

FINAL REPORT

INVESTIGATION TO DETERMINE THE EFFECTS OF
 LONG-TERM BED REST ON G-TOLERANCE AND ON
 PSYCHOMOTOR PERFORMANCE

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Responsible Investigator

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FORWORD

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ABSTRACT

Fourteen young men were confined to bed for 28 days. They were randomly divided into three subject groups of 5, 5 and 4 individuals. One group exercised, another did pressure breathing and the third did both. Each subject was exposed to a re-entry acceleration profile in the -Gx position while performing a three dimensional tracking task prior to the bed rest and at the conclusion of the bed rest. Tilt table tolerance and blood volumes were determined in a similar sequence.

Cardiovascular deconditioning manifested by plasma volume decrements of 20% and decreased tolerance to passive tilting resulted in all subjects and was not differentially affected by the exercise, pressure breathing or the combination maneuvers.

Performance on the tracking task during acceleration was not affected by the cardiovascular deconditioning.

CONTENTS

	Page
INTRODUCTION	1
EXPERIMENTAL DESIGN	1
SUBJECTS	2
METHODS AND PROCEDURES	2-12
Physical Conditioning and Deconditioning	2-6
The Centrifuge Studies	6-8
Pressure Breathing and Exercise	8
Blood Volume	8
Tilt Table	8-10
Catecholamine and Catecholamine Metabolite Studies	10-12
RESULTS	12-44
Physical Conditioning-Deconditioning	12
Centrifuge Studies	16
Blood Volume	16
Tilt Table Studies	16
Catecholamine and Catecholamine Metabolite Studies	22
DISCUSSION OF RESULTS	45-47
CONCLUSIONS	47
REFERENCES	48

TABLES

<u>Number</u>		<u>Page</u>
1.	Physical Working Capacity of Subjects as Estimated by Astrand Procedure and Measured Directly by Maximal O ₂ Consumption Test.	14.
2a.	Mean Max. Strength El Flexors	15.
2b.	Mean Max. Strength Rectus Abdominis	15.
3.	Average Tracking Error Scores For the Last 3 Practice Trials	17.
4.	Average Tracking Error Scores At 1 G	18.
5.	Average Tracking Error Scores At 6 G	19.
6.	Average Tracking Error Scores At 8 G	20.
7.	Average Tracking Error Scores Pre (1) and Post (2) Bed Rest	21.
8.	Epinephrine Plus Norepinephrine	23.
9.	Percent Epinephrine	24.
10.	Metanephrine Plus Normetanephrine	25.
11.	Vanillylmandelic Acid $\mu\text{gm/hr.}$ Urinary Excretion	26.
12.	$(M + NM)/VMA$ Urinary Excretion	27.
13.	$(E + N)/(M + NM)$ Urinary Excretion	28.
14.	$\mu\text{gm/hr.}$ Urinary Excretion	29.
15.	Epinephrine Plus Norepinephrine $\mu\text{gm/hr.}$ Urinary Excretion	30.
16.	Percent Epinephrine Urinary Excretion	31.
17.	Metanephrine Plus Normetanephrine $\mu\text{gm/hr.}$ Urinary Excretion	32.
18.	Vanillylmandelic Acid $\mu\text{gm/hr.}$ Urinary Excretion	33.
19.	$(M + NM)/VMA$ Urinary Excretion	34.
20.	$(E + N)/(M + NM)$ $\mu\text{gm/hr.}$ Urinary Excretion	35.
21.	Epinephrine Plus Norepinephrine $\mu\text{gm/hr.}$ Urinary Excretion	36.
22.	Percent Epinephrine Urinary Excretion	37.

TABLES (Continued)

<u>Number</u>		<u>Page</u>
23.	Metanephrine Plus Normetanephrine μgm/hr. Urinary Excretion	38.
24.	Vanillylmandelic Acid μgm/hr. Urinary Excretion	39.
25.	(M + NM)/VMA Urinary Excretion	40.
26.	(E + N)/(M + NM) Urinary Excretion	41.
27.	Differences Between Supine and Highest Pulse Rate During Tilt	42.
28.	Tilt Table - Pulse Rate Averages	43.
29.	Blood Volume Data	44.

DIAGRAMS

A.	Total Time Acceleration Profile	9.
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INTRODUCTION

The primary purpose of the experimental effort was to study the effect of an extended period of bed rest on the ability to perform a complex tracking task when exposed to a simulated re-entry acceleration. Secondly, information concerning the attendant cardiovascular deconditioning(10) and how this might be altered by exercise and pressure breathing was obtained.

Some urgency in organizing the experimental program was realized because of the necessity of completing the effort in the university summer recess period. Further, the mock-up of the re-entry couch for use on the centrifuge as well as the tracking task were not immediately available at the outset. These factors led to some compromises of the experimental design, however, the effort did meet the primary goals of investigation.

EXPERIMENTAL DESIGN

The general format of the experiment can conveniently be divided into three phases. Phase One consisted of:

1. 2-4 weeks of intensive physical conditioning.
2. Familiarization rides on the human centrifuge.
3. Learning and practicing the required tracking tasks.
4. Collection of urine specimens for catechol amine determinations.
5. Obtaining tilt table tolerances data.
6. Measurement of blood volumes.

In Phase Two the subjects were divided into three experimental groups. The three experimental groups were confined to bed for 28 days and randomly assigned to perform: a) isotonic exercises, b) pressure breathing and, c) isotonic exercises and pressure breathing. Some measurements were made during the period of bed rest such as measurements of venous tone, skeletal muscle strength, and 24 hour urine samples were collected periodically for hormone studies.

In Phase Three the subjects were brought on stretchers to the human centrifuge where they performed the tracking tasks while exposed to a programmed acceleration profile. All subjects also undertook tilt table tolerance test. Time prevented follow-up studies of the subject after the final data collection effort was completed.

SUBJECTS

Subjects for the experiment were male university students ranging in age from 18 to 24 years. They were selected on the basis of good physical and mental health as judged by appropriate medical examinations, interviews with a clinical psychologist and the completion of the Minnesota Multiphasic Personality Inventory. The medical examination was based on the one required for the Air Force flight personnel.

METHODS AND PROCEDURES

Physical Conditioning and Deconditioning

As each subject became available he was introduced into a four hour daily physical conditioning program. The exercise program was designed to improve circulo-respiratory function (referred to as "physical work capacity") and muscle strength and muscle tonus of the skeletal musculature. The workouts were broken up into two - 2 hour bouts, 10:00-12:00 A.M. and 3:00-5:00 P.M. Each 2 hour bout was in turn divided into one hour of weight training and one hour of hard interval running. Training was brought about in a progressive manner under the direct supervision of two trained physical educators. Since all subjects did not become available at the same time, the period of training varied from a minimum of two weeks to a maximum of four weeks.

Evaluation of training progress was accomplished by weekly administration of the physical work capacity test designed by Astrand (1). The 900 kpm/min load was found suitable for all subjects. The maximum O_2 consumption was also measured directly for each subject at the end of training.

Muscle tonus is frequently suggested as a possible component of a multi factor explanation for the maintenance of cardiovascular tone during changing g loads such as imposed by the orthostatic tolerance test. Unfortunately, however, an operational definition of muscle tonus has not been available, and in the past it has been evaluated by such non-quantitative methods as palpation. Others have used maximum strength as a criterion of tonus but this parameter can also be challenged on at least two grounds: 1) maximum strength is a measure confounded with psychological parameters such as motivation and willingness to bear pain, and 2) whether or not any relationship between strength and muscle tonus exists is yet to be demonstrated by objective means.

For reasons set forth above, one of us has developed electromyographic equipment and techniques for the quantitative appraisal of electrical activity in muscle tissue. In brief, the equipment consists of a high gain, differential, voltage amplifier which drives a voltage controlled oscillator. The

output of the VCO in pulses per sec. is linearly related ($\pm 1.0\%$) to the integral of EMG voltage arising in the muscle sampled. By the simple expedient of counting (electronically) the pulse output of the VCO a direct readout of the muscles' electrical activity may be had for any given period of time.

Using this equipment, it has been found in agreement with other investigators (2) (7) that resting muscles in normal healthy individuals exhibit electrical silence if the subject is well relaxed (4). Furthermore, this ability to achieve electrical silence seems quite unrelated to either the maximum strength, or the firmness of the resting muscle. However, it has been found that the regression of EMG integral upon force of voluntary isometric contraction is linear (9) and that furthermore the slope of this line is typical for any one muscle in any one subject. Indeed, a pilot study indicated that the slope of the line is related to the measured maximal strength of the muscle by $r=.73$ (6). For these reasons an operational definition of muscle tonus for the purpose of this study was set up as follows: "Muscle tonus is considered to be best reflected by the ratio of force of contraction per unit electrical activity of the subject muscle group." Or it might be stated that the smaller the increment in electrical activity required for a given increment of force required of the muscle the better the "tonus" of that muscle. Thus, the flatter the slope of the plot of EMG potentials as a function of force of contraction, the better the "tonus." Henceforth in this report the term muscle tonus will be used in this context.

Physical Work Capacity Testing

Subjects were instructed not to smoke for one hour previous to the test and no tests were scheduled for one hour after a meal. The bicycle ergometer used was of the Von Döbeln type. The saddle and handlebars were adjusted to suit each individual's height. A 6 min. 900 kpm work test was administered with heart rate taken stethoscopically every minute. The mean of the last two rates was taken as the working pulse for the load under consideration and the working capacity in terms of O_2 consumption/min. was estimated from the Astrand nomogram (1). All tests were performed at 50 pedal r.p.m. in cadence with a metronome.

Maximum O_2 Consumption

Maximal O_2 consumption is accepted as the best single measure of physical working capacity. Consequently, in addition to its estimation by the Astrand test, it was also measured directly at the end of the training program, immediately prior to entering the bed rest phase. This measure was also made on the Von Döbeln type bicycle ergometer and each subject had had at least two rides previous to the testing program. The

procedure used was similar to that of the Mitchell, Sproule and Chapman (11) modification of the Taylor, Buskirk, and Henschel method (12). The Sjostrand test, consisting of two consecutive 6 min. bicycle rides of 450 and 900 kpm/min., was used as a warm up procedure and this also provided a prediction of aerobic capacity which was used to set up the first workload. The subject was connected to an "Otis McKerrow" high velocity two way breathing valve and gas collection was effected by the Douglas Bag method. Volume measurement was made by Tissot type gasometer and duplicate samples of expired air were analyzed by Haldane technique. Calculations were based on apparent change of N_2 percentage to correct expired to inspired volume.

The first test-ride was set up for approximately 300 kpm/min. above the aerobic capacity predicted for the subject by the Sjostrand test warm up and subsequent rides were increased by increments of 300 kpm/min. until no further increase could be tolerated. Subjects rested between test rides until their resting pulse had returned within 12 beats of their normal resting value. When more than three rides were necessary to achieve a plateau a second day of testing was scheduled for that subject.

Each ride was of 4 minutes duration. During the first minute the Douglas Bag was flushed out and the sample was taken during the last minute. In some few cases where the workload was very high, a 30 sec. sample was taken from 3:00-3:30.

The maximal O_2 intake was taken as the value at which the intake turned downward with increasing load or that value which showed less than a 150 ml/min. increment.

Muscle Tonus Testing Procedure

In order to provide a suitable electrical environment for the electromyographic testing program, a metal skinned trailer was outfitted as a testing laboratory which thus provided a virtual "shielded room." To provide a measured amount of force of contraction, a hydraulic system was set up in which the subject applied force isometrically against a piston actuator which was transmitted to a "dead weight tester." Thus a very accurately known force was applied and held by the subject with no need for monitoring any readout device. This allowed the investigator to control the angle of the joint (and consequently the length of the muscle) more closely.

Four muscle groups were evaluated: 1) R. elbow flexors, 2) R. rectus abdominis, 3) R. external oblique and 4) R. gastro-soleus. In all cases surface electrodes were used and the skin was abraded with 2-0 garnet paper at the electrode site until the interelectrode resistance was below 5000 ohms using EKG Sol electrode cream. For each muscle group a subject held an isometric contraction 10 sec. against increasing

weight loads with 30 sec. rest between loads. During each 10 sec. observation period an "Anadex" electronic counter counted the pulse output of the Biotronics "EMG Monitor" and the analog EMG signal was monitored for artifact by oscilloscope. The procedure for each muscle was as follows:

1. Right elbow flexor group

- a) body position -- supine, knees up
- b) elbow at 90° -- forearm vertical
- c) piston actuator -- midway between styloid process of radius and middle of antecubital space on radial aspect
- d) electrodes -- one EKG precordial cup type on point midway between axillary fold and antecubital space on volar midline of biceps. EKG plate electrode on volar aspect of R. wrist
- e) forces used -- 5 - 10 - 15 - 25 - 35 - 45 - 55 - 65 pounds

2. Right rectus abdominis

- a) body position -- supine, arms across chest
- b) piston actuator -- on a line between and 3/4 of the distance from the anterior superior iliac spine to the proximal border of the patella
- c) electrodes -- EKG cup midway between the umbilicus and the symphysis pubis just lateral to the linea alba. Indifferent cup just lateral to the anterior superior iliac spine
- d) forces used -- 15 - 25 - 35 - 45 - 55 - 65 pounds

3. Right external oblique

Everything identical to procedure of R. rectus abdominis, except active electrode over McBurney's point.

4. Right gastro-soleus

- a) body position -- supine, arms across chest
- b) knee held locked in extended position by pressure above knee by assistant. Ankle joint in anatomic position. Foot resting on 4" padded block
- c) piston actuator -- under ball of foot

- d) electrodes -- EKG cup $1/3$ of the distance distally from the middle of the popliteal space to the surface of the floor, in the dorsal midline. EKG plate on medial aspect of ankle.
- e) forces used -- 25 - 45 - 65 - 85 - 105 - 125 pounds

At the end of the EMG runs for the elbow flexor and abdominal groups, an all-out strength effort was required and the hydraulic pressure was transmitted to an 0 - 200 p.s.i. gauge by switching a 3-way valve. Since the surface area of the piston actuator was 1.00 square inches the reading was directly in pounds of force. The gauge was equipped with a maximum reading hand and was calibrated weekly against the dead weight tester.

The Centrifuge Studies

For the purpose of reducing apprehension, subjects were given a series of familiarization rides on the centrifuge in both the positive (G-2) and transverse (G-4) configurations. Time limitation did not allow for as extensive a familiarization program as would be most desirable. The subjects did willingly and with some competitive spirit enter into the task of learning the required tracking tasks while becoming familiar with the sensations associated with transverse accelerations.

The transverse accelerations were achieved using a mock-up of the Gemini re-entry couch. A seven degree back angle was used. Suitable mounting was provided for the tracking task.

The task used on the centrifuge was the DYG 779A1 Space Vehicle Rate Simulator supplied by Manned Space Craft Center. This provides an electronic simulation of the simplified Euler's equations of motion for manned space capsule with parameter values adapted to the Mercury Capsule.

The problem presented is a typical retro-rocket firing sequence. It consists of the torques and corresponding angular velocities in pitch, roll and yaw caused by unequal retro-rocket thrusts. By flying a control stick, a pilot can correct to zero the vehicle rates presented by the rate meters on the simulator.

The working system is divided into three parts:

The programmer

The computer-indicator

The control stick

The programmer provides random signals representing the retro-rocket torques and the timing sequence for the program.

The computer-indicator provides the displays for the three orthogonal velocities and the necessary electronics to mechanize Euler's equations. The display is an orthogonal representation of pitch, roll and yaw rates. Roll and yaw rates are indicated by horizontally moving vertical lines, roll being the upper half. Pitch rates are presented by a vertically moving horizontal line and extending across the entire scale face. Each axis is scaled for a $60^\circ/\text{sec}$. maximum rate. The stick provides the signals for cancelling the vehicle rate signals. The stick is a side arm controller. Pitch is a forward and backward motion of the hand-grip; roll is left and right, yaw is a twist. Each mode is connected to a variable resistor so that the control signal is linear with respect to stick displacement.

The unit at rest is in a trim mode. This allows all inputs to be set at zero.

When the system is initiated it begins a reset mode that lasts for five seconds. This allows preparation time between the start and the retro-rocket disturbance sequence. At the end of five seconds the unit begins the "operate" mode. During this period the pilot manipulates the control stick in order to cancel the disturbance torque signals and resulting cross torque signals to try and hold the rate indicators to zero. This mode lasts 21 seconds.

At the end of this mode the unit begins the error mode. During this period an error meter presents the total integrated error during the operate mode. This mode lasts four seconds. The unit then returns to its rest mode.

A total time of 30 seconds was required for the completion of one complete sequence including the reset, operate and error modes. There were five separate variations of the operate mode such that the subject was required to complete 5 sequences before completing.

It was not possible to record the performance of the subjects and therefore errors for each mode were read by an observer and manually recorded.

Time was a factor in training the subjects and because of this not all subjects were trained to proficiency with the full three axis task. Five of the subjects demonstrated a superior learning ability for the task and were trained for full three axis performance. The remaining nine subjects were trained for two axis performance, namely pitch and roll. Subjects were required to demonstrate consistent performance prior to the test centrifuge ride that was conducted just prior to the initiation of the bed rest period.

The acceleration profile used for the test runs had to account for the time required for the completion of one full cycle (five variations of the operate mode) of the task programmer. Accordingly, the run commenced by rapid onset of

acceleration to 6G. When this acceleration was achieved, the programmer was started and the subject completed one full cycle of the task. The total time at 6G was at least 150 sec. The acceleration was then reduced to 3G. Starting at 3G the acceleration was increased to 8G, maintained, and then decreased to one G such that the subject completed one full cycle of the task during the course of the acceleration curve. At least two operate modes of the program were completed at maximum acceleration. This type of profile provided for testing at a steady acceleration and also for testing in a changing acceleration field. The total time of acceleration experienced by the subject was more than 6 minutes. (See diagram A).

Pressure Breathing and Exercise

Pressure breathing was accomplished with standard A-13A breathing masks. Compressed air was supplied through an A-14 demand regulator modified such that a mask pressure of 60 mm of mercury could be achieved. Subjects performing pressure breathing did so four times a day for thirty minutes of each occasion. The mask pressure was adjusted to 60 mm of mercury in steps as the subject became accustomed to the pressure.

Exercise was accomplished by means of a conventional exercising band stretched between the soles of the feet and the hands. The band was stretched by the subject at such a rate that the resting pulse rate was doubled during the period of exercise. The exercise was performed for $\frac{1}{2}$ four times a day.

Subjects doing both the exercise and the pressure breathing routines performed each routine four times a day.

Blood Volume

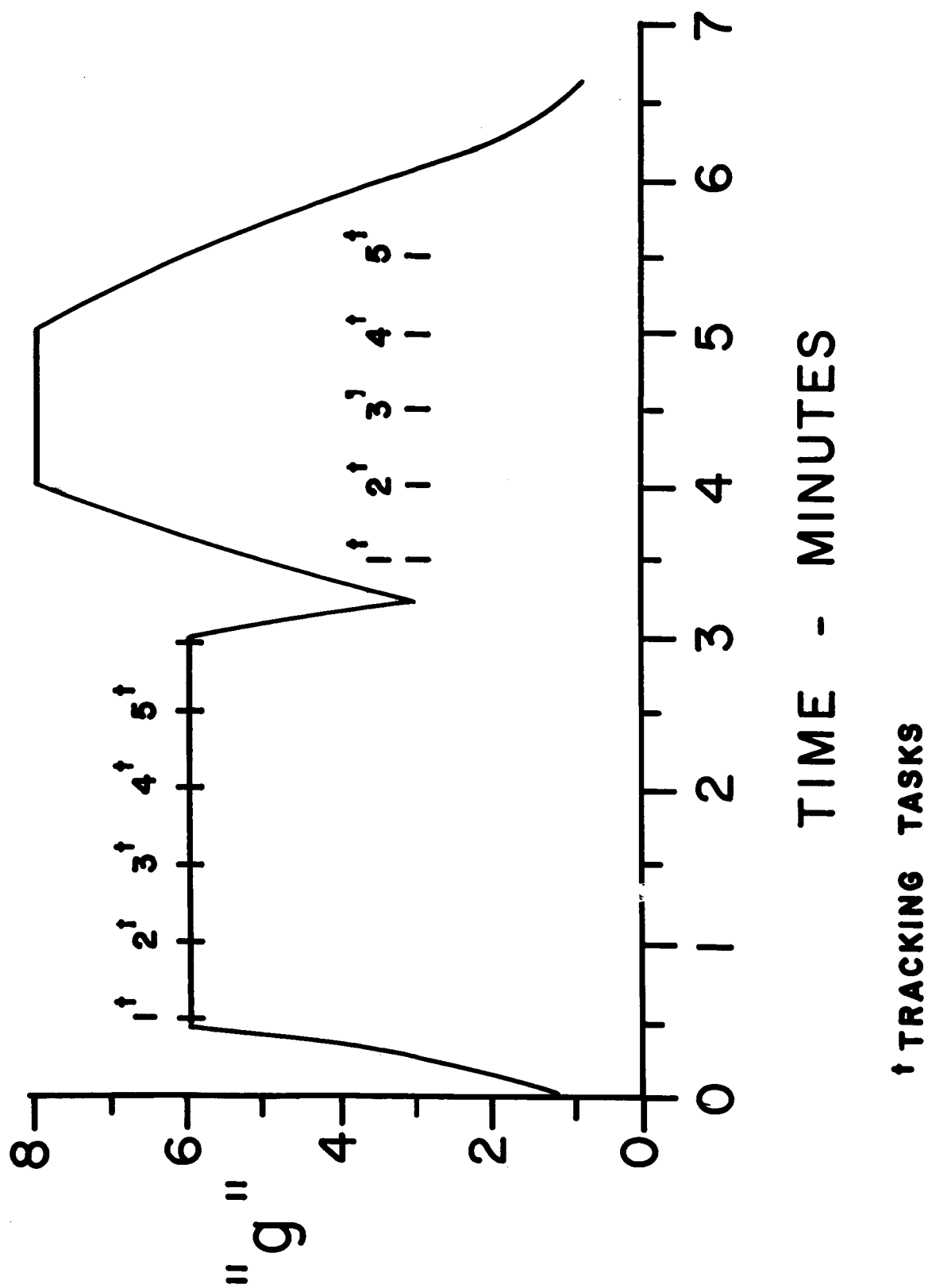
Blood volumes were determined on the basis of the hematocrit and an estimation of the plasma volume. Plasma volumes were estimated by the Evans Blue dye technique.*

The subject was recumbent for a $\frac{1}{2}$ hour prior to the estimation. The procedure was carried out in the morning approximately 3 hours after breakfast. The subjects were either at bed rest or on limited activity in ward quarters on the days blood volume measurements were made.

Tilt Table

The subject was secured to the tilt table by means of a modified parachute harness. Necessary adjustments were made so that the body weight could be supported by the crotch straps without causing discomfort during the head up position. The

* Ref. early bed rest project - AF report

DIAGRAM A

feet were not supported by a foot rest. After these preparations were made, the subject was allowed to rest while pulse rates were counted at 2 minute intervals. Rates were determined on the basis of 20 second counts. Tilting was accomplished when four successive pulse counts varied by no more than three beats per minute.

Subjects were tilted to the 75 degree head up position. Pulse rates were determined on the basis of 20 second counts started on the minute for 10 minutes beginning at the end of the first minute of tilting.

Catecholamine and Catecholamine Metabolite Studies

Prolonged bed rest increases syncope and presyncopal signs and symptoms with orthostasis on the tilt table. In humans, sympathetic nervous system function is an important part of the complex homeostatic mechanisms required to maintain blood pressure with changes in posture. Norepinephrine, although secreted by the adrenal medulla, is primarily the sympathetic neuro-transmitter substance. If significant changes take place in the autonomic nervous system with prolonged bed rest, then changes in the urinary excretion of catecholamines and their metabolites might be seen.

Methods

Urine specimens were collected on a "control" day and on three days when the subjects were at bed rest. On the control day the subjects were ambulatory. They were instructed not to lay down but were allowed to sit. On each of three test days the subjects were at bed rest except for limited bathroom privileges. The "control" day was August 5, 1964, and the three "bed rest" days on which specimens were collected were August 11, 18, and 28, 1964. On each collection day, each subject's uring was collected in four aliquots: 7:00-12:00, 12:00-19:00, 19:00-24:00, and a "sleeping" specimen 24:00-7:00. Urine was voided at the end of each collection period. When the subject voided during a collection interval the urine was saved in a container immersed in ice water and the specimen obtained at the end of the collection period added.

At the end of each collection period the volume of each specimen was determined, preservative added and the specimen frozen. The preservative used was two parts by weight sodium metabisulfite and one part sodium fluoride. 0.05 grams of this powder was added for each 10 ml. of urine.

Epinephrine (E) and Norepinephrine (N)

The free (unconjugated) catecholamines were determined, amberlite CG-50 (ammonium ion form) being used for the initial separation. The catecholamines were oxidized with potassium

ferricyanide at pH 5.5 and tautomerized to form indoles by the addition of an alkaline ascorbate solution stabilized with ethylenediamine. Internal standards of both epinephrine and norepinephrine were used for each determination. All the oxidations were done in duplicate. Fluorescence measurements were made with a modified Farrand filter fluorometer with the use of two sets of interference filters, one with an excitation wavelength of 390 millimicrons and a fluorescence wavelength of 500 millimicrons and a second set with wavelengths of 430 and 520 millimicrons respectively.

Metanephrine (M) and Normetanephrine (NM)

The total of free plus conjugated metanephrine and normetanephrine was determined. These metabolites were hydrolyzed with heat and acid. Epinephrine and norepinephrine were removed by passage of the urine through an alumina column, and the metanephrine and normetanephrine isolated by adsorption on and elution from amberlite CG-50 in the ammonium ion form. The oxidation was carried out in two steps, the initial step at pH 3.5 and the final oxidation at pH 5.5. These oxidations were all done in duplicate with tautomerization and fluorescence reading methods identical with those for epinephrine and norepinephrine. Internal standards for metanephrine and normetanephrine were used for each determination.

Vanillylmandelic Acid (VMA)

The initial separation was carried out on a Dowex 1X4 anion-exchange column with the resin in the acetate form. After this the VMA was extracted into ethyl acetate and re-extracted into a carbonate solution. The carbonate extract was divided into three aliquots. Vanillylmandelic acid was added to one aliquot to serve as an internal standard. This and another aliquot were oxidized with sodium periodate. An unoxidized aliquot served as a blank. These aliquots were extracted with toluene, which was re-extracted into a carbonate solution. The absorbency was determined at 360 and 333 millimicrons. By reading at these two wavelengths and with solution of two simultaneous equations it was possible to correct for the presence of parahydroxymandelic acid, which would otherwise have interfered.

Calculations

The calculation of all these results, which in each case required solving two simultaneous equations, was carried out by entering the fluorometer or spectrophotometer readings and other data on IBM cards, used to calculate and print out the urinary excretion results in micrograms per hour. After verification of the card entry the same cards were grouped and used to calculate ratios and the various statistics.

"Fortran" computer programs were used for these calculations, which were carried out with a Honeywell 800 computer.

For each of these parameters and various ratios between them, means and standard deviations were determined for various groups, and the p values for the significance of the difference of the means were determined. For the ratios the p values were from data corrected for skewness of the distribution curves by logarithmic transformation.

RESULTS

Physical Conditioning-Deconditioning

Physical Work Capacity

The results of the physical work capacity (PWC) testing are shown in Table 1. Weekly progress in the PWC is shown in the conditioning period which preceded the bed rest phase, and the mean level reached just before going to bed, 43.0 ml/kg agrees reasonably well with the directly measured mean maximum O₂ consumption value of 46.1 ml/kg. According to the norms of Swedish men for this age group (1) this subject population would be considered average in PWC at the end of their conditioning period.

Immediately after the deconditioning period of bed rest the PWC decreased to a value of 38.5 ml/kg (mean of 2 consecutive daily measurements) which falls on the borderline of the "low" and "fair" ratings by the Astrand norms.

Muscle Tonus

In order to evaluate the repeatability of the measure as described above, three subjects who were in neither conditioning nor deconditioning programs were tested and retested with two weeks of normal activity intervening. The results are shown in Table 2. It would be difficult to plot separate regression lines for "before" and "after" measures for any of the four muscles tested.

On this basis, some small but meaningful changes seem to have occurred in the experimental subjects.

Elbow Flexors

All three experimental sub groups showed improvement in muscle tonus as evidenced by the flatter slope of the mean EMG potentials during the bed rest phase of the study. The first run was accomplished in the first week of actual bed rest and the second test run was performed during the first week out of bed. The third test run occurred after approximately two weeks out of bed and although less clearcut, seems to indicate a reversion toward pre-bed-rest measures.

Abdominal Muscles

It should be pointed out that the method of testing actually used the hip flexor muscles as prime movers. Yet the involvement of the abdominal group seems to be proportional to the effort expended by the hip flexors. This can best be explained by the fact that muscles which usually function synergically are at best difficult to innervate separately.

In any event, evaluation of the abdominal group by voluntary contraction of the hip flexor group seems to be justified, although the plots which result are likely to be less typical.

The reason for inclusion of the abdominals in the testing program was to allow evaluation of a differential effect of the three different bed rest training plans. The expected difference seemed to occur between the exercise and the pressure breathing sub groups in that the "exercise only" group which performed no abdominal work fell off in tonus of these muscles during bed rest while the pressure breathing group whose abdominals were forced to work in expiration for two hours daily did indeed show evidence of improvement. The results for the subgroup which did both exercise and pressure breathing are less clear but some improvement did seem to occur in the external oblique muscle while the results for the rectus abdominis are unclear.

Gastro-soleus Muscles

There is no clear evidence of changes having occurred during bed rest in this muscle group. However, in all three subgroups a small but definite improvement seems to have taken place in the first two weeks of normal activity.

Strength

The results of the mean maximum strength changes in the elbow flexors and rectus abdominis are shown in Fig. 2A and 2B. Unfortunately, measurements could not be made on the gastro-soleus group since almost all subjects could exceed the range of the gauge. The results are interesting in that each succeeding run yielded higher mean strength values.

TABLE 1. Physical Working Capacity of Subjects as Estimated by Astrand
Procedure and Measured Directly by Maximal O₂ Consumption Test.

	S	AGE	HT. (cm)	WT. (kg)	Pre Bed Rest Weekly Work Cap. Est. by Astrand Test in mc/kg				MAX O ₂ CONS.	Post Bed Rest Working Gap by Astrand	
					1	2	3	4		1	2
1.	M.B.	20	182	78.8	—	—	46	38	52.0	37.0	
2.	J.B.	22	196	78.5	34	40	42	48	51.1	42.0	
3.	J.C.	24	194	88.0	—	—	43	38	41.5	41.5	
4.	S.E.	20	180	72.8	33	36	40	47	51.7	40.5	
5.	R.F.	23	183	74.0	34	33	36	40	45.6	35.5	
6.	G.H.	19	180	76.0	30	32	35	38	45.5	34.0	
7.	C.H.	20	185	87.7	32	37	37	40	40.3	35.5	
8.	K.J.	21	179	86.5	—	29	37	36	35.3	33.0	
9.	R.J.	20	183	75.5	41	—	47	49	50.7	40.0	
10.	W.M.	20	193	88.0	—	—	35	33	42.6	42.0	
11.	A.P.	23	192	92.8	—	—	37	45	40.2	32.5	
12.	K.U.	20	180	81.0	31	36	40	43	51.1	39.5	
13.	W.W.	21	180	69.6	36	39	40	45	48.5	39.5	
14.	A.Y.	20	196	90.4	47	58	56	62	49.5	45.5	
M		20.9	186.0	81.4	35.3	37.8	40.6	43.0	46.1	38.5	

TABLE 2 (A) MEAN MAX. STRENGTH EL FLEXORS

RUN 1		RUN 2		RUN 3		RUN 4	
EXERCISE ONLY							
1.	126	116	131				
2.	110	127	139				
3.	78	86	115				
4.	116	111	116				
5.	123	137	140				
M = 110.7		M = 115.5		M = 128.2			
PRESSURE BREATHING ONLY							
6.	110	112	102				
7.	119	120	125				
8.	135	157	136				
9.	122	101	163				
10.	123	114	138				
M = 121.8		M = 132.9		M = 132.8			
EXERCISE AND PRESSURE BREATHING							
11.	140	153	166				
12.	114	136	132				
13.	94	120	137				
14.	127	134	141				
M = 118.9		M = 135.7		M = 143.9			
M = 116.9		127.4		134			

TABLE 2 (B) MEAN MAX. STRENGTH RECTUS ABDOMINIS

EXERCISE ONLY							
1.	135	136		133			
2.	103	119		133			
3.	68	84	M = 104.2	96	M = 119.2		
4.	83	68		103			
5.	116	114		131			
M = 102.0							
PRESSURE BREATHING ONLY							
6.	119	128		150			
7.	--	--		--			
8.	132	123	M = 117.0	112	M = 138.2		
9.	124	123		161			
10.	90	84		130			
M = 116.3							
EXERCISE AND PRESSURE BREATHING							
11.	105	127		143			
12.	84	103	M = 119.0	135	M = 132.9		
13.	117	124		125			
14.	118	122		128			
M = 106.0							
M = 107.6		112.7		129			

Centrifuge Studies

The results are summarized in Tables 3 through 7.

1. On the pre-bed-rest runs, nine of fourteen subjects performed better at 8 g's than 6 g's. (64%)
2. On the post-bed-rest runs, eight of fourteen subjects performed better at 8 g's than 6 g's.
3. Thirteen of the fourteen subjects performed better at both the 6 and 8 g's in the post-bed-rest runs than in the pre-bed-rest runs.
4. There is no significant difference in performance in the static runs between the pre and post bed-rest trials. (Seven scored slightly better, 6 slightly worse and one had the same score).

Tilt Table Studies

The results are summarized in Tables 27 and 28. All subjects showed an increased pulse rate response to passive tilting. There was no significant difference between any of the experimental groups. The extent of cardiovascular deconditioning due to the period of bed rest was not, as demonstrated by the passive tilt, modified by the exercise and pressure breathing maneuvers.

Blood Volume Studies

The blood volume data are summarized in Table 29. All subjects experienced highly significant reductions in blood volumes although nine of twelve subjects did show an increase in the hematocrit.

TABLE 3.

AVERAGE TRACKING ERROR SCORES
FOR THE LAST 3 PRACTICE TRIALS

<u>SUBJECT</u>	<u>TRIAL 1</u>	<u>TRIAL 2</u>	<u>TRIAL 3</u>
1	6.8	6.6	7.4
2	10.8	12.9	11.2
3	12.2	11.5	11.4
4	6.1	15.5	5.6
5	9.6	14.0	7.3
6	11.1	7.4	10.4
7	14.7	14.9	15.0
8	10.0	9.4	6.6
9	14.9	17.6	16.4
10	5.1	5.3	4.7
11	5.2	7.2	5.5
12	6.4	8.0	5.8
13	5.3	5.3	3.9
14	6.5	9.2	4.5
MEAN	8.9	10.3	8.3

TABLE 4.

AVERAGE TRACKING ERROR SCORES

At 1 G

<u>SUBJECT</u>	<u>PRE-BED REST</u>	<u>POST BED REST</u>	<u>DELTA</u>
1	5.2	3.4	- 1.8
2	5.2	5.2	0
3	8.0	5.4	- 2.6
4	2.6	2.8	+ .2
5	4.1	5.6	+ 1.5
6	6.5	4.2	- 2.3
7	6.2	8.4	+ 2.2
8	4.7	2.3	- 2.4
9	8.3	9.6	+ 1.3
10	3.1	2.3	- .8
11	2.8	3.9	+ 1.1
12	3.3	3.4	+ .1
13	2.2	1.9	- .3
14	2.9	1.7	- 1.2
MEAN	4.6	4.3	- .36

TABLE 5.

AVERAGE TRACKING ERROR SCORES

At 6 G

<u>SUBJECT</u>	<u>PRE-BED REST</u>	<u>POST BED REST</u>	<u>DELTA</u>
1	8.9	9.8	+ .9
2	12.3	5.5	- 6.8
3	18.5	7.6	-10.9
4	6.1	4.7	- 1.4
5	9.6	8.9	- .7
6	13.4	6.6	- 6.8
7	24.3	13.8	-10.5
8	17.5	5.3	-12.2
9	14.3	9.2	- 5.1
10	8.7	2.9	- 5.8
11	11.7	7.7	- 4.0
12	19.1	6.0	-13.1
13	6.5	3.7	- 2.8
14	14.4	3.6	-10.8
MEAN	13.2	8.8	- 6.4

TABLE 6.

AVERAGE TRACKING ERROR SCORES

AT 8 G

<u>SUBJECT</u>	<u>PRE-BED REST</u>	<u>POST BED REST</u>	<u>DELTA</u>
1	10.4	6.7	- 3.7
2	12.9	6.0	- 6.9
3	19.4	10.5	- 8.9
4	5.3	3.0	- 2.3
5	5.6	7.2	+ 1.2
6	18.3	6.4	-11.9
7	21.2	11.2	-10.0
8	10.5	5.4	- 5.1
9	14.1	9.4	- 4.7
10	5.3	3.3	- 2.0
11	9.2	6.9	- 2.3
12	12.5	5.7	- 6.8
13	6.9	3.1	- 3.8
14	11.9	3.7	- 8.2
MEAN	11.7	6.3	- 5.4

TABLE 7.
 AVERAGE TRACKING ERROR SCORES
 PRE (1) and POST (2) BED REST

Subject	6G(1)	6G(2)	8G(1)	8G(2)	POST STAT (1)	POST STAT (2)
1	8.9	9.8	10.4	6.7	5.2	3.4
2	12.3	5.5	12.9	6.0	5.2	5.2
3	18.5	7.6	19.4	10.5	8.0	5.4
4	6.1	4.7	5.3	3.0	2.6	2.8
5	9.6	8.9	5.6	7.2	4.1	5.6
6	13.4	6.6	18.3	6.4	6.5	4.2
7	24.3	13.8	21.2	11.2	6.2	8.4
8	17.5	5.3	10.5	5.4	4.7	2.3
9	14.3	9.2	14.1	9.4	8.3	9.6
10	8.7	2.9	5.3	3.3	3.1	2.3
11	11.7	7.7	9.2	6.9	2.8	3.9
12	19.1	6.0	12.5	5.7	3.3	3.4
13	6.5	3.7	6.9	3.1	2.2	1.9
14	14.4	3.6	11.9	3.7	2.9	1.7
Mean =	13.2	8.8	11.7	6.3	4.6	4.3

Catecholamine and Catecholamine Metabolite Studies

The results are summarized in Tables 8 through 13. In these tables there are two major groups, with five subjects in each group. There were four collection periods on each of four days, or 16 collections for each group. The mean and standard deviation values in the tables are all determined from five or less individual values.

In order to obtain larger groups for statistical purposes the samples were pooled as follows. The daytime control (ambulatory) values were pooled, for both the "pressure breathing" and "exercise" groups. Similarly the night values for the control (ambulatory) day were pooled. With both the "pressure breathing" and "exercise" groups the values for a given time period on each of the three rest days when samples were collected and pooled. Table 14 indicates how the data was pooled. This pooled data is in Tables 15 through 20.

The high values of the ratio of $(M + NM)/VMA$ in the exercise group (see Tables 12 & 19) was primarily due to specimens from two of the five subjects RF and MB. Therefore, the data from these two subjects was compared with that from the other three. These results are summarized in Tables 21 through 26.

BED REST STUDY TABLE 8.

EPINEPHRINE PLUS NOREPINEPHRINE		ugm/hr. Urinary Excretion			
PRESSURE BREATHING		CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
	7:00 - 12:00	1.43 $\pm$.34	1.18 $\pm$.26	1.52 $\pm$ 1.00	1.10 $\pm$.60
	12:00 - 19:00	2.68 $\pm$ 1.11	1.96 $\pm$.85	1.24 $\pm$.75	1.32 $\pm$.87
	19:00 - 24:00	2.20 $\pm$ 1.1	1.30 $\pm$.05	1.11 $\pm$.60	1.43 $\pm$.71
	24:00 - 7:00 Night	1.54 $\pm$.66	1.12 $\pm$.51	1.05 $\pm$.68	1.16 $\pm$.69
	7:00 - 12:00	2.18 $\pm$.57		1.38 $\pm$.16	2.18 $\pm$ 1.15
	12:00 - 19:00	2.51 $\pm$ 1.81	1.45 $\pm$.41	1.39 $\pm$.18	1.21 $\pm$.74
	19:00 - 24:00	2.77 $\pm$ 1.62	1.23 $\pm$.89	1.32 $\pm$.45	1.84 $\pm$.75
EXERCISE	24:00 - 7:00 Night	1.23 $\pm$.44	1.50 $\pm$.58	0.84 $\pm$.24	1.50 $\pm$.60

BED REST STUDY TABLE 9.

PERCENT EPINEPHRINE

Urinary Excretion

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
PRESSURE BREATHING	7:00 - 12:00	21 $\pm$ 13	48 $\pm$ 17	23 $\pm$ 14
	12:00 - 19:00	27 $\pm$ 13	17 $\pm$ 10	29 $\pm$ 14
	19:00 - 24:00	39 $\pm$ 10	19 $\pm$ 10	22 $\pm$ 4
	24:00 - 7:00 Night	27 $\pm$ 9	27 $\pm$ 24	31 $\pm$ 20
EXERCISE	7:00 - 12:00	26 $\pm$ 11		19 $\pm$ 11
	12:00 - 19:00	28 $\pm$ 6	35 $\pm$ 11	27 $\pm$ 13
	19:00 - 24:00	39 $\pm$ 14	48 $\pm$ 13	30 $\pm$ 17
	24:00 - 7:00 Night	26 $\pm$ 20	21 $\pm$ 10	21 $\pm$ 3

BED REST STUDY TABLE 10.

METANEPHRINE PLUS NORMETANEPHRINE

 $\mu\text{gm/hr.}$ Urinary Excretion

PRESSURE BREATHING

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
7:00 - 12:00	9.8 $\pm$ 4.6	10.0 $\pm$ 2.3	11.3 $\pm$ 9.9	12.4 $\pm$ 6.1
12:00 - 19:00	13.2 $\pm$ 3.2	12.2 $\pm$ 4.9	11.4 $\pm$ 3.6	10.6 $\pm$ 2.9
19:00 - 24:00	12.8 $\pm$ 5.3	9.9 $\pm$ 1.8	10.1 $\pm$ 6.2	11.3 $\pm$ 3.8
24:00 - 7:00 Night	11.1 $\pm$ 4.0	12.5 $\pm$ 0.7	11.8 $\pm$ 3.6	14.0 $\pm$ 3.6
7:00 - 12:00	16.5 $\pm$ 3.8		14.1 $\pm$ 8.4	17.0 $\pm$ 10.0
12:00 - 19:00	13.5 $\pm$ 4.9	13.9 $\pm$ 5.9	14.9 $\pm$ 8.1	16.8 $\pm$ 8.0
19:00 - 24:00	12.7 $\pm$ 2.9	12.7 $\pm$ 6.7	20.3 $\pm$ 9.5	22.4 $\pm$ 9.0
24:00 - 7:00 Night	10.2 $\pm$ 1.9	20.7 $\pm$ 20.8	10.6 $\pm$ 1.7	12.9 $\pm$ 5.1

EXERCISE

BED REST STUDY TABLE 11.

VANILLYLMANDELIC ACID $\mu\text{gm/hr.}$ Urinary Excretion

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
PRESSURE BREATHING	7:00 - 12:00	126 $\pm$ 51	185 $\pm$ 32	155 $\pm$ 104
	12:00 - 19:00	159 $\pm$ 33	170 $\pm$ 29	155 $\pm$ 33
	19:00 - 24:00	158 $\pm$ 52	153 $\pm$ 53	124 $\pm$ 63
	24:00 - 7:00 Night	127 $\pm$ 33	149 $\pm$ 70	140 $\pm$ 57
EXERCISE	7:00 - 12:00	193 $\pm$ 31		200 $\pm$ 20
	12:00 - 19:00	160 $\pm$ 40	154 $\pm$ 64	158 $\pm$ 27
	19:00 - 24:00	205 $\pm$ 50	106 $\pm$ 56	152 $\pm$ 55
	24:00 - 7:00 Night	123 $\pm$ 19	153 $\pm$ 28	118 $\pm$ 20

BED REST STUDY TABLE 12.

(M + NM) / VMA

Urinary Excretion

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64	
PRESSURE BREATHING	7:00 - 12:00	.08 $\pm$.03	.06 $\pm$.02	.08 $\pm$.03	.07 $\pm$.02
	12:00 - 19:00	.09 $\pm$.04	.07 $\pm$.02	.07 $\pm$.01	.07 $\pm$.02
	19:00 - 24:00	.08 $\pm$.03	.07 $\pm$.04	.08 $\pm$.02	.09 $\pm$.03
	24:00 - 7:00 Night	.09 $\pm$.03	.10 $\pm$.06	.09 $\pm$.02	.10 $\pm$.03
EXERCISE	7:00 - 12:00	.09 $\pm$.02		.07 $\pm$.03	.12 $\pm$.07
	12:00 - 19:00	.08 $\pm$.01	.10 $\pm$.04	.09 $\pm$.04	.13 $\pm$.08
	19:00 - 24:00	.07 $\pm$.03	.14 $\pm$.06	.19 $\pm$.22	.13 $\pm$.04
	24:00 - 7:00 Night	.08 $\pm$.02	.14 $\pm$.15	.09 $\pm$.02	.08 $\pm$.02

BED REST STUDY TABLE 13.

(E + N)/(M + NM)

Urinary Excretion

PRESSURE BREATHING

EXERCISE

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
7:00 - 12:00	.17 $\pm$.07	.13 $\pm$.06	.17 $\pm$.05	.09 $\pm$.05
12:00 - 19:00	.21 $\pm$.11	.16 $\pm$.04	.12 $\pm$.07	.12 $\pm$.08
19:00 - 24:00	.18 $\pm$.08	.13 $\pm$.03	.12 $\pm$.03	.13 $\pm$.07
24:00 - 7:00 Night	.14 $\pm$.03	.09 $\pm$.04	.08 $\pm$.03	.08 $\pm$.04
7:00 - 12:00	.14 $\pm$.04		.12 $\pm$.05	.20 $\pm$.25
12:00 - 19:00	.19 $\pm$.10	.12 $\pm$.05	.11 $\pm$.05	.11 $\pm$.13
19:00 - 24:00	.26 $\pm$.22	.10 $\pm$.04	.07 $\pm$.03	.10 $\pm$.07
24:00 - 7:00 Night	.12 $\pm$.05	.11 $\pm$.07	.08 $\pm$.02	.14 $\pm$.11

BED REST STUDY TABLE 14.

 $\mu\text{gm/hr.}$ Urinary Excretion

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
PRESSURE BREATHING	7:00 - 12:00	x	x	x
	12:00 - 19:00	x	x	x
	19:00 - 24:00	x	x	x
	24:00 - 7:00 Night	x	x	x
EXERCISE	7:00 - 12:00	x	x	x
	12:00 - 19:00	x	x	x
	19:00 - 24:00	x	x	x
	24:00 - 7:00 Night	x	x	x

This table shows how the data of Tables 1 thru 6 is grouped to form Tables 7 thru 13.

BED REST STUDY TABLE 15.

EPINEPHRINE PLUS NOREPINEPHRINE $\mu\text{gm/hr.}$ Urinary Excretion

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
PRESSURE BREATHING	7:00 - 12:00	2.11 $\pm$ 1.00	1.29 $\pm$.72	
	12:00 - 19:00		1.5 $\pm$.83	
	19:00 - 24:00		1.3 $\pm$.55	
	24:00 - 7:00 Night	1.54 $\pm$.66	1.1 $\pm$.60	
EXERCISE	7:00 - 12:00	2.49 $\pm$ 1.36	1.7 $\pm$ 1.0	
	12:00 - 19:00		1.3 $\pm$.47	
	19:00 - 24:00		1.5 $\pm$.71	
	24:00 - 7:00 Night	1.23 $\pm$.44	1.3 $\pm$.57	

BED REST STUDY TABLE 16.

		PERCENT EPINEPHRINE		Urinary Excretion	
		CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
PRESSURE BREATHING	7:00 - 12:00	29 $\pm$ 13	30 $\pm$ 18		
	12:00 - 19:00		21 $\pm$ 11		
	19:00 - 24:00		24 $\pm$ 13		
	24:00 - 7:00 Night	26 $\pm$ 9	30 $\pm$ 19		
EXERCISE	7:00 - 12:00	31 $\pm$ 12	19 $\pm$ 9		
	12:00 - 19:00		31 $\pm$ 13		
	19:00 - 24:00		33 $\pm$ 16		
	24:00 - 7:00 Night	26 $\pm$ 20	20 $\pm$ 8		

BED REST STUDY TABLE 17.

METANEPHRINE PLUS NORMETANEPHRINE $\mu\text{gm/hr.}$ Urinary Excretion

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
PRESSURE BREATHING	7:00 - 12:00	11.9 $\pm$ 4.4	11.4 $\pm$ 6.9	
	12:00 - 19:00		11.4 $\pm$ 3.7	
	19:00 - 24:00		10.5 $\pm$ 4.3	
	24:00 - 7:00 Night	11.1 $\pm$ 4.0	12.8 $\pm$ 3.1	
EXERCISE	7:00 - 12:00	14.2 $\pm$ 4.0	15.4 $\pm$ 8.7	
	12:00 - 19:00		15.2 $\pm$ 7.0	
	19:00 - 24:00		17.2 $\pm$ 7.3	
	24:00 - 7:00 Night	10.1 $\pm$ 1.9	14.7 $\pm$ 12.3	

BED REST STUDY TABLE 18.

VANILLYLMADELIC ACID $\mu\text{gm/hr.}$ Urinary Excretion

PRESSURE BREATHING

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
7:00 - 12:00	147 $\pm$ 45	169 $\pm$ 69		
12:00 - 19:00		160 $\pm$ 25		
19:00 - 24:00		137 $\pm$ 54		
24:00 - 7:00 Night	127 $\pm$ 33	146 $\pm$ 47		
7:00 - 12:00	186 $\pm$ 43	191 $\pm$ 70		
12:00 - 19:00		151 $\pm$ 41		
19:00 - 24:00		147 $\pm$ 46		
24:00 - 7:00 Night	123 $\pm$ 19	143 $\pm$ 35		

EXERCISE

BED REST STUDY TABLE 19.

(M + NM) / VMA

Urinary Excretion

PRESSURE BREATHING

EXERCISE

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
7:00 - 12:00	$.08 \pm .03$	$.07 \pm .03$		
12:00 - 19:00		$.07 \pm .02$		
19:00 - 24:00		$.08 \pm .03$		
24:00 - 7:00 Night	$.09 \pm .03$	$.09 \pm .03$		
7:00 - 12:00	$.08 \pm .03$	$.09 \pm .06$		
12:00 - 19:00		$.11 \pm .05$		
19:00 - 24:00		$.12 \pm .04$		
24:00 - 7:00 Night	$.08 \pm .02$	$.10 \pm .08$		

BED REST STUDY TABLE 20.

(E + N)/(M + NM)

 $\mu\text{gm/hr.}$ Urinary Excretion

PRESSURE BREATHING

EXERCISE

	CONTROL (Day 1) 8-5-64 Ambulatory	REST (Day 2) 8-11-64	REST (Day 3) 8-18-64	REST (Day 4) 8-28-64
7:00 - 12:00	$.18 \pm .08$	$.13 \pm .06$		
12:00 - 19:00		$.13 \pm .05$		
19:00 - 24:00		$.13 \pm .05$		
24:00 - 7:00 Night	$.14 \pm .03$	$.09 \pm .03$		
7:00 - 12:00	$.19 \pm .14$	$.15 \pm .16$		
12:00 - 19:00		$.11 \pm .08$		
19:00 - 24:00		$.09 \pm .04$		
24:00 - 7:00 Night	$.12 \pm .05$	$.11 \pm .07$		

BED REST STUDY TABLE 21.

EPINEPHRINE PLUS NOREPINEPHRINE $\mu\text{gm/hr.}$ Urinary Excretion

EXERCISE

	CONTROL (Day 1) 8-5-64 Ambulatory	MB + RF	JB + AY + BW
7:00 - 12:00	2.49 $\pm$ 1.36	1.20 $\pm$.43	2.20 $\pm$ 1.10
12:00 - 19:00		1.20 $\pm$.29	1.40 $\pm$.55
19:00 - 24:00		1.10 $\pm$.37	1.70 $\pm$.81
24:00 - 7:00 Night	1.23 $\pm$.44	1.30 $\pm$.66	1.30 $\pm$.54

BED REST STUDY TABLE 22.

EXERCISE

PERCENT EPINEPHRINE		Urinary Excretion	
	CONTROL (Day 1) 8-5-64 Ambulatory	MB + RF	JB + AY + BW
7:00 - 12:00	31 $\pm$ 12	18 $\pm$ 4	20 $\pm$ 13
12:00 - 19:00		29 $\pm$ 11	31 $\pm$ 14
19:00 - 24:00		30 $\pm$ 15	35 $\pm$ 18
24:00 - 7:00 Night	26 $\pm$ 20	18 $\pm$ 10	22 $\pm$ 7

BED REST STUDY TABLE 23.

METANEPHRINE PLUS NORMETANEPHRINE $\mu\text{gm/hr}$. Urinary Excretion

EXERCISE

	CONTROL (Day 1) 8-5-64 Ambulatory	MB + RF	JB + AY + BW
7:00 - 12:00	14.2 $\pm$ 4.0	17.8 $\pm$ 8.7	13.4 $\pm$ 9.1
12:00 - 19:00		19.7 $\pm$ 7.2	12.9 $\pm$ 5.9
19:00 - 24:00		18.1 $\pm$ 8.3	16.5 $\pm$ 7.0
24:00 - 7:00 Night	10.1 $\pm$ 1.9	20.4 $\pm$ 18.0	10.9 $\pm$ 3.8

BED REST STUDY TABLE 24.

VANILLYLMANDELIC ACID $\mu\text{gm/hr.}$ Urinary Excretion

EXERCISE

	CONTROL (Day 1) 8-5-64 Ambulatory	MB + RF	JB + AY + BW
7:00 - 12:00	186 $\pm$ 43	156 $\pm$ 73	219 $\pm$ 60
12:00 - 19:00		135 $\pm$ 58	159 $\pm$ 30
19:00 - 24:00		125 $\pm$ 56	163 $\pm$ 32
24:00 - 7:00 Night	123 $\pm$ 19	147 $\pm$ 45	140 $\pm$ 28

BED REST STUDY TABLE 25.

EXERCISE

	(M + NM) / VMA		Urinary Excretion
	CONTROL (Day 1) 8-5-64 Ambulatory	MB + RF	JB + AY + BW
7:00 - 12:00	$.08 \pm .03$	$.13 \pm .06$	$.06 \pm .02$
12:00 - 19:00		$.16 \pm .04$	$.08 \pm .04$
19:00 - 24:00		$.15 \pm .04$	$.10 \pm .02$
24:00 - 7:00 Night	$.08 \pm .02$	$.14 \pm .13$	$.08 \pm .02$

BED REST STUDY TABLE 26.

EXERCISE

	(E + N) / (M + NM)		Urinary Excretion
	CONTROL (Day 1) 8-5-64 Ambulatory	MB + RF	JB + AY + BW
7:00 - 12:00	.19 $\pm$.14	.08 $\pm$.05	.21 $\pm$.20
12:00 - 19:00		.07 $\pm$.03	.14 $\pm$.09
19:00 - 24:00		.07 $\pm$.02	.11 $\pm$.05
24:00 - 7:00 Night	.12 $\pm$.05	.08 $\pm$.05	.13 $\pm$.11

TABLE 27.

Differences Between Supine and Highest Pulse Rate During Tilt

E X E R C I S E			
	1	2	3
Wilson	11	44	20
Fouts	10	51	26
Young	29	48	20
Berg	18	40	52
Brockman	23	50	24
	18.2	46.6	28.4

E X E R C I S E A N D P R E S S U R E B R E A T H I N G			
Johnston	11	19	20
Hoffman	7	36	20
Jeremiah	8	37	8
Ulrich	16	46	32
	10.5	34.5	20.0

P R E S S U R E B R E A T H I N G			
Pilmanis	16	48	20
Holm	14	30	20
Michelutti	11	36	
Ellickson	11	24	16
Colloran	22	34	12
	14.8	34.4	17.0

TABLE 28.

TILT TABLE - PULSE RATE AVERAGES

SUBJECT	E X E R C I S E					
	S1	T1	S2	T2	S3	T3
Wilson	75	82.3	86	121.4	80	82.2
Fauts	66	72.2	96	137.1	80	101.2
Young	51	66.9	72	104.6	60	76.8
Berg	62	74.7	88	115.8	64	109.2
Brockman	53	72.8	70	106.2	64	86.4
	61.4	73.8	82.4	117.0	69.6	91.2

	E X E R C I S E A N D P R E S S U R E B R E A T H I N G					
Johnston	63	71.4	72	86.2	68	85.6
Hoffman	71	74.4	68	94.0	72	85.6
Jeremiah	78	81.6	92	120.9	84	88.0
Ulrich	62	69.3	74	91.0	72	98.7
	68.5	74.2	76.5	98.0	74	89.5

	P R E S S U R E B R E A T H I N G					
Pilmanis	66	72.1	84	121.2	74	91.4
Holm	59	68.4	60	86.2	72	82.8
Michiellutte	77	84.4	72	98.0		
Ellickson	55	62.3	66	82.2	58	68.9
Colloran	62	75.8	86	109.2	68	74.0
	63.8	72.6	73.6	99.4	68.0	79.5

TABLE 29
BLOOD VOLUME DATA

BEFORE BED REST				AFTER BED REST		
<u>EXERCISE</u>	Body Weight (Lbs.)	Htc.	<u>ML Blood</u> Kg.	Body Weight	Htc.	<u>ML Blood</u> Kg.
Wilson	151	49.5	69.0	138	49.0	52.0
Fouts				158	47.4	65.2
Young	200	46.7	94.0	191	48.27	56.0
Berg	174	48.5	74.0	174	50.0	54.0
Brockman	171	49.7	83.0	?166	50.0	59.0
AVERAGE	174	48.6	78.2	167.2	49.3	55.2
<u>EXERCISE AND PRESSURE BREATHING</u>						
Johnston	160	49.5	81.3	165	47.9	64.0
Hoffman	171	49.4	81.5	?168	50.0	71.0
Jeremiah	187	45.4	69.0	?183	45.5	53.0
Ulrich	178	45.4	84.0	176	44.1	58.3
AVERAGE	174	47.4	78.9	173	46.9	61.5
<u>PRESSURE BREATHING</u>						
Pilmanis	202	47.8	78.0	201	49.0	69.0
Holm	189	49.1	87.0	185	51.3	63.6
Michelutti				188	46.0	56.9
Ellickson	158	46.3	90.2	154	48.5	72.0
Colloran	192	49.5	79.0	185	51.5	47.5
AVERAGE	185.2	48.2	83.5	181.2	50.1	63.0

-Sig N.S. -Sig

DISCUSSION OF RESULTS

Physical Conditioning-Deconditioning

Physical Work

In general, it would seem from the data on physical work capacity that the subjects started the experiment in a state of "low work capacity" and after two to four weeks of rigorous conditioning attained an "average" PWC, which then regressed to a borderline value between "low" and "fair" after four weeks of bed rest. However the best norms available, which have been used here, have been developed from Scandinavian populations (1). It seems quite likely that these norms may be too high for American populations because of the fact that Scandinavians use bicycles for transportation. Consequently the muscles involved could be expected to be more efficient on the bicycle ergometer.

For these reasons it is suggested that the subjects of this experiment were actually in better than "average" condition and quite probably approached the physical condition of prospective astronauts at the end of the conditioning program.

The mean decreases in PWC associated with the four weeks of bedrest were approximately 4.5 ml/kg of maximal O₂ consumption, a fall from the pre bedrest value of 43.0 to 38.5 ml/kg. This is in close agreement with the results of other investigators. Lamb et al (8) in a space cabin simulator confinement experiment found pre and post values of 36.8 ml/kg and 31.5 ml/kg respectively on 16 subjects confined for 14-30 days. Birkhead et al (3) put four subjects to bed for 42 days. Their subjects had a maximal O₂ of 40.6 ml/kg before and 35.4 ml/kg after bed rest and 18 days retraining.

The EMG data on the subjects' muscle tonus do not seem to indicate any general trend toward deconditioning. On the contrary, the data show a small but consistent improvement in the elbow flexor group during bedrest. This is not surprising since two of the three groups exercised this muscle group. The improvement of the elbow flexors in the pressure breathing group can be rationalized on the basis that the pressure breathing in stimulating the abdominals brought about some degree of co-contraction of the elbow flexors.

Changes in the abdominal muscles seem to be in the directions expected. The "exercise only" group did not exercise the abdominals and the data show decreased tonus, while the "pressure breathing only" group seems to show some improvement in the abdominals during bed rest. The data for the rectus abdominis on the "exercise and pressure breathing" group are confused, but the data for the external oblique show the expected improvement.

The data from the gastro-soleus show no obvious change in slope during bed rest but the expected reconditioning effect is apparent during the first two weeks following bed rest (2nd to 3rd run). It is difficult to explain the lack of change in slope for this muscle group during bed rest since it is one of the extensor groups essential to the erect posture. Previous work by one of us has shown its continuous involvement in maintaining even the "easy standing posture" (5).

The strength measures show improvement which is probably due in large part to one of two contaminating factors:

- 1) a "learning" how to manipulate the piston actuator and/or
- 2) a changing motivation level. However, these measures do corroborate the conclusion that the experimental procedures were successful in preventing any significant decreases in skeletal muscle tonus. Consequently, in view of the fact that a decreased cardiovascular tolerance to 70° tilt was observed, it seems unlikely that skeletal muscle tonus can be a significant factor in the maintenance of the orthostatic response.

Catecholamine and Catecholamine Metabolism

Catecholamines are metabolized by two major routes. These routes differ in that the initial deactivation is either by the enzyme monoamine oxidase, yielding metanephrine or normetanephrine. Although O-methylation is the major route for circulating amines, oxidative deamination may be the principal means for initial deactivation of norepinephrine at nerve endings. Metanephrine and normetanephrine are formed from epinephrine and norepinephrine respectively, independent of the enzyme monoamine oxidase. Vanillylmandelic acid requires monoamine oxidase for its formation. The ratio of the 3-methoxy-catecholamine metabolites to vanillylmandelic acid is inversely proportional to monoamine oxidase activity. The ratio of $(E+N)/(M+NM)$ is related to the relative amount of oxidative deamination. With decreased oxidative deamination the relative amount of O-methylation is increased and the ratio is decreased. This is true for both normal and hypertensive subjects taking monoamine oxidase inhibitors.

Circulating catecholamines are metabolized more by O-methylation and less by oxidative deamination than are the endogenous catecholamines released at nerve endings. Therefore, release of catecholamines into the circulation before they are deactivated can result in an increase in the ratio of $(M+NM)/VMA$.

The daytime values for $(E+N)$ while at rest are not significantly higher than the sleeping values, indicating that the known decrease in catecholamines excretion with sleep is probably postural. Although marked increases of catecholamine excretion with exercise have been reported, the effect of posture on this response needs further evaluation.

The results of the catecholamine studies failed to indicate any correlation of significance with either the pressure breathing or exercise requirements. The patterns of excretion followed those expected for a group of healthy young men confined to bed.

CONCLUSIONS

All of the subjects exhibited the now classical signs of cardiovascular deconditioning as evidenced by reduction of plasma volume and tilt table intolerance. The exercise maneuvers and the pressure breathing either applied separately or together, failed to ameliorate either the reduction in plasma volume or reduced tolerance to passive tilting. The exercise tests indicated some reduction in the ability to perform at a high work level although the objective measures of muscle strength did not show significant decrements. These results are consistent with the earlier observations of Meehan and Jacobs(10).

The performance under transverse acceleration indicated that the bed rest did not result in performance decrements. This implies that the cardiovascular deconditioning did not interact with the ability of the subject to effectively execute the tracking task used in these experiments.

REFERENCES

1. Astrand, I. "Aerobic Work Capacity in Men and Women with Special Reference to Age." Acta Physiologica Scandinavica, Vol. 49 (Suppl. 169) 1-92, 1960.
2. Basmajian, J.V. and A. Latif. "Integrated Actions and Functions of the Chief Flexors of the Elbow." Journal of Bone and Joint Surgery, Vol. 39A:1106-1118, 1957
3. Birkhead, N.C., J.J. Blizzard, J.W. Daly, G.J. Haupt, B. Issekutz, Jr., R.N. Meyers, and K. Rodahl. "Cardiodynamic and Metabolic Effects of Prolonged Bed Rest." Technical Documentary Report No. AMRL-TDR-63-37, May, 1963.
4. de Vries, H.A. "Effects of Exercise upon Residual Neuromuscular Tension in Normal Subjects." Research Quarterly in print.
5. de Vries, H.A. "Muscle Tonus in Postural Muscles." Submitted to American Journal of Physical Medicine.
6. de Vries, H.A. "Prediction of Muscular Strength by Quantitative Electromyography." Submitted to American Journal of Physical Medicine.
7. Jacobson, E. Progressive Relaxation, Ed. 2, The University of Chicago Press, Chicago, p.299, 1938
8. Lamb, L.E., R.L. Johnson, P.M. Stevens, and B.E. Welch. "Cardiovascular Deconditioning from Space Cabin Simulator Confinement." Aerospace Medicine, Vol. 35:420-428, 1964.
9. Lippold, O.C.J. "The Relation Between Integrated Action Potentials in a Human Muscle and its Isometric Tension." Journal of Physiology, 117:492-499, 1952.
10. Meehan, J.P. and H.I. Jacobs, Relation of Several Physiological Parameters to Positive G Tolerance. WADC Technical Report 58-665, Astia Document No. AD 209387, January, 1959.
11. Mitchell, J.H., B.J. Sproule, and C.B. Chapman. "The Physiological Meaning of the Maximal Oxygen Intake Test." Journal of Clinical Investigation, 37:538-547, 1958.
12. Taylor, H.L., E. Buskirk, and A. Henschel. "Maximal Oxygen Intake as an Objective Measure of Cardio-Respiratory Performance." Journal of Applied Physiology, Vol. 8:73-80, 1955.