SKYLAB FOLLOW-ON STUDIES

National Aeronautics and Space Administration

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TABLE OF CONTENTS

TABLE AND FIGURES

SKYLAB FOLLOW-ON ACTIVITIES

I. Skylab Medical Experiments

A. Summary of Pertinent Findings

The Skylab medical experiment results demonstrated that man could adapt and function effectively in the weightless environment of space for extended periods of time. Crew health and well-being were maintained by adequate dietary intake, programmed daily inflight personal exercise, and appropriate sleep, work and recreation periods. Table I lists those findings which require additional research to understand causative mechanisms and in some cases may require the development of remedial or preventative measures for mission durations in excess of 9-12 months.

Cephalad Body Fluid Shifts - Anthropomentric measurements made before, during, and after flight, supplemented by subjective comments (full feeling of the head, nasal and ocular congestion), photographs, and center of mass determinations documented an expected headward fluid shift. This fluid shift remained throughout flight, but was ameliorated by cycle ergometer exercise inflight, and was immediately reversible (2-3 hours upon reexposure to the one-g environment. It is possible that this observed cephalad fluid shift upon exposure to the weightless environment may be responsible for, or at least contributed to, other physiological alterations noted in the Skylab Program.

Space Motion Sickness - Under operational conditions, six of the nine crewmen experienced motion sickness. However, the administration of antimotion sickness drugs makes it difficult to determine the individual

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SKYLAB MEDICAL EXPERIMENT FINDINGS

- CEPHALAD BODY FLUID SHIFTS
- SPACE MOTION SICKNESS
- BONE AND MUSCLE ALTERATION
- CARDIOVASCULAR DECONDITIONING
- FLUID AND ELECTROLYTE CHANGES
- REDUCED RED CELL MASS AND PLASMA VOLUME

Table I

susceptibility and severity of incidents. With this in mind, it appears that the Skylab 2 crewmen did not experience clear-cut symptoms inflight and only the Scientist Pilot experienced seasickness after recovery. Among the Skylab 3 crew, the Pilot experienced motion sickness shortly after orbital insertion. The remaining Skylab 3 crewmen experienced motion sickness only after entering the workshop (1,2). In Skylab 4, both the Commander and Pilot exhibited symptoms even with doses of anti-motion sickness medication. In general, Skylab motion sickness symptoms persisted for 3 to 4 days with complete recovery by Mission Day 7.

Bone and Muscle Alterations - Moderate inflight losses of calcium, phosphorous and nitrogen were observed during the Skylab Program (3). The observed losses of nitrogen and phosphorous appear to be associated with reduction in leg muscle tissue (4). Typically, inflight urinary calcium excretion rapidly doubled its ground-based level and plateaued at levels analogous to the losses observed in bedrest (5). There was no indication of a decrease in calcium excretion toward the end of the 84-day Skylab 4 mission.

Cardiovascular Deconditioning - Provocative lower body negative pressure (LBNP) tests conducted inflight have shown that the Skylab crewmen exhibited cardiovascular deconditioning which was adaptive in nature and which tended to stablize after 4 to 6 weeks. These changes however, did not impair crew health or the ability to function effectively in the zero-g environment. Table II summarizes the incidents of presyncopal episodes observed during LBNP exposure in three Skylab missions. A total of 13 presyncopal episodes were evidenced. They generally occurred during

NASA-S-74-4498

SKYLAB 2, 3, AND 4

M092, LOWER BODY NEGATIVE PRESSURE

MISSION DAYS	NO. OF EARLY TERMINATIONS OF LBNP TESTS
4 - 14	5
15 - 28	4[a]
29 - 42	1
43 - 56	1
57 - 70	1
71 - 83	1

[a]THREE OF 4 BETWEEN DAYS 15 TO 20

Table II

tests conducted 7 hours or more after arising from sleep. No significant inflight decrement in work capacity or physiological response to both submaximal and maximal levels of exercise was observed. Postflight, however, all crewmen evidenced both orthostatic intolerance and diminished response to exercise. The etiology for both the orthostatic intolerance and reduced response to exercise appears to be related to a decreased effective circulating blood volume (postflight relative to preflight) with consequent decreased venous return and cardiac output. The Skylab crews exhibited an approximate 30 percent decrease in cardiac output immediately postflight (6). Recover was for the most part rapid, requiring 4 to 5 days for the Skylab 3 and 4 crews and approximately 21 days for the Skylab 2 crew. Increased inflight exercise by Skylab 3 and 4 crewmen is thought to be a factor in their improved recovery rate (7, 8, 9). Based on crew comments after each successive flight, time allocated for daily personal exercise was extended from 0.5 hours per crewmen in Skylab 2 to 1.0 hours per crewman in Skylab 3 and 1.5 hours per crewman in Skylab 4.

In an attempt to provide the Skylab crewmen with some protection against anticipated decreased effective circulating blood volumes upon return to the one-g environment, individually sized cardiovascular counter-pressure garments were provided and were donned prior to reentry. As seen in Figure 1, the garment had built-in lateral capstans in each leg which, when inflated to gage pressure 170-180 mm. Hg produced a pressure gradient which ranged from 85-90 mm. Hg at the ankles to 10mm. Hg at the waist. The efficacy of these garments in reducing postlfight postural hypotension

SKYLAB CARDIOVASCULAR COUNTER PRESSURE GARMENT

Figure 1

effects is demonstrated in Table III. The pressurized garments afforded a 1-20 BPM reduction in heart rate together with a 5-15 mm. Hg increase in pulse pressure.

Fluid and Electrolytes - Significant biochemical changes were observed during Skylab. These changes returned to normal shortly after reexposure to the one-g environment. Basically, the observed changes were indicative of a successful adaptation to the combined stresses of weightlessness. This adaptation permitted reestablishment of the homeostasis of the internal milieu to new levels appropriate to the zero-g condition. However, as stated previously, no such adaptation occurred with respect to the catabolism of the musculoskeletal system. Changes in endocrinological parameters clearly indicate that the astronauts were stressed by their exposure to weightlessness. The overall effect on fluid and electrolyte homeostasis over a prolonged period of time remains conjectural at this point.

Reduced Red Cell Mass and Plasma Volume - Red cell mass decreases averaging approximately 10 percent have been measured regularly among crewmen returning from space flight. Analyses of data from the Skylab red cell mass determinations indicated the red cell mass drops occurred within the first 30 days of flight and that a gradual recovery of red cell mass deficits began approximately 60 days after launch. The plasma volume changes shown in Table IV are expressed as the mean percent change from the pre-mission value observed for each of the three Skylab crews. As can be seen, the plasma volumes decrease and do not return to normal

EFFICACY OF CARDIOVASCULAR COUNTER PRESSURE GARMENT (FIVE MINUTE MEANS)

	STANDING INFLATED	STANDING, DEFLATED
HEART RATE	103 ± 4	121 ± 5
SYSTOLIC BLOOD PRESSURE	124 ± 11	113 ± 8
DIASTOLIC BLOOD PRESSURE	70 ± 6	66 ± 10
PULSE PRESSURE	54 ± 9	43 ± 8

Table III

PLASMA VOLUME
(PERCENT CHANGE FROM PREMISSION VALUE)

SKYLAB 2		
CDR		- 2.5
SPT		-10.3
PLT		-12.3
	MEAN	- 8.4
SKYLAB 3		
CDR		-18.4
SPT		- 9.1
PLT		-11.8
	MEAN	-13.1
SKYLAB 4		
CDR		-15.7
SPT		-19.2
PLT		-12.9
	MEAN	-15.9

Table IV

values with extension of the mission. The Skylab 2 (28-day) plasma volume decrease was less than those for Skylab 3 (59-day) and Skylab 4 (84-day) but still greater than during Apollo (-5% mean). For the most part, plasma volume values reverted back to or exceeded normal pre-mission values within 14 days after flight. The transient nature of these changes appears to indicate successful adaptation to weightlessness.

B. Results Not Presented in the 1974 Skylab Life Sciences Symposium

1. Stereophotogrammetry

Biostereometric analysis of body form on the nine Skylab astronauts, preflight and postflight, reveals a loss of volume of one to one and one-half liters from the legs, much of which is replaced during the first four days postflight (10). It is estimated that about one-third of this loss represents partial atrophy of the leg muscles due to relative disuse in zero gravity, the remainder being due to a deficit in body fluid. Reduction in volume of the abdomen has been noted also, and this probably represents a small loss of body fluid, combined with a loss of body fat in all but two of the crewmen. Difficulties in distinguishing between the upper arm and the shoulder region have prevented any useful conclusions being drawn from the measurement of arm volume.

Analysis of the coordinate data on body form was accomplished; however, much more detailed analyses and conclusions may be possible in the future. In contradiction to any other form of anthropometry, the stereoscopic photographs of the Skylab astronauts are a permanent detailed

record of body form, which may be reexamined at some future date to answer new qustions, or to take advantage of the increased accuracy resulting from advances in techniques.

2. Hematology and Immunology

Cellular Immune System - The functional capacity of the cellular immune system was evaluated based upon the ability of purified lymphocyte cultures to undergo blastoid transformation in response to an in vitro mitogenic challenge.

There was a significant depression of the lymphocyte response to phytohemagglutinin (PHA) stimulation on the day of recovery (R+0), as measured by RNA and DNA synthesis rates (11). This finding was characteristic of all three missions and did not appear to be related to mission duration. The capacity of the lymphocytes to respond to PHA was recovered rapidly and by R+3 was within the established preflight limits.

The absolute white cell count was typically elevated at recovery, but rapidly returned to preflight levels. Differential counts indicated that this elevation was due to an absolute increase in the number of neutrophils with the lymphocyte absolute count not changing significantly. These results are consistent with the high control levels measured in the crews at recovery.

The medical significance of these changes in the cellular immune system is not clear at this time. It is difficult to predict what a reduced lymphocyte responsiveness, of this magnitude and short duration means with respect to the immune competence of the returning crews.. The

Skylab crews were maintained in isolation for 7 days postflight, thus, their potential for contact with infectious agents during that time was significantly reduced.

Hemoglobin (Hb) - If the relative Hb concentration-calculated as percent of the preflight mean and averaged for each crew - are examined, a downward trend with time is evident (Figure 2). It is perhaps significant to note that the inflight Hb level drops below the preflight level (100%) only after day 60 - about the same time that the red cell mass begins to be replenished (based upon a composite of the data from all three missions).

3. Endocrinology

Hydroxylysine - Hydroxylysine glycosides, free hydroxylysine and total hydroxylysine were measured in urine samples of Skylab 4 crewmembers by ion exchange chromatography, usine either whole, prefiltered urine; urine hydrolyzed with 6 N HCl for 24 hours at 100°C; or whole, prefiltered urine applied to a special cation exchange resin.

The results obtained indicate that in the three crewmembers, the amounts of total hydroxylysine and peptide-bound hydroxylysine excreted in the preflight and inflight periods were statistically higher than those excreted during the postflight period. The other types of hydroxylysine measured, namely free hydroxylysine and glycosylated hydroxylysine, did not show any statistically significant variation. Thus, at the present, we are not yet in the position of stating whether an increased degradation of collagen might initiate during the preflight period of

NASA-S-74-4964

SKYLAB 3 AND 4

RELATIVE HEMOGLOBIN CONCENTRATION IN-FLIGHT

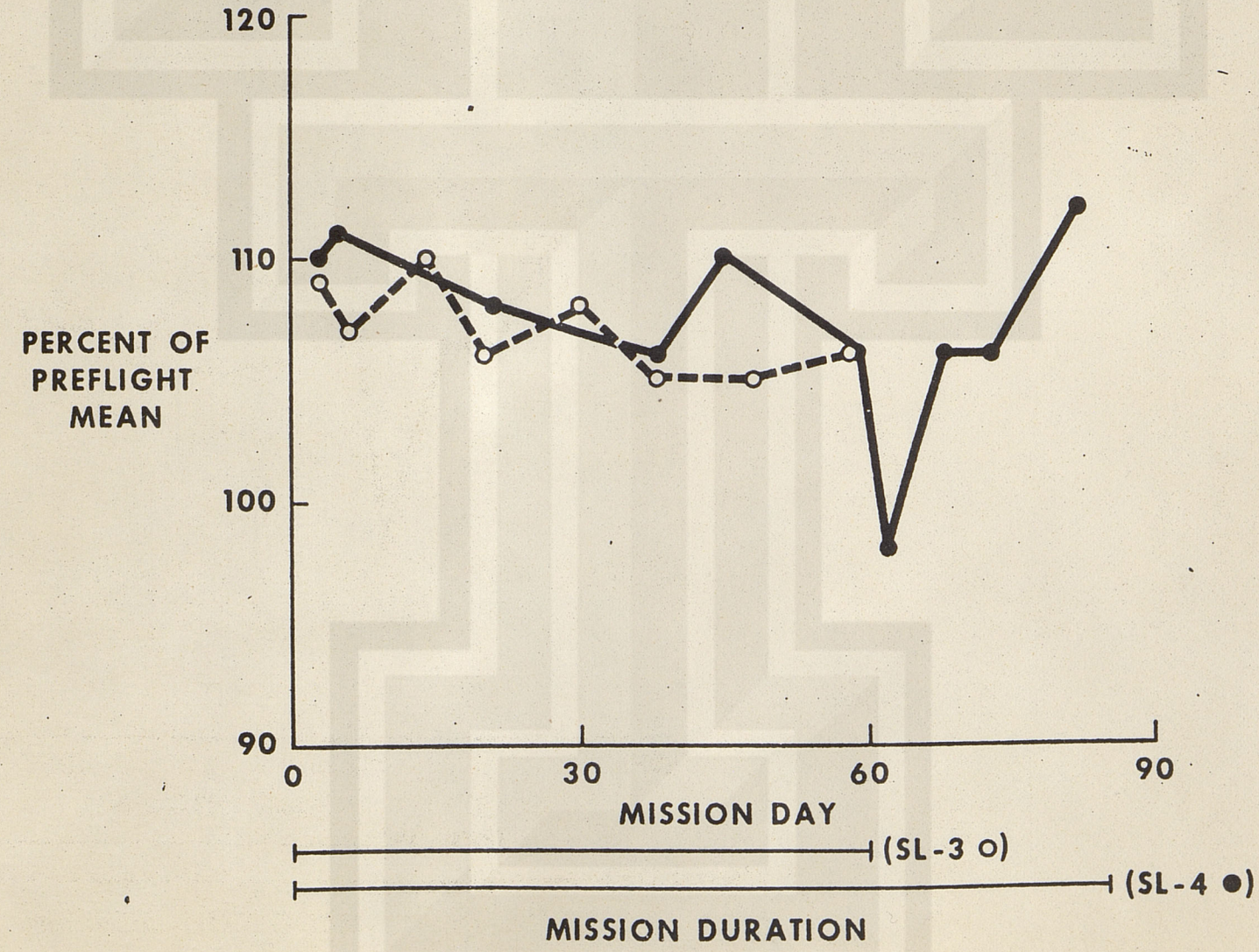

Figure 2

intense training and continue during flight, to revert to normal values in the postflight period.

Elastin - Studies were conducted to evaluate the degradation of elastin pre-, during, and postflight. The results demonstrated, at least with the analytical method employed, no increased degradation of elastin during flight.

Scopalamine - Dexedrine Study - One of the drugs used to prevent motion sickness in six crewmen during Skylab was dexedrine (5mg) plus scopalamine (.4mg). In order to investigate the effect, if any, of this drug on the physiological changes noted during flight, this drug was given to five subjects three times daily at 0800, 1200, and 1600 for four days. Control data were collected 3-4 days prior to taking the drug, during the drug exposure, and for 8-9 days after discontinuing the drug. The same biochemical measurements as were made on the Skylab crew samples were performed on the study samples.

When the days that the subject were given the drug are compared to the control days, consistent elevations were observed in urinary cortisol, epinephrine and antidiuretic hormone. General decreases were noted in urine volume and norepinephrine with no consistent changes shown in aldosterone excretion.

The biochemical results of the Skylab crewmen on the days that they took this drug will be considered in relation to the influences noted in these test subjects. Further work designed to consider which of the two compounds present in the drug were responsible for these findings is in progress.

II. Skylab Follow-on Studies

A. Bedrest Studies

1. Head-down Tilt Studies

Marked headward fluid shifts were demonstrated by volumetric leg measurements (and other data) on Skylab crewmen. Because of the significant role of fluid shifts on cardiovascular responses, head-down tilt studies have been performed on ground-based subjects in preliminary feasibility studies. Intuitively this should be a better analog of zero gravity than the accepted practice of supine (horizontal) bedrest. Accordingly, head-down tilt studies have been conducted both for short duration (2 hours) periods using 10° head-down tilt at JSC and for extended periods (7 days) at 5° head-down tilt at the USPHS Hospital (San Francisco). These data are in preliminary stages of reduction and for the most part, the number of subjects tested is not yet sufficient to demonstrate statistical validity.

Initial short duration results indicate that leg volume may be reduced more after head-down tilt than after comparable time in the supine position. Measurements of leg blood flow by occlusive cuff plethysmography suggest that head-down tilt results in a greater decrement in blood flow than is seen in comparable supine studies. Neither condition, however, reproduces the augmentation of leg blood flow such as was seen during flight on Skylab 4 crewmen.

Systolic time interval measurement provides yet another index of the effects of fluid shifts and resulting myocardial

preload on cardiodynamics. Four tests have been completed with paired supine and 10° head-down tilt protocols. Though an expected decrease in Pre-ejection Period/Left Ventricular Ejection Time (PEP/LVET) ratio easily differentiates between sitting and supine positions, no appreciable distinction between supine and 10° head-down tilt can be made from the few data points obtained.

On the other hand, one vectorcardiographic parameter (QRS magnitude), which increased quite significantly on Skylab crewmen, seem to show no consistent magnitudinal changes in either supine or head-down tilt conditions, while certain other parameters (P, ST and J vector magnitudes) appear to change opposite to that observed on Skylab crewmen. Statistical inferences cannot yet be made.

Pulmonary function tests revealed evidence of increased pulmonary fluid volume during head-down tilt (static lung volumes decreased and airway closing volume increased) as compared with the sitting position, however, no statistical difference was noted between head-down tilt and supine position (12).

Longer periods of head-down tilt (7 days) at a different inclination (5°), have revealed essentially nothing different from supine control states for the same periods.

2. Impact Loading Study

A bedrest study designed to determine the importance

of direct physical stress (weight-bearing) in maintaining the integrity of bone is currently being conducted. This study consists of a 6-week ambulatory control period during which calcium, phosphorus and nitrogen balance are measured along with urine hydroxyproline and creatinine. In addition, baseline calcanial mineral density is determined by gamma ray transmission scanning using technetium labeled EHDP*.

The second phase is an 18-week bedrest period during which the six subjects are randomly selected for either no therapy (2 subjects) or treatment by impact loading (4 subjects). Impact loading is accomplished by means of a device which exerts a given amount of static compression upon the subject and then administers an impact load upon the heel of each foot. The impact loading is performed in four hourly segments (one every two seconds at a loading force of 25 pounds), scattered throughout each day on each individual.

The third phase is a 2 to 4 week reambulatory period during which recovery of balance and bone mineral density will be measured.

Preliminary results, based upon only two weeks of available balance data, indicate that two of three subjects receiving impact loading have less than 100 mg Ca/day increase in urine compared to two controls who are excreting greater than 140 mg CA/day. A rise in urinary phosphorus output also shows that there is a greater increase of phosphate output in the two controls than in the impact loading subjects.

*Disodium etidronate (disodium-ethane-1-hydroxy-1, 1-diphosphonate).

3. Fourteen-day Bedrest Study

A 14-day bedrest study was conducted to compare the physiological, biochemical and hematologic changes resulting from bedrest with those observed during Skylab missions. Bedrest has long been used as a simulation for the weightless condition; however, definitive data concerning specific changes could not be validated without long-duration in-flight medical results. This study was designed to identify those changes and effects that are similar, and further studies could provide useful information concerning the basic mechanisms involved in these changes.

The testing program pre- and post-bedrest was similar to that of Skylab and included lower body negative pressure tests, bicycle ergometry tests, and postural equilibrium and vestibular studies. Fluid and electrolyte shifts were documented with isotope studies and urine analysis. Red cell mass, plasma volume, total body water, extracellular fluid, total body exchangeable potassium and the urinary excretion of potassium, sodium nitrogen, calcium, ADH and aldosterone measurements comprised part of the studies.

Following the fourteen-day strict bedrest period, the subjects were moved in the supine position to the test area where all tests were conducted. Post-bedrest testing continued for 7 days on most experiments. Diet control, urine and fecal collection, and blood sampling continued for 14 days post-bedrest.

The results of the bedrest study experiments have not been sufficiently analyzed to be presented in detail; however, preliminary examinations of the data have been made.

Both red cell mass and plasma volume decreased during bedrest. Measurements taken on the final day of bedrest showed a mean red cell mass decrease of 4.9% for the six subjects. Results of tests made approximately two weeks after bedrest showed a continuing mean decrease to 6.5%. The red cell mass change was of a magnitude and time course (in 4 of 6 subjects) similar to that seen during Skylab. As in Skylab 2, the red cell mass did not recover during the first two weeks post-bedrest. The plasma volume decline was more gradual and less consistent. After one day of bedrest, the mean plasma volume decrease for the six subjects was 2.8%. On the final day of bedrest it was 6.9%, and approximately two weeks after completion of the fourteen day bedrest period the mean plasma volume showed a 7.4% increase. Analyses of red cell shape and of the cellular immune function are still in progress. Hematological parameters showed the influence of change in vascular fluid compartments but were unchanged otherwise.

The subjects went on a controlled metabolic diet and collection began of all urine and fecal samples three weeks before bedrest, throughout bedrest, and for two weeks after bedrest. During bedrest, the results show increases in the urinary excretion of sodium, potassium, chloride, calcium, magnesium, phosphorous, and uric acid. Decreases were observed in norepinephrine and epinephrine excretion during bedrest. After bedrest, retention in most electrolytes was observed for the first few days

then a more general return toward normal. Post-bedrest decreases were measured in urinary volume, cortisol and epinephrine. The results of these biochemical measurements are similar to Apollo findings. More correlation between these data and data collected during the first 2 weeks of Skylab flights is required before a direct comparison can be made.

In the exercise response testing, it was observed that immediately post-bedrest there was significant tachycardia both during rest and during exercise which in the latter case led to a decrease oxygen pulse. Cardiac output levels during exercise was similar both pre- and post-bedrest for most of the test subjects. When combined with the increased heart rate there was a calculated decrease in stroke volume. Diastolic blood pressure responses post-bedrest indicated an increased peripheral resistance which may have been in response to a decrease vascular volume. The time course for return of the changes was rapid with most of the change absent by the R+1 test. In general, these findings are qualitatively similar to those observed postflight during the Apollo program. A more detailed analysis of the data is required to comfirm these initial impressions and to evaluate bedrest as an analog to weightless when studying the response to exercise.

The neurophysiological data collected on the six subjects employed in this study included a static test of postural equilibrium (Rail Standing Test), motion sensitivity as measured on the Skylab astronauts, and electromyographic testing. To date, the results from the pre- and post-testing have indicated that there was little, if any, real change in any

of the subjects' ability to balance on the rails used in the postural ataxia test. Motion sensitivity post tests suggested that on the first day out of bed there was slight decrease in the subjects' motion sicknes threshold. However, it is felt that these results may be confounded because the subjects were exposed to both the LBNP and the ergometer prior to testing in the rotating chair. By the 7th day post-bedrest, all of the subjects had either regained their pre-bedrest levels of sensitivity or had demonstrated a somewhat increased tolerance in the motion sensitivity test. The EMG data was taken from the gastrocnemius muscle and included an Achilles tendon reflex, a voluntary response or voluntary flexional foot movement, and an involuntary response or experimenter induced dorsoflexion of the subject's foot. The results indicate that response latencies associated with these movements did not change as a function of bedrest. Amplitude changes, however, were observed in the monosynaptic potentials on the first day out of bed. Most of these increased potentials had returned to normal after the subjects had been mobile for two days. It was concluded that the difficulty some of the subjects experienced in walking the first day out of bed could be explained by the observed changes in EMG amplitudes.

B. Parabolic Flight Studies

A major difficulty with the investigation of space motion sickness is that the overall syndrome in all of its complexities is largely bound to a specific stimulus condition, namely 0-g. Although very important in their own right, studies conducted in a 1-g field have not and may never yield information completely valid for the 0-g situation. It is necessary, therefore, to utilize unique experimental

devices and techniques which more closely approximate the 0-g environment. The KC-135 0-g aircraft represents such an approach. Properly controlled measurements made during the 0-g phase of parabolic flight have a high probability of yielding new information relevant to the open question of the causes, prediction, and prevention of space motion sickness.

The objectives of this program are:

1) To conduct tests during the 0-g phase of parabolic flight fundamental to gaining increased understanding of the processes underlying 0-g motion sickness.

2) To develop and validate ground-based methods for the prediction and prevention of susceptibility to motion sickness during parabolic flight which have a potential for application to weightless space flight. Included will be the evaluation of adaptation (training) procedures and anti-motion sickness drugs.

3) To evaluate motion sickness susceptibility during parabolic flight as a predictor of susceptibility during weightless space flight.

To accomplish these program objectives, studies are currently underway or are planned which incude the measurement of perilymph/endolymph fluid pressure changes in the vestibular system, investigation of semicircular canal/otolith interaction, otolith function, and changes which may occur within the central nervous system and the autonomic nervous system as a function of weightlessness. These studies are designed to investigate how predictive tests may be developed as well

as looking at how basic vestibular mechanisms may be influenced during both periods of 0-g and increased g forces.

C. Skylab Data Integration

A continuing effort is being made to integrate and correlate all of the medical experiment data collected during the three Skylab missions. The details of this program will be presented in another paper.

In general, the approach is to utilize automated data bases with detailed statistical and graphical capabilities. After evaluation of physiological adaptative processes across investigative systems, computer simulations (utilizing large, complex system analysis programs) are run to determine the feasibility of new and or modified hypotheses.

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