the previous section exemplify the general alterations in electrolytic balance which occur during weightless flight. Changes in fluid volume and water balance are also important concomittant factors. Electrolytic changes have been among the most reliable effects observed postflight. For example, total body gamma spectometry has revealed significant potassium losses. Decreases in sodium and chloride levels due to elevated excretion are frequently observed as well. Electrolyte alterations closely parallel changes in body weight loss and gain. Postflight increases in ADH (anti-diuretic hormone) and aldosterone levels consistent with the retention of electrolytes has been observed, paralleling the pattern of rapid recovery of in-flight weight loss in the immediate postflight period.

As other authors have described (15, 22), these changes in electrolytic balance suggest a model of man's overall adaptation to zero gravity conditions as shown in Figure 2 and detailed in Table 6. In essence, the theory states that the lack of hydrostatic pressure in weightlessness encourages absorption of tissue fluid and initially increases blood volume circulation. The stretch receptors of the atria are stimulated initiating impulses to the hypothalamus-hypophysis (via the Gauer-Henry reflex) to inhibit release of ADH (aldosterone release is also inhibited). Decreased ADH and aldosterone then produces diuresis of sodium and potassium through the action of the kidneys leading to plasma volume reduction and subsequently production of a secondary aldosteronism. Extracellular alkalosis resulting from the diuresis of potassium produces an intracellular exchange of potassium and hydrogen. This loss of cellular potassium (verified by postflight urinary analyses) could mean a loss of muscle cell potassium and may also explain the cardiac arrhythmias sometimes reported through a loss of potassium in the heart muscle. However, this latter possibility is strictly speculative.

Additional factors in this process should also be noted. For example, the Space Sciences Board (23) notes the importance of decreased renal sympathetic activity as a variable influencing increased urine flow rate and sodium excretion. This loss of sodium in turn activates the renin-aldosterone, sodium control loop resulting in a decrease in aldosterone secretion by the adrenal cortex and an increase in sodium loss.

Figure 2. Hypothesized Course of Adaptation to Weightlessness.



Berry (14), Pestov and Gerathewohl (15)

Table 6. Overview of Current Hypothesized Course of Adaptation to Weightlessness.

<u>Event</u>	<u>Response of Body</u>
Entry into zero gravity. Redistribution of circulating blood volume.	→ Body attempts to reduce volume. ADH decreases, aldosterone production decreases. ↙
Loss of water, sodium, potassium (loss of body weight).	→ Decrease in plasma volume. Aldosterone produced. ↙
Increased sodium. Potassium loss continues. Cell: acidotic; extracellular fluid: alkalotic.	↙ Intracellular exchange of potassium and hydrogen ions. → Decrease in bone density and muscle mass, possibly including cardiac muscle. ↙
Respiratory and renal compensation. Halt to weight loss trend.	→ Stabilized with new cardiovascular load. New body fluid and electrolyte balance.

While this overall picture provides a reasonable view of how physiological adaptation to weightlessness occurs, it unfortunately has not been completely supported by the available flight data, especially those of Skylab. During Skylab 3 and 4 ADH secretion was uniformly decreased as predicted. However, during Skylab 2 it was elevated. Also, contrary to the model's prediction aldosterone secretion was consistently high. Despite these differences, sodium and potassium were excreted at high levels during all missions. This indicates other humoral and hemodynamic factors not included in the model are involved. Nevertheless, this theory comes the closest yet to providing a working foundation for understanding man's adaptation to space.

Although the dehydration and electrolyte loss occurring in space apparently pose no problems during routinely brief flights, few conclusions can be drawn regarding their importance during longer duration missions. However, if the loss of potassium does reflect loss of general muscle cell (and heart) potassium and continues at elevated rates, severe consequences, both in flight and following return to earth could result.

VESTIBULAR SYSTEM

During the Apollo and Skylab Programs, an alarmingly high percentage of astronauts reported some symptoms of "space sickness" related to the lack of gravity. Likewise, Soviet investigators have reported in detail vestibular side effects experienced by four cosmonauts upon insertion into weightlessness (24, 25, 26, 27, 28, 29, 30, 31). The experiences of Titov during the 1961 Vostok 2 flight

(6) provides a good example. Immediately after entering weightlessness, Titov had the illusion of flying upside down. Soon after he became dizzy and reported vertigo, loss of appetite, and nausea.

In analyzing these and other symptoms, most investigators have found it useful to distinguish between two distinct, but related categories of vestibular reactions. Graybiel (32) makes the dichotomy between: 1) vestibular I (VI) manifestations which are reflex phenomena emanating from the vestibular system or from systems which normally receive vestibular activity and 2) vestibular II (VII) manifestations known as delayed epiphenomena or more commonly as motion sickness. VI responses include such phenomena as nystagmus, illusions of seen motion, postural illusions (i.e., feelings of inversion), dizziness, and vertigo. VII reactions include nausea and vomiting, stomach and head awareness, pallor and cold sweating, headaches, drowsiness, locomotor ataxia, and loss of appetite among others. The primary etiology of these symptoms is also of vestibular origin (otolith and semi-circular canals), but secondary causal factors operate as well. Conflict between visual inputs and psychological factors such as expectancy are usually the most important of these variables. VI reactions will occur in response to acceleratory stimuli independent of whether motion sickness develops and are not themselves evidence of motion sickness.

Currently, the major behavioral theory regarding vestibular functions in space relies upon the notion of sensory conflict. Reason and his associates (33) have succinctly summarized the essence of this approach: "Motion sickness is due to a discord or confusion created in spatial integrating centers of the brain by

conflicting position and motion information arriving simultaneously from the various spatial senses, principally the vestibular system, the eyes, and the non-vestibular proprioceptors." The main thesis of Reason's approach (34, 35) is that all situations which provoke motion sickness are characterized by a condition of sensory rearrangement in which the motion signals transmitted by the eyes, the vestibular system and the non-vestibular proprioceptors are at variance not only with one another, but also with what is expected on the basis of past experience. For the purposes of discussion, Reason subsumes most sickness provoking sensory conflicts into two general categories:

Visual (A) - inertial (B) rearrangement: where inertial includes both the vestibular and non-vestibular proprioceptors; here the conflict is between sense modalities and

Canal (A) - otolith (B) rearrangement: here the conflict lies within one modality, between the two vestibular receptor systems.

A mismatch of information from either of these categories can lead to sickness due to one of the following three types:

Type I: when A and B simultaneously signal contradictory or uncorrelated information

Type II: when A signals in the absence of an expected B signal

Type III: when B signals in the absence of an expected A signal

From these two kinds of sensory rearrangement and three conflict types, Reason and Brand derived six basic circumstances under which motion sickness may develop. These are illustrated in Table 7 along with various examples from everyday and laboratory experiences.

Table 7. Some Everyday and Laboratory Examples of the Six Kinds of Sensory Rearrangement that can Provoke Motion Sickness

	Visual (A) -- Inertial (B)	Canal (A) -- Otolith (B)
Type 1 (A and B)	<ol style="list-style-type: none"> 1. Watching waves over the side of a ship. 2. Looking out of the side or rear windows of a moving vehicle. 3. Making head movements while wearing some optical device that distorts vision. 	<ol style="list-style-type: none"> 1. Head movements made about some axis other than that of bodily rotation - cross-coupled angular accelerations. 2. Low frequency oscillations: between 0.1-0.3 Hz.
Type 2 (A not B)	<ol style="list-style-type: none"> 1. "Cinerama sickness". 2. Operating a fixed-base vehicle simulator with a moving visual display - "simulator sickness." 3. "Haunted-Swing" type of fairground device. 	<ol style="list-style-type: none"> 1. Weightless flight - "space sickness". 2. Calorific stimulation of the outer ear. 3. Positional alcoholic nystagmus associated with alcohol and heavy water.
Type 3 (B not A)	<ol style="list-style-type: none"> 1. Reading a map in moving vehicle. 2. Riding in a vehicle without external visual reference. 3. Being swung in an enclosed cabin. 	<ol style="list-style-type: none"> 1. Rotation about an Earth-horizontal axis. 2. Any rotation about an off-vertical axis. 3. Counter-rotation.

For our purposes it is most pertinent to consider Type 2 conflicts in which the canal signals in the absence of the otoliths. In space there is no gravitoninertial vector, therefore no baseline against which the otoliths can signal head position (tilt). The otoliths are functionally deafferented due to the effects of weightlessness. However, the semi-circular canals are not adversely affected by zero gravity and continue to send impulses regarding angular accelerations. When the astronaut quickly moves his head, the semicircular canals transmit signals indicating angular acceleration, however, no confirming information is received from the otoliths. In addition, sensory conflict exists at the time of rapid head movement between visual system input and vestibular input. That is, the eyes signal movement which agrees with the output of the canals, but no corroborating impulses are received from the otoliths. This confusion in turn leads to the unpleasant symptoms of motion sickness previously outlined.

The sensory conflict hypothesis has proved very useful in providing a foundation for organizing the available empirical data and certainly has relevance to space flight conditions. For instance, it clarifies why such a discrepancy in symptomatology between astronauts and cosmonauts existed early in the history of the space program. Initially, Soviet crewmen reported considerable difficulty related to space sickness (both VI and VII reactions), while no reports of these symptoms occurred for American crewmen prior to the Apollo missions. The Mercury and Gemini capsules were considerably smaller relative to the Vostok and Vokhod vehicles thus restricting movement to a greater degree. With less

movement ability, less potential for sensory conflict between visual/canal impulses and otolith impulses existed. In the Apollo vehicles (which were of comparable size to the earlier Soviet vessels) considerably more opportunity existed for generating sensory conflict. As a result, space sickness did occur among 9 of the 25 astronauts. The results of Skylab prove even more interesting in relation to the sensory conflict theory. While aloft, Skylab crewmen were subjected to transitions in moving between the Command Module and the larger workshop. In this situation, two separate adaptations had to be made. Two astronauts were motion sick when based in the Command Module. After adapting to this situation, the science pilot of Skylab 3 also became motion sick upon entering the workshop. This result coupled with the fact that two other crewmen developed their first symptoms upon entering the workshop highlights two important points. First, it lends support to the sensory conflict theory. The increased movement allowed by the larger area of the workshop provided more opportunity for sensory conflict due to increased activity (particularly of the head), resulting in a higher incidence of sickness. More importantly these results illustrate the lack of protective adaptation one situation provides for another. Adapting to the Command Module was not a satisfactory prophylactic for preventing sickness inside the workshop. These results closely agree with those obtained from ground-based experiments indicating that adaptation is situation specific. We possess an expectancy of events within each and every different environment based on previous sensory experience. Adapting to conflicts within one environment does not prevent conflict within another.

While space sickness has proved to be a decrement to performance and well being in space there are certain encouraging factors with regard to long term missions. Adaptation occurs within about two or three days and can be advanced through various head movement exercises (to be described in a later section). Another point is that not all crewmen have experienced the problem of sickness in space suggesting the possibility of pre-selecting candidates already immune to difficulties. Unfortunately, until more is known about the specific mechanisms involved in how sensory conflict actually produces the physiological symptoms, methods for selection will be limited. This point will be detailed in a later section.

Temporary space sickness may not pose a particularly limiting problem to future space travelers. However, the readaptation to earth's gravity may prove more debilitating as the length of stay (and thus the weightlessness altered sensory expectation of how environmental stimuli should appear) increases. Just as sensory conflict produced by weightlessness can adversely affect physiology and behavior, the process of readapting to earth's 1g atmosphere can produce a reverse sensory conflict. This is illustrated by one of the Skylab astronauts who upon returning home, fell after his wife turned out the lights in the living room (thus depriving him of a visual frame of reference).

One final point is that various anti-motion drugs have proved effective in decreasing the severity of space sickness symptoms. However, these compounds merely serve to prolong the period of adaptation and provide less than complete relief. This point will be discussed later.

Ground based simulation studies of motion sickness have proved very worthwhile in illuminating problems involved in actual weight-

less space sickness. These techniques and a more detailed discussion of possible countermeasures will be described in a subsequent section of this chapter.

RADIATION EFFECTS

Thus far the radiation doses received by space crews have been well within the tolerance levels. No demonstrable effects have been related to these radiation exposures except for a small, statistically insignificant number of chromatid type aberrations observed during the Gemini and Apollo mission. However, these did not appear correlated with length of mission. Satellite bioexperiments involving plants have shown that radiation during weightless flight can increase abortive cell division in plant cells. Furthermore, an abnormally high number of chromosomal rearrangements in Drosophila larva reproductive cells has been noted as well as increased developmental and behavioral abnormalities in Habrobracon. Spaceflight conditions may increase the germinating capacity of a variety of seeds and produce increases in the number of chromosomal aberrations. However, many experiments remain inconclusive or of borderline significance. For example, it is still debatable whether cosmic radiation can and does increase the number of dominant lethals in the fruit fly or chromosomal deletions and crossovers in human cells.

The possibility of radiation produced biologically hazardous conditions was most prominently brought to attention by the sighting of light flashes on board the Apollo 11 spacecraft (36). Astronauts reported seeing light flashes during periods of darkness in the spacecraft. This was reported in one eye at a time and even with both eyes closed. One possible explanation of this is that they are generated by high-energy, high atomic particle radiation

(atomic number $Z \geq 6$) traversing the head or eyes. Following these initial reports on board Apollo 11, the remaining Apollo crews were specifically requested to focus on any such sensations during their missions. With few exceptions, they all reported low level, borderline threshold sensations.

It is uncertain what if any danger these high-Z particles pose during short-term missions. However, such particles, depending upon their occurrences in various regions of space and their numbers could represent a serious problem on long-duration flights particularly to the nondividing cells of the nervous system and other controlling cells. One distinct problem in evaluating this possibility is the lack of consistency among investigators as to what constitutes a harmful dosage under what conditions. In the Soviet Union, the dose standards for short-term space flights up to 30 days has been set at 15 rem.* A permissible dose of 25 rem was used by the United States for the Apollo flights. For longer term missions the figures become even more diverse. Grigor'yev and associates (37) suggest a maximum allowable dosage of 220 rem for 1 year, 250 rem for two years, and 375 rem for three years. However, other authors such as Olling (38) suggest considerably higher recommended allowable dosages (300 rad per year of flight). These figures can be compared with those of Warren and Grahn (39) who report tentatively calculated maximum and minimum doses of sun flare activity radiation present during different phases of solar activity. From Table 8 it is clear that as the length of stay in space increases dramatically, even the minimum doses may

*The unit rem stands for roentgen equivalent man and is a computation based on rad (radiation absorbed dose) X RBE (relative biological effectiveness) and corrects for specific ionization of different types of radiation. See Figure 3 for further explanation.

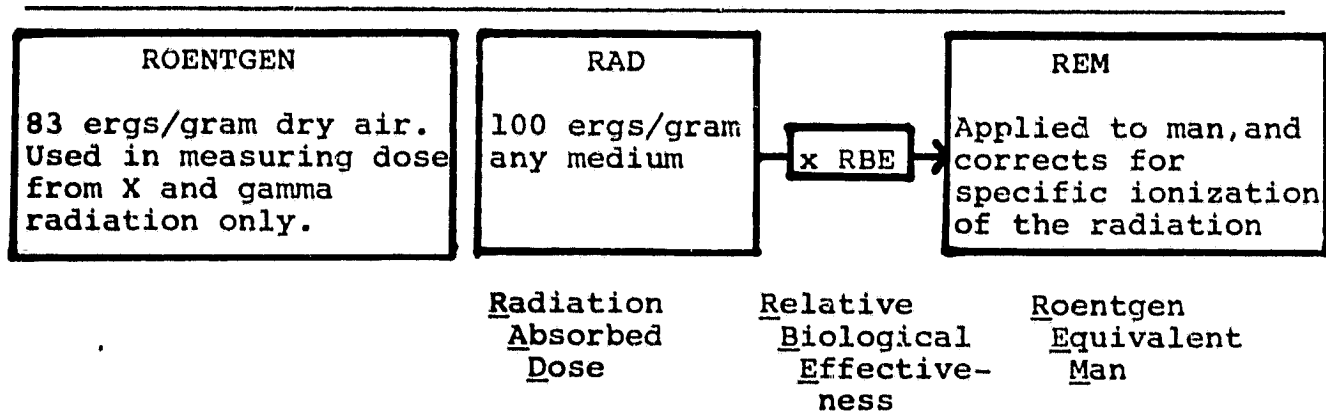
Table 8. Maximum and Minimum Mission Doses* for Best and Worst Launch Dates During a Single Period of Solar Activity.

<u>Mission Duration</u>	<u>Maximum Dose (rads)</u>	<u>Minimum Dose (rads)</u>
4 years	3492	2439
3 years	3229	974
2 years	2781	526
1.5 years	2415	176
1 year	2110	15
9 months	1963	2
6 months	1963	0
3 months	1962	0
1.5 months	1492	0
1 month	1452	0
2 weeks	1452	0
1 week	1452	0

*Surface dose inside 1 g/cm² uniform aluminum shielding.

Warren and Grahn (39)

Figure 3. Relationship Among Principal Units Used in Describing Radiation Exposure.



Warren and Grahn (39)

exceed those recommended by the most liberal of authors. Considerably more research is needed before these discrepancies can be resolved. This does appear to be an area where much more consideration of effects during long-term exposure is necessary.

MICROBIOLOGICAL CHANGES

Under earth's gravitational conditions, airborne microflora remain suspended in inverse proportion to their size. However, in zero-gravity no settling occurs and a considerably larger number of particulate matter remains stabilized in the air. The change in distribution of microbe-bearing particles in weightlessness where no settling of larger particles occurs and the small size and close proximity of the human population may have clinical significance for the development and transmission of problems related to microbiology. For example, during the Apollo mission series staphylococcus aureus obtained at one preflight sampling site on one crewman, spread to most sites on all three crewmen producing some clinical infection (40, 41). Similar findings were reported for Skylab missions as well (42).

It is important to note that some organisms become less resistant to antibiotics following flight as reported following the Soyuz 9 mission (43). The origins of these changes is unclear, but factors such as confinement rather than weightlessness are more likely involved.

Microbial samples pre- and post-flight have demonstrated the presence of a number of clinically significant micro-organisms during the Apollo and Skylab missions. Berry (22) has summarized those observed during the Apollo series as shown in Table 9.

**Table 9. Microflora of Possible Medical Importance Identified
Postflight in Apollo Crews**

Staphylococcus - aureus	Moraxella - species
epidermis	Corynebacterium - species
faecalis	Enterobacter - aerogenes
Klebsiella - aerobacter	Haemophilus - parahaemolyticus
enterobacter	Herella - vaginicola
pneumoniae	E. coli (Throat)
Proteus - mirabilis	β - Streptococcus
Pseudomonas - aeruginosa	Mycoplasma
Serratia - species	Candida - albicans
Mima - polymorpha	

Berry (22)

The following summary points can be made regarding overall pre- to post-flight changes in microflora as outlined by Berry (22):

1. Anaerobic bacteria decreased in number
2. Aerobic bacteria increased in number and type
3. Microorganisms isolated at more body sites
4. Organisms tend to spread across crewmembers (especially Staphylococcus Aureus)
5. Fungal isolates decreased in number
6. Higher carrier states for mycoplasma indicated

While most of these findings are of minor significance to short-term missions, they may be of more concern during long-duration flight. Microbial shifts related to space flight may produce unexpected changes observed only after much longer exposures.

RESEARCH APPROACHES

The preceding sections have outlined some of the by-products of extended weightless flight. Given the potential seriousness of some of these effects for long term missions, it is important to consider what strategies have been explored in investigating these phenomena under flight and earth-based space simulation conditions. One technique is to produce brief periods of weightlessness through aircraft flights using a Keplerian trajectory (44). This method is suitable for obtaining quantitative measurements since the gravitational conditions can be identical to space flight conditions. It is also effective in studying vestibular functioning and body fluid shifts which occur almost immediately during weightlessness (whereas cardiovascular and musculoskeletal changes require more sustained exposure). Unfortunately, zero gra-

vity can only be simulated for a few seconds to a minute. Furthermore, the "pull-outs" which occur immediately after weightlessness produce high-g exposure causing a high incidence of motion sickness. Other disadvantages include weather-dependent scheduling, limited flight craft volume and problems of interrupted training procedures.

Since there is true weightlessness only in space flight and during brief parabolic maneuvers, other techniques for simulating zero-g effects have been developed. The major techniques include neutral buoyancy (whole body immersion in water) (45, 46) and prolonged bed rest (47).

WATER IMMERSION

The water immersion technique has been used for several purposes (48) including the study of physiological responses. These studies have included cardiovascular, respiratory, metabolic, and musculoskeletal responses to immersion (49, 50, 51, 52, 53, 54, 55, 56). Usually, large steel tanks with below surface viewing ports have been used as the training facility. Diving equipment may be used for total body water immersion. As a technique for simulating weightlessness, immersion has the advantage of allowing subjects six-degrees-of-freedom within a normal center of mass range. This has particularly good applications for the study of performance under conditions similar to those of weightlessness. As a technique for assessing physiological reactions, immersion provides a fair index of changes produced in space due to a lack of hydrostatic pressure. The buoyant support provided the limbs and trunk of the

subject reduces the physiological effort required for normal posture and support. Indeed, subjects who have experienced both immersion and Keplerian flight have reported that the sensations are similar.

For physiological studies, the subject is normally seated in a "bathtub" mode, immersed to neck level in neutral temperature ($33.5 \pm 0.5^{\circ}$ C) water or saline without any support equipment. Under these conditions, prolonged water immersion produces circulatory alterations resulting in orthostatic intolerance as measured by tilt-table tests (57). Blood volume is reduced under these conditions, which undoubtedly contributes to the orthostatic intolerance. The ability to reliably produce these effects as an analog to space flight has contributed greatly to our understanding of how weightlessness may produce cardiovascular changes. Furthermore, the water immersion technique has been a useful tool for the testing of various countermeasures which might be used to combat cardiovascular alterations during sustained exposure to weightless space flight (see Countermeasures section at end of this chapter).

Water immersion also produces body fluid volume shifts in a fashion similar to weightlessness. Circulating plasma volume initially increases, followed by a decrease in total plasma volume exceeding 10% of control subjects (58). The diuresis which accompanies water immersion follows a pattern similar to that seen in space. That is, the intrathoracic vascular stretch or "volume" receptors are stimulated by an increase in both total and intrathoracic blood volume which reflexively inhibits ADH release. While the diuresis is predominantly free-water (solute excretion is not necessarily the same as under weightless conditions) the mechanism appears similar to that of space flight. That is, less hydrostatic

pressure results in less cardiovascular effort encouraging a greater absorption of tissue fluids monitored by the volume receptors as an increase in total plasma volume. This in turn results in diuresis.

While immersion has proved to be a valuable aid in simulating the effects of weightlessness, particularly with regard to cardiovascular alterations and body fluid volume shifts, the unnatural external environment of immersion produces some important experimental difficulties and is therefore distinct from the true weightless state in several respects. These are enumerated below as outlined by McCally and Wunder (59):

1. The high specific heat of water results in abnormal heat exchange with the environment. This means that body temperature must be very carefully monitored if temperature artifacts are not to confuse such studies. Additional artifacts may be induced through the restriction of normal cutaneous water losses and ventilation by the use of rubber suits.
2. Immersion in water exposes subjects to ambient pressures of greater than 1 atmosphere.
3. During immersion the ambient pressure over the body is distributed as a gradient, increasing as the depth of immersion increases. This may cause anatomical distortion of the chest and lungs, as the intrapulmonic pressure is uniform.
4. Hydrostatic pressure gradients persist in fluid-filled compliant systems (e.g., the heart, great vessels, and pulmonary vasculature) that are contained in the air-filled, uniformly pressured, thoracic cavity.
5. For comfortable or "eupneic" breathing, breathing air is supplied at a pressure negative to ambient pressure at midchest or right atrial level, producing all the physiological consequences of negative pressure breathing.
6. Viscous resistance to body segment motion is present during immersion.
7. Immersion of human subjects is technically difficult for prolonged periods (days), and although occasionally attempted, immersion is not applicable to most unanesthetized animals.

While water immersion as a tool for the study of simulated weightlessness-induced physiological alterations was particularly important during the early days of the manned space flight program, it is no longer regarded as the major research instrument it once was. Immersion effects on respiratory mechanisms, blood volume distribution, and thermal equilibrium make interpretation of experimental results more ambiguous than other methods. More appropriate experimental tools such as bed rest and cast immobilization have been developed which are closer models to the simulation of weightlessness-induced biomedical changes. Still, immersion remains a useful technique for the comparative evaluation of countermeasures for deconditioning effects. Also, as will be discussed in the next chapter on Performance Factors in Long-Duration Space Flight, immersion continues to be important in simulating the problems of motor and kinematic performance of freely moving, suited men within space vehicles and extra-vehicular activity simulations.

HYPOKINESIS-HYPODYNAMIA

Current knowledge suggests that a hypokinetic-hypodynamic state induced by various techniques is the most appropriate ground-based method with which to study the effects of prolonged weightlessness. Considerable data has been generated using plaster cast immobilization (60), chair rest (61, 62), and confinement (63, 64, 65, 66). However, the major source of information has come from studies of bed rest (67, 68, 69, 70, 71, 72, 73, 74, 75). As such, the present discussion of the effects of hypokinesis-hypodynamia will focus primarily on bed rest as an analog to weightlessness.

Many ground-based experiments have been conducted to determine the effects of simulated weightlessness on the musculoskeletal system (20, 60, 76, 77), intravascular hydrostatic pressure (78) and other cardiovascular mechanisms (79, 80, 81), metabolism (82, 83, 84, 85), fluid and water balance (86, 87, 88, 89), and other related parameters (90, 91, 92). In most cases the lack of activity imposed by bed rest has effectively simulated many of the effects that weightlessness produces due to the lack of hydrostatic pressure and the lack of stress upon the body. Within 24 to 48 hours following recumbancy, there is a loss of fluid volume. This effect is due to an initial shift of volume from the periphery (legs) to the chest which is interpreted by central mechanoreceptors as a relative increase in volume. This stimulates the process of ADH inhibition and consequential diuresis in a manner similar to that observed under weightless conditions.

Fluid loss in turn serves as one of the reasons for decrease in body weight observed during prolonged bed rest. It is also involved in the deconditioning of the cardiovascular system since decreased blood volume along with decreased blood pressure can result in diminished reactivity or sympathetic tone of vessels (particularly veins).

The lack of stress upon the musculoskeletal system during prolonged bed rest effectively simulates the lack of stress inherent in weightlessness. When the human body is maintained in the horizontal position, gravitational forces are not exerting pressure upon the support structure in the same way as experienced in the vertical position. As a result, muscles tend to atrophy from disuse and bones tend to demineralize from lack of stress, combining

with cardiovascular and metabolic alterations to decrease work tolerance and capacity.

The lack of need for active opposition to gravitational forces during bed rest leads to other effects as well. There is a decrease in energy exchange and oxygen transport requirements in the system with a systematic decrease in basal metabolism. This decreased energy metabolism is in turn a reason for decreased food consumption. Thus, the fluid volume shift and elimination of weight stress produced by bed rest are responsible for a large number of reactions which resemble those obtained from flight experiments. Table 10 abbreviated from that presented by Pestov and Gerothewohl (15) summarizes some of the effects observed under weightless and hypokinetic-hypodynamic conditions.

VESTIBULAR FUNCTIONING INVESTIGATIVE TECHNIQUES

While water immersion and bed rest techniques have proved valuable in simulating many aspects of space flight, the ever present force of gravity does not make them particularly useful models of vestibular functioning in weightlessness. Instead, several other techniques have been developed to investigate the mechanisms behind vestibular alterations during space travel.

Historically, the shipboard force environment was the first to receive serious attention in the study of vestibular involvement in motion sickness. The study of wave characteristics demonstrated that magnitude of accelerations was not an eliciting factor in the production of motion sickness, however time between acceleration was (93).

Table 10. Comparison of Physiological Response to Weightlessness and Ground-Based Simulation.

Reactions to Weightlessness	Reactions to Ground-Based Simulations
Pulse frequency: slowing of normalization following action of G-forces; subsequent tendency toward slowing, increase in variability (possible arrhythmias of the bigeminal type); in final stage of long SF, slight increase	With PBR* following initial decrease in frequency of pulse, increase in frequency (lack of training)
Arterial pressure: moderate decrease, followed by stabilization, tendency toward decrease in pulse pressure.	In PBR, initial decrease followed by increase (sympathetic effect)
Bone tissue: demineralization (according to the data from x-ray photometry) due to loss of Ca^{++}	Similar changes in experiments with PBR
Muscles: decrease in volume and strength	Similar changes in experiments with PBR
Dehydration (decrease in plasma volume, followed by loss of intracellular fluid)	Similar changes in experiments with PBR
Decrease in weight (mass) of the body	Similar changes in experiments with PBR
Protein metabolism: increase in blood urea content, increased excretion of creatinine with urine, negative nitrogen balance	Similar changes in PBR
Reduced excretion of 17-oxycorticosteroids in flight, increase in excretion following flight	Similar relationship in experiments with simulation of weightlessness
Blood: neutrophilic leukocytosis, lymphopenia, or lymphocytosis, eosinopenia, increase in ROE [?], changes in coagulatory and anticoagulatory systems of blood; thrombocytes - decrease or absence of changes	Similar changes in experiments with PBR
Deterioration of tolerance to transverse G-forces during launch	Similar changes in experiments with PBR

Table 10. Continued

Reactions to Weightlessness	Reactions to Ground-Based Simulations
Gas exchange: decrease (according to data from analysis of regenerative substance) during the SF; increase during post-flight period	Decrease in the PBR
Decrease in food consumption	Characteristic of PBR
Orthostatic instability	Develops also under conditions of terrestrial experiments involving simulation of weightlessness
Decrease in physical working capacity	Consequence of hypodynamia
*PBR - Prolonged bed rest.	

Adapted from Pestov and Gerathewohl (15)

A logical extension of the earlier research on acceleration effects was the laboratory use of vertical and horizontal oscillations. However, it was soon discovered that head position played an important role in the production of symptoms (94) and so studies began to focus more on angular accelerations. The Angular Acceleration Susceptibility (AAS) Test has been a standard in assessing factors related to motion sickness. As an example, Miller and Graybiel (95) investigated the role of the semicircular canals in motion sickness using a special motor driven Barany-type chair. The chair was accelerated to a velocity of 30 or 60 rpm within approximately 4 seconds with acceleration maintained for 150 seconds. The chair was then decelerated to a stop within 4 seconds and remained stationary until the accumulative time totalled 300 seconds. Tolerance to this 300 second procedural cycle (acceleration, constant velocity; deceleration, static hold) serves as a good index of susceptibility to motion sickness involving simple angular acceleration without any significant gravitoinertial force changes. Coriolis Acceleration Susceptibility (CAS) has also been investigated using a rotating chair (Stille rotational chair) by adding the requirement of standardized head movement during rotation (96, 97).

Coriolis acceleration problems have also been investigated using the Slow Rotation Room (SRR) located at the Naval Aerospace Medical Research Laboratory in Pensacola, Florida. A large room rotating at velocities between approximately 4 to 14 rpms is used to simulate angular velocity and to investigate prolonged exposures and sudden transitions between the rotating and nonrotating states.

The SRR has been important in demonstrating the following points relevant to sudden transitions between gravitational states:

1. persons remaining symptom-free during exposure to an incremental adaptation schedule (counterclockwise rotation) experienced motion sickness when the direction of rotation was reversed (98)
2. non-symptom-free persons required to adapt to rotation in one direction, showed transference of that adaptation when rotation proceeded in the opposite direction (100)
3. head movements executed on return to zero velocity, after achieving symptom-free adaptation in an incremental fashion, would elicit symptoms of motion sickness (99)

At least one other important variation on the rotating environment has been used to study the role of vestibular functioning in motion sickness. The Off-Vertical Rotation Susceptibility (OVR) Test also makes use of a Stille rotary chair. However, the chair is tilted so that its rotational axis is displaced from the gravitational vertical. This procedure is particularly useful for assessing the otolithic systems. In the SRR and CAS tests described above, the canalicular system is initially affected, but exposure to rotation at other than gravitational upright initially disturbs the otolithic system.

While the use of rotating environments has proved relevant in studying various aspects of motion sickness, there are certain inherent disadvantages in its application to the study of a weightless environment. Most notably, it does not produce the same effect on the vestibular systems as weightlessness. The lack of gravity in space essentially deafferents the otolithic system, while having no effect on semicircular canal impulses. No such effect can be produced through ground-based studies (except through surgical deafferentation in animal subjects or the study of humans

with defective anatomy). Also, the rotating environments of earth do not permit assessment of man under unrestrained walking and working conditions. Furthermore, for some functions, susceptibility under ground-based conditions has proved to be a poor indicator of susceptibility aloft (32). These limitations in the study of vestibular functioning on earth have been somewhat offset by the use of parabolic flight as a complementary source of data.

Studies dealing with susceptibility to motion sickness in the weightless phase of parabolic flight have been mainly of two types. In one, the subjects are required to make standardized head movements while restrained in their seats. In the second type of study, subjects also make standardized head movements, but while being rotated in a chair device. Under these conditions, each subject serves as his own control with comparisons made between susceptibility under terrestrial rotation conditions and during parabolic flight (with rotation). It is encouraging to note that insofar as the studies have used similar methods, the findings from parabolic flight agree with findings on astronauts (101) and cosmonauts (102) in orbital flight.

BIOMEDICAL USES OF ANIMALS

Aside from ground-based simulation studies of hypodynamic effects and the use of Keplerian trajectories for the study of brief weightlessness states, one other important source of information regarding the effects of space flight exists: the use of animal models under operational conditions. Animals have played a significant role in serving as precursors to man in space. It is

anticipated that animal flights will continue to serve as a useful measure of the effects of weightlessness through the use of longer duration missions emulating those which man might eventually attempt. Table 11 displays a chronological listing of vertebrate experiments conducted suborbital and orbital. The American programs have utilized primates as the animal of choice while the Russians have used dogs.

In the early days of the space program animals were used to assess the feasibility of manned space travel. From 1946 to 1954, a large number of balloon flights were used to test the effects of cosmic radiation upon central nervous system tissues. Over 30 flights were conducted between 1950 and 1954, using mice, hamsters, cats, dogs, and monkeys for durations up to 28 hours. Between 1947 and 1957, heavily instrumented rockets were tested, frequently using animals to assess acceleration and environmental parameter effects upon physiology and performance.

As progress was established toward the first manned space flights of the Mercury Program, chimpanzees were put into orbital flight to test missile-vehicle control systems and to demonstrate that a species similar to man could tolerate short-term weightlessness without adverse effects.

As the focus of the space program began to center on actual man-in-flight missions, animals still continued to play an important role in the accumulation of flight related data. Pocket mice were included on Apollo 17 and Skylab 3 missions.

By the 1960's, animal flights had become an important source of biomedical data. Missions such as Biosatellite and Kosmos demonstrated

Table 11. Vertebrate Experiments in Space.

<u>Year</u>	<u>Mission</u>	<u>Species Carried</u>
1946-1952	Balloons and Ballistic Rockets	Mice, Rats and Cats
1957	Soviet Sputnik	Dog (Layka)
1958	Jupiter Ballistic Missile	Squirrel Monkey (Old Reliable)
1958	Jupiter Ballistic Missile	Rhesus Monkey (Able) and Squirrel Monkey (Baker)
1959	Little Joe Ballistic Missile	Rhesus Monkey (Sam)
1960	Soviet Sputniks 4 & 5	Dogs, Small Laboratory Animals
1960	Little Joe Ballistic Missile	Rhesus Monkey (Miss Sam)
1961	Soviet Sputniks 6 & 7	Dogs, Small Laboratory Animals
1961	Mercury Ballistic Flight	Chimpanzee (Ham)
1961-Nov.	Mercury Ballistic Flight	Chimpanzee (Enos)
1966	Soviet Kosmos 110	Dogs
1967	Soviet Kosmos 212	Tortoises
1968	Soviet Zond 5	Tortoises
1969	Soviet Zond 6 & 7	Tortoises
1969-June	Biosatellite III	Pigtail Monkey (Bonnie)
1970	OFO-A	Frogs
1972-Dec.	Apollo 17	Pocket Mice
1973-July	Skylab 3	Pocket Mice, Fish
1973	Soviet Kosmos 605	Rats and Tortoises
1974	Soviet Kosmos 690	Rats
1975	Soviet Kosmos 782	Rats, Fish, Turtles
1977	Soviet Kosmos 936	Rats

the usefulness of animals for obtaining data more detailed and controlled than permitted by the multi-purpose flights of the astronauts/cosmonauts.

Just as animals have preceeded man in previous high risk flights, it seems logical that long duration animal flights will be an important source of information regarding the effects of long duration space flight. This might take the form of either an unattended long-term animal mission or missions involving a central space laboratory which can be periodically monitored by humans. The first notion has been favorably received and marked by several attempts, which unfortunately, never came to fruition. At least two long duration (6-12 months) nonhuman primate missions have previously been entertained, with feasibility studies conducted and prototype hardware constructed. The Orbiting Primate Experiment (OPE) described by Walton Jones (103) was originally intended to be part of the Apollo Applications Programs. The purpose of the mission was to study the physiological effects of long-term weightlessness on the vestibular organs and to investigate the microscopic changes which might occur in these organs.

A technical feasibility demonstration model of the life support system of the capsule was constructed and tested at the Naval Aerospace Medical Research Institute. With the exception of some minor problems, the model functioned well. Due to other financial considerations at the time, the mission was not approved beyond the planning stages.

More recently, the Biomedical Experiment Scientific Satellite (BESS) was proposed as a long-term animal flight experiment

facility which would have flown small laboratory animals and eventually a nonhuman primate (104). Again while feasibility and design studies were executed with promising results, the project did not come to fruition.

While a mission such as the OPE or BESS could prove quite valuable, there are some inherent problems in flying animal subjects for long periods either completely or relatively unattended. If the animal becomes ill or the equipment fails to function properly the probability of successfully completing the mission is substantially reduced. This was unfortunately demonstrated in the Biosatellite III flight of 1969 (105) during which a planned 30 day mission was cancelled after 8 days when the pigtailed monkey on board began to show diminished physiological response. The monkey died shortly after recovery of the capsule apparently due to the stress of over-instrumentation. Problems of equipment failure also plagued the mission.

Perhaps a more promising approach to the study of animals and man under long-term exposure to weightlessness is the concept of an orbiting space laboratory. Initially animals could be exposed to flight conditions for long periods while a rotating human crew periodically monitored the status of the subjects. In a later phase, the craft could be used to study human responses to long term weightlessness before any actual long-term space flights were attempted. Certainly the outstanding accomplishments of our Skylab missions demonstrate the promise of this approach. This possibility may be achieved through the forthcoming Space Shuttle/Space Lab program. Although an orbiting Life Science laboratory is planned,

the flight duration initially will only be 7 to 14 days. It is conceivable that considerably longer periods will be generated in later missions. Such missions would certainly prove valuable in enhancing our knowledge of the effects of sustained exposure to weightlessness.

COUNTERMEASURES

As indicated in an earlier section, it is not entirely clear what effects long term exposure to weightlessness will have on the various systems of the body. Space flights to date have not entailed any serious physiological threat to the safety of crew members. However, certain symptoms indicative of potential dangers have been observed: orthostatic intolerance, loss of exercise tolerance and muscle power, diuresis with reduction in fluid volume and circulating blood volume and perhaps red blood cell mass, loss of skeletal calcium, etc. It appears that these changes represent the body's homeostatic adaptation to changes in gravity. If they reach a steady state optimal for functioning in zero-gravity and maintain an asymptotic level which poses no health problems during extended weightlessness, many of our present concerns will be relieved. Under these circumstances the factor of critical importance would be adaptation of the system to transitional changes in gravity, i.e., from 1-g to 0-g upon insertion into space and from 0-g to 1-g upon re-entry to earth's atmosphere. This would entail the possible need for various countermeasures which could attenuate the stresses of these transitions, but need only be used prior to transitions rather than throughout the entire flight. On the other

hand, there is some evidence that certain physiological changes due to weightlessness may not reach steady state prior to the point of irreversibility (bone decalcification). Should this be the case, in-flight countermeasures would be a necessity to ensure safety throughout the mission. This controversy points out the need for biomedical research in all areas to determine the limits of exposure to zero-gravity (or its simulation) to better assess what countermeasures are necessary and sufficient for long duration space travel. Currently, countermeasures are being developed using a wide range of techniques. Table 12 reprinted from Vinograd and Manganeli (106) and Table 13 reprinted from Pestov and Gerathewohl (15) summarize the methods which have been employed.

CARDIOVASCULAR SYSTEM PROTECTION

Given that the lack of hydrostatic pressure seems to be the major cause of altered cardiovascular functioning during 0-g, the logical prevention of this condition should involve creating an artificial counteractive pressure. Initially, various venous occlusion cuffs were employed as in the Gemini flights (107). These cuffs which enclose the extremities (usually the upper part of the thighs) were intended to reduce return of venous blood to the heart thus simulating conditions of the human in a vertical position on earth. Unfortunately, numerous laboratory tests have failed to demonstrate reliable protective effects (108, 109, 110). The inflated cuffs used during space flights also yielded no significant reduction of orthostatic intolerance (107).

Table 12. Countermeasures to the Effects of Weightlessness.

Exercise	Tumbling
Medication	Electrical stimulation of muscles
Diet	Exercise and LBNP
LBNP	Exercise and venous occlusion cuffs
Gradient positive pressure	Exercise and positive pressure breathing
G-Suit	Exercise and bone stress
Venous occlusion cuffs	Exercise and hypoxia
Positive pressure breathing	Venous occlusion cuffs and medication
Valsalva maneuver	Venous occlusion cuffs and leotards
Bone stress	Hypoxia, LBNP and exercise
Double trampoline	Centrifugation

Vinograd and Maganelli (106)

Table 13. Countermeasures to the Effects of Weightlessness.

Partial adaptation to weightless state	
Physical exercise	Acceleration
Calisthenics All kinds of sports Tumbling, diving, zero-G training Isometric and isotonic contractions Bicycle and hand ergometers Head movements during zero-G	On-board centrifuge Trampoline Oscillating support Vibrating bed Space station rotation
Controlled environment	Drugs and medication
Hypoxia Low temperature Diets	Aldosterone Antidiuretic hormone Plasma expanders 9 α -fluorohydrocortisone
Pressure	Counteractives
Pressure breathing Positive pressure cuffs Elastic garments Lower body negative pressure Anti-G suit	Glucose Pitressin Anabolic hormones Electrostimulation
Complete adaptation	
Preconditioning of organism to subgravity level or zero-G state; reconditioning organism to force of normal terrestrial gravitation	

Pestov and Gerathewohl (15)

More promising possibilities include the application of lower body negative pressure (LBNP) or gradient positive pressure. LBNP involves the use of a device that produces slight negative air pressure around the lower half of the body. This encourages caudal pooling of blood, which increases transudation of fluid, rehydration, and restoration of tissue tension in the lower extremities. Studies of subjects exposed to water immersion and bed rest simulating weightlessness have responded well to the LBNP technique (111, 112, 113, 114). For example, Cramer (115) found that intermittent application of -70mm HG restored orthostatic tolerance following five days of water immersion and bed rest. Experiments on board Skylab demonstrated encouraging results as well. In-flight LBNP data proved useful both for predicting the early post-flight status of orthostatic tolerance and for assessing in-flight crew health status. At rest, in-flight Skylab 4 crewmembers showed typically increased mean resting heart rates, systolic blood pressures, and pulse pressures and decreased diastolic and mean arterial pressures relative to pre-flight measurements. Thus, LBNP used as an intermittent stressor shows substantial promise as a prophylactic technique against zero-gravity effects on the cardiovascular system. It can be used to develop tolerance to blood shifts and ensure adequate venous return to the heart.

Another similar approach which has been explored is the use of gradient positive pressure applied to the upper part of the body. While LBNP draws blood to the lower part of the body by reducing pressure in that part, gradient positive pressure en-

tails increasing the pressure applied to the upper part of the body thereby encouraging greater pooling in the lower part. This technique was employed immediately following the Apollo 17 mission (5) and in associated bed rest studies with promising results.

Re-entry stress may be attenuated through the use of G-suits (71, 110, 116). G-suits feature an elastic undergarment that exerts counterpressure on the lower half of the body thereby reducing the blood volume alterations in that area. This serves to counteract the tendency toward blood pooling following weightlessness. The combination of LBNP during flight and the use of G-suits immediately post-flight should prove to be an effective countermeasure to the re-entry problems of the cardiovascular system due to blood shifts. G-suits have been shown to be effective in counteracting orthostatic stress following prolonged bed rest.

MUSCULOSKELETAL SYSTEM PROTECTION

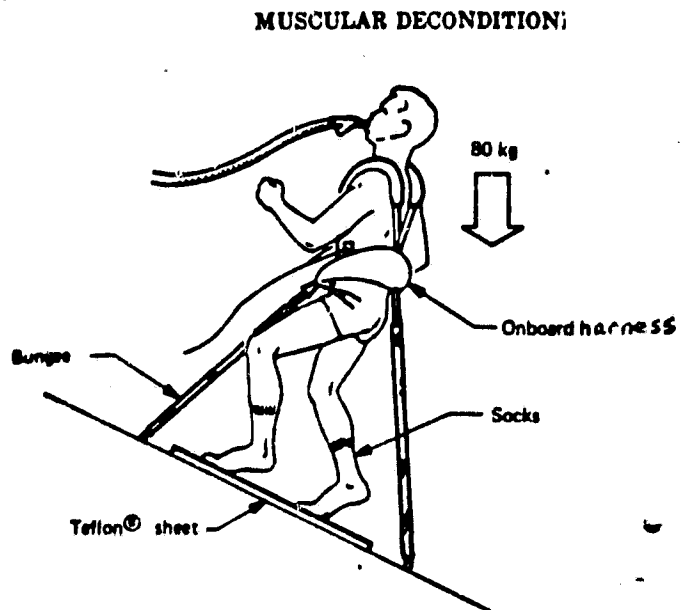
Considerable research has been devoted to the development of an exercise regime to prevent the deconditioning of the muscle system during weightless flight. There seems little doubt about the desirability of its use in weightlessness. However, the question of the nature, intensity, and the overall effect of the regime is still under debate. Isometric and isotonic exercise has been used with positive benefits on both American (2, 4, 5) and Soviet (116, 117) missions. The programs used in Skylab 2, 3, and 4 have been the most comprehensive and effective to date and serve as a good example of the benefits associated with exercise.

Four different types of exercises were used. These included a bicycle ergometer (used in all missions), a treadmill shown in Figure 4 (used in Skylab 4), and the MK-I (shown in Figure 5) and MK-II devices (both used in Skylabs 3 and 4). A summary of crew averages of exercise related data is shown in Table 14. The data for Skylab 4 is particularly impressive, indicating that exercise prevented loss of weight, leg strength and volume quite effectively. Similar results for other muscle groups were obtained as well.

While exercise has proved to be a valuable in-flight aid to the protection of the muscle system, it is less clear whether its effects extend to other systems as well. For example, there is considerable data to indicate it does not deter skeletal losses (118, 119). Its usefulness in preventing cardiac deconditioning is also unimpressive. Exercise alone is not effective in combating cardiac anomalies (110, 120), but according to some investigators may be helpful as an adjunctive therapy if the procedure raises the heart rate above 120 beats per minute (22). Physical exercise is thought to have some psychological benefits. This point will be dealt with in a later chapter.

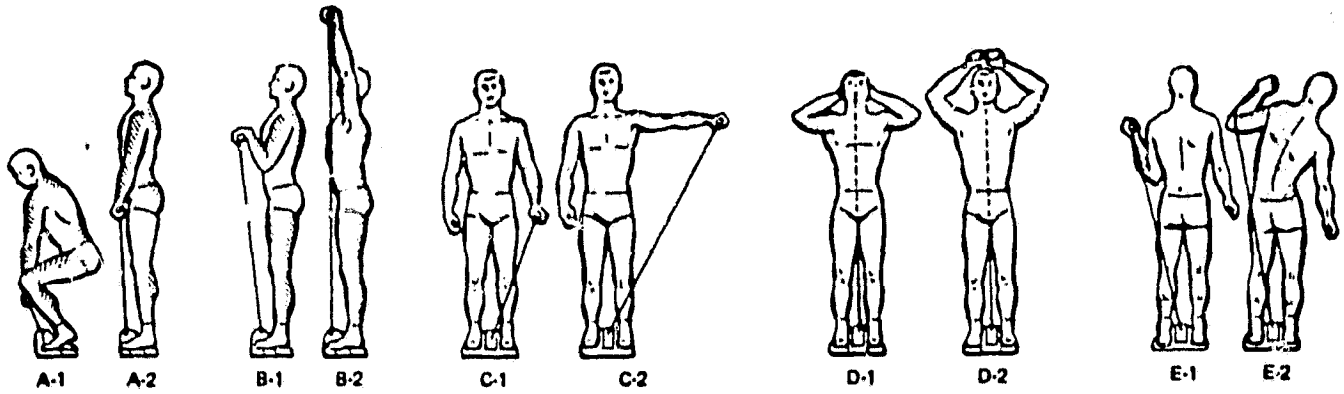
While in-flight exercise may be beneficial to at least the muscular system there is considerable disagreement regarding the value of pre-flight physical fitness conditioning beyond that of the average healthy person. Klein, Wegmann, and Kuhlinski (121) report that under extreme environmental conditions, athletes are more adversely affected than non-athletes. For example, under high altitude conditions, the aerobic work capacity of athletes decreased by

Figure 4. Skylab Treadmill.



Thornton and Rummel (2)

Figure 5. Exercise Positions of the Skylab MK-I.



Thornton and Rummel (2)

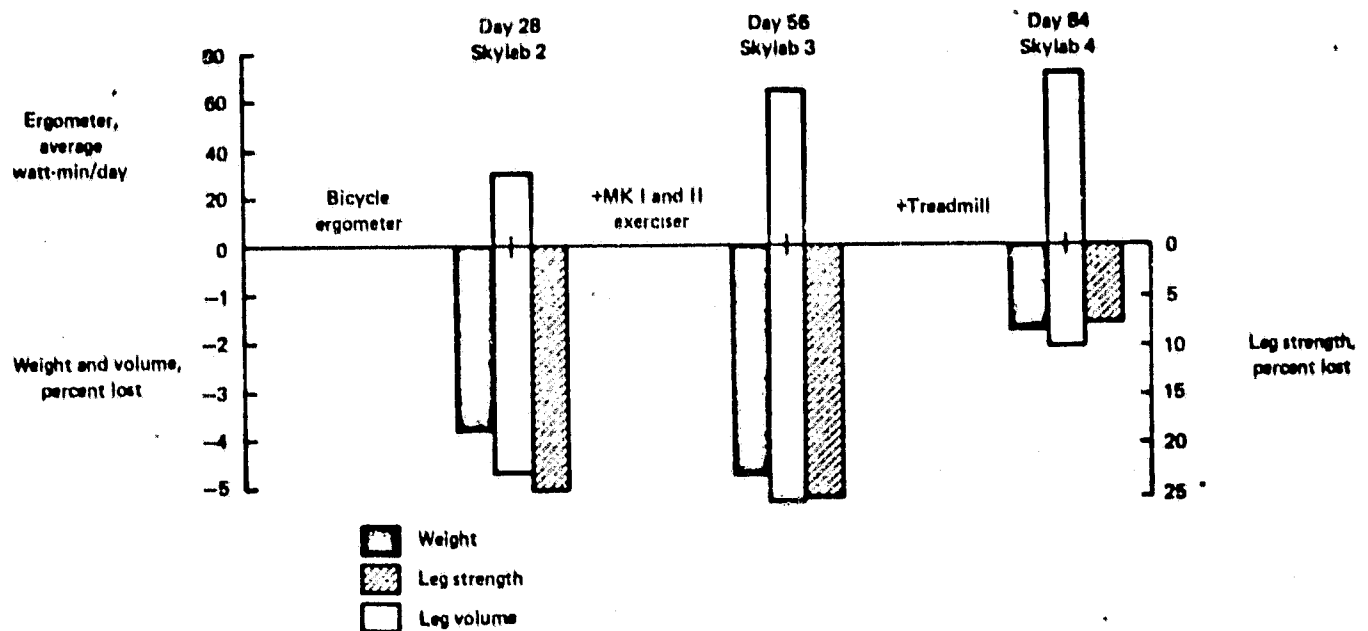
Table 14. Exercise Related Quantities on Skylab Missions.

Skylab crew	Change in leg extension forces <i>F</i> -15 to <i>R</i> +1, percent/day	Change in leg volume <i>F</i> -15 to <i>R</i> +5, percent/day	Change in lean body mass <i>F</i> -15 to <i>F</i> +1, percent/day	Change in body weight <i>F</i> -1 to <i>R</i> +0, percent/day	Average daily ergometer exercise/ body weight watt-min/kg
2	-0.89	-0.160	-0.089	-0.13	31.3
3	-0.44	-0.088	-0.019	-0.08	65.0
4	-0.09	-0.023	-0.011	-0.02	71.0

† Bicycle ergometer.

‡ Bicycle ergometer, MK-I and MK-II exercisers.

• Bicycle ergometer, MK-I and MK-II exercisers, treadmill.



a factor of 10.1% while non-athletes showed decrements of only 8.7%. This greater reduction for athletes was highly significant. During a 20 minute head-up 90° tilt test, 5 out of 12 athletic subjects fainted, while 4 of 12 non-athletes fainted. At the same time, Luft and associates (122) found during Lower Body Negative Pressure a highly significant difference in tolerance of 42% favoring non-athletes.

Klein et al. (122) point out that under conditions of simulated weightlessness (immersion), athletes show a significantly greater reduction in aerobic work capacity following six hours of water immersion than do non-athletes. Also, following immersion all endurance trained athletes fainted during a 10 minute vertical tilt, while the untrained subjects tolerated the tilt without any abnormal effects.

These results are supported by the in-flight findings of Skylab 4. According to pre-flight aerobic capacity, the Scientist Pilot (SPT) and the Pilot (PLT) were in "good" to "excellent" physical condition as estimated by the Cooper Scale (123), while the Commander (CMD) was only classified as of "fair" fitness. During the mission, the SPT and PLT clearly demonstrated poorer responses to provocative gravitational stress: a higher increase of heart rate and calf volume, and a greater reduction of pulse pressure during LBNP (124). Also, during post-flight LBNP stress, the SPT and PLT showed a higher degree of orthostatic intolerance even though they exercised in flight more than the CMD. This suggests that physical exercise is more successful in the less trained individual in attenuating ortho-

static intolerance induced by weightlessness. Simulated weightlessness studies have also demonstrated this result (125). Intermittent swimming exercise during immersion improves the circulatory responses during subsequent tilt table tests more in non-athletes than athletes.

These results strongly suggest that the view of exercise in the pre-conditioning of astronauts and cosmonauts emphasized as a non-specific method for increasing resistance to spaceflight is inappropriate. Particularly with regard to the cardiovascular system, athletic endurance training may not only be useless but disadvantageous. It seems more appropriate to maintain crew members within the normal range given for a non-athletic population during pre-flight, while stressing an exercise program (such as that used in Skylab 4) during actual space flight. This is certainly an important area that deserves further research.

In contrast to the cardiovascular and muscle systems, relatively little progress has been made toward the development of skeletal loss countermeasures. As indicated earlier, physical exercise has not proven effective in reducing decalcification. This has been demonstrated by the results of Skylab 4 and by the efforts of the Soviets who employed a Prophylactic Load Suit (PLS) during the 30 day Salyut 4 space station mission. The PLS was designed to load the bones and muscles of the legs and torso and had been shown to be effective during five days of water immersion. However, results of the Salyut 4 flight demonstrated no prevention of calcium loss in a weightless environment.

Other procedures which have been used in treating disuse bone calcium loss include dietary supplementary calcium (Hulley et al., unpublished data), injections of calcitonin to stimulate bone calcium uptake (126), and more recently, the use of in vivo electrical stimulation of the bone (127, 128). Unfortunately, all of these procedures have yielded questionable results. Some researchers report positive benefits, others negligible effects, and in most cases some slight effects but in only certain subjects. The positive benefits of each of these countermeasures when applied to ground-based disuse models of weightlessness has at best been a deterrent to the rate of calcium loss, rather than a preventive prophylaxis. To date, there has not been an effective countermeasure for the prevention of calcium loss in a weightless environment. Certainly this is an area where considerably more research is needed.

VESTIBULAR "SPACE SICKNESS" PREVENTION

Vestibular effects manifested as space motion sickness have, in several cases, been severe enough to hinder performance during the first three to four days of space flight. Treatment of these symptoms has not been particularly effective in preventing debilitation, but have provided some relief. The use of various anti-motion sickness drugs have been used since the early days of the manned space program. While the exact type of medication and dosage has varied slightly, only drugs with a parasympatholytic or sympathomimetic action (and some of the antihistamines) have been notably effective. For example, the astronauts on board Skylab 2 and 3 used capsules containing .35 milligrams of 1-scopolamine and 5 milligrams d-ampetamine, while the Skylab 4 crew

also carried 25 milligrams promethazine hydrochloride + 50 milligrams ephedrine sulfate capsules. While these drugs effectively raise the stimulus threshold for eliciting motion sickness response, they only serve to postpone the onset of symptoms elicited by conditions of extreme provocation. The use of anti-motion sickness drugs brings into issue the entire concept of space pharmacology. There are some important questions to be addressed regarding drug action under weightless conditions. Stated simply, does a given drug affect the body in space in a manner similar to its action on earth. Due to changes in blood pressure, fluid volume, and metabolism the time course of drug action may be significantly altered as well as its overall effects. Also, since there are major biomedical alterations throughout the body, one cannot necessarily assume that the particular system to be treated will react to the drug in the same way as on earth. This issue is somewhat akin to the antedotal notion that alcohol effects the brain more rapidly at high altitudes making air travelers more susceptible to intoxication. Given the tremendous amount of pharmacological research which has been directed toward the treatment of in-flight alterations (130), it seems critical that research also be directed toward understanding the ramifications of a drug-weightlessness interaction.

Beyond the use of pharmacological agents, perhaps the only way to confer protection is through the natural process of adaptation. This can be accelerated somewhat through the use of certain head movements which intensify the stimulus conflict involved in the production of symptoms. This can be an annoying process and one

that is certain to cause maximal debilitation for a given individual. However, if the intensity of the stimuli is high, the latencies associated with the appearance and disappearance of symptoms is brief. This poses a certain dilemma for the space sick astronaut. He can either intensify those actions which increase the onset and severity of symptoms, but also result in faster adaptation or he can reduce the severity of the symptoms through various methods which unfortunately results in a more prolonged period of adaptation. There are certain techniques which do decrease the frequency and severity of symptoms. The use of anti-motion sickness medication is one of them. Also, restricting head movements, closing one's eyes, or fixating on the horizon or some stable object are others. Related to this is the finding that adapting the supine position markedly reduces the risk of motion sickness (129), probably because it necessarily restricts independent head motions. Finally, there are a number of antidotal and research observations which indicate that focusing on an engaging task requiring mental activity can help in reducing susceptibility. Unfortunately, depending on the nature of the task, performance may be reduced due to the presence of these symptoms.

During the missions thus far flown, space sickness has been only a fairly annoying problem but with adaptation occurring within a few days. However, as the complexity of missions and spacecrafts increases, the problems of adapting could become more severe. For example, protective adaptation tends to be highly specific to a particular environment or stimulus. Consequently

as more living and working areas are added to spacecraft (as in Skylab) it may be necessary for passengers to endure more than one adaptation process.

Currently, there are at least two promising approaches which may help this situation. One is the use of assessment techniques to select only those crew members with a high tolerance to space sickness. This possibility will be explored further in the chapter on Testing, Selection, and Training. Another possibility is to pre-train astronauts to control those autonomic responses which reduce space sickness through the use of autogenic training and biofeedback. One such program is presently being conducted by Cowings and associates (131, 132, 133) with promising results. Cowings and associates have shown that subjects given biofeedback training designed to gain control of respiration rate, heart rate, and blood volume pulse demonstrated significantly higher tolerance to Coriolis acceleration following training than during pre-treatment tests.

This type of training has particularly good potential for dealing with control of space motion sickness because it deals specifically with the final common path of the autonomic manifestations of motion sickness. The method should work equally well under ground-based simulation conditions and in weightlessness, thereby eliminating the problem of transferring protection from one type of environment to another. What is learned on earth would be directly transferrable to operational conditions. Also, what is useful in one area of the spacecraft could be used during transitions into other locations on-board.

NONSPECIFIC COUNTERMEASURES

Within the total system of preventative measures, it is necessary to consider factors which can have a general ameliorative effect on the adverse consequences of space flight. A reduction in the stress related aspects of the craft and flight is one important source of nonspecific prevention. While this topic will be dealt with in more detail in the following chapter, suffice it to say that stress can be a contributing factor in the production of many of the symptoms discussed throughout this chapter.

The habitability of the craft can be assumed to be an important area in promoting weightlessness tolerance. Even the type of clothing used can be important. Light clothing used during the 14 day Gemini flight decreased adverse effects of weightlessness compared to the heavy space suits used in the 8 day flight (134). Social conditions will become increasingly important as the length of stay increases. Interpersonal relations may well serve to increase tension and stress or may help eliminate frustrations and anxieties depending upon the individuals and the circumstances. These possibilities will be dealt with in more detail in later chapters.

The diet of the crew will be another source of deconditioning prevention. Increased calcium and potassium dietary supplements may be somewhat helpful with certain weightlessness-associated imbalances. According to ground-based studies, the addition of phosphates to food decreases both urine excretion and calcium losses in the blood. Also, prolonged hypodynamia studies indicate increased excretion of vitamins, suggesting that space

diets should include increased vitamin saturation. While the content of the diet is important, it is also crucial that the diet be appetizing and palatable to ensure stimulation of appetite diminished from weightlessness. Other features of the diet should also be investigated. Soviet scientists recently tested a wide range of preparations in reducing psychophysical problems related to prolonged exposure to stress and sensory deprivation (135). Additives which tended to reduce unfavorable changes in brain activity and individual behavior included: ascorbic acid, glucose, phytin, lipocerebrin, calcium pangamate, thiamine bromide, methionine, calcium pantothenate, nicotinic acid, riboflavin, glutamic acid, andelenium.

Another intriguing possibility for increasing nonspecific resistance to weightlessness may be acclimatization to high altitude. In simulated weightlessness studies, hypoxia prevented erythrocyte mass decrements and encouraged decreased electrolyte excretion, total urinary nitrogen, and reduction in bone substance demineralization (136, 137, 138, 139). Apparently, physiological reactions to hypoxia are similar to those of physical training in flight with respect to the counteraction of hypodynamic symptoms.

ARTIFICIAL GRAVITY

Another possibility which has been suggested as a countermeasure to the effects of weightlessness is the use of artificially produced gravity on board the spacecraft. This could be accomplished either through rotation of the entire vehicle or the inclusion of an on-board centrifuge.

Artificial gravity produced by craft rotation has the greatest apparent validity as a countermeasure for preventing physiological deconditioning and to the degree that it approximates a normal, linear gravitational environment may produce a more comfortable living arrangement for long duration space crews. Unfortunately, a rather large vehicle is necessary in order to produce axial rotation simulating earth-type gravitational conditions. A short-radius rotating craft (SRRC) does not give a very good approximation to linear gravity and may yield a number of undesirable phenomena to an even greater extent than do long radius rotation vehicles. Under SRRC conditions, astronauts may anticipate a certain degree of locomotor difficulty, spacial disorientation, and motion sickness. These effects are due to the same type of intersensory conflict thought to be involved in motion sickness experienced under weightless conditions. There exists a conflict between the gravitational vertical and the vertical direction indicated by a flat floor. This visual-proprioceptive conflict regarding the vertical-horizontal frame of reference leads to a conflict of sensory information consequently enhancing the possibility of motion sickness. However, the most dramatic problems involve whole body movements (particularly the head) subject to Coriolis forces. An angular movement of the head about any axis not parallel to the rotational axis of the vehicle will generate a highly unusual stimulus to the vestibular system. The semicircular canals respond to the cross-coupled torque as well as the actual head movement, thus generating signals that the head has moved in a direction other than the actual direction of movement. This information conflicts

with the subject's knowledge of the direction attempted and with the accompanying proprioceptive and visual information. As pointed out in an earlier section of this chapter, this type of conflict in sensory information seems to be a precipitating factor in the production of space motion sickness symptoms.

One important issue regarding the use of a rotational vehicle artificial gravity system is how adaptation to such a system would procede. Earth-based rotational studies using vertical axis rotation have shown that adaptation can occur within about 24 hours at angular velocities at least as great as 6.0 rpm (140, 141, 142, 143). However, the rotation in a weightless spacecraft is significantly different from that in an earth based room (144). On earth, the inter-sensory discordances accompanying most movements are consistent. The subject experiences the same effects during any movement regardless of his position within the room or the direction he is moving or facing. In a rotating spacecraft, pitch and roll head movements, angular limb movements, and horizontal translation will have dramatically different effects depending upon the crew members' orientation. Since the intersensory discordances are not consistent under artificial gravity conditions, adaptation to rotation may be expected to occur to a lesser degree than demonstrated in earth-based room rotation studies. Also, the form of the adaptation may be different (vestibular habituation, perceptual-motor adaptation, and conditioned visual suppression of conflicting information are all possibilities suggested by Ramsey (145)).

In considering the possibility of rotating vehicle artificial gravity systems, the question of how much g-load is sufficient is certainly of importance. It may prove sufficient to use a rotation which produces something less than the 1-g force of earth but greater than the null gravity of weightlessness. By varying the degree and radius of rotation, it would be possible to generate several gravitational loads within the range of $0g \leq X \leq 1g$. Table 15 shows the rotation radii and angular velocities necessary to generate three levels currently considered acceptable (14). Note that the shorter the radius of rotation, the greater is the angular velocity requirement and the Coriolis force. A maximum Coriolis force of 20 percent of apparent weight is considered the limit which can be tolerated without resulting discomfort (14). With higher angular velocities or shorter radii of rotation than those shown in Table 14 even simple head movement can produce discomfort due to severe Coriolis forces. These factors impose some severe design and construction limitations on the use of rotational vehicle artificial gravity systems. However, as a countermeasure to the biomedical effects of sustained exposure to weightlessness, the production of artificial gravitational forces may prove desirable.

Another approach for producing artificial gravity is the possibility of on-board centrifuge devices. Much of the centrifuge work was done in connection with the development of the Manned Orbiting Research Laboratory vehicle (146). Centrifugation is in the form of $+G_z$ spin around or close to the axis of the heart. It has been demonstrated that four 7.5 minute exposures to a

+4G_z level at the foot largely prevents orthostatic intolerance produced by immersion. However, discomfort in the legs and feet, and petechiae in the feet have also been reported.

The most recent attempts to test the centrifuge system in space produced some promising results. In the Cosmos 936 flight of 1977, rats were exposed to centrifugation during 18.5 days of weightless space flight. While the final results are still being analyzed, preliminary analyses show that the lifespan of centrifuged animals was slightly greater, but statistically significant due to decreased hemolysis (147). Hemolysis increased threefold in non-centrifuged flight animals, but was significantly less in those subjects exposed to centrifugation.

The bone system also seemed to be positively affected (147). Bone strength was shown to be significantly greater among rats exposed to centrifugation than controls exposed to weightlessness alone. Unfortunately, no protection was afforded against losses in bone formation.

While these and other results of the Cosmos 936 flight are based on a small sample of subjects, the results are encouraging and support the need and usefulness for further research using on-board centrifuge systems.

It should be noted that current data do not indicate the necessity of artificial gravity. But if the length of stay in space increases and other countermeasures do not prove sufficient the introduction of such a system may be warranted. The cost of artificial gravity would be high in both monetary and engineering terms, and as mentioned earlier, may solve some problems only to

be replaced by others. Both engineers and biomedical specialists are trying to perfect other measures to circumvent the need for artificial gravity (149).

LOOKING TOWARD THE FUTURE

SUMMARY, CONCLUSIONS, RECOMMENDATIONS

While the duration of stay in space so far has not resulted in any medical problems of a critical nature, there have been indications that longer exposures may produce more severe problems. One major area of research directed at future long-duration travel should be the determination of time course and end points of the processes involved in the symptoms observed to date: cardiovascular deconditioning, musculoskeletal disuse atrophy, body fluid volume shifts, exercise and work capacity decrements, etc. Until it is known to what level these systems may degrade during extended flight, it will not be possible to determine what, if any, countermeasures must be taken, and what the limits of stay in space may be. This is an area that deserves highest priority.

A corollary to this issue revolves around the desirability of in-flight adaptation to weightlessness within some systems. In some instances, our concern need not be the changes which occur in-flight, but how to minimize the adverse aspects of re-adaptation to earth's gravity. In the case of the cardiovascular and musculoskeletal systems, it may eventually be demonstrated that the systems do reach adaptive asymptote and pose no problem to the individual as long as they remain in space. Concern, then, would center only on the problem of re-entry and those problems

associated with how the systems can re-adapt to their initial levels of functioning. Certainly these questions are critical and only confounded more as the required duration in space increases. For other systems, research is greatly needed to assess how the duration of exposure to weightlessness affects both with respect to in-flight adaptation and post-flight readaptation. Part of these answers may be achieved through the use of ground-based simulation studies using techniques including water immersion and bed rest among others. However, the feasibility of conducting 12 to 24 month studies using these procedures is poor. The longest human bed rest study to date has been 9 months, the longest animal immobilization experiments average about six months, while nothing of any considerable duration has (or probably will be) attempted with other simulation techniques such as immersion, parabolic flight, etc. A better solution is to expose animals to long term weightlessness under rigidly controlled experimental conditions. This would yield maximum data with less problems of interpretation than those available from astronauts involved in multi-purpose missions. The possibility that the Space Shuttle - Spacelab concept could be enlarged to include flights of greater duration is intriguing. It is hoped that such a possibility will be seriously considered.

Aside from the general need for more research involving a longer time space, there is still considerably more basic research needed to better understand the processes inherent in the different systems of the body and how they are affected by weightlessness. The vestibular system is a good example of this. We need to

determine how the physical symptoms of space motion sickness are actually produced by sensory conflict. Ground-based studies can certainly be of use here. As a possible countermeasure to the problem, autogenic training and biofeedback deserve a closer look. Past work provided some promising results, however many important questions remain to be addressed. While biofeedback is useful in learning to control central mechanisms related to space motion sickness, how efficiently can it be used? Can crewmembers be given a few, intensive training sessions or will its use require briefer sessions scheduled across a longer time period? How well is the learned response control retained? Given the potentially hectic training schedules of crewmembers, can the requisite training be given many months before the flight and still be useful during the mission? If not, how soon before the mission does the training need to be given? Also, how effective can the procedure be expected to be? What are the limits of biofeedback; how many systems can be conditioned; how many simultaneously? While the initial results of this work demonstrate a reduction in the severity of the symptoms and the time of onset, can biofeedback be used to actually prevent symptoms altogether? These are all questions that require further research. It is suggested that biofeedback and autogenic training be given more attention than previously demonstrated.

The importance of exercise to physiological maintenance is a topic that needs further resolution. What should be the nature of pre- and in-flight conditioning regimes and how should they be integrated? The evidence at present indicates there may be a disadvantage to using highly pre-trained athletic individuals in

spaceflight because of the greater severity of problems associated with deconditioning. Also, controversy remains regarding the usefulness of in-flight exercise for systems other than the muscles. It is important to assess more closely the generalized benefits of the exercise regime so as to maximize its effectiveness within the appropriate systems. This is still an open issue. Until more research can be conducted to clarify this question, it probably remains safer to stress physical conditioning appropriate to the non-athletic individual both pre- and in-flight.

The effects of radiation during spaceflight is another topic that needs further clarification. While no significant detrimental effects have yet been demonstrated in human subjects exposed to short duration missions, radiation may well prove a crucial issue when flight lengths are increased. Determining appropriate maximum allowable dosages for flights of varying durations needs more clarification than now available. The use of plant and animal studies seems to be an appropriate means of researching this topic. It is hoped that continued efforts will be directed toward understanding the effects of different types and quantities of radiation as they relate to manned space flight.

One important expansion needed in almost all physiological considerations is how weightlessness affects various types of individuals. As missions expand to include both men and women of all ages, it is important to consider how these basic factors may interact with space weightlessness. Certainly as regards the very young, adverse effects may be expected to be more dramatic because of the vulnerability of the maturing systems. Stress placed upon

an organism not yet fully developed can be expected to produce more severe consequences than when applied to the adult. It would be useful to expand our in-flight animal studies to include young and maturing members of the species. Also, we should begin more fully detailing any differential effects between sexes. Given that with one exception, women have never flown in space, it is evident that future research efforts must include assessment of both sexes. Since mixed crews are planned for the Space Shuttle - Spacelab flights, the need for this consideration is real and immediate.

Although it is unclear at present exactly which biomedical problems may be of real concern for longer duration flights, it is essential that work continue on the development of new and better countermeasures. Until we know for certain that a biomedical alteration under conditions of long duration exposure to weightlessness does not pose a hazard, it is better to regard such changes as problems to be minimized or eliminated. Many important techniques in this area need to be refined and tested under actual spaceflight conditions. It appears that our single weakest area at present is the lack of effective countermeasures to retard or reverse skeletal disuse atrophy. There is presently no known effective technique for reversing the decalcification process or its attendant complications. While research on the possibility of stressing the bone with compensatory electrical current has demonstrated some significant results, other researchers report inconsistent or negligible effects. It is important to more fully test this new technique both with animals and humans to better determine its benefits. Certainly, new and better techniques are needed in

this area. It is hoped that research will be directed toward this problem both to assess its time course and the end point of atrophy, as well as the possibilities for reversal.

Considerable research has been devoted to cardiovascular deconditioning countermeasures, much of it successfully. The use of LBNP and g-suits has proved quite effective in reducing post-flight deconditioning anomalies. The question now is whether these methods will prove equally effective for use with substantially longer missions. The use of autogenic training and biofeedback could be brought to this area as well as that of the vestibular and other systems. Much research demonstrates that these techniques are effective in allowing subjects to monitor and regulate various functions of the cardiovascular system (i.e., heart rate, blood pressure, etc.). It seems worthwhile to examine these methods as possible countermeasures to the deconditioning symptoms produced by weightlessness. Little, if any, research has been devoted to this possibility so far.

Certainly, one countermeasure that future research must continue to explore is the use of artificial gravity systems of 1g or less. Under what conditions can artificial gravity be used and how does it positively or negatively affect the overall function of the individual? Is it possible to supplement the zero gravity experience of the mission crew with periodic exposure to artificial gravity and thereby adequately compensate those biomedical alterations produced by weightlessness? Or is it more effective in the long run to use a large scale artificial gravity system operating all the time? If artificial gravity is an effective deterrent to

biomedical alterations, what level and direction of G force is required? These are critical questions that must be addressed for future long term missions if our biomedical observations indicate that some system changes do continue unaborted beyond a reasonably safe level. Furthermore, an understanding of how the vestibular system as well as other physiological systems function under artificial gravity is needed.

Certainly, the development of nonspecific countermeasures directed toward the general amelioration of adverse consequences of space flight is of the utmost importance. As will be detailed in later chapters, the general habitability, social milieu, and overall functioning of the craft and crew will play a substantial role in the successful completion of a mission. These are all factors that play a major indirect part in determining the physiological and psychological well being of each crew member. Given that little direct research in this area has been conducted, it is certainly a wide open, broad field requiring considerably more attention.

In closing it is perhaps useful to consider the many advantages which weightlessness may someday provide to mankind. While we are currently battling with all of the disadvantages of zero gravity, a note of optimism should be welcomed. The lack of gravity in space may eventually be beneficial to cardiac patients. The decreased demand placed on the heart and musculature may be quite useful to those patients weakened by age or illness. Null gravity may eventually serve a similar purpose in the care and treatment of burn victims by reducing pressure at the site of injury. A space

environment would also be an ideal situation for the muscularly disabled individual. Mobility would no longer be dependent on artificial measures and the individual no longer committed to a wheel chair or prosthetic devices.

While all these and other possibilities spark the mind and offer support for our ventures into space, we must first deal with those aspects of this alien environment which pose a danger. The greatest of these dangers at present seems to revolve around how long the individual remains in space.

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