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STATUS OF U.S. RESEARCH IN
COUNTERMEASURES AGAINST UNDESIRABLE
EFFECTS OF WEIGHTLESSNESS

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* PLEASE NOTE: This paper contains unpublished data.

It seems clear that the advancement of manned space flight will entail progressively longer duration flights, fuller and more demanding task schedules, and more varied onboard personnel to eventually include ancillary crew and passengers as well as pilots. As we move into this era of growth, it will be increasingly important for us to have available a set of techniques, ideally simple ones, by means of which the untoward effects of space flight on man can be effectively prevented or corrected. Our success in developing such countermeasures will play a large role in determining permissible flight durations, magnitude and complexity of task accomplishment, and the extent to which medical selection criteria can be safely relaxed to provide a more varied and specialized crew complement with broader capability.

Over the past several years, much research has been accomplished by the US and the USSR to identify and evaluate effective techniques and regimens. To date in the US program, we have been observing space flight effects to determine their magnitude and whether there is a necessity for a countermeasure against any particular system response. While minimal exercise regimens, dietary regulation of electrolytes and antinotion sickness drugs have been used on occasion in our flight crews, the flight durations thus far encountered (through 14 days) have not elicited a requirement for constant use of any countermeasures. However, the advent of Skylab, which in this present calendar year will attempt

to quadruple our own maximum crew stay time experience from 14 to 56 days and more than double the USSR's Salyut maximum duration of 24 days, establishes the requirement for us to examine the present status of our knowledge of potential countermeasures.

Over a decade of manned space flight experience and an even longer period of ground-based research involving simulated weightlessness by bed rest and water immersion have established that among the most consistent and important effects of weightlessness are a reduction of circulatory responsiveness to gravity in the Z axis, and a more gradual atrophic response of the musculoskeletal system. These effects have been identified by a variety of studies and indices which include reduction of tolerance to tilt table stress, LBNP, passive standing and g_z (ground-based studies), decreased exercise tolerance, occurrence of cardiac arrhythmias, decreased bone density, and negative mineral and nitrogen balance during weightlessness or its simulation.

Additional findings have shed some light on possible controlling mechanisms of these manifestations. These can be generally identified as body fluid compartment and electrolyte shifts, hormonal changes involving ADH, aldosterone, renin, angiotensin and catecholamines, and body mass and volume decreases which appear to be primarily relatable to fluid losses. They have led to the currently prevailing concept that at least a significant part of the alteration of orthostatic response after weightlessness is due to body fluid losses and fluid compartment shifts. The

changes which occur are thought to be initiated by a more uniform distribution of circulating blood throughout the body after release of the blood sequestered in the lower portions of the body by the hydrostatic pressure imposed by gravity. The resultant relative increase in the volume of circulating blood in the upper portions of the body causes an increased venous return to the heart, triggering a regulatory response through vagus auricular sensors (Gauer Henry Reflex). ADH and aldosterone outputs are decreased, renal tubular resorption decreased, urinary output increased and circulating fluid volume decreased until a new homeostatic level is achieved.

Specific findings relatable to the development of circulatory changes in weightlessness or its simulation (orthostatism) include negative water, sodium, and potassium balances, decreased plasma volume, decreased intracellular fluid, decreased ADH, decreased aldosterone (not confirmed), increased renin levels, increased ACTH, decreased cortisol, unchanged 17 hydroxy-corticosteroid output (reports vary), variable or unchanged catecholamines, and decreased norepinephrine. Cardiovascular measurements during 0g simulation have shown a decreased stroke volume, increased resting heart rate, unchanged cardiac output and cardiac index, decreased systolic and pulse pressures, decreased peripheral resistance and decreased pulmonary resistance.

Musculoskeletal changes due to 0g and 0g simulation are reflected in

the consistent occurrence of increased urinary outputs of calcium, phosphorous and hydroxyproline; negative calcium, phosphorus and nitrogen balance; decreased bone density as measured by photon absorption and x-ray techniques; and a decrease of muscular endurance, size and strength. Findings having broader implications than these two problem areas, alone, include increased triiodothyronine (T_3), unchanged thyroxine (T_4), and unchanged growth hormone levels.

These circulatory and musculoskeletal effects are particularly important because of the consistency with which they occur, because of the fact that their severity appears to be a function of duration of exposure to weightlessness, and because they are key elements of the functional integrity and safety of man not only during flight, but during re-entry and post flight as well. Although this paper will be directed to countermeasures in these two areas, no attempt to diminish the importance of countermeasures in other areas is any way intended or implied. On the contrary, it continues to be most important for us to develop similar techniques to counteract equilibrium dysfunction, sleep disturbances, circadian dysrhythmias, sensations of heaviness, disturbances of gait, and changes which we feel may be anticipated but have not yet been encountered or identified in association with space flight.

It should also be pointed out that while countermeasures research entails a large amount of study oriented to the body systems, problem definition and

countermeasure evaluation must be done on the basis of response of the integrated human (or animal) organism. It is for this reason that the term "circulatory effects" is used here to denote altered responsiveness to gz, recognizing that this response is attributable to neuroendocrine, renal and cardiovascular changes attended by significant fluid and electrolyte shifts.

Candidate countermeasures can be described as consisting of two categories: 1) those which prevent untoward effects by a form of pre-stress training and 2) those which support the deficient function artificially through the stressful period until readaptation to a satisfactory level takes place. For convenience, they will be referred to here as preventive and supportive, respectively. These terms are applied in the physiological sense since they are both preventive of symptoms. An example of a preventive countermeasure is lower body negative pressure (LBNP) which, by more or less simulating gravity, in effect trains the body to respond to gravity. A supportive countermeasure is, in essence, a form of physiological crutch, the anti-gravity suit (anti-g suit), for example, which supports the physiologically deficient system through re-entry g's and, if necessary, through the readaptive period after return to 1g. The distinction is important because the techniques are opposites with respect to both circulatory and musculoskeletal changes. Preventive techniques apply gentle stress, whereas supportive techniques alleviate it. As an example, negative pressure directs the circulation downward in the case of LBNP, upward in the case of the anti-g suit.

COUNTERMEASURES

CANDIDATE TECHNIQUES (IN ORDER OF DISCUSSION)

1. LOWER BODY NEGATIVE PRESSURE (CIRC.; POSSIBLE M-Sk.)*
2. EXERCISE (CIRC. AND M-Sk.)
3. MEDICATIONS AND DIETARY CONTROL (CIRC. AND M-Sk.)
 - A. CIRCULATORY
 1. BY INCREASING CIRCULATING BLOOD VOLUME
HYDRATION; ELECTROLYTES; STEROIDS
 2. CARDIOVASCULAR STIMULATION
SYMPATHOMIMETIC AMINES; PITUITARY HORMONES; CAFFEINE;
STRYCHNINE; STIMULANT-TRANQUILIZER COMBINATIONS;
(K SUPPLEMENTS vs. CARDIAC ARRHYTHMIAS)
 - B. MUSCULOSKELETAL
 1. DIETARY SUPPLEMENTS
CALCIUM; PHOSPHORUS; PROTEIN; VITAMINS; AND COMBINA-
TIONS THEREOF - NOTABLY COMBINED CALCIUM AND
PHOSPHORUS SUPPLEMENTS
 2. HORMONES
CALCITONIN; ANABOLIC STEROIDS
 3. MINERAL BINDING SUBSTANCES
FLUORIDES
4. BONE STRESS (M-Sk.)
5. ANTI-G SUIT (CIRC.)
6. COMBINED THERAPY (CIRC. AND M-Sk.)
7. GRADIENT POSITIVE PRESSURE (CIRC.)
8. VENOUS OCCLUSION CUFFS (CIRC.)
9. DOUBLE TRAMPOLINE (CIRC. AND M-Sk.)
10. VALSALVA MANEUVER (CIRC.)
11. POSITIVE PRESSURE BREATHING (CIRC.)

* CIRC. - CIRCULATORY
M-Sk. - MUSCULOSKELETAL

FIGURE 1

A comprehensive list of candidate countermeasures, all of which have had at least some ground-based study, is given in Figure 1. The problem area which each is thought to prevent or correct is indicated. Two techniques have been omitted, the use of an onboard centrifuge, and spacecraft rotation for artificial g. The onboard centrifuge, because of its complexity, cost and propensity to cause vestibular symptoms without offering evidence of greater effectiveness than other methods, has been abandoned. Spacecraft rotation, besides its significant impact on engineering complexity, cost, flight operations and vestibular function, is in reality not a countermeasure at all. It is, instead, an Earth gravity substitute which truly successful research in countermeasures will render unnecessary.

A year ago, a summary of available literature on countermeasures research was prepared and the relative effectiveness of each listed technique was given for each study cited.⁽³²⁾ This document has not yet been published, but was given to the USSR Working Group at the May 1972 meeting. An update is currently in progress and should be available in April of this year. The discussion following will include new and previously unpublished US research in attempting to evaluate the weight of current evidence concerning the relative merits of each candidate listed.

LOWER BODY NEGATIVE PRESSURE

Lower body negative pressure (LBNP) has been studied by several

investigators over the past eight years.⁽³²⁾ More recent reports from the USSR^(9, 10) and two very recently completed, but as yet unreported, US studies by Hyatt⁽²⁰⁾ and Hulley⁽¹⁷⁾ have supplemented our knowledge of this promising technique. The effectiveness of LBNP in ameliorating orthostatic circulatory changes is uniformly reported very favorably. The chief issue remaining to be resolved is the establishment of an optimum regimen of administration. In the future, our attack on this problem might be aided to a great extent by the use of indicators such as the circulatory index described by Suvarov and Beleda,⁽²⁹⁾ and the index of resistance to skeletal change worked out by Hulley, et. al.⁽¹⁶⁾

Hyatt⁽²²⁾ in a just completed study evaluated LBNP as a circulatory countermeasure in three subjects exposed to 28 days of bed rest. His regimen consisted of the application of LBNP four hours each day of the last seven days of bed rest at a sustained level of -30 mm Hg. In all three subjects, plasma volumes and extracellular fluid volumes were decreased just prior to LBNP (on the 21st day of bed rest) and were restored to pre-bed rest levels at the end of the 28-day period. All test subjects showed no degradation of orthostatic response, using LBNP as a test, after the 28 days of bed rest. Of additional interest in this study is the fact that a second control group of three bed rested subjects on whom LBNP tests (using the standard NASA Apollo testing technique) were performed every three to four days showed no beneficial

effect; ergo, the testing, itself, produced no beneficial effect.

Hulley⁽¹⁷⁾ is now in process of reducing the data derived from a six week bed rest experiment designed to determine what effect LBNP and other techniques might have as a countermeasure to prevent musculoskeletal changes. At this point it appears that LBNP will not prove to be particularly effective for this purpose in any of the three regimens evaluated. These were -30 mm Hg for four hours each day (1) delivered intermittently two minutes on, one minute off each day of the six week period, (2) delivered at a sustained -30 mm Hg level each day of the six week period, and, (3) given by sustained application during the fourth week, only.

Genin and Pestov^(9, 10) have recently reported the results of their use of LBNP in three subjects during a 30-day bed rest experiment. LBNP was applied for 2 1/2 to 3 hours on each of the last five days of bed rest. It was gradually administered to a sustained level of -30 to -60 mm Hg, each period of application. Plasma volumes were partially restored in two subjects. Orthostatic tolerance was maintained at pre-bed rest levels in one, improved over control levels in the second, and unchanged over control values in the third.

These same investigators also reported that the application of -25 mm Hg LBNP sustained throughout an entire 18-hour period of water immersion resulted in maintenance, and even improvement, of orthostatic tolerance. Body fluid and weight losses were minimum.

Pestov⁽²⁶⁾, et. al., reported marked effectiveness of LBNP in preserving orthostatic tolerance and fluid balance when applied to eight subjects at -24 mm Hg throughout 18 hours of water immersion. It was similarly effective in preserving orthostatic tolerance in nine subjects in a 30-day bed rest study. Here, LBNP was applied once daily during the last five days on an increasing schedule which progressed from -13 mm Hg for 10 minutes on the 26th day to -18 mm Hg for 30 minutes on the 29th day, with a free regimen on the final day which ranged from -9 to -57 mm Hg for up to 40 minutes. However, 30-day bed rest subjects treated with a diminishing schedule of LBNP throughout the 30-day period were not benefited as measured by orthostatic tolerance. This schedule began with a regimen of -27 mm Hg for 3 hours twice daily from days 1-19, and ended with an interrupted schedule of -13 to -27 mm Hg for a total of 1 1/2 hours twice daily.

Voskresenskii, et. al.⁽³³⁾ in another 30-day bed rest study reported no beneficial effect on orthostatic intolerance when LBNP was applied daily at -25 to -30 mm Hg for 3 hours twice daily during the full 30 days. On the other hand, they noted a very beneficial effect when they applied LBNP on only the last 5 days, using a regimen of -50 to -55 mm Hg for 2 1/2 hours daily. The authors conclude that daily LBNP is fatiguing and can lead to a general asthenia, but LBNP is very effective if applied only during the last five days.

The only space flight test of LBNP to date was carried out aboard Salyut.

Although a full assessment of its physiological effectiveness cannot be made, it is of interest that the cosmonauts reported that LBNP was subjectively more tolerable and pleasant in space than on the ground. It imparted the sensation of returning to Earth. (9, 10)

COMMENT: Considering the total evidence presented, LBNP appears to be the most effective single circulatory countermeasure of the preventive type presently available. At the same time, evidence seems to be emerging that it is of little value in preventing musculoskeletal effects. By a happy coincidence, it appears to be more desirable physiologically as well as operationally to begin the application of LBNP 5 to 7 days before re-entry, not earlier, although it seems reasonable to expect that the exact optimum pre-re-entry period may vary to some extent with duration of weightlessness and degree of deconditioning.

A flat or increasing daily "dosage" seems more likely to be effective than a diminishing one, but the administration of a sufficient level and duration the last day or two prior to re-entry is probably a more important factor. A sustained negative pressure of about -30 mm Hg for 2 1/2 to 4 hours for the final 5 to 7 days of a bed rest period of about 30 days appears to be effective and well tolerated. Schedules of this type and even shorter and more practical ones should be investigated for space flight with the goal of maintaining physiological effectiveness while minimizing use of crew

time. Even the application of the technique during sleep would require an observer, thus impacting the crew activity schedule.

EXERCISE

Exercise has been the subject of a great many investigations since it offers potential effectiveness in preventing both circulatory and musculoskeletal changes due to weightlessness. Unfortunately, past literature⁽³²⁾ is quite confusing, primarily because of the wide variations of types of exercise employed, kinds and durations of simulations, and measurement techniques used to determine responses. On reviewing the US literature, the general impression is gained that orthostatic changes are not favorably influenced by exercise, alone. The Russian literature of the past seems to indicate that circulatory responses are benefited to a significant degree. The complex treadmill exercise apparatus employed by the USSR investigators in the 70-day bed rest study may well be the reason for this difference. One investigator, Korobkov⁽²³⁾, reported that isometric exercise performed with Valsalva, similar to the weightlifters' technique, during a 40-day bed rest study showed promise of circulatory benefit.

On the other hand, both isotonic and isometric exercise as counter-measures have appeared to have some favorable effect, although rather widely variable, on muscle integrity, work capacity, mineral balance, and bone density. It may be fair to tentatively conclude that the degree of benefit reported has been a function of the amount of exercise and the brevity and discontinuity of the weightlessness simulation.

More recently, Greenleaf⁽¹¹⁾, one of the investigators participating in a bed rest-centrifugation study at NASA's Ames Research Center in 1971, reported the results of his use of isotonic exercise. The experiment consisted of two two-week periods of bed rest separated by a two-week recovery period, preceded by a control period, and followed by a final recovery period. The eight subjects were studied for their responses to three g levels in the z axis in a human centrifuge preceding and following each of the two bed rest periods. The gz levels were 2.1, 3.2 and 3.8, applied in random order. Isotonic leg exercises were carried out at 1/2 maximal oxygen uptake for 1/2 hour each day through two weeks of bed rest. No improvement of gz tolerance was noted.

Hulley⁽¹⁶⁾ carried out studies of three subjects during and after 24 to 30 weeks of bed rest using horizontal exercise with the exergerie as the test countermeasure. This instrument consists of a rope and pulley which has a resistance of eight pounds. It was used at the rate of one pull per second and produced an average increase of heart rate of 31 beats per minute. The subjects exercised in this fashion three times a day for a total of 80 minutes daily throughout the period of bed rest. The technique was without effect on calcium and phosphorus balance, urinary hydroxyproline output, or bone density as measuring by photon absorption (gamma ray transmission scanning). The investigator postulates that it is possible that the amount and duration of exercise might have been insufficient, but adds that no more would have been acceptable to the subjects judging from complaints received.

Very recently, a second bed rest-centrifuge study was carried out at the NASA Ames Research Center. Since the data are incompletely reduced, the results can only be given in terms of present indications. The papers issuing from this multifaceted study should be completed within the next several months. In the experiment, seven subjects underwent a two-week control period followed by three two-week bed rest periods which were separated by three-week recovery periods. The series was followed by a one-week final recovery period. As in the earlier study described above, gz responses were evaluated aboard a human centrifuge before and after each bed rest period employing the same gz levels, again in random fashion. Greenleaf, et. al.⁽¹²⁾, investigated the effectiveness of isotonic and isometric exercise as compared with no exercise in each subject, one routine during each bed rest period. Isotonic exercise was performed on a Collins ergometer at 60% maximal O₂ uptake, and isometric exercise was carried out utilizing 25% maximal extension force alternately, one minute on and one minute off. All exercise was performed in the supine position for 1/2 hour twice a day. Findings available so far seem to indicate that neither form of exercise produced a favorable effect as measured by LBNP, plasma volume, ataxia tests, or fibrinolytic response. Diminished tolerance to gz after bed rest was not significantly altered by either isometric or isotonic exercise. Hand grip endurance appeared to be favorably affected by isotonic and slightly less by isometric exercise. Maximal oxygen uptake values suggest a moderate attenuation of the usual post-bed rest decreases by both forms of exercise.

Lancaster, et. al.⁽²⁵⁾, in a report of their eight subject five-week bed rest study indicate that exercise employing a total body ergometer 20 minutes three times a day at a level of 600 KCAL per day resulted in little protection from changes in LBNP tolerance, but good protection from decreased exercise tolerance.

van Beaumont, et. al.⁽³¹⁾, found that ergometer exercise 30 minutes a day during an eight subject, 21-day bed rest study effectively alleviated reductions of plasma protein and albumin levels, and moderately diminished plasma volume losses. Exercise was carried out at 50% maximal O₂ uptake.

Genin and Pestov^(9, 10) reported protection against loss of equilibrium and muscle coordination, and evidence of a level of protection against neuromuscular, orthostatic, bone, metabolic, autonomic, and physical performance changes in 70-day bed rest studies utilizing exercise. It may be significant that in addition to the bicycle ergometer and expanders, this exercise employed the use of a special "complex trainer," which is a motor driven vertical treadmill to which the horizontally supported subject is pressed by a shock absorber system with a force of 50 KG. The quantity of the exercise load was not given.

COMMENT: The usefulness of exercise as a countermeasure seems now to be even more clearly dependent on the kind of exercise used. This, in turn, has a bearing on the amount of exercise an individual can comfortably perform.

One might anticipate that appropriate exercise will be of appreciable value in maintaining work tolerance and post-flight coordination and stability. The muscles used will clearly be aided in maintaining their strength and endurance. USSR reports have stated that circulatory responses may be benefited to some extent, US reports have not confirmed this and results may depend on the kind of exercise employed. One might conclude that skeletal integrity is apparently affected to only a small degree at best, at least for the simulation durations studied. Review of the bulk of the literature on the subject suggests that exercise of the whole body appears to be more effective than bicycle ergometry or other more localized forms of exercise with respect to both circulatory and musculoskeletal responses. Current evidence indicates little difference between isometric and isotonic exercise, but where both of these were studied comparatively, exercise levels may have been too low. Isotonic exercise may be preferable to isometric, however, in that it may be capable of providing greater degrees of activity in a manner which is acceptable to the subjects, by involving more of the body musculature simultaneously.

With respect to future studies of exercise as a countermeasure, the accumulated evidence to date suggests that such research might proceed most profitably by emphasizing tests of whole body techniques at high, but comfortable, activity levels. Once the physiological benefits are better established, experiments to define optimal regimens can proceed on a firmer basis. Such efforts

would be considerably enhanced by a better standardization of durations of bed rest and evaluative measurement techniques, which would lead to the derivation of earlier and sounder conclusions.

MEDICATIONS AND DIETARY CONTROL

Medications and dietary control have been studied fairly extensively as countermeasures. An attempt to categorize the approaches employed appears in Figure 1. Past work in this very broad area has been directed at the prevention and therapy of a wide range of potential effects of space flight. With respect to circulatory responses, countermeasure strategies in this general category have included (1) augmentation of circulating blood volume, primarily by hydration, electrolyte replacement, and steroids; and (2) pharmaceutical stimulation of the cardiovascular system, i.e., evaluation of peripheral resistance, cardiac output, venous return, general central nervous system activity, and combinations thereof using such medications as the sympathomimetic amines, pituitary hormones, caffeine, strychnine, and combinations of stimulants and tranquilizers. One might add to this the specific use of potassium dietary supplements to prevent cardiac arrhythmias as carried out on Apollo 16 and 17⁽²⁾.

Musculoskeletal countermeasures have included (1) dietary supplements with calcium, phosphorus, dietary protein, and vitamins; (2) endocrine substances such as calcitonin and anabolic steroids; and (3) specific medications such as mineral binding pharmaceuticals.

Recently Hyatt⁽²¹⁾, added to his earlier investigations of the potential usefulness of 9-alpha-fluorohydrocortisone as a circulatory countermeasure. In a series of 28 day bed rest studies involving a total of seven test and six control subjects, three dosage schedules were employed; 0.2 mgm twice daily for the entire 28 days; 0.5 mgm twice daily during only the last seven days of bed rest; and 1.0 mgm twice daily during only the last two days of bed rest. The resultant data indicate that the medication can restore plasma volumes to pre-bed rest levels as measured by RHISA¹²⁵, but that it invariably produced hypokalemia unless massive doses of potassium supplements were given. Furthermore, these hypokalemic subjects always developed syncope in response to post-bed rest tilt or LBNP despite their normal plasma volumes.

Another study carried out by Hyatt, et. al.⁽¹⁹⁾, resulted in interesting related findings, although it was not, per se, a countermeasure experiment. After the observations of inflight cardiac arrhythmias and post-flight depletions of body potassium (measurements of exchangeable potassium using ⁴²K) in Apollo 15, this team of investigators undertook to determine the effects of low potassium intake. Two test subjects were placed on a diet restricted to 15 meq of potassium per day during a 12-day bed rest simulation of the flight. Body potassium losses of 3.3% and 6.5% (measured by balance techniques) and 14.5% and 10.5% (measured by ⁴²K) resulted in the two subjects by the end of the test period. Of particular interest, hypokalemia did not develop, cardiac arrhythmias

were not observed, and post-test tilt and exercise responses were not different from control post-bed rest values.

During the first Ames Research Center bed rest-centrifugation study referred to earlier, Greenleaf, et. al.⁽¹¹⁾, studied the effects of rehydration on gz tolerance. They administered 1.0 to 1.9 liters of a slightly hypertonic drink (saline grapefruit) to some of the subjects on the last day of the second bed rest period, prior to centrifugation. The resultant data led them to conclude that the rehydration provided in this manner slightly improved +gz tolerance to 2.1 g but not to 3.2 g or 3.8 g.

In the musculoskeletal area, Hulley, et. al.⁽¹⁴⁾, experimented with the effects of dietary phosphorus supplementation in five subjects placed at bed rest for 24 to 30 weeks. The supplement added 1.3 Gm of elemental phosphorus per day to the daily dietary intake of 1.6 Gm elemental phosphorus, and 1.0 Gm elemental calcium. During the 12-week periods of administration, the hypercalcuria of bed rest was entirely prevented and a positive phosphorus balance was produced. However, calcium balance was only slightly less negative than control values owing to increased fecal calcium. Bone density losses, measured by gamma ray transmission, were unaffected by the supplement. Magnesium excretion responses were similar to those of calcium excretion. : •

Hulley, et. al.^(15, 16), and Hantmann, et. al.⁽¹³⁾, also studied the skeletal protection afforded by simultaneous calcium and phosphorus supplementation.

Five of six healthy subjects studied during 19 weeks of bed rest, on a strictly stable diet providing 1.0 Gm calcium and 1.7 Gm phosphorus per day, were given additional dietary mineral to provide a total daily calcium intake of 1.8 or 2.3 Gm, and a total daily phosphorus intake of 3.0 Gm. This mineral supplementation with calcium lactate and K_2HPO_4 , respectively, was administered during either the first or the last eight weeks of the bed rest period. The results showed a very promising response. Calcium balance became significantly less negative and urinary excretion of calcium and hydroxyproline returned to pre-bed rest levels. Os calcis density determinations were less clear. Three of the five individuals showed essentially no decrease in bone densities during the eight weeks of treatment. The other two received this regimen during the last eight weeks of the total bed rest period, possibly reflecting the antecedent mineral losses. This is not difficult to understand considering the long delay with which bone density changes seem to follow changes in calcium balance.

In the same study, Hulley, et. al.^(15, 16), and Hantmann, et. al.⁽¹³⁾, investigated the possible salutary effects of calcitonin on bone resorption by administering 100 MRC units of synthetic salmon calcitonin subcutaneously each morning to two of the six subjects through the first eight weeks of their 19 week bed rest periods. It did not alter the negative mineral balance response to bed rest or decrease the elevated urinary calcium and hydroxyproline excretions.

Because of the promising effects of calcium and phosphorus supplements in preventing skeletal mineral loss, Hulley, et. al.⁽¹⁸⁾, repeated the study in five subjects maintained at bed rest for seventeen weeks. Three were test subjects and two were untreated controls. Using the same regimen to produce a total daily intake of 2.2 Gm calcium and 3.0 Gm phosphorus, the investigators extended the treatment period to the full 17 weeks of bed rest. This resulted in complete prevention of negative calcium and phosphorus balance during the first 12 weeks, after which there was an apparent escape from this protective effect. Os calcis densities were preserved in two of the three test subjects.

Genin and Pestov^(9, 10) found that pharmacological stimulants, referring specifically to caffeine, tea, strychnine, and phenamine, given throughout the period of 0g simulation and one hour before LBNP testing were ineffective in altering measured physiologic responses, but did seem to prevent syncope.

In a 120-day bed rest study of six test subjects and four controls Krupina⁽²⁴⁾, Petukhov⁽²⁷⁾, and Yakovleva⁽³⁴⁾ reported that nerobol (an anabolic steroid) given daily affected fluid and electrolyte balance and protein metabolism very favorably, but had no effect on electromyograms of the musculature of the lower leg, or on intranasal circulation. Pituitrin given on an interrupted schedule throughout bed rest, and DOCA given on days 72 to 90 had no effect on any of these measurements with the exception of a moderately favorable influence on the EMG.

COMMENT: Ground-based research studies so far generally present no convincing evidence of a medication or dietary regimen which offers promise as a preventive countermeasure against circulatory disturbances due to weightlessness. On the other hand, it is suggested that cardiovascular stimulants carefully administered, especially the sympathomimetic amines should prove to be of value as supportive countermeasures, i.e., if administered to achieve peak activity during re-entry or other periods of circulatory stress. The indications for CNS stimulants would be expected to be approximately the same in space flight as on Earth.

The failure of the cortisone derivative, 9-alpha-fluorohydrocortisone, to alleviate diminished orthostatic resistance despite its effectiveness in maintaining plasma volume is both interesting and, in the opinion of the author, fortunate. It is interesting because it adds further evidence that factors other than decreased circulating blood volume are also importantly involved in the etiology of the characteristic orthostatic response, confirming Gemini 7 and later flight findings. Furthermore, the results of these studies suggest that hypokalemia can also play a role in reducing orthostatic tolerance. This tends to be supported by Apollo 15 findings which showed that the two astronauts in whom post-flight circulatory changes were more marked, while not actually hypokalemic, did exhibit post-flight serum potassium values at the bottom edge of normal (3.6 meq) as compared with the third crew member whose post-flight level was 3.9 meq. Pre-flight values

for all three were 4.3 to 4.5 meq (normal range 3.6 to 5.0 meq). Finally, it is interesting because this cortisone derivative, which is considered to influence electrolyte balance less than others, produced hypokalemia so rapidly and at such low dosages under bed rest conditions.

The failure of 9- α -fluorohydrocortisone is deemed fortunate because the cortisone derivatives with all of their adverse potential, viz., osteoporosis, hyperglycemia, euphoria, decreased resistance to infection, peptic ulcer, etc., can now be more emphatically removed from further consideration as a counter-measure.

Hyatt's study of low potassium intake offers evidence that hypokalemia is not easily produced by dietary restriction despite depletion of whole body potassium. Yet, hypokalemia is produced easily by steroids. These studies also suggest that orthostatic tolerance is not inclined to be affected adversely by reduction of whole body potassium, whereas, according to his steroid studies, it is affected adversely by hypokalemia. This could be explained by the hypothesis that hypokalemia does not develop until depletions of whole body potassium become more severe.

The marked effectiveness of dietary calcium and phosphate supplements in protecting skeletal integrity is a very important finding, and one which clearly warrants further study. This technique offers the great additional advantages of acceptability, safety, and ease of administration in flight.

According to the reports of USSR investigators, the anabolic steroid, nerobol, appears to be sufficiently promising to warrant further study. However, the medication is not known in the US, and no further comment can be made here without much more knowledge of its pharmacological action, safety, and side effects.

Past research employing other dietary approaches seem to indicate that a high protein intake offers no special advantages as measured by nitrogen balance studies.⁽³²⁾ One study by Udalov, et. al.⁽³⁰⁾, reports that a vitamin enhanced diet low in protein effectively maintained nitrogen balance in bed rested human subjects, suggesting that vitamin enrichment may be predominantly important. Some corroborative study may be useful.

Future research to determine the relative benefits of both established and new medications as countermeasures must continue to investigate side effects as thoroughly as favorable ones for the regimens employed. Although a similar comment can be made with respect to any proposed technique, this point is considered to be particularly important when dealing with pharmaceuticals.

BONE STRESS

Bone stress in the form of regularly applied g simulating forces to the skeletal structure to prevent bone changes has been investigated further in more recent studies.

Hulley, et. al. (15, 16, 17), and Hantmann, et. al. (13), conducted an evaluation of passively applied longitudinal skeletal stresses equal to 80% body weight to three of the six subjects in the 19-week bed rest study referred to earlier in which calcium and phosphorus supplements and calcitonin were also investigated. Skeletal compression was passively applied during the first or last eight weeks of the total bed rest period by means of a gravity acceleration simulation suit (GASS), a development of Dr. James D. Gatts⁽⁸⁾ in the early to mid-1960's. As modified for this purpose, the device consisted of a harness and motor-driven springs which applied 1/3 of the total force to the shoulders and 2/3 to the waist along the Z axis of the bed rest subject, pressing him against a foot board. The force was applied at a frequency of 45 times per minute, which the subject received alternately on one foot, then the other, as if walking. The technique was administered twice daily for a total of four hours per day. The investigators reported that negative mineral balance was not substantially improved by this technique and that it proved fatiguing to the subjects. They offered the suggestions that better results might be achieved if greater active muscular involvement, and a gravity simulated hydrostatic pressure differential were also introduced. This conclusion is, in general, supported by the findings of Genin and Pestov^(9, 10) in their work with the complex trainer.

More basic studies of the roles and mechanisms of bone stress in the maintenance of bone integrity are currently being conducted in the US, but they are still at a very early stage.

COMMENT: It may be tentatively concluded that for practical purposes bone compression, alone, does not offer much skeletal protection. However, it may prove valuable in combination with other techniques, i.e., the same principal might well be profitably incorporated into an exercise routine.

THE ANTI-GRAVITY SUIT

The anti-gravity suit (anti-g suit) is, by comparison with other proposed techniques, a well-known entity, having been used in aviation for many years to protect the circulation against multiple gz forces. The term anti-g suit is used here to convey use of the same principle as protection against g forces in the Z axis, whether against multiples of G or post-flight orthostatism. As pointed out above, it is a supportive device for use during g stress rather than a preventive conditioner to be applied prior to g exposure. By means of a system of air bladders or capstans over the lower portion of the body it applies a pressure gradient to the column of blood in the opposite direction to the imposed force, i.e., in the -z direction. The elastic leotard is a variant of the same principle, applying the same kind (but not amount) of pressures by virtue of the elasticity of its material instead of air pressure.

Because its characteristics and capabilities are quite well known, the anti-g suit has not been the object of much additional study in the US.

In an informal evaluation carried out recently by NASA personnel at the Ames Research Center, aircraft pilots were exposed to 2 and 3 gz levels after

one week of bed rest with and without anti-g suits worn during centrifugation. Data are incompletely reduced at the present time, but preliminary indications are that post-bed rest heart rate responses to centrifugation were very effectively assisted by the anti-g suit. Additional work is being carried out at this Center, but these studies are not yet complete.

The effectiveness of elastic leotards over the lower half of the body in supporting the circulation in 1g post flight was evaluated in one of the Apollo 16 astronauts. While original plans called for his donning them while still in the spacecraft after splashdown, operational requirements prompted their alteration. As a result, the garment was donned on the carrier about four hours later. Despite the fact that three leg sizes were available to compensate for anticipated decreases in calf circumference, the garment was difficult to get into. Five minute passive standing tests with recording of blood pressure every 30 seconds and heart rate continuously showed some protective effect. Detailed reduction of the data and collation with blood volume data are still in progress.

In Apollo 17, another form of anti-hypotensive garment was tested on one of the crew members. This device, developed at the NASA Manned Spacecraft Center, is a pressurized garment which fits over the lower half of the body. Air pressure is delivered by means of capstans in such a way as to supply a pressure gradient which ranges from 65 mm Hg at the ankles to 10 mm Hg at the waist. The astronaut donned and pressurized the garment while still in the spacecraft

after splashdown and continued wearing it until the 5 minute passive standing test was carried out aboard the carrier three hours later. This test was repeated with the suit deflated immediately afterward. Conclusions are uncertain at this time since the resultant data have not yet been reduced.

Recent USSR reports ^(9, 10) indicate that the anti-g suit was protective to tilt and LBNP tests, but not completely so in subjects fatigued by the daily application of LBNP during 30 days of bed rest. On the other hand, when used during orthostatic tests after LBNP conditioning on only the last five days of the bed rest period, responses were not only maintained, but improved over control responses.

COMMENT: Judging from past experience and research experiments, it seems clear that the anti-g suit can be expected to provide excellent circulatory support during gz exposure after weightlessness. There are some indications ^(9, 10), however, that under certain circumstances the support provided by this technique, alone, may be slightly less than complete. Further investigation is still required. One very useful avenue of research would be to develop predictive indices with which to prognosticate during weightlessness the relative efficacy of the anti-g suit during re-entry.

COMBINATION COUNTERMEASURES

Combinations of various countermeasures appear to show the greatest promise of all, as one would anticipate. A variety of combinations have been

studied in the past, some more favorably reported than others. It is likely that in some instances where combinations were reported as effective, one or more of the approaches of the combination may not have contributed significantly to the overall benefit.

In the 19-week, six subject study of Hulley, et. al.^(15, 16), and Hantmann, et. al.⁽¹³⁾, two test subjects received a combination of all three countermeasures which were investigated during that study; calcium and phosphorus supplements, synthetic salmon calcitonin, and longitudinal skeletal compression. As in the other tests, these subjects were treated during eight weeks of the total bed rest period, in this case the first eight weeks. A distinct skeletal benefit was obtained by using this combination, but it was no more pronounced than that derived from dietary calcium and phosphorus supplementation, alone. A fuller comparative study may be undertaken in the future if warranted by favorable progress in experimental work with the other two individual techniques.

Genin and Pestov^(9, 10) reported that the combination of LBNP and exercise using the complex trainer was more protective against post-bed rest orthostatic intolerance than either measure alone. They further concluded from their studies that the appropriate use of LBNP (only the last several days of bed rest) combined with use of the anti-g suit during orthostatic testing procedures was more beneficial than either countermeasure, alone. Finally,

as a result of their entire series of studies, they recommended for Salyut a combination of LBNP, physical training using a special trainer, the medication, "secophene" before termination of O_2 , and use of the anti-g suit.

COMMENT: In attempting to assess the present state-of-the-art of combined preventive therapy for space flight, the distinction must be made between combinations directed at only one effect, such as circulatory and those directed at more than one effect, i.e., circulatory, musculoskeletal, equilibrium, etc., a distinction not always easily made. In a practical sense, it is reasonable to assume that the actual "prescription" of countermeasures for space flight will include more than one ingredient because flight personnel, i.e., the whole man, will exhibit more than one physiological change. There appears to be no reason why this should apply any less to preventing the adverse responses of space flight than it does to treating disease in clinical medicine. In both cases, the primary concern is the well being of the total person.

In addition to the recent research described above, past experiments with combined therapy to prevent circulatory changes have included combinations of venous cuffs and steroid (9-alpha), cuffs and leotard, hypoxia with isometric exercise and LBNP, and exercise in dual combination with LBNP, cuffs, hypoxia, and positive pressure breathing. For several reasons the results are difficult to evaluate.

Many of these studies were done at a time when the capabilities and characteristics of the individual techniques were less well known than they are now, and the combinations used were, from our present vantage point, less than optimal. Because of this, comparative appraisal of responses to combined vs. individual component techniques, where it was ventured at all, was estimated on the basis of a much weaker data base than we now have. Retrospectively, merits attributed to a combined treatment were often more likely to be attributable to only one, and demerits of some combinations might have been anticipated. Another factor obscuring the assessment of this research is that muscular exercise, which was utilized in most combinations, was administered in a wide variety of ways, most of which were inadequate according to present indications. Thus, our subsequent progress, which was based on these earlier studies, has been significant, and has given us the advantage of some degree of 20/20 hindsight.

Of the techniques used in these research efforts, more recent findings have led to the de-emphasis of venous occlusion cuffs, 9-alpha, hypoxia, and positive pressure breathing as candidate circulatory countermeasures. The more promising techniques remaining are LBNP, whole body exercise, and the anti-g suit (leotards can be considered a modification), the anti-g suit being a supportive technique. Of five reports of studies using LBNP and exercise in combination ^{1, 3, 7, 27, 34)}, three used whole body exercise and all of them

reported substantial benefit which was greater than either used alone. Whether the total effect was additive or synergistic is a somewhat esoteric question to the more practically oriented, but continuing research in basic physiology may shed further light on the problem. Other candidates, such as rehydration, may provide useful adjuvant treatment.

Combined countermeasures to prevent musculoskeletal changes have, in addition to the recent studies discussed above, included exercise in dual combination with LBNP, cuffs and bone stress (with 1g applied in the form of quiet standing), and in triple combination with hypoxia and LBNP. The reports of these studies have indicated, overall, either no or moderate improvement. Difficulties in interpreting these data were similar to those encountered in terms of circulatory responses. All things considered, whole body exercise appears to be the exercise of choice to provide adequate activity for effectiveness. It is suggested that techniques to add a hydrostatic pressure gradient to either bone stress, or whole body exercise, or both, may provide synergistic benefit. It is conceivable that all three principles might be combined effectively into a single set of exercise routines. Calcium and phosphorus supplementation combined with any or all of these principles would appear to offer the greatest skeletal protection, since it emerges as by far the most promising single skeletal countermeasure so far reported.

From the practical standpoint, all current evidence favors the inclusion of

appropriately administered whole body exercise aboard extended duration manned space flights because of benefit to both circulatory and musculoskeletal responses, and enhancement of a feeling of well being. Future research must continue to evaluate combinations of the most promising single countermeasures, both known and as yet unknown. To be most productive, such research should include quantitative comparative assessments of the relative values of the techniques used in combination vs. singly, and must be cognizant of possible antagonisms and side effects.

OTHER MEASURES

Other candidate countermeasures will be discussed only briefly since little or no recent information is available.

The gradient positive pressure suit (reverse gradient garment) is a suit which applies positive pressure to produce the same effect on the circulation as LBNP, i.e., opposite to the anti-g suit. Combined with positive pressure breathing, it directs a downward force on the column of blood exerting a resultant effect which is thought to more nearly reproduce the pressure gradients caused by standing in $1g^{(4)}$. Further studies of this concept are currently in progress.

Venous occlusion cuffs have not been investigated further in the US in recent years. Although past water immersion studies have demonstrated their effectiveness in maintaining orthostatic tolerance to tilt, experimental in-flight

use aboard Gemini 5 and 7 failed to show post-flight benefit. Recent USSR reports^(9, 10) similarly indicate that the effectiveness of the cuffs during 18 hours of water immersion could not be duplicated in 30-day bed rest subjects. These findings, the fact that the technique is excessively cumbersome for space flight, and the availability of better methods have led to its de-emphasis in the US.

The double trampoline device is a concept proposed in 1964 to study on Earth the effects of exercising in weightlessness in such a way as to produce short hydrostatic pressure gradients in alternate directions on the column of blood.^(5, 6) In space, such exercise would not necessarily call for two opposing trampolines, but only reproduction of the up and down jumping motion by any means. From the description of the USSR's "complex trainer"^(9, 10, 28) this device might permit such motions. No further evaluation of this concept has yet been undertaken in the US, although it is tentatively planned.

Finally, Valsalva routines, and positive pressure breathing, per se, have not been pursued any further because earlier studies failed to show promise of potential value.

SUMMARY AND CONCLUSIONS

An attempt has been made to review and assess the current status of research concerned with the development of countermeasures to prevent unfavorable cardiovascular and musculoskeletal responses in man when

exposed to extended periods of weightlessness in space. The results of recent research were given, and current status discussed in the presentation of each candidate technique. Conclusions may be summarized as follows:

1. At this point in time, the most promising single countermeasures appear to be:

Circulatory - LBNP, whole body exercise, and anti-g suit.

The anti-g suit is regarded as a supportive, rather than preventive countermeasure.

Musculoskeletal - Dietary calcium and phosphorus supplements, and whole body exercise. Exercise has been most effective in maintaining muscular integrity (muscle strength and endurance, work tolerance, etc.), but has so far shown relatively small effect on skeletal changes.

2. Although there now appears to be adequate experimental evidence that whole body exercise is more effective than others, further research into specific whole body exercise maneuvers may enhance its value. Specifically, maneuvers designed to impart a hydrostatic pressure gradient and bone stress, i.e., tumbling, jumping, may prove to be additionally beneficial to the maintenance of both circulatory and musculoskeletal (especially skeletal) integrity.

3. Research in countermeasures is of primary importance to the progress of man's ability to explore space. Both new and older concepts must continue to be evaluated by quantitative and comparative assessment. Progress can be enhanced by a better degree of standardization of simulation techniques and their durations, and of evaluative measurement techniques. The use of predictive indices, such as venous compliance, and those described by Hulley, et. al.⁽¹⁶⁾ with respect to skeletal changes, and Suvorov and Beleda⁽²⁹⁾ with respect to circulatory changes, may also add quantitative accuracy as well as insight to these studies.

4. Combined techniques not only appear to be most effective for protection against each of these two problem areas, but also are most likely to be flown because no single countermeasure except gravity, itself, is likely to be optimally effective against both circulatory and musculoskeletal changes. Investigations of combinations of techniques must include comparative evaluations of the combined vs. the individual countermeasures, and must carefully examine possibilities of antagonisms and side effects.

5. In a practical sense, techniques will be recommended for flight not only on the basis of effectiveness, but also on the basis of safety, relative

non-interference with crew activities, and minimal requirement for special procedures and personnel, in addition to the usual array of optimal hardware considerations (reliability, accuracy, stowability, interface compatibility, weight, volume, power, etc.). The selection of candidate countermeasures for research must continue to be tempered to these ultimate requirements.

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March 16, 1973

Dr. Sherman P. Vinograd
Associate Master Director, Bio-Research
NASA Headquarters
Code MMR
Washington, D.C. 20546

Dear Sherm,

Thanks so much for the copy of your review of countermeasures. I found it well written, informative, and accurate. This synthesis of available information with critical commentary and in compact form is exactly what is needed to improve communication in the scientific community in general and within NASA in particular -- I only hope they read it!

My comments are few and relatively trivial:

Page 12, paragraph 2: Although the overall bed rest period was 24-30 weeks, they were only on exercise for 12. It might be better to use this figure in the text.

Page 18 or page 22: Hypercalciuria precipitated by renal calculus formation is a hazard during bed rest (Ann. Surg. 129:177, 1949) and a potential complication of space flight -- I predict we may learn this the hard way some day. I believe it is worth commenting on this fact on one of these pages, and on the fact that phosphate removed the hazard, not only by reducing urinary calcium but also through other mechanisms (Amer. J. Med. 45:693, 1968).

Page 22, paragraph 2: The complications attributed to cortisone derivatives are only seen when pharmacological quantities of glucocorticoids are given. Use of 0.1 to 0.2 of 9 α fluorohydrocortisone, ^{an} essentially pure mineralocorticoid, would in my opinion not have any of these potential hazards.

Dr. Vinograd
Page 2

March 16, 1973

Page 38, reference 13: Delete "Accepted for Publication."
Insert "J. Clin. Endocr. Metab., in Press (May 1973)."

Page 38: I suggest you delete reference 17, referring
to 18 for all unpublished statements in the text. You
might wish to include the following as reference 17:
Special Symposium Volume, Clinical Aspects of Metabolic
Bone Disease, Henry Ford Hospital, Detroit, June 25-29,
1972, (Excerpta Medica (in Press)).

This contains much the same material as the Vienna talk,
but it has the advantage that it will be in print this
spring. All reference in the text to 16 could be to 17
in addition.

I have no objection to your publishing our material in this review
article format. In fact, I wish you speedy success in such an
endeavor.

With best personal regards.

Sincerely,

Steve

Stephen B. Hulley, M.D.
Director, Metabolic Unit

®

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17 September 1962

*A TECHNICAL PROPOSAL OF THE
BIOSCIENCES OPERATION*

**CONCEPT DEVELOPMENT OF
A PROGRAM FOR**

**COUNTERMEASURES
FOR THE EFFECTS
OF PROLONGED
WEIGHTLESSNESS**

GENERAL  ELECTRIC

MISSILE AND SPACE DIVISION
VALLEY FORGE SPACE TECHNOLOGY CENTER
P.O. BOX 8555, PHILA. 1, PA.

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I SUMMARY

The Missile and Space Division of the General Electric Company proposes a twelve month program directed at the initial development of an appropriate countermeasures program which may be subject to detailed orbital testing prior to lunar orbit landing attempt.

The principal investigator for the program will be Richard W. Lawton, M.D.

II INTRODUCTION

The study of the physiological effects of prolonged weightlessness--indeed, any scientific study of man in space--must take into account the vehicle capabilities, the mission constraints, the operational circumstances surrounding the mission and the requirement for repetitive measurements as a function of time, as well as the necessity for measurements on a number of subjects because of the large range of individual differences likely to be encountered among even the most highly-selected astronauts. An effective program of study must be woven within and among these variables, must be adaptable to alterations in flight schedules and must profit by experience as it is gained. On the basis of projected NASA vehicle programs, the following sequential development of the experimental study of weightlessness seems likely:

A. MERCURY (< 24 HOURS)

A major element in the initial Mercury flights will be the appearance of physiological derangements related to stress. A principle task will be to separate and characterize these stress effects (as exhibited by the cardiovascular and perhaps the gastrointestinal system). Under the operational constraints of limited space and limited fuel, simple exploratory tests will attempt to highlight labyrinthine effects. Head motions, during various modes of vehicle stability and instability, and coordination, as measured by task performance, will be evaluated.

With the passage of time, stress effects may be expected to wane somewhat. Particularly, multiple exposures of the same astronaut would result in a clearer picture of the physiological status relevant to zero G. The advent of a 24-hour flight will permit the initiation of studies directed toward the characterization of sleep states under weightlessness.

B. GEMINI (TWO DAYS)

Beginning with the Gemini flights, clear evidence of weightlessness effects may be obtained. The adequate fuel stores (for rendezvous maneuvers) may permit quantitative labyrinthine threshold measurements. Sleep studies may be extended to include diurnal

considerations. A special disarticulating space suit will permit timely blood and urine sampling in orbit. The presence of additional space will permit observations of man-on-man or man-on-animals. The development of a special tape recorder will permit the separation of the biological experimental instrumentation from the vehicle monitoring system. Experimental studies should be extended to include the evaluation of some aspects of the cardiovascular system and the investigation of the effects of simple exercise and other supportive regimens.

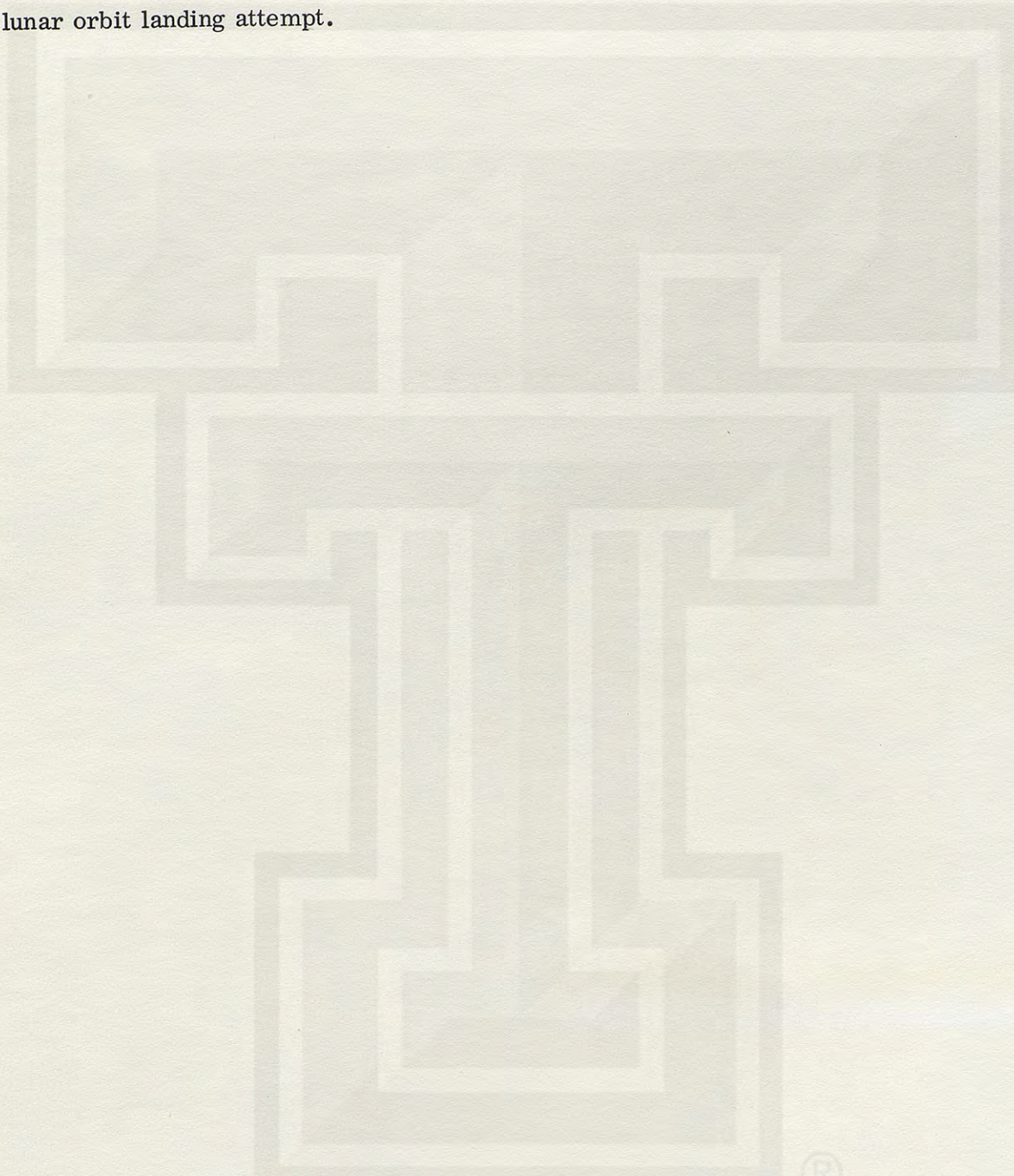
C. GEMINI AND APOLLO (ORBITAL: 7-14 DAYS)

The long-term effects of weightlessness, if they are to appear, should be evident for flights lasting one to two weeks. Because of the nature and urgency of the lunar program, it is likely that a regimen of countermeasures will be developed and pursued vigorously during this period. Although experience will still be largely derived from ground-based laboratory studies, it is likely that such a regimen will successfully prevent the appearance of important zero-g effects. Operational constraints may dictate that no crew member be used as a "control." A principle guide to the efficiency of the countermeasure program will rest with an evaluation of the musculoskeletal and cardiovascular system including orbital methods as well as "before and after" measurements.

D. MANNED ORBITAL SPACE STATION

It is thus apparent that a scientific study of the effects of the space environment on man can only be pursued with a vehicle of appropriate capability, with a number of subjects, consistent with the individual differences to be expected, relieved of the operational and mission constraints of the lunar program. While a countermeasure program may be entirely successful for flights of the duration of the lunar mission, it will only be by the experimental characterization of the effects themselves that such regimens may be optimized and space flight-time extended. If initial attempts at countermeasures fail, a detailed study of the physiological effects of prolonged weightlessness must precede the lunar-landing attempt.

This proposal is directed at the initial development of such an appropriate counter-measure program which may be subjected to detailed orbital testing prior to the lunar orbit landing attempt.



III BACKGROUND

An analysis of the possible effects of prolonged weightlessness (see attached review) emphasizes the interrelation of activity and cardiovascular and musculoskeletal effects as studied at bed rest or under conditions of submersion. Relatively minor but probably highly specific types of activity may indeed totally obscure the consequences of exposure to zero g over a prolonged period. For the biologist this presents difficult problems in experimental design if physiological effects are to be measured. However, for the lunar operational mission, performance and physiological well-being may be readily assured if appropriate activity is employed.

Because of volume restrictions in both the Gemini and Apollo vehicle, consideration must be given to the specificity of such activity because generalized activity will probably not be possible. In addition, generalized exercise may result in excessive use of attitude control fuel as well as weight restrictions will prevent the utilization of extensive equipment. An optimal exercise regimen must thus be highly specific and utilize minimal and relatively simple equipment. Such a regimen should effectively support both the musculoskeletal and the cardiovascular system.

A. MUSCULOSKELETAL SYSTEM

Few analyses have been performed relevant to the kinematics of weightlessness. Baume and Kuehnegger have explored analytically kinematic implications under conditions of lunar gravity. Exercise regimens proposed do not, however, take into account vehicle constraints. In contrast to such an analytical approach, a wealth of empirical information exists in the literature of physical medicine, physiotherapy and rehabilitation which have not been tapped. A perusal of this literature may be expected to yield information on generalized versus specific exercises depends upon certain types of muscular development, a preflight training schedule may have to be established.

B. CARDIOVASCULAR SYSTEM

The nature of the factors maintaining the integrity of the cardiovascular system are relatively poorly understood. It is apparent that a major factor is activity. For instance, prolonged standing at rigid attention frequently results in fainting in soldiers. Braveline has recently pointed out that the intermittent distension of the venous system may successfully prevent postural hypotension following submersion. Equivalent elevations in venous pressure can be obtained by positive pressure breathing and thus simplify the equipment required.

In addition to supporting the peripheral vascular system during zero g, measures directed at the support of the heart itself may be required. Bed rest data suggest a diminution in heart size and an increase in pulse rate may occur with a decline in stroke volume. Extremity cuffing or positive pressure breathing must be examined with respect to the long term effects on cardiac activity as well as peripheral vascular effects. Data must be sought in the literature of physical medicine and the physiology of exercise to answer such questions.

Although some aspects of the integrity of the cardiovascular system for re-entry deceleration may be evaluated by means of tilt table tests or centrifuge exposure, further study is required to develop validity. Attempts to develop correlations between acceleration tolerance and tilt table responses as well as with a variety of other parameters have been generally disappointing.

IV PROPOSED PROGRAM

The Missile and Space Division of the General Electric Company proposes a 12 month three part study resulting in the development of recommendations for exercise procedures, exercise equipment and exercise validation methods applicable to NASA's current and future manned space flight programs. The principal investigator will be Dr. Richard W. Lawton.

A. PROCEDURES RECOMMENDATIONS

The current study of the musculoskeletal and cardiovascular effects of prolonged weightlessness will be extended including consideration of kinematics at zero g. The literature of physical medicine and the physiology of exercise will be searched for empirical approaches to the problem. A supportive regimen will be recommended which is consistent with vehicle and mission constraints as determined by the NASA.

B. EQUIPMENT RECOMMENDATIONS

On the basis of weight, space and power and as the result of the procedures recommendations, the equipment necessary for the support of such a regimen will be recommended.

C. VALIDATION RECOMMENDATION

Procedures and techniques for earth-based and orbital evaluation of the proposed supportive regimen will be recommended.

D. SCHEDULE RECOMMENDATION

The proposed twelve month program will require 1200 hours of professional labor, to be provided by Dr. Lawton and personnel of his Biosciences Operation. Outside consultants will be used as required.

V PERSONNEL (BIOGRAPHIES)

RICHARD W. LAWTON, M.D., Manager, Biosciences and Human Factors

B.A. - Dartmouth College, 1942

M.D. - Cornell Medical College, 1944

Rotating internship - Mary Hitchcock Memorial Hospital, Hanover, New Hampshire, October 1944 - July 1945.

Military Service - Lt. (j.g.) Medical Corps; U.S. Naval Hospital, San Diego, California; 1st Marine Division, China, 1945 - 1946.

From 1946 to 1948 Dr. Lawton was a Fellow in the Physiological Sciences at Dartmouth Medical School where he studied calorimetry and plethysmography of the hand, the cardiovascular and respiratory effects of ganglionic blockade in cats and began studies on the elasticity of body tissues (with Professor A. L. King, Department of Physics).

In 1948 Dr. Lawton was appointed Instructor of Physiology at Cornell University Medical College where he continued studies of human and animal calorimetry under Dr. Eugene DuBois and Dr. James D. Hardy. Under a U.S. Public Health Service grant, studies were conducted on the mechanical properties of the rat lung, the thermodynamics and static and dynamic elasticity of the aorta. He was appointed Assistant Professor in July, 1952.

Dr. Lawton became Associate Professor of Physiology at the University of Pennsylvania School of Medicine in July, 1954 and was appointed Head of the Physiology Division of the Aviation Medical Acceleration Laboratory of the Naval Air Development Center, Johnsville, Pa. where he conducted studies of human tolerance to acceleration stress, the cardiovascular effects of acceleration in experimental animals and the physiological requirements for space flight.

Dr. Lawton joined General Electric in July 1958 as Manager of Bioastronautics. He was promoted in October 1959 to Manager of Life Support Systems, supervising the Department activities in the biosciences, human factors, life support equipment and bioinstrumentation. He has played an active role in the Discoverer biomed capsule program, the USAF Space Cabin study and the Apollo study. The hardware responsibilities of his group have included the development of an environmental test chamber for chimpanzees, a food preservation unit design for space flight application, a space suit design study for extravehicular use and the construction of a remote primate brain stimulator. He supervises an active in-house applied research program encompassing studies of displays and controls for space vehicle operation, the biological effects of abnormal space vehicle environments and the effects of magnetic fields on biological subjects.

Dr. Lawton is Adjunct Associate Professor of Physiology at the University of Pennsylvania School of Medicine. He is a Consultant to the Scientific Advisory Board of the U.S. Air Force in the field of bioinstrumentation. He is a member of the Human Factors and Bioastronautics Committee of the American Rocket Society and the Committee on Industrial Health and Safety of the Aerospace Medical Association. He is a member of the Human Factors Society, the Council on Basic Sciences of the American Heart Association, the American Astronautical Association, the American Physiological Society, Sigma Xi and the Harvey Society.

Dr. Lawton is licensed to practice medicine in New Hampshire, New York and Pennsylvania.

Publications:

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Measurements on the Elasticity of the Isolated Rat Lung.	American Journal of Physiology, Vol. 167, No. 1 (2)*	1951
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With:	(1)* Allen L. King
	(2)* Doyle Joslin
	(3)* Allen L. King
	(4)* Lawrence R. Prouty and James D. Hardy
	(5)* None
	(6)* Leon C. Greene

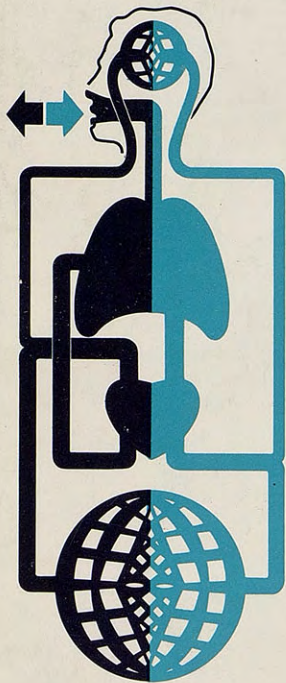
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With:

- (1)* Philip J. Dorman
- (2)* Philip J. Dorman
- (3)* Leon C. Greene, George H. Kydd
- (4)* George H. Kydd, Leon C. Greene, Richard J. Crosbie
- (5)* Leon C. Greene, George H. Kydd, Lysle Peterson, Richard J. Crosbie
- (6)* Carter C. Collins

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(2)* Allen L. King
(3)* Armand J. Gold, Harry Hance, Murray Kornhauser
(4)* Murray Kornhauser



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